

Nutrición Hospitalaria



ÓRGANO OFICIAL DE LA SOCIEDAD ESPAÑOLA DE NUTRICIÓN PARENTERAL Y ENTERAL
 ÓRGANO OFICIAL DEL CENTRO INTERNACIONAL VIRTUAL DE INVESTIGACIÓN EN NUTRICIÓN
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Perspectiva	150 palabras	1.200 palabras	2	10
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Artículo especial

Tecnología de alimentos y evolución en los alimentos de textura modificada; del triturado o el deshidratado a los productos actuales

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Resumen

Las dietas trituradas son unas de las dietas más utilizadas en hospitales y residencias de ancianos. Estas dietas elaboradas de manera tradicional pueden tener un bajo valor nutricional, especialmente suelen tener bajo contenido en energía y proteínas. Su uso continuado puede provocar déficits nutricionales y comprometer el estado nutricional del paciente.

Durante las últimas décadas hemos visto cómo la tecnología ha evolucionado y ahora es posible encontrar en el mercado productos industriales con un completo valor nutricional y una textura adecuada para la deglución del paciente. Estos productos son fáciles de preparar y servir, por lo que su inclusión en las cocinas hospitalarias aporta grandes ventajas.

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Introducción

La trituración de alimentos con el fin de modificar su consistencia es una práctica muy habitual en centros sanitarios. Estas dietas de textura modificada están indicadas principalmente en pacientes con problemas de masticación o deglución¹.

Las dietas trituradas son unas de las dietas terapéuticas más utilizadas en un hospital y pueden suponer alrededor de un 10-15% de las dietas servidas. Si hablamos de residencias de la tercera edad las cifras pueden aumentar hasta el 15-26%².

A pesar de que las dietas trituradas elaboradas de manera tradicional pueden mejorar la capacidad de deglutir, a menudo son poco apetecibles y adecuadas

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TEXTURE-MODIFIED FOODS; FROM GROUNDING OR DEHYDRATION TO CURRENT PRODUCTS

Abstract

Texture modified diets are among the most used in hospitals and nursing homes. These traditionally prepared diets may have a low nutritional value and particularly tend to have low energy and protein content. The continued use of these diets can lead to nutritional deficiencies and compromise the patient's nutritional status

Over the last decades, we have witnessed the evolution of technology and evolved and nowadays it is possible to find on the market industrial products with a complete nutritional value and a suitable texture for deglutition among inpatients. These products are easy to prepare and serve, so that their inclusion in the hospital kitchens provides great advantages.

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debido a su apariencia, consistencia, sabor y valor nutricional. Estos purés están elaborados siguiendo recetas que a menudo se modifican para adaptarse a las necesidades del enfermo, haciendo difícil la consecución de todo el valor nutricional de los ingredientes.

La industria ha desarrollado tecnología que permite la fabricación de dietas de textura modificada de manera industrial y con ello potenciar la salud, mejorar la calidad de vida y ofrecer mejores productos a nivel nutricional a los pacientes con necesidad de tomar dietas trituradas. Hemos observado con el paso del tiempo cómo se ha evolucionado desde la elaboración casera de las cremas y purés hasta el desarrollo de productos en polvo para reconstituir en agua o más recientemente productos pasteurizados listos para su consumo. Estos productos tienen un correcto y constante valor nutricional, son de fácil preparación, aceptable sabor, presentan una textura homogénea que facilita la deglución y minimizan el riesgo higiénico.

Aún así es necesario realizar estudios que comparen la dieta tradicional con los nuevos preparados a nivel nutricional y sensorial.

Tecnología de alimentos: desarrollo de productos alimenticios

Se pueden clasificar los alimentos según el tratamiento de conservación que hayan recibido (tabla I). La 1ª gama está constituida por alimentos frescos como hortalizas, verduras, frutas, carnes, pescados y huevos y otros alimentos conservados mediante métodos tradicionales como la deshidratación, salazón y fermentación.

La 2ª gama está formada por alimentos sometidos a un tratamiento térmico, generalmente una esterilización, tras lo cual se ha envasado herméticamente en envases de vidrio o en latas. A estos productos se les llama conservas o semiconservas.

La 3ª gama la forman los alimentos conservados en refrigeración o congelación.

La 4ª gama está constituida por hortalizas y frutas frescas a las que se les realiza una serie de operaciones (pelado, cortado, lavado) y posteriormente se envasan en atmósferas protectoras y refrigeradas. De este modo disponemos de estos alimentos listos para su consumo y conservando sus cualidades de frescor. Estos productos son más perecederos que crudos y sin procesar ya que las operaciones de troceado aumentan su deterioro.

Finalmente, en los últimos años la industria alimentaria ha desarrollado una serie de productos denominados de 5ª gama. Estos productos han recibido un tratamiento térmico por calor, están listos para su consumo y es necesaria su comercialización a temperatura de refrigeración para una correcta conservación. La investigación e innovación en este campo con la incorporación de nueva maquinaria y el desarrollo de nuevos envases hace posible el desarrollo de productos con texturas y sabores óptimos que permanecen hasta el consumo final del producto.

Centrándonos en el tema que nos ocupa, la industria alimentaria ha desarrollado nuevos productos desde productos en polvo para reconstituir en agua o más recientemente productos pasteurizados listos para su consumo. Estos productos se están introduciendo en el sector de la hostelería, tanto en cocinas hospitalarias como en sistemas de catering o en los programas de "Meal on wheels"³ desarrollados en otros países para suministrar comida a pacientes en su domicilio que no son capaces de adquirir y/o preparar su propia comida. Indudablemente aportan una serie de ventajas. La elaboración de las cremas y túrmix de manera tradicional supone disponer de un gran almacén para la conservación de toda

la materia prima utilizada, y de los equipos necesarios para la realización de los purés con todas las garantías sanitarias. Esto aumenta las necesidades de personal y tiempo para su elaboración. El avance en la tecnología y la disposición de productos de 5ª gama ha facilitado la organización de las cocinas ya que se elimina la fase de preparación y elaboración del plato y sólo es necesario un calentamiento previo a su consumo.

La posibilidad de disponer de productos de calidad nutricional y que suponen un menor riesgo microbiológico sin duda presenta ventajas respecto a la elaboración de triturados naturales. Además estos productos son fáciles de preparar y servir y son compatibles tanto con cocinas con sistemas de producción en línea caliente (sistema de producción tradicional en el que se elabora la comida y se mantiene en caliente hasta el momento de su consumo) como cocinas que utilizan la línea fría (sistema de producción en el que se difiere el momento de elaboración de la comida del momento de su consumo, manteniéndola en Tª de refrigeración).

Limitaciones y riesgos de la dieta triturada

El uso continuado de las dietas trituradas convencionales puede producir déficits nutricionales. De hecho se ha considerado la dieta por túrmix un factor de riesgo de desnutrición en pacientes hospitalizados⁴. Este tipo de dietas pueden presentar menor contenido nutricional⁵⁻⁷ y su ingesta es menor a la recomendada⁷. De hecho tal es la preocupación por este tema que se han publicado trabajos para mejorar la calidad y la apariencia de las dietas trituradas⁸.

En la literatura hay diversos estudios que evidencian las deficiencias nutricionales de las dietas trituradas. Wright et al.⁹ compararon la dieta basal con la dieta triturada del hospital en un grupo de 55 pacientes. Inicialmente el contenido de energía y proteínas era similar en ambas dietas pero la ingesta de la dieta triturada era claramente inferior. Dahl et al.¹⁰ determinaron el contenido proteico de los purés realizados en centros de larga estancia, la ingesta proteica de los pacientes y la calidad de las proteínas ofrecidas en estas dietas. Como resultados obtuvieron que la cantidad media de energía y proteínas aportadas al día eran de 1.074 ± 202 kcal y 54 ± 19 g respectivamente. Para conseguir alcanzar los requerimientos de los pacientes, había que aportar 3.000 ml de volumen, lo que no era ingerido por los pacientes. Moreno et al.⁵ demostraron que las dietas para pacientes con disfagia eran nutricionalmente inadecuadas ya que tenían bajo aporte calórico, proteico y eran deficitarias en algún micronutriente (hierro, calcio y vitamina C). En un estudio canadiense¹¹, los autores evaluaron dos grupos de ancianos institucionalizados. Al grupo control se les proporcionaba la dieta triturada convencional y al grupo de intervención una dieta triturada reformulada. Evaluaron a los pacientes a las 6 y 12 semanas. Al finalizar las 12 semanas, el grupo de intervención había aumentado el aporte calórico y el proteico de manera

Tabla I

Clasificación de los alimentos según el tratamiento recibido

1ª gama.	Alimentos frescos.
2ª gama.	Conservas o semiconservas
3ª gama.	Alimentos envasados al vacío o en atmósfera modificada.
5ª gama	Alimentos tratados térmicamente, con envasado aséptico y conservación a temperatura de refrigeración.

significativa, lo que produjo una mejoría en el estado nutricional de los pacientes.

Los nuevos productos preparados parece que mejoran esta situación. Rubio et al.¹² realizaron un estudio comparando la dieta triturada hospitalaria con un preparado en polvo hiperproteico e hipercalórico. Encontraron que a pesar de que la ingesta del preparado fue menor que la del puré tradicional, la porción ingerida aportaba más energía y proteínas. Los pacientes con dieta triturada convencional no alcanzaban los requerimientos en un 83% vs un 38% de los pacientes con el preparado industrial.

Amurund et al.¹³ evaluaron y compararon dietas de textura modificada comerciales y caseras en una residencia de ancianos. Evaluaron la ingesta dietética, el peso y la aparición de úlceras por presión durante un periodo de 28 días. Los pacientes con dietas de textura modificada comerciales tuvieron una ingesta mayor pero no hubo cambios significativos en el peso ni en las úlceras por presión. De Luis D et al.¹⁴, demostraron que la utilización de productos nutricionales modificados de textura y listos para su uso produce un incremento en la ingesta de esos pacientes con mejoría en parámetros bioquímicos y antropométricos y de la calidad de vida.

Keller¹⁵ no encontró cambios en la ingesta al introducir dietas de textura modificada comerciales.

Otro de los aspectos claves en las dietas trituradas es la textura. Existen distintas definiciones de textura, por lo que se están realizando estudios para describir con parámetros físicos las distintas consistencias¹⁶. En teoría todos los alimentos pueden ser triturados, pero en la práctica se observa que hay purés con menor aceptación debido al resultado final¹⁷. Las mejores preparaciones se obtienen de alimentos de consistencia similar, ya que al triturarlos la mezcla es más homogénea (tabla II). Hay que tener especial cuidado al triturar elementos duros o fibrosos para evitar que en el puré final queden hebras, huesecillos,..., que hagan el puré poco seguro para el paciente.

Los purés elaborados de manera tradicional tienen una textura variable dependiendo de la cantidad de agua e ingredientes que utilizemos en su preparación y pue-

Tabla II

Platos triturados de consistencia homogénea¹⁶

- Verduras poco fibrosas con patata y zanahoria.
- Puerro y patata (*vichyssoise*).
- Calabacín con queso.
- Pollo con verduras y arroz o pasta.
- Ternera con verduras y arroz o pasta (*vichyssoise*).
- Huevo con verduras.
- Pescado blanco con verduras.
- Champiñones, calabaza, espárragos.
- Gazpacho.
- Ajoblanco.
- Frutas.

de ser en algunos casos inaceptable para el paciente⁵. Con los nuevos productos disponibles en el mercado, nos aseguramos la misma textura de manera constante.

Y por último, pero no por ello el menos importante, uno de los grandes riesgos de la dieta triturada es la seguridad alimentaria. El riesgo higiénico que presenta la elaboración de la dieta triturada no es nada despreciable debido a la alta manipulación necesaria en su preparación (tabla III). El pelado, troceado, lavado, cocinado, mezclado y triturado de los ingredientes aumentan las posibilidades de realizar unas malas prácticas de manipulación que provoquen que el resultado final no sea un alimento sanitariamente seguro. La higiene en cada etapa debe extremarse. La materia prima debe ser de gran calidad, alcanzar más de 65° C en el interior del alimento durante el cocinado, y extremar las precauciones en la trituración de los alimentos. Además estos alimentos no se deben exponer a temperaturas microbiológicamente peligrosas, principalmente desde los 15° C a 45° C, ya que esas temperaturas son las óptimas para el crecimiento bacteriano de la mayoría de los microorganismos patógenos (fig. 1). En un estudio de la Agencia de Salud Pública de Barcelona¹⁸, se controlaron las dietas trituradas de comedores geriátricos. Obtuvieron como resultado que en un 33% de los comedores se elaboraban los purés con más de 2 horas de antelación a su consumo y no se mantenían a temperaturas adecuadas hasta el mismo. En otro estudio¹⁹, se evidenció que si bien la temperatura alcanzada durante la cocción era correcta, la temperatura varió significativamente desde el mantenimiento a la distribución de la dieta.

Este riesgo está minimizado con el uso de las nuevas dietas disponibles en el mercado, ya que los productos liofilizados al ser en polvo eliminan el riesgo de crecimiento bacteriano y los productos listos para su uso utilizan un envasado aséptico tras el tratamiento térmico que dota al producto de mayor seguridad.

Aceptación por el consumidor y propiedades organolépticas

Una dieta perfectamente diseñada no es válida si a quien va dirigida no se la come. No existen muchos trabajos en la literatura que evalúen la aceptación de la dieta triturada. De Luis et al. han evaluado la aceptación de dietas de textura modificada a partir de productos liofilizados. En un primer estudio²⁰ comparaba la dieta triturada convencional con una dieta a base de productos liofilizados en 22 pacientes hospitalizados.

Tabla III

Factores de riesgo higiénico en las dietas trituradas

- Ingredientes ricos en sustratos para el crecimiento bacteriano.
- Alto valor de a_w .
- Elevada manipulación de alimentos.
- Dificultad en mantener a una temperatura segura el alimento durante todo el procesado.

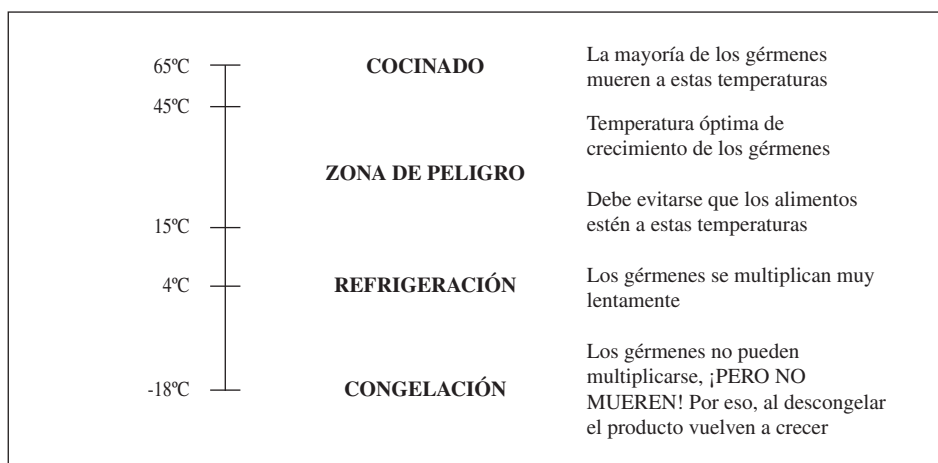


Fig. 1.—Crecimiento microbiano según el tratamiento térmico.

En general los productos liofilizados obtuvieron mejor puntuación que los productos convencionales en cuanto a su textura, color, olor y sabor. En el segundo estudio²¹, compararon la aceptación de la dieta triturada convencional y la de productos liofilizados y obtuvieron los mismos resultados.

En nuestro hospital²² hemos realizado varios estudios de evaluación del residuo que queda en la bandeja una vez que vuelve a la cocina tras la ingesta del paciente. Se ha realizado en dos ocasiones, una con productos liofilizados y otro con productos listos para tomar. Evaluamos más de 1.000 bandejas durante 14 días. El 15% de las bandejas evaluadas correspondían a dieta por túrmix. Entorno al 50% de los pacientes ingerían más del 75% de la ración emplatada, tanto de las cremas que componían el primer plato como las túrmix que componían el segundo. Los resultados obtenidos con ambos tipos de dietas trituradas fueron equiparables. Si bien es cierto que las cremas y purés listas para su consumo tenían una ligera mejor aceptación que los elaborados a base de producto deshidratado.

Reglamentación en materia de Seguridad Alimentaria

Como consumidores queremos poder confiar en los productos alimenticios que comemos. En la actualidad disponemos de un alto grado de protección legal en cuanto a seguridad alimentaria. Esta protección es en parte debida al desarrollo del marco jurídico con un enfoque global “desde la granja a la mesa” con el objetivo de proporcionar alimentos seguros. Las medidas legislativas adoptadas están destinadas a reducir, eliminar o evitar riesgos para la salud de los consumidores.

El sector de la restauración ha estado regulado²³ por diversas disposiciones de carácter específico como el Real Decreto 512/1977, de 8 de febrero, por el que se aprueba la Reglamentación técnico-sanitaria para la elaboración, circulación y comercio de platos preparados, modificado por el Real Decreto 3139/1982, de 12 de noviembre; la Orden de 21 de febrero de 1977 sobre normas higiénico-sanitarias para la instalación

y funcionamiento de industrias dedicadas a la preparación y distribución de comidas para consumo en colectividades y medios de transporte; y el Real Decreto 2817/1983, de 13 de octubre, por el que se aprueba la Reglamentación técnico-sanitaria de los comedores colectivos y sus modificaciones posteriores.

Estas disposiciones han servido para regular un sector que ha mejorado las condiciones higiénicas de los establecimientos así como se han desarrollado buenas prácticas de manipulación de alimentos para ser aplicadas por los profesionales de la restauración.

Más recientemente, y como consecuencia de los avances tecnológicos, se ha publicado más normativa enfocada en establecer medidas de control para prevenir la aparición de problemas derivados de unas malas prácticas de manipulación. Como punto de partida se puede establecer la creación del Libro Blanco sobre la Seguridad Alimentaria, aprobado por la Comisión Europea en el año 2000. Uno de los objetivos que se establecían era que la protección de la salud de los consumidores alcanzase el nivel más elevado posible. Para ello se propusieron una serie de medidas legislativas en las que se concretaban los principios de seguridad alimentaria, la responsabilidad de los distintos operadores económicos, la trazabilidad de los productos, el análisis de los riesgos y la aplicación del principio de cautela.

Para desarrollar y poner en práctica dichos principio fueron promulgadas una serie de disposiciones que componen el llamado “Paquete de Higiene”. Estos nuevos reglamentos combinan y simplifican las exigencias de higiene de la anterior normativa. Su innovación es la realización de una política de higiene única, y aplicable a todos los alimentos, junto con la introducción de instrumentos eficaces para gestionar la seguridad alimentaria y cualquier crisis alimentaria. Dicho Paquete de Higiene está compuesto por:

- Reglamento (CE) 178/2002 por el que se establecen los principios y los requisitos generales de la legislación alimentaria, se crea la Autoridad Europea de Seguridad Alimentaria y se fijan los procedimientos relativos a la seguridad alimentaria.

- Reglamento (CE) 852/2004 de higiene de los productos alimenticios.
- Reglamento (CE) 853/2004 de higiene de los productos de origen animal.
- Reglamento (CE) 854/2004 por el que se establecen normas específicas para la organización de controles oficiales de los productos de origen animal destinados al consumo humano.
- Reglamento (CE) 882/2004 sobre controles oficiales efectuados para garantizar la verificación del cumplimiento de la legislación en materia de piensos y alimentos y la normativa sobre salud animal y bienestar de los animales.

Hay que destacar la legislación alimentaria nacional con respecto a este tema. El Real Decreto 640/2006, de 26 de mayo, por el que se regulan las disposiciones comunitarias en materia de higiene, de la producción y comercialización de productos alimenticios contribuye a la correcta aplicación del Paquete de Higiene así como establece normas de aplicación para algunos aspectos que no se contemplan en los citados reglamentos. Además dicho Real Decreto deroga distintas normativas nacionales relacionadas con la higiene, producción y comercialización de productos alimenticios. También derogó los criterios microbiológicos recogidos en el Reglamento (CE) 2073/2005. Y más tarde el Real Decreto 135/2010 derogó los criterios microbiológicos de la legislación nacional.

Mucho más reciente es la Ley 17/2011, de 5 de julio, de Seguridad Alimentaria y Nutrición que fija el establecimiento de instrumentos que contribuyan a generar un alto nivel de seguridad de los alimentos y la prevención de riesgos derivados del consumo de alimentos, desarrollo de estrategias que fomenten la educación para la salud en el ámbito de la nutrición, la coordinación de las administraciones públicas competentes en seguridad alimentaria y nutrición y la regulación de los procedimientos de actuación en supuestos de crisis o emergencias.

Como puede apreciarse, la legislación alimentaria está constantemente actualizándose para adaptarse y garantizar las necesidades de seguridad alimentaria de todos los consumidores.

Conclusiones

Las dietas trituradas son unas de las dietas más utilizadas en hospitales y residencias de la 3ª edad. Estas dietas están indicadas principalmente para enfermos con problemas de masticación y/o deglución.

Las dietas trituradas elaboradas de manera tradicional pueden ser deficitarias nutricionalmente, principalmente en energía y proteínas, lo que aumentaría el riesgo de desnutrición en estos pacientes.

Los productos disponibles en el mercado presentan una serie de ventajas frente a las dietas trituradas de manera tradicional ya que son fáciles de preparar y servir, aseguran un valor nutricional y una textura adecuada, y el riesgo sanitario es menor al necesitar

menos manipulación. En general la aceptación de estos productos es buena y su ingesta es adecuada.

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Revisión

Consumption of functional foods in Europe; a systematic review

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Abstract

Objective: To assess differences in functional foods consumption between European countries.

Design: Systematic review. The literature search was conducted in Medlars Online International Literature (MEDLINE), via PubMed® and Scopus. Twenty two studies were identified to examine the differences in functional food consumption between European countries.

Results: Figures on consumers of functional foods reveal differences across European countries. Functional foods are popular in most of European countries like Finland, Sweden, the Netherlands, Poland, Spain and Cyprus, but not so in other countries like Denmark, Italy and Belgium. A high percentage of adolescents in the European Mediterranean countries (Spain and Cyprus, but not Italy) consume functional foods. Evaluation of functional foods consumption according to gender is difficult, because results differ from one study to another.

Conclusions: Functional foods have become very popular in Europe in recent years, but still huge differences exist between Europeans on consumption of functional foods. Further research is needed to find out the reasons behind these differences and to understand consumers' needs for functional foods.

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Keywords: *Functional foods. Food fortification. Food consumption. Europe. Systematic review.*

Introduction

Diet-related diseases such as obesity, cancer, diabetes and cardiovascular disease have been increasing¹ and in this view, functional foods play an important role by

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CONSUMO DE ALIMENTOS FUNCIONALES EN EUROPA; UNA REVISIÓN SISTEMÁTICA

Resumen

Objetivo: Evaluar las diferencias en el consumo de alimentos funcionales entre los países europeos.

Diseño: Revisión sistemática. La búsqueda bibliográfica se realizó en Medlars Online International Literature (MEDLINE), vía PubMed®, y Scopus. Se identificaron veintidós estudios que examinaron las diferencias en el consumo de alimentos funcionales entre los europeos.

Resultados: Existen diferencias en la proporción de consumidores de alimentos funcionales entre los países europeos. Así, mientras los alimentos funcionales son muy populares en la mayoría de los países europeos como Finlandia, Suecia, Países Bajos, Polonia, España y Chipre, en algunos países como Dinamarca, Italia y Bélgica no lo son tanto. Un elevado porcentaje de adolescentes europeos mediterráneos (España y Chipre, pero no Italia) consume alimentos funcionales. La evaluación del consumo de alimentos funcionales en función del género es difícil, pues los resultados varían de estudio a estudio.

Conclusiones: En los últimos años se ha extendido el consumo de alimentos funcionales en Europa, pero dicho consumo muestra grandes diferencias entre los europeos. Más investigaciones serán necesarias para averiguar las razones subyacentes tras estas diferencias y entender las necesidades de los consumidores de alimentos funcionales.

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Palabras clave: *Alimentos funcionales. Alimentos fortificados. Consumo de alimentos. Europa. Revisión sistemática.*

reducing or preventing risk of diseases.² Regarding to health message of functional foods, markets for these products has been growing steadily.^{3,4} The biggest functional foods markets are in Japan and the USA; however, European markets far behind them,^{3,5} and in European functional food market, Germany, France, the United Kingdom and The Netherlands have higher consumption of functional foods than other European countries.³

Consumer's acceptance and attitude towards functional foods determine the markets size and success. While Americans accept and consume functional foods more easily, Europeans' approaches are more critical⁶ and questioning of functional foods.⁷ It has

been reported that Danish consumers have more negative attitudes toward functional foods than American and Finnish consumers.⁸ By contrast, Finnish consumers have the most positive attitudes toward functional foods⁽⁵⁾. In addition to consumer's acceptance, the study for comparison between European and American consumer's awareness of functional foods also shows the differences between Europe and the USA. Labrecque et al.⁹ reported that awareness of functional foods among French consumers is lower than Americans and Canadians.

In the literature, there are studies comparing consumers acceptance and awareness of functional foods between Europeans and Americans;^{5,9} however, studies evaluating the differences in the functional food consumption of European countries are scarce. The aim of the present study is to systematically review the functional food consumption in European countries.

Methods of this review

The literature search was conducted through September 2013 in Medlars Online International Literature (MEDLINE), via PubMed[®] and Scopus. The MeSH dictionary in PubMed was used to identify search terms for this review. The keywords used in the search were “functional food”[Major] AND (“intake”[Mesh] OR “consumption”[Mesh] OR “food habits”[Mesh], OR “diet” [Mesh]) AND (“Mediterranean”[Mesh], OR “Europe”[Mesh], OR “adults”[Mesh], OR “child”[Mesh], OR “elder”[Mesh],OR “age groups”[Mesh], OR “demography”[Mesh], OR “socioeconomic factors”[Mesh]).

The selection process for the articles is shown in figure 1. In total, 425 articles (403 via PubMed, and 22 via Scopus) were selected by reading the title or abstract (by AEO). Among the latter, review articles, systematic reviews, articles in other language rather than English, articles that are not conducted in Europe,

articles that are not included a validated method for assessing dietary intake at the individual level and articles which are not included the number and percentage of the functional food consumer in the population were excluded (n = 402). Finally, a total of twenty three articles were chosen for the present review. Author and year of publication, age range of the population, number and gender of participants, sampling size, country in which the study was carried out and methods were collected from these articles. In addition to these data, number and percentage of the functional food consumers in each study were found. Full-text articles were assessed by 2 authors (AEO and JAT). Any matter of doubt was discussed by at least two of the reviewers (AEO, MMB, AP, and JAT).

Twelve articles¹⁰⁻²¹ represented the functional food consumption of the population; however other studies gave information about the food consumption²²⁻²⁵ or dietary patterns²⁶ or consumption of specific food group²⁷⁻³³ of the study population. In these studies functional foods were determined according to the definition of Diplock et al.:² *A food can be regarded as 'functional' if it is satisfactorily demonstrated to affect beneficially one or more target functions in the body, beyond adequate nutritional effects, in a way which is relevant to either the state of well-being and health or the reduction of the risk of a disease. The beneficial effects could be either maintenance or promotion of a state of well-being or health and/or a reduction of the risk of a pathologic process or a disease.*

Results

The characteristics of studies selected for this systematic review are shown in table I. In these studies the number of participants varied from 395³¹ to 48763.²⁷ The range of the response rate was 33%²⁷-99%.¹³ In two studies the response rate^{17,20} and in one study¹⁷ the

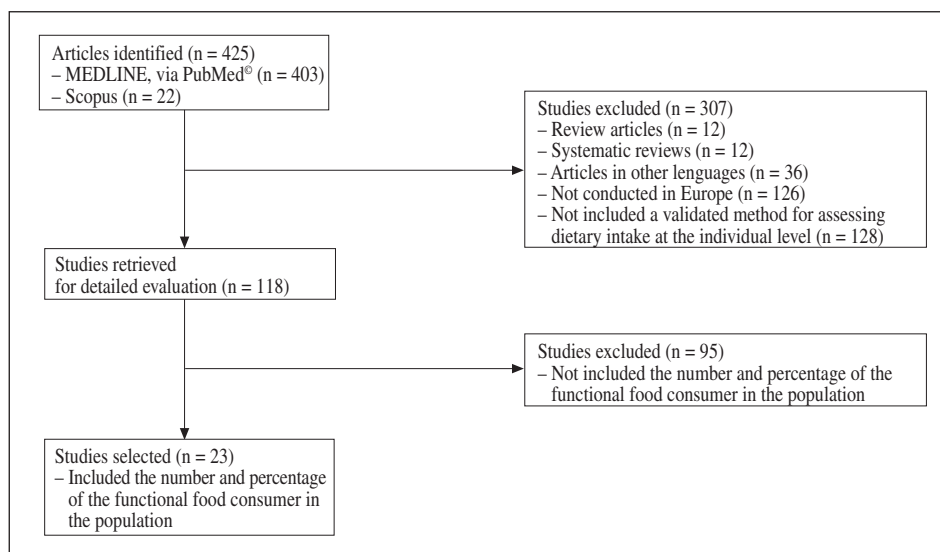


Fig. 1.—Flow chart for selection of articles for the present review.

Table I
Description of the studies included in this review

Author(s)	Method	Country	Study year	Sample size (Response rate, %)	Age range
Schätzer et al. ³³	Self-administered questionnaire	Austria	2006	2704 (52.7)	19-64 y
Mullie et al. ¹⁵	Semi-quantitative food-frequency questionnaire (FFQ)	Belgium	2007	1852 (37)	20-59 y
Mullie et al. ¹⁹	Semi-quantitative food-frequency questionnaire (FFQ)	Belgium	2007	1852 (37)	20-59 y
Lazarou et al. ²⁶	Semi-quantitative food-frequency questionnaire (FFQ)	Cyprus (The CYKIDS)	2004-2005	1140 (72)	9-13 y
Tjønneland et al. ²⁷	Food frequency questionnaire (FFQ)	Denmark	1993-1997	48763 (33)	50-64 y
Lahti-Koski et al. ²⁴	Self-administered questionnaire	Finland (FINRISK)	1982-1997	24604 (79)	25-64 y
Anttolainen et al. ¹⁰	Questionnaire (Health-lifestyle)	Finland	1996-1998	23657 (79)	35-84 y
Hirvonen et al. ¹⁸	24-hour dietary records	Finland (FINDIET)	2007	981 (90)	25-64 y
Urala et al. ¹¹	Special questionnaire	Finland	1999	958 (n.d.)	17-81 y
Lukasiewicz et al. ³⁰	24-hour dietary records	France	1994-2002	2323 (86)	35-60 y
Annunziata and Vecchio ¹⁷	Special questionnaire	Italy	n.d.	400 (n.d.)	18-75 y
Ferraroni et al. ³¹	Food frequency questionnaire (FFQ)	Italy	1990-1991	395 (87%)	>35 y
Trevisan et al. ²⁹	Special questionnaire	Italy	1978-1987	15649 (83%)	30-59 y
de Jong et al. ¹²	Self-administered questionnaires	Netherlands	2000	1183 (76)	19-91 y
de Jong et al. ¹³	Food frequency questionnaire (FFQ)	Netherlands	2003	2379 (99)	28-76 y
van de Vijver et al. ³²	Food frequency questionnaire (FFQ)	Netherlands	2006	4237 (85)	55-69 y
Aranceta et al. ²²	Food frequency questionnaire (FFQ)	Spain (Basque Country)	1990	2348 (73)	25-60 y
Ciprián et al. ²¹	Food frequency questionnaire (FFQ)	Spain (Valencia Comm)	1994	1863 (74)	>15 y
Serra-Majem et al. ^{23,25}	24-hour dietary records	Spain (EnKid)	1998-2000	3850 (70)	2-24 y
Núñez-González et al. ²⁰	Special questionnaire	Spain (Canary Islands)	2009-2010	1112 (n.d.)	>18 y
Landström et al. ¹⁴	Food questionnaire	Sweden	2005	972 (48)	17-75 y
Lindström et al. ²⁸	Cross-sectional study	Sweden	1994	11834 (39)	45-64 y
Wadolowska et al. ¹⁶	Closed-question questionnaire	Poland	2005	1005	15-75 y

n.d.: no data.

year of the study was not mentioned. While two studies involved only men,¹⁵ and one study involved only adolescents,²⁶ most of the studies showed an age range of 2-91 y.

Food consumption of respondents was determined by different questionnaires. In total, five food frequency questionnaires (FFQ), one of them was validated, three validated semi-quantitative food frequency questionnaires (s-FFQ), three self-administered questionnaires (two of them were validated), one cross-sectional study, one food questionnaire, three 24-h dietary recalls, four special questionnaires and one validated closed question questionnaire were used to assess food consumption.

The functional food consumption was reported in twelve studies,¹⁰⁻²¹ and eight of them showed different functional food consumption,^{4,12,14-17,20,21} whereas two of them presented consumption of stanol-enriched margarines.^{10,13} In one study low-fat food consumption was reported¹⁹ and in another study fortified food consumption was presented.¹⁸ Two studies showed functional foods consumption only in men.^{15,19}

Nine articles reported different food group consumption like fruits and vegetable, whole grain, or alcohol. While two studies reported fruit and vegetable intake,^{28,33} one study reported tea and coffee con-

sumption³¹ and two studies reported alcohol consumption.^{29,37} One study reported relationship between body mass index and food choices.²⁴ One study assessed the association of whole-grain intake with BMI,³² and another one reported alcohol intake and BMI relation.³⁰ Rest of the studies reported food pattern of the study population.^{21,22,23,25,26}

Milk and dairy products

Six studies reported consumption of low-fat/skimmed milk, milk with n-3 fatty acid or milk fortified with Ca or with vitamins A and D. In Finland while 42.3% of respondents consumed low-fat milk only 8.8% of them consumed skimmed milk;²⁴ however in Belgium only 7.4% of the respondents consumed low-fat milk¹⁹ (table II). Total percentage of the adults who consumed low-fat/skimmed milk in Finland was higher than those in Spain in where only ≤ 30% of the adults consumed functional milk products like milk low in lactose, milk products low in fat or milk enriched with vitamins and/or minerals.^{20,21} In Italy functional milk products consumption (milk with n-3 fatty acids) was lower than in Finland, Belgium and Spain, only 5% of

Table II
Number and percentage of the functional food consumers in different European countries

Country	Functional food	Men		Women		Total	
		n	%	n	%	n	%
<i>Austria</i> ³³	Fruits and vegetables	290	27.2	694	43.0	984	36.4
<i>Belgium</i> ¹⁵	Fortified margarines	488	26.3	n.d.	n.d.	488	26.3
	Fermented dairy products	87	4.7	n.d.	n.d.	87	4.7
	Nuts	259	14.0	n.d.	n.d.	259	14.0
	Black tea	551	29.8	n.d.	n.d.	551	29.8
	Red wine	190	10.2	n.d.	n.d.	190	10.2
	Fatty fish	228	12.3	n.d.	n.d.	228	12.3
	Fruits	354	19.1	n.d.	n.d.	354	19.1
	Vegetables	492	26.6	n.d.	n.d.	492	26.6
<i>Belgium</i> ¹⁹	Low-fat mayonnaise	93	5.0	n.d.	n.d.	93	5.0
	Low-fat yogurt	320	17.3	n.d.	n.d.	320	17.3
	Low-fat milk	137	7.4	n.d.	n.d.	137	7.4
	Low-fat cheese	65	3.5	n.d.	n.d.	65	3.5
	Low-fat cottage cheese	95	5.1	n.d.	n.d.	95	5.1
	Low-fat meat	401	21.7	n.d.	n.d.	401	21.7
<i>Cyprus (The CYKIDS)</i> ²⁶	Semi skimmed milk	352	66.0	422	69.5	774	67.9
	Yogurt	240	45.1	256	42.2	496	43.5
	Whole grain bread	113	21.2	118	19.5	231	20.3
	Breakfast cereals	273	51.2	293	48.2	566	49.7
<i>Denmark</i> ²⁷	Red wine	12973	55.7	13891	55.5	26864	55.1
<i>Finland (FINRISK)</i> ²⁴	Low-fat milk	5065	42.7	5339	41.9	10404	42.3
	Skimmed milk	875	7.4	1287	10.1	2162	8.8
	Sour milk	10697	90.2	11846	92.9	22543	91.6
	Coffee	11740	99.0	12675	99.4	24415	99.2
	Tea	10455	88.2	11573	90.8	22028	89.5
<i>Finland</i> ¹⁰	Plant sterol ester margarine	577	5.1	518	4.2	1095	4.6
<i>Finland (FINDIET)</i> ¹⁸	Voluntarily fortified foods ¹	305	74	315	65	620	67.5
<i>Finland</i> ¹⁰	Probiotic juice and yoghurt	n.d.	n.d.	n.d.	n.d.	287	30.0
	Cholesterol lowering products	n.d.	n.d.	n.d.	n.d.	169	18.0
	Products with added calcium	n.d.	n.d.	n.d.	n.d.	451	47.0
	Products with added fibre	n.d.	n.d.	n.d.	n.d.	465	49.0
	Low-salt products	n.d.	n.d.	n.d.	n.d.	670	70.0
<i>France</i> ³⁰	Wine	954	90.4	984	77.6	1938	83.4
<i>Italy</i> ¹⁷	Milk with n-3 fatty acids	n.d.	n.d.	n.d.	n.d.	20	5
	Probiotic yoghurt	n.d.	n.d.	n.d.	n.d.	48	12
	Vitamin enriched juices	n.d.	n.d.	n.d.	n.d.	21	7
	Enriched breakfast cereals	n.d.	n.d.	n.d.	n.d.	60	15
	Low cholesterol butter	n.d.	n.d.	n.d.	n.d.	12	3
	Spread with added calcium	n.d.	n.d.	n.d.	n.d.	16	4
<i>Italy</i> ³¹	Coffee	80	61.5	161	60.8	241	61.0
	Decaffeinated coffee	120	92.3	243	91.7	363	91.9
	Tea	93	71.5	183	69.1	276	69.9
<i>Italy</i> ²⁹	Red wine	5650	62.9	4090	61.3	9740	62.2
<i>Netherlands</i> ¹²	Yogurt with lactic acid bacteria	n.d.	n.d.	n.d.	n.d.	383	32.4
	Cholesterol lowering margarine	n.d.	n.d.	n.d.	n.d.	78	6.6
	Lemonade or sweets with extra vitamins and minerals	n.d.	n.d.	n.d.	n.d.	435	36.8
	Foods with extra Ca	n.d.	n.d.	n.d.	n.d.	324	27.4

Table II (cont.)
Number and percentage of the functional food consumers in different European countries

Country	Functional food	Men		Women		Total	
		n	%	n	%	n	%
Netherlands ³²	Whole grain (all grain without bran and germs)	727	35.0	938	43.5	1665	39.3
	Total brawn bread (sum of brown, wholemeal and rye bread)	1913	92.1	2018	93.5	3931	92.8
	All grain (bran, germs, muesli, porridge, brown rice and cooked grains)	765	36.8	1051	48.7	1816	42.9
Netherlands ¹³	Phytosterol/-stanol-enriched margarines	48	4.0	67	5.7	115	4.8
Spain (Basque Country) ²²	Red wine	793	69.4	470	39.0	1263	39.5
Spain (Valencia Community) ²¹	Low-fat milk	151	18.1	313	31.9	464	25.0
	Vitamins A+D enriched milk	65	7.9	125	12.8	190	10.6
	Calcium enriched milk	28	3.4	68	7.0	96	5.3
	Fibre enriched foods	146	17.5	269	27.6	415	23.0
	Two yoghurts	107	12.9	159	16.2	266	14.3
	Coffee	344	41.3	399	40.7	743	39.9
	Red wine	177	21.3	68	6.9	245	13.2
	Iodized salt	239	29.4	335	34.8	574	32.3
Spain (EnKid) ^{23,25}	Cereal or cereal product for breakfast	1380	84.7	1669	87.6	3049	86.3
	Two yoghurts and/or 40 g cheese	850	52.2	897	47.1	1748	49.5
Spain (Canary islands) ²⁰	Milk products ²	n.d.	n.d.	n.d.	n.d.	331	29.8
	Cereals ³	n.d.	n.d.	n.d.	n.d.	341	30.7
	Drinks ⁴	n.d.	n.d.	n.d.	n.d.	463	41.6
	Eggs ⁵	n.d.	n.d.	n.d.	n.d.	75	6.7
	Fats ⁶	n.d.	n.d.	n.d.	n.d.	197	17.7
Sweden ¹⁴	Probiotic fruit-drinks	169	39.5	276	50.7	445	45.8
	Probiotic milk-products	217	50.8	326	59.9	543	55.9
	Portion-sized yoghurt with muesli	20	4.7	47	8.6	67	6.9
	Juice with added vitamins or minerals	208	48.6	265	48.7	473	48.7
	Cholesterol-lowering products	112	26.3	162	29.7	274	28.2
	Fibre-rich bread with n-3 fatty acids	157	36.7	256	47.1	413	42.5
	Egg with n-3 fatty acids	14	3.3	23	4.2	37	3.8
Sweden ²⁸	Fruit Juice	2987	55.5	2925	45.3	5912	50.0
Poland ¹⁶	Cholesterol lowering spreads or drinks	n.d.	n.d.	n.d.	n.d.	201	20.0
	Energy drinks	n.d.	n.d.	n.d.	n.d.	70	7.0
	Food with added vitamins and/or minerals	n.d.	n.d.	n.d.	n.d.	201	20.0
	Fruit and/or vegetables	n.d.	n.d.	n.d.	n.d.	834	83.0
	High fibre foods	n.d.	n.d.	n.d.	n.d.	382	38.0
	Probiotic yoghurt drinks	n.d.	n.d.	n.d.	n.d.	372	37.0
	Weight loss products	n.d.	n.d.	n.d.	n.d.	40	4.0

n.d.: no data.

¹Yogurts fortified with vitamins or minerals, juice fortified with vitamins or minerals, Ready-to-eat breakfast cereals fortified with vitamins or minerals, Energy and wellness drinks fortified with vitamins or minerals, Quarks fortified with vitamins or minerals

²Milk products: easily digestible milk (or milk low in lactose), milk enriched with vitamins and/or minerals, skimmed milk with soluble fiber, milk with royal jelly, milk with modified fatty acids (omega 3), milk products low in fat, pro-biotic foods (yoghurt and fermented milk) and yoghurt with phytosterols.

³Cereals: fortified breakfast cereals, whole-meal cereals and energy bars.

⁴Drinks: juices and enriched drinks, stimulating drinks and isotonic drinks.

⁵Eggs: Docosahexanoic acid-enriched (DHA), low in cholesterol eggs.

⁶Fats: enriched margarine, margarine rich in phytosterols and sunflower oil rich in oleic acid.

the adults consumed milk with n-3 fatty acids.¹⁷ In one study, semi-skimmed milk consumption of adolescents was investigated, and reported that 66% of boys and 69.5% of girls consumed low fat milk in Cyprus.²⁶

Consumption of fermented milk products was reported in ten studies. Finland had the highest consumption percentage of fermented milk products, 91.6% of the respondents consumed sour milk.²⁴ Also in Sweden probiotic milk products were consumed in high ratio (55.9%), while yogurt with muesli was consumed by only 6.9% of the respondents.¹⁴ De Jong et al.¹² reported that 32.4% of the Dutch respondents consumed yogurt enriched with lactic acid bacteria and Wadolowska et al.¹⁶ reported that 20% of the Polish respondents consumed probiotic yogurt drinks; however in Spain,²¹ Italy¹⁷ and Belgium,¹⁵ fermented dairy products were not popular. While in Spain 14.3% (12.9% of men and 16.2% of women) and in Italy 12% of the respondents consumed probiotic yogurt, in Belgium less than 5% of the respondents consumed these products. In Belgium, 17.3% of the respondents consumed low-fat yogurt.¹⁹ Lazarou et al.²⁶ reported that 43.5% of the children consumed yogurt in Cyprus, while in Spain almost 50% of the children consumed yogurt.^{23,25}

Infusions

Coffee and/or tea consumption was reported in four studies. In Finland coffee and tea consumption was higher than in other countries and no gender difference was reported.²⁴ Coffee consumption, especially decaffeinated coffee, also in Italy was high. Coffee with caffeine consumed by 61% of Italian respondents, almost 92% of them consumed decaf coffee.³¹ Spanish people also show high coffee consumption (39.9%), higher in men (41.3%) than among women (40.7%). While almost 70% of male respondents consumed tea in Italy,³¹ 29.8% of the male respondents in Belgium consumed black tea.¹⁵

Cholesterol-lowering products

Consumption of cholesterol lowering products (phytosterol/stanol-enriched foods) was reported in six studies. Cholesterol lowering margarine/drink was a popular functional food in Belgium, Sweden, Poland and Spain where the percentage of consumption were 26.3%,¹⁵ 28.2%,¹⁴ 20%¹⁶ and 17.7%²⁰ respectively; however, in Finland and The Netherlands cholesterol lowering products were consumed by 4.6%¹⁰ and 6.6%¹² of the respondents. In Finland, 18% of the respondents consumed cholesterol lowering products.¹¹

Red wine

Five studies reported consumption of red wine. France had the highest proportion for red wine consumption

with 83.4% of the respondents.³⁰ In Italy (62.2%) and Denmark (55%) more than half of the respondents consumed red wine,^{27,29} while in Spain 13.2%-39.5% of the respondents consumed red wine.^{21,22} In France and Spain there was a gender difference in the consumption of red wine, male respondents more likely to consume red wine in these countries; however, in Denmark and Italy no gender difference was observed. In Belgium red wine consumers was reported as 10.2% of the respondents;¹⁵ since this study represented functional foods consumption of military men, comparison of genders for red wine consumption was not possible.

Cereals

Breakfast cereals or fibre rich bread consumption was reported in six studies. In Cyprus and Spain breakfast cereal consumption of adolescents was investigated. In these two Mediterranean countries children had similar and high percentage of breakfast cereal consumption, 49.7%²⁶ and 49.5%^{23,25} respectively, and boys had slightly higher consumption proportion than girls.

Landström et al.¹⁴ reported that 42.5% of Swedish respondents consumed fibre rich bread with n-3 fatty acid, while 92.8% of the Dutch respondents consumed total brown, wholemeal or rye bread.³² Whole and all grain consumption of Dutch respondents were also reported as 39.3% and 42.9% of respondents, respectively.^{16,32} Wadolowska et al.¹⁶ reported that high fibre foods were consumed by 38% of the Polish respondents. In Italy only 15% of the respondents consumed enriched breakfast cereals.¹⁷

Fruit and vegetables

Fruit and vegetables consumption was reported in three studies. In Austria 36.4% of the respondents consumed fruits and vegetables and it is clearly seen that females more likely to consume these products.³³ In Poland 83% of the respondents consumed fruits and vegetables.¹⁶ In Belgium consumption of fruits and vegetables were investigated separately. While 26.6% of the respondents consumed vegetables 19.1% of them preferred to consume fruits.¹⁵

In five studies consumption of fruit juice were investigated. In Sweden almost half of the respondents (48.7%) consumed juice with added vitamins or minerals.¹⁴ In another study reported that 50% of the Swedish respondents consumed fruit juice.²⁷ Another common functional food among Swedish respondents was probiotic fruit drinks which was consumed by 45.8% of the respondents.¹⁴ Consumption of vitamin enriched juices was not popular in Italy, only 7% of the respondents consumed these products;¹⁷ however in Spain juices and enriched drinks were consumed almost 42% of the respondents.²⁰

Other functional foods

Consumption of other functional foods like eggs with n-3 fatty acids, spread with added Ca, low-fat mayonnaise, low fat cheese, low cholesterol butter, nuts, energy drinks, vitamin or mineral enriched foods, fibre enriched foods, iodized salt, and weight loss products was also investigated among European citizens. While fatty fish was consumed by 12.3% of the Belgium respondents, nuts were consumed by 14% of them.¹⁵ Low-fat products like mayonnaise and cheese were consumed by 5% of the Belgium respondents; however, low fat meat was consumed 22% of them.¹⁹ Consumption of low cholesterol butter and spread with added calcium in Italy were investigated and reported that less than 5% of the respondents consumed these products.¹⁷ Consumption of different functional foods (yogurts fortified with vitamins or minerals, juice fortified with vitamins or minerals, ready-to-eat breakfast cereals fortified with vitamins or minerals, energy and wellness drinks fortified with vitamins or minerals, quarks fortified with vitamins or minerals) were investigated in Finland and it was reported that total 67.5% of the respondents consumed these products.¹⁸ Probiotic juice and yogurt, products with added fibre and low-salt products were also commonly consumed by Finnish.¹¹

Consumption of functional eggs was mentioned in two studies. While in Sweden only 3.8% of respondents consumed eggs with n-3 fatty acids,¹⁴ in Spain 6.7% of the respondents consumed eggs with n-3 or low in cholesterol.²⁰ Vitamin enriched foods like lemonade or sweets were popular in The Netherlands, almost 40% of the respondents consumed these products.¹⁵ In the same study it was reported that almost 30% of the study population consumed foods with extra calcium.¹⁵ Products with added calcium were also popular in another north European country, almost half of the study population consumed calcium fortified products in Finland.¹¹ However, in Poland 20% of the respondents consumed vitamin and/or mineral enriched foods, whereas energy drinks and weight loss products were consumed by only 7% and 4% of the respondents respectively.¹⁶ In Spain, 32.3% of respondents consumed iodized salt, and 23.0% of them consumed fibre enriched foods.²¹

Discussion

While in most of the north European countries like Finland, Sweden and The Netherlands, functional foods are consumed by a high percentage of the population,^{10,12,13,18,24,32} in Belgium percentage of functional foods' consumers is not as high as in the north European countries.^{15,19} On the other hand, in most of the other European countries, fortified margarines were consumed by less than 10% of the populations,^{10,12,13,17} but in Belgium 26% of the study population consumed these products.¹⁵ It is also surprising that fermented dairy

products, one of the most popular functional foods,³⁴ is consumed by less than 5% of the study population in Belgium. The studies conducted in Belgium represented only specific group of population, military men, it might be the reason that results from this north European country differs from other northern countries.

Results from Mediterranean countries, like Spain, Italy and Cyprus, also show differences. Spanish and Cypriots are more likely to consume functional foods than Italians. Functional foods, except coffee, tea and red wine, are not as popular in Italy as in other European countries.^{17,29,31} When the functional food consumption of young population in Mediterranean countries was investigated, results show that in Spain and Cyprus a high percentage of adolescents consumed functional foods.^{23,25,26}

It is clearly seen that there are differences between functional food consumers' percentage across the countries. Menrad³ reported that functional foods are more popular in the Central and Northern European countries than in Mediterranean countries; however, it is not possible to make a generalization between northern and southern countries. Furthermore, in East Europe functional foods consumption has become popular,¹⁶ and functional food market has been growing in Poland.³⁵ European countries differ in their nutrition and health claims of functional foods³⁶ and also popularity of functional foods differs from country to country.

Bech-Larsen and Grunert⁸ reported that Finnish consumers have positive attitudes toward functional foods, whereas Danish consumers have negative attitudes toward functional foods. High acceptability of functional foods in Finland might be the result of the government's support of functional foods.¹⁴

It is difficult to evaluate functional food consumption according to gender, because results varied from study to study. In some studies, it was reported that females were more interested in functional food,^{14,37,38} however, some studies reported that different products might be attractive for one or the other gender.^{12,39} In fact, results of some studies conducted in same country represent different outcomes. According to Lathi-Koski et al.²⁴ females were more likely to consume functional foods than males in Finland; in contrast Anttolainen et al.¹⁰ and Hirvonen et al.¹⁸ reported that male consumers were more interested functional foods than females. Similarly, Landström et al.¹³ pointed out that Swedish women more likely to consume functional foods than men, but another study conducted in Sweden reported that males consumed functional foods more than female did.²⁸

Functional foods offer a new kind of health message due to the specific effects of functional components,⁴⁰ and consumer aspects of functional foods lay on the grey area between food and medicine.⁷ The lack of legal definition and regulation for functional foods could affect the consumer attitude to functional foods.¹⁴

Lately, it has been evaluated the knowledge of, interest in and predisposition towards FFs in Spanish di-

eticians and experts in human nutrition, and how these professionals rate the potential benefits and risks associated with consuming functional foods. This study yielded that functional foods are generally accepted by nutritional professionals. However, further study is required into the discrepancies between dieticians and experts in human nutrition regarding the view that it is “dangerous” to consume certain functional foods and regarding their evaluation of whether the public know in which situations certain functional foods should be consumed.⁴¹

Conclusions

Functional foods have become very popular in Europe in recent years, but still huge differences exist between Europeans with consumption of functional foods. Further researches are necessary to find out reasons behind the differences and understand consumers' needs for functional foods.

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Authors' contributions

AEO and JAT contributed to the design of the strategy for the literature search, double screened and selected the retrieved documents. AP and MMB provided previous literature searches and analysis. AEO and JAT prepared the main outline of the manuscript, and all authors contributed to the preparation of the manuscript.

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Revisión

Efecto del consumo de té verde o extractos de té verde en el peso y en la composición corporal; revisión sistemática y metaanálisis

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Resumen

Introducción: La cafeína y las catequinas contenidas en el té verde podrían tener un efecto termogénico que favorece la pérdida de peso y de grasa corporal. El objetivo del presente estudio es evaluar la magnitud del efecto del té verde o de sus extractos (cafeína y catequinas) sobre el peso corporal y la composición corporal.

Material y métodos: Se realizó una revisión sistemática y metaanálisis para determinar la magnitud del efecto del té verde o de sus extractos sobre el peso corporal (kg), índice de masa corporal (IMC) (kg/m²), masa grasa (%), y perímetro de cintura (cm), o de cadera (cm). Se incluyeron estudios publicados entre los años 2000 y 2013, recuperados de PubMed/Medline con las siguientes características: ensayos controlados aleatorizados (ECA) de grupos paralelos (intervención y placebo), con asignación aleatoria, doble cegado, y un seguimiento mínimo de 12 semanas, en individuos sanos de cualquier género, de edades superiores a los 18 años, con IMC de 25-40 kg/m². De cada estudio incluido se estableció su calidad y riesgo de sesgos, y se realizó el análisis estadístico, con el software RevMan Cochrane Collaboration 5.1.6, según el modelo de efectos aleatorios con un intervalo de confianza del 95% (IC 95%). Se estimó que el efecto era estadísticamente significativo en $p < 0,05$, y se evaluó la homogeneidad de los estudios mediante el índice I².

Resultados: La estrategia de búsqueda recuperó 154 estudios, de los cuales solamente 5 pudieron ser incluidos en el análisis cuantitativo. El análisis reveló una diferencia media (DM) estadísticamente no significativa de pérdida de peso, tanto en el análisis de subgrupos: individuos asiáticos -0,81 kg (95% IC: -2,76 a 1,13; $P = 0,41$; $I^2 = 0\%$; $n = 210$), individuos caucásicos -0,73 kg (95% IC: -3,22 a 1,75; $P = 0,45$; $I^2 = 0\%$; $n = 91$); como en su conjunto: -0,78 kg (95% IC: -2,31 a 0,75; $P = 0,32$; $I^2 = 0\%$; $n = 301$). Tampoco se observó una DM estadísticamente significativa de disminución del IMC, tanto en el análisis de subgrupos: individuos asiáticos -0,65 (95% IC: -1,85 a 0,54; $P = 0,29$; $I^2 = 0\%$; $n = 71$), individuos caucásicos -0,21 (95% IC: -0,96

EFFECT OF GREEN TEA OR GREEN TEA EXTRACT CONSUMPTION ON BODY WEIGHT AND BODY COMPOSITION; SYSTEMATIC REVIEW AND META-ANALYSIS

Abstract

Introduction: Caffeine and catechins contained in green tea may have a thermogenic effect favoring weight and body fat loss. The aim of this study is to evaluate the magnitude of the effect of green tea or its extracts (caffeine and catechins) on body weight and body composition.

Material and methods: A systematic review and meta-analysis was conducted to determine the magnitude of the effect of green tea or its extracts on body weight (kg), body mass index (BMI) (kg/m²), fat mass (%), and waist and hip circumference (cm). We included studies published between 2000 and 2013, retrieved from PubMed/Medline with the following characteristics: randomized controlled trials (RCTs) of parallel groups (intervention and placebo), randomized, double-blind, and a minimum 12-week follow-up, in healthy individuals of either gender, 18 years or older, with a BMI of 25-40 kg/m². Quality and risk of bias was assessed for every included study, and the statistical analysis was performed with the Cochrane Collaboration RevMan 5.1.6 software, according to the random effects model with a confidence interval of 95% (95%). It was established that the effect was statistically significant at $p < 0.05$, and the homogeneity of the studies was assessed using the I² index.

Results: The search strategy retrieved 154 studies, of which only five could be included in the quantitative analysis. The analysis revealed a not statistically significant mean difference (MD) in weight loss in the analyzed sample and subgroups: Asian individuals -0.81 kg (95% CI: -2.76 to 1.13; $P = 0.41$; $I^2 = 0\%$, $n = 210$), Caucasians -0.73 kg (95% CI: -3.22 to 1.75; $P = 0.45$; $I^2 = 0\%$; $n = 91$), as well as in the sample as a whole: -0.78 kg (95% CI: -2.31 to 0.75; $P = 0.32$; $I^2 = 0\%$; $n = 301$). No statistically significant decrease was revealed in BMI in the analyzed sample and subgroups: Asian individuals -0.65 (95% CI: -1.85 to 0.54; $P = 0.29$; $I^2 = 0\%$; $n = 71$), -0.21 Caucasians (95% CI: -0.96 to 0.53; $P = 0.58$; $I^2 = 22\%$; $n = 91$), as well as in the sample as a whole: -0.31 kg (95% CI: -0.88 to 0.27; $P = 0.30$; $I^2 = 0\%$; $n = 162$), nor for the waist circumference 0.08 cm (95% CI: -0.39 to 0.55; $P = 0.73$; $I^2 = 3\%$; $n = 301$) or hip (95% CI: -1.14 to 0.93; $P = 0.85$; $I^2 = 0\%$; $n = 210$). In the evaluation of the effect on the percentage of fat mass (FM%), MD was found not statistically significant for population subgroups:

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a 0,53; P = 0,58; I² = 22%; n = 91); como en su conjunto: -0,31 kg (95% IC: -0,88 a 0,27; P = 0,30; I² = 0%; n = 162), ni para el perímetro de cintura 0,08 cm (95% IC: -0,39 a 0,55; P = 0,73; I² = 3%; n = 301) o cadera (95% IC: -1,14 a 0,93; P = 0,85; I² = 0%; n = 210). En la evaluación del efecto sobre el porcentaje de masa grasa (%MG), no se halló una DM estadísticamente significativa para los subgrupos de población: individuos asiáticos -0,76 (95% IC: -1,59 a 0,08; P = 0,08; I² = 0%; n = 169), individuos caucásicos -0,76 (95% IC: -2,22 a 0,70; P = 0,31; I² = 36%; n = 93); pero sí una pequeña, aunque estadísticamente significativa, disminución en su conjunto -0,76 (95% IC: -1,44 a -0,09; P = 0,03; I² = 0%; n = 260).

Discusión: El efecto estadísticamente significativo del té verde sobre el %MG de toda la muestra no fue clínicamente relevante, hecho remarcado en los resultados de otros metaanálisis.

Conclusión de los autores: La ingesta de té verde o de sus extractos no ejerce efectos estadísticamente significativos sobre el peso de adultos con sobrepeso u obesidad. Se observa un pequeño efecto sobre la disminución del porcentaje de masa grasa, pero no es clínicamente relevante.

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Palabras clave: *Té verde. Sobrepeso. Obesidad. Cafeína. Catequinas.*

Introducción

La obesidad es una enfermedad¹ que se está convirtiendo en la epidemia del siglo XXI y en uno de los problemas que más preocupa a los Sistemas de Salud de los Países Desarrollados. Según un informe de la Organización para la Cooperación y el Desarrollo Económico (OCDE), en España, dos de cada tres hombres tienen sobrepeso y una de cada seis personas padece obesidad², situándose la prevalencia alrededor del 25%³. Esta enfermedad representa un importante factor para el desarrollo de comorbilidades que aumentan sustancialmente la mortalidad de la población, disminuyen su calidad de vida y suponen un gasto sanitario muy elevado⁴⁻⁸. Pese a que el control de la ingesta energética y el aumento de la actividad física siguen siendo los pilares fundamentales en el tratamiento del sobrepeso y la obesidad^{8,9}, existe un aumento en el interés de nuevas estrategias para la pérdida de peso. En este sentido, y a causa de los escasos requisitos que según la legislación vigente deben cumplir los llamados “productos dietéticos”¹⁰, existen en el mercado un sinnúmero de productos alimenticios con supuestos beneficios para la pérdida de peso que no han sido testados clínicamente y de los que, en consecuencia, no se conoce su eficacia y seguridad¹¹.

Tanto la disminución de la ingesta energética como el aumento del gasto energético son puntos clave para conseguir un balance energético negativo y, en consecuencia, para traducirse en una disminución del peso corporal. En este sentido, algunos autores han reportado que la cafeína puede tener un efecto termogénico¹²⁻¹⁴, que podría ejercer cierto efecto en el aumento del gasto energético basal, aunque la Autoridad Europea de Seguridad Alimentaria

Asian individuals -0.76 (95% CI: -1.59 to 0.08; P = 0.08; I² = 0%; n = 169), Caucasians -0.76 (95% CI: -2.22 to 0.70; P = 0.31; I² = 36%; n = 93), but a small, although statistically significant, decrease in the overall effect was found -0.76 (95% CI: -1.44 to -0.09; P = 0.03; I² = 0%; n = 260).

Discussion: The statistically significant effect of green tea on the FM% of the entire sample was not clinically relevant, a fact also highlighted in the results of other meta-analysis.

Conclusion of the authors: Green tea or gree tea extracts intake or its extracts exerts no statistically significant effect on the weight of overweight or obese adults. There is a small effect on the decrease in the percentage of fat mass, but it is not clinically relevant.

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Keywords: *Tea. Overweight. Obesity. Caffeine. Catechin.*

considera que este efecto no está probado¹⁵. Asimismo, se ha detectado que el efecto termogénico del té verde no puede atribuirse únicamente a su contenido en cafeína, observándose que la mezcla de cafeína y catequinas-polifenoles (sustancias presentes en el té verde) puede tener un efecto mayor sobre el gasto energético que una cantidad equivalente de cafeína^{16,17}.

Pese a que se han publicado varias revisiones de la literatura científica sobre el papel potencial que puede tener el té verde como coadyuvante en la pérdida de peso y en la prevención del *weight cycling* (conocido como “efecto yoyó”)¹⁸⁻²⁰, su revisión de forma sistemática y crítica es menos abundante²¹⁻²³. Aunque se dispone de revisiones sistemáticas y metaanálisis²¹⁻²³, existen importantes consideraciones de inclusión y exclusión de estudios (consumo basal de cafeína y catequinas y cuantificación del consumo de ambas sustancias, control de su ingesta en los grupos control, alteraciones y enfermedades que pueden afectar espontáneamente al peso de los individuos sujetos a estudio, duración de la intervención o control de otros aspectos terapéuticos, como la dieta y el ejercicio físico) así como de análisis de subgrupos (individuos caucásicos y individuos asiáticos) que, según la opinión de los autores de esta revisión, podrían ejercer como factores de confusión. Asimismo, los autores de sendas revisiones^{21,22} (excepto Jurgens TM et al. 2012²³) no establecen una clara diferencia entre los resultados estadísticamente significativos y los resultados clínicamente relevantes.

La presente investigación (revisión sistemática y metaanálisis) analiza la magnitud del efecto del consumo de té verde o sus extractos (cafeína y catequinas) sobre el peso corporal y en la composición corporal de ambos

sexos, mayores de 18 años y menores de 60 años con un IMC entre 25 y 40 kg/m², obtenidos de ensayos clínicos controlados (intervención y placebo), aleatorizados de no menos de 12 semanas de seguimiento, a cuyo grupo placebo no se hayan administrado sustancias que pudieran generar efectos de confusión.

Material y métodos

Criterios de inclusión

Tomando como base las características de los metaanálisis publicados hasta la fecha²¹⁻²³, la presente revisión consideró los siguientes criterios para la selección de estudios: ser ensayos clínicos con un mínimo de dos grupos paralelos (grupo intervención y grupo placebo) con asignación aleatoria, doble cegado, y con un seguimiento mínimo de 12 semanas. En los estudios se debía poder evaluar el consumo habitual de cafeína y la etnicidad de la muestra, ya que el consumo basal de té (diferente en función de la etnia) podría afectar a la magnitud del efecto²².

La muestra debía ser de individuos de ambos géneros, mayores de 18 años con un IMC entre 25 y 40 kg/m², que no padecieran enfermedades que pudieran influir espontáneamente en el peso corporal, no estar bajo prescripción de ningún medicamento y ser no fumadores.

Al grupo intervención (GI) debía administrársele té verde (bebida) o extracto de té verde (pastillas, cápsulas o cualquier otra presentación) con una cantidad de cafeína y catequinas cuya dosis pudiera cuantificarse, y que no contuviese ninguna otra sustancia que pudiera ejercer efectos sobre el peso corporal o su composición. Al grupo placebo (GP) debía administrársele una bebida, pastilla o cápsula (o cualquier otra presentación) idéntica a la suministrada al GI que no contuviese las sustancias sujetas a estudio (cafeína o catequinas) o principios activos que pudieran tener efectos significativos sobre la pérdida de peso o sobre la saciedad. Entre ambos grupos debía existir una condición isocalórica y de control de la actividad física que posibilitase identificar de forma inequívoca que la diferencia entre dichos grupos era debida únicamente al efecto del té verde. No se aceptaron como sistemas adecuados para la pérdida de peso las dietas de muy bajo contenido calórico (*very low calorie diets*), debido a sus efectos sobre la masa libre de grasa y a su posible efecto sobre el gasto energético basal²⁴, pudiendo ejercer por tanto como efecto de confusión.

Los estudios incluidos debieron ofrecer, como mínimo, el resultado de la variación de la masa corporal (kg), la variación del IMC (kg/m²), o la variación de la masa grasa (expresada en porcentaje respecto a la masa corporal o de forma absoluta en kg). También se evaluaron, si aparecían, los siguientes datos antropométricos: variación de la masa libre de grasa (kg), perímetro de la cintura (cm), perímetro de la cadera (cm) o el ratio de perímetros cintura/cadera.

Estrategia de búsqueda para la obtención de estudios

Búsqueda de estudios publicados entre el 1 de enero de 2000 hasta el 1 de enero de 2013, ambos incluidos. Se buscaron estudios en la base de datos PubMed/Medline, no excluyéndose ninguna lengua. La estrategia de búsqueda fue la siguiente: (“green tea”[All Fields] OR “green tea extract AR25 “[Substance]) AND (“Body Mass Index”[Mesh] OR (“Body Weight”[Mesh] OR (“body”[All Fields] AND “weight”[All Fields]) OR “body weight”[All Fields]) OR “Body Weight Changes”[Mesh] OR (“Weights and Measures”[MeSH Terms] OR (“weights”[All Fields] AND “measures”[All Fields]) OR “weights and measures”[All Fields] OR “weight”[All Fields]) OR “Body Composition”[Mesh] OR (“Body Fat Distribution”[Mesh] OR “Adipose Tissue”[Mesh] OR “fat mass”[All Fields]) OR (“Muscles”[MeSH Terms] OR “muscles”[All Fields] OR “muscle”[All Fields] OR “fat free mass”[All Fields]) AND (“Obesity”[Mesh] OR “obesity”[All Fields]) OR (“Overweight”[Mesh] OR “overweight”[All Fields]))

No se incluyeron límites de especie (humano o animal), diseño de estudio (ensayos clínicos controlados aleatorizados u otros), o edades para aumentar la sensibilidad de la búsqueda y hacer el cribado de forma manual.

Debido a que no se han encontrado estudios sobre el grado de solapamiento de estudios incluidos en diferentes bases de datos en materia de nutrición humana y dietética, únicamente se explotó dicha base de datos.

Asimismo, se buscaron más estudios potencialmente relevantes mediante el sistema que el manual *Cochrane* define como *pearling* (o “encontrar perlas”) revisando los estudios incluidos en los dos metaanálisis publicados hasta la fecha^{21,22}. No se analizó el metaanálisis publicado por Jurgens TM et al. 2012²³, ya que en el momento de la obtención de dicha publicación, el presente metaanálisis ya estaba en fase de análisis de los datos.

Obtención y tratamiento de datos y análisis

El proceso de selección fue realizado por dos revisores independientes. De los artículos recuperados mediante la estrategia de búsqueda especificada anteriormente se excluyeron de forma manual los que no fueran estudios de intervención (revisiones, estudios epidemiológicos, guías de práctica clínica, cartas al editor, comentarios), ensayos clínicos no controlados y aleatorizados, o estudios con características o contenidos claramente no relevantes para la presente revisión. Se obtuvieron los textos completos de todos los estudios preseleccionados, con la finalidad de poder aplicar los criterios de inclusión/exclusión descritos, y eliminar aquellos estudios que no los cumplieran, indicando sus razones. Finalmente se seleccionaron los estudios que permitieran un análisis cuantitativo de las medidas antropométricas indicadas anteriormente.

Los estudios seleccionados para su análisis cuantitativo fueron clasificados en función de si se trataba de una intervención cuyo objetivo era la pérdida de peso, o bien el mantenimiento o prevención de la ganancia de peso corporal después de una intervención de pérdida de peso. En los estudios de pérdida de peso, el punto inicial correspondió con los valores medidos en tiempo cero, mientras que en los estudios de mantenimiento del peso corporal, los valores iniciales correspondieron a los valores medidos justo después de una breve fase de pérdida de peso. El punto final se correspondió siempre con los valores medidos justamente después de la intervención. En los casos en que existieron diferentes grupos intervención con dosis de cafeína diferentes, se comparó el efecto de cada grupo intervención con el efecto en el grupo control. Asimismo, se clasificaron los estudios en función de la etnicidad de sus participantes y en función del consumo de cafeína pre-intervención. De cada estudio incluido en la revisión se extrajeron datos referentes a: los métodos (tipo de diseño, cegado, duración), los participantes (géneros, IMC medio, rango de edades, etnicidad), la intervención (dosis y sustancias ofrecidas al grupo intervención y al grupo placebo), y los resultados (valores de las medidas antropométricas).

En relación a los resultados, se extrajeron las medias y las desviaciones estándar de los datos antropométricos de interés para la presente revisión, que fueron copiados en una hoja de *Excel* para realizar operaciones intermedias de homogenización de datos, y posteriormente trasladados al sistema de análisis estadístico de datos cuantitativos del programa *Review Manager 5.1.6*, propiedad de la *Cochrane Collaboration*²⁵.

Asimismo, de cada estudio se estableció si existía un riesgo alto, bajo o incierto de los siguientes tipos de sesgo propuestos por la *Cochrane Collaboration*: generación de las secuencias aleatorias (sesgo de selección), ocultamiento de la asignación (sesgo de selección), cegado de los participantes y del personal responsable de la intervención (sesgo de realización), cegado de la evaluación de los resultados (sesgo de detección), datos de resultados incompletos por abandonos (sesgo de desgaste), e información selectiva (sesgo de información).

La estimación de la magnitud del efecto de las variables de datos continuos fue agregada en el presente metaanálisis mediante la diferencia media (y de sus desviaciones estándar) de los valores iniciales y finales del grupo intervención y del grupo control (respectivamente).

En el caso de que los autores de los estudios originales hubieran omitido datos de interés para la actual revisión, o que el estudio estuviera escrito en una lengua distinta al español, inglés, francés, italiano, portugués, o alemán, se contactó con dichos autores para obtener los datos necesarios.

Para determinar la heterogeneidad entre estudios (subgrupos y total), se utilizó el índice I^2 propuesto por la *Cochrane Collaboration*. Un valor $I^2 < 25\%$ se consideró como heterogeneidad leve, entre 25% y 75% heterogeneidad media y $> 75\%$ heterogeneidad alta.

El análisis de los datos continuos se realizó en base al modelo de efectos aleatorios (*random-effects model*) con un intervalo de confianza del 95% (CI 95%), tanto para el estudio del efecto de subgrupos como para el efecto total. Los valores negativos para el efecto observado, indican que el efecto favorece al grupo intervención, mientras que el valor cero o los valores positivos, indican que no existe efecto, o bien que el efecto observado es favorable al grupo control. Se estimó que el efecto era estadísticamente significativo en $p < 0.05$.

Resultados

Descripción de los estudios recuperados

La estrategia de búsqueda en PubMed/Medline reportó 144 estudios relacionados con la ingesta de té verde o sus extractos y el peso corporal, y 10 más fueron hallados e incorporados a través de otros sistemas de obtención de estudios, descritos anteriormente. Después de leer los 154 estudios potenciales para la inclusión en la presente investigación, 101 fueron eliminados por no tratarse de ensayos controlados aleatorizados, 2 por no estar realizados exclusivamente en humanos, y 22 artículos por no ser relevantes para la revisión actual. De los 29 estudios preseleccionados, 21 fueron eliminados por no cumplir con todos los criterios de inclusión. De los 8 restantes, únicamente 5 contenían los datos adecuados para llevar a cabo el análisis cuantitativo (fig. 1).

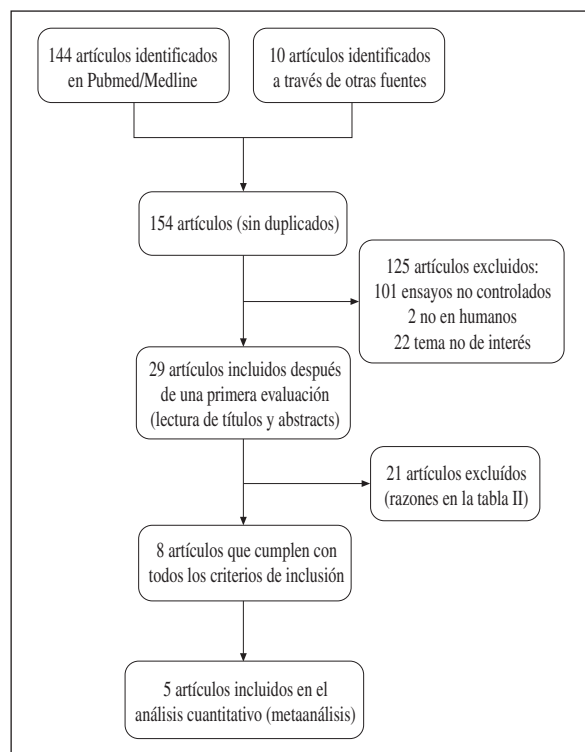


Fig. 1.—Diagrama de flujo del proceso de selección de estudios.

Tabla I
Estudios incluidos en el análisis cuantitativo y sus principales características

Ref.	Autores/as	Año	Métodos	Participantes	Grupos	Medidas de resultado	Caféina basal
26	Wang H et al.	2010	ECA Grupos paralelos Doble ciego Duración 12 sem.	Géneros: hombres y mujeres; IMC: > 25; Edades: 18 a 55; No individuos caucásicos	GI1: 1 té verde/día: 458 mg catequinas/104 mg caféina GI2: 1 té verde/día: 468 mg catequinas/126 mg caféina GI3: 1 té verde/día: 886 mg catequinas/198 mg caféina GP: té verde sin caféina ni catequinas Todos: Dieta mantenimiento de peso	Peso (kg); Masa grasa (%); Masa grasa (kg); Masa libre de grasa (kg); Perímetro cintura (cm); Perímetro cadera (cm)	Bajo (< 200 mg)
27	Hursel R et al.	2009	ECA Grupos paralelos Doble ciego Duración 12 sem.	Géneros: hombres y mujeres; IMC: > 25; Edades: 18 a 60; Individuos caucásicos	GI: 6 cápsulas de extracto de té verde (ETV)/día: 270 mg catequinas/150 mg caféina GP: 6 cápsulas de aceite vegetal Todos: Dieta mantenimiento de peso (normo o hiperproteica)	Peso (kg); IMC (kg/m ²); Masa grasa (%); Masa grasa (kg); Masa libre de grasa (kg); Perímetro cintura (cm)	Bajo (< 100 mg)
28	Auvichayapat P et al.	2008	ECA Grupos paralelos Doble ciego Duración 12 sem.	Géneros: hombres y mujeres postmenopáusicas; IMC > 25; Edades: 40-60; No individuos caucásicos	GI: 3 cápsulas extracto de té verde (ETV)/día: 140.85 mg catequinas/86.58 mg caféina GP: 3 cápsulas de celulosa Todos: Dieta de 8373.6 kJ/día para mantenimiento del peso Actividad física: rutina habitual (sedentarios)	Peso (kg); IMC (kg/m ²); Masa grasa (%); Perímetro cintura (cm); Perímetro cadera (cm); Ratio cintura/cadera	Bajo (no identificada cantidad exacta < 300 mg)
29	Hsu CH et al.	2008	ECA Grupos paralelos Doble ciego Duración 12 sem.	Géneros: mujeres; IMC: > 25; Edades: 16 a 60; No caucásicas	GI: 3 cápsulas de extracto de té verde (ETV)/día: 491 mg catequinas/27.3 mg caféina GP: 3 cápsulas de celulosa Todos: Dieta normal para mantenimiento del peso	Peso (kg); IMC (kg/m ²); Perímetro cintura (cm); Perímetro cadera (cm)	Bajo (no identificada cantidad exacta < 300 mg)
30	Kovacs EM et al.	2004	ECA Grupos paralelos Doble ciego Duración 13 sem.	Géneros: hombres y mujeres; IMC: > 25; Edades: 18 a 60; Individuos caucásicos	GI: 6 cápsulas de extracto de té verde (ETV)/día: 573 mg catequinas/104 mg caféina GP: 6 cápsulas placebo (no se identifica) Todos: Dieta de mantenimiento de peso (después de un periodo de pérdida de peso con VLCD)	Peso (kg); IMC (kg/m ²); Masa grasa (%); Masa grasa (kg); Masa libre de grasa (kg); Perímetro cintura (cm); Ratio cintura/cadera	Alto (>300 mg/día)

ECA: Ensayo controlado aleatorizado; IMC: Índice de masa corporal; GI: Grupo intervención; GP: Grupo placebo.

Tabla II
Relación de estudios excluidos y razón(es) para su exclusión

<i>Ref.</i>	<i>Autores/as</i>	<i>Año</i>	<i>Razón(es) de exclusión</i>
31	Brown AL et al.	2011	El grupo intervención recibe una bebida sin cafeína.
32	Stendell-Hollis NR et al.	2010	El grupo control recibe una bebida con igual contenido en cafeína que el grupo intervención.
33	Belza A et al.	2009	El grupo intervención recibe una sustancia (tirosina), además de las sustancias de interés.
34	Brown AL et al.	2009	El grupo intervención recibe una bebida sin cafeína.
35	Frank J et al.	2009	Seguimiento de menos de 12 semanas. El grupo control recibe una bebida con igual contenido en cafeína que el grupo intervención.
36	Maki KC et al.	2009	El grupo control recibe una bebida con igual contenido en cafeína que el grupo intervención.
37	Nagao T et al.	2009	La muestra contiene sujetos diagnosticados de diabetes mellitus tipo 2, y el grupo control recibe una bebida con igual contenido en cafeína que el grupo intervención.
38	Matsuyama T et al.	2008	La muestra contiene sujetos con edades comprendidas entre 6 y 16 años de edad, y el grupo control recibe una bebida con igual contenido en cafeína que el grupo intervención.
39	Takeshita M et al.	2008	El grupo intervención recibe una bebida sin cafeína.
40	Hill AM et al.	2007	El grupo intervención recibe una bebida sin cafeína.
41	Nagao T et al.	2007	El grupo control recibe una bebida con igual contenido en cafeína que el grupo intervención.
42	Chan CC et al.	2006	No es un estudio doble ciego, y la muestra contiene sujetos diagnosticados de síndrome poliquístico de ovario.
43	Fukino Y et al.	2005	No es un estudio doble ciego y que la muestra contiene sujetos diagnosticados de Diabetes tipo 2
44	Harada U et al.	2005	El grupo control recibe una bebida con igual contenido en cafeína que el grupo intervención.
45	Kozuma K et al.	2005	El grupo intervención recibe una bebida sin cafeína.
46	Nagao T et al.	2005	La muestra contiene sujetos con un IMC considerado normopeso, y el grupo control recibe una bebida con igual contenido en cafeína que el grupo intervención.
47	Maron DJ et al.	2003	El grupo intervención recibe una bebida con contenido en cafeína cuya cantidad no está adecuadamente descrita.
48	Chantre P et al.	2002	No hay grupo placebo-controlado.
49	Tsuchida T et al.	2002	El grupo control recibe una bebida con igual contenido en cafeína que el grupo intervención.
50	Hase T et al.	2001	El grupo control recibe una bebida con igual contenido en cafeína que el grupo intervención.
51	Nagao T et al.	2001	El grupo control recibe una bebida con igual contenido en cafeína que el grupo intervención.

En la tabla I se enumeran los estudios incluidos en el análisis cuantitativo y sus principales características²⁶⁻³⁰. En la tabla II se enumeran los estudios excluidos y se indica la razón por la que fueron eliminados³¹⁻⁵¹.

Solamente 5 estudios contenían la información adecuada para realizar el análisis cuantitativo²⁶⁻³⁰.

Se evaluó el riesgo de sesgo en todos los estudios incluidos en nuestro análisis. En la figura 2 se ofrece el

análisis de evaluación de sesgo propuesto por *Cochrane Collaboration*²⁵.

Efecto de la intervención

Efecto del té verde en el peso corporal total (fig. 3): 5 estudios evaluaron la relación entre la ingesta de té verde o sus extractos y su efecto en el peso corporal

Wang, 2010	Kovacs, 2004	Hursel, 2009	Hsu CH, 2008	Auvichayapat, 2008	
			+		Generación de secuencias aleatorias (sesgo de selección)
	+		+	+	Ocultamiento de asignación (sesgo de selección)
+	+	+	+	+	Cegado de participantes y personal (sesgo de realización)
+	+	+	+	+	Cegado de evaluación de resultados (sesgo de detección)
+	+	+	+	+	Datos incompletos por abandono (sesgo de desgaste)
+	+	+	+	+	Información selectiva (sesgo de información)

Fig. 2.—Resumen del riesgo de sesgo de los estudios incluidos en el análisis cuantitativo.

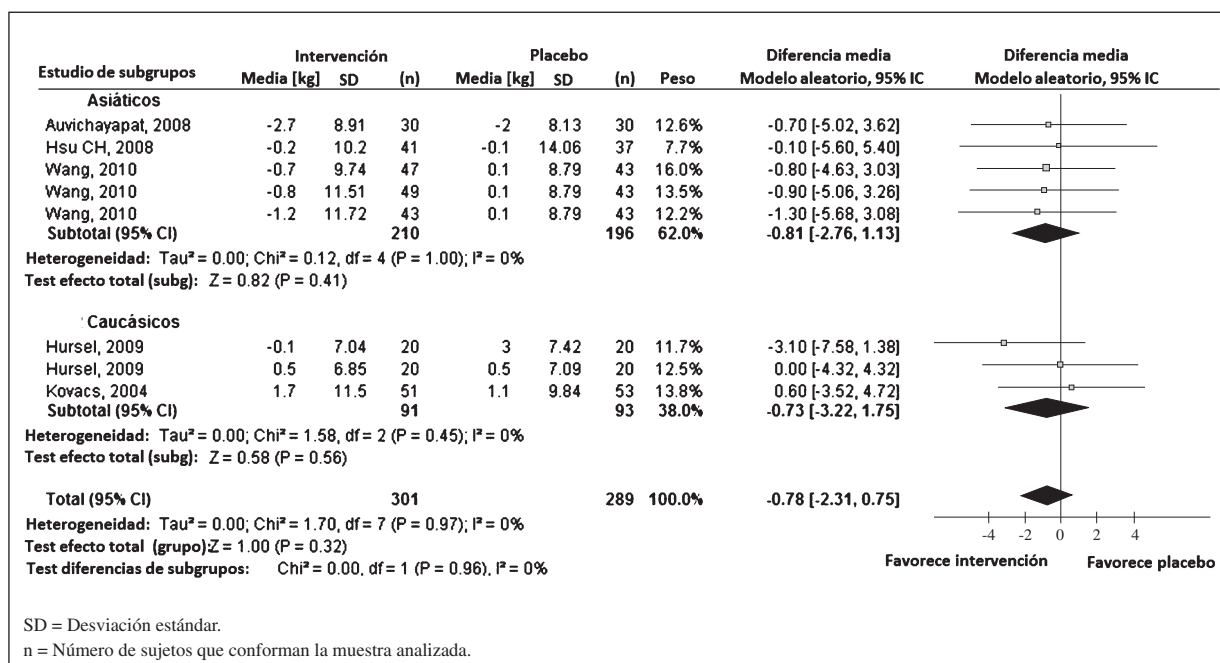


Fig. 3.—Efecto del consumo de té verde en el peso corporal total (kg); subgrupos individuos asiáticos e individuos caucásicos.

total (n = 301), 3 estudios en individuos asiáticos (n = 210) y 2 estudios en individuos caucásicos (n = 91). El análisis estadístico en el subgrupo de individuos asiáticos reveló una diferencia media (DM) estadísticamente no significativa de pérdida de peso de -0,81 kg (95% IC: -2,76 a 1,13; P = 0,41; I² = 0%; n = 210). El análisis estadístico en el subgrupo de individuos caucásicos reveló una DM estadísticamente no significativa de pérdida de peso de -0,73 kg (95% IC: -3,22 a 1,75; P = 0,45; I² = 0%; n = 91). El análisis del efecto total, reveló una DM estadísticamente no significativa de -0,78 kg (95% IC: -2,31 a 0,75; P = 0,32; I² = 0%; n = 301).

Efecto del té verde en el IMC (fig. 4): 4 estudios evaluaron la relación entre la ingesta de té verde o sus extractos y su efecto en el IMC (n = 162), 2 estudios en individuos asiáticos (n = 71) y 2 estudios en individuos caucásicos (n = 91). El análisis estadístico en el subgrupo de individuos asiáticos reveló una diferencia media (DM) estadísticamente no significativa de disminución del IMC de -0,65 (95% IC: -1,85 a 0,54; P = 0,29; I² = 0%; n = 71). El análisis estadístico en el subgrupo de individuos caucásicos reveló una DM estadísticamente no significativa de disminución del IMC de -0,21 (95% IC: -0,96 a 0,53; P = 0,58; I² =

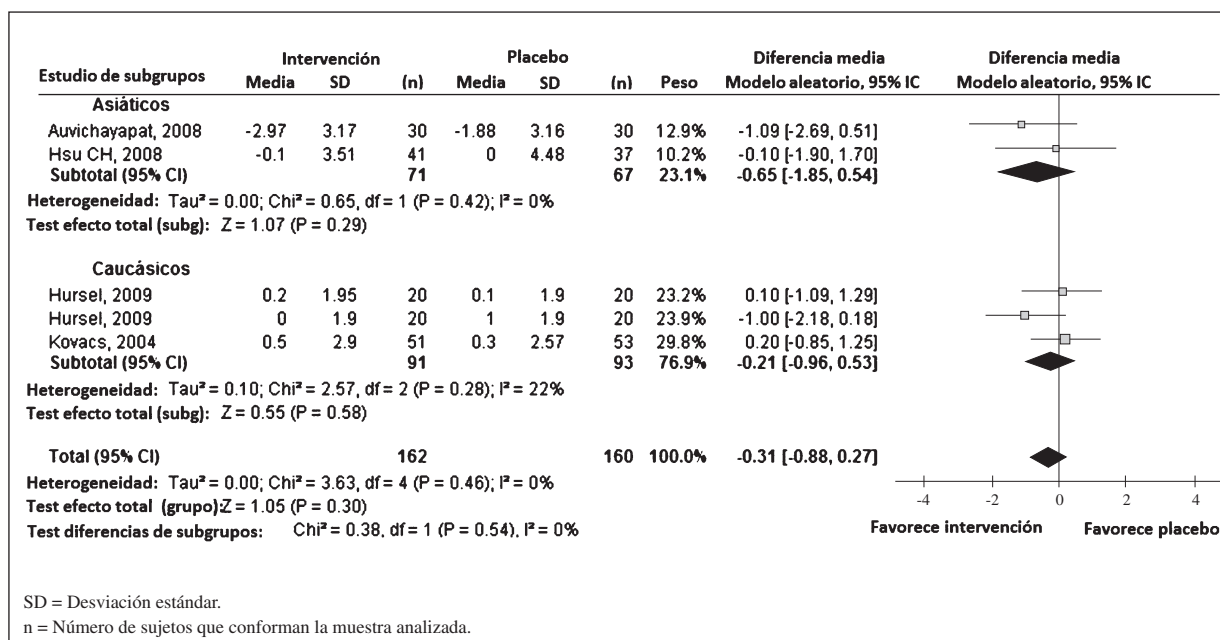


Fig. 4.—Efecto del consumo de té verde en el IMC; subgrupos individuos asiáticos e individuos caucásicos.

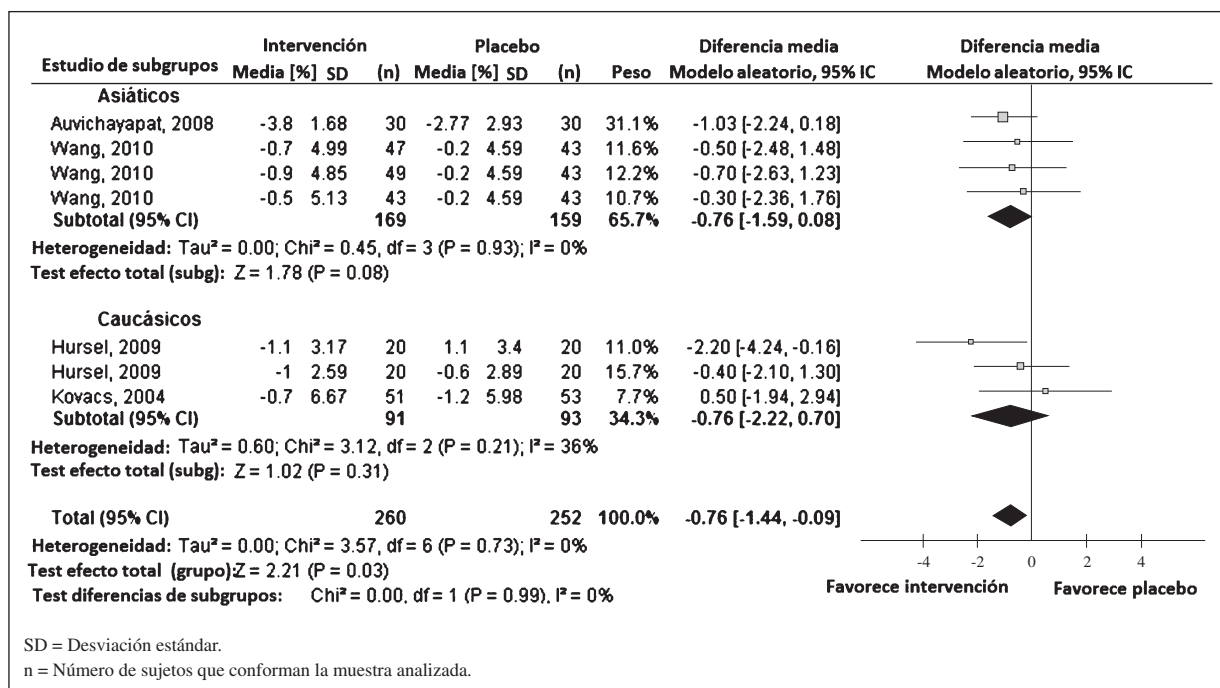


Fig. 5.—Efecto del consumo de té verde en el porcentaje de grasa corporal (%); subgrupos individuos asiáticos e individuos caucásicos.

22%; n = 91). El análisis del efecto total, reveló una DM estadísticamente no significativa de disminución del IMC de -0,31 kg (95% IC: -0,88 a 0,27; P = 0,30; I² = 0%; n = 162).

Efecto del té verde en el porcentaje de masa grasa (%MG) (fig. 5): 4 estudios evaluaron la relación entre la ingesta de té verde y su efecto en el %MG (n = 260), 2 estudios en individuos asiáticos (n = 169) y 2 estudios en individuos caucásicos (n = 93). El análisis estadístico en el subgrupo de individuos asiáticos re-

veló una diferencia media (DM) estadísticamente no significativa de disminución del %MG de -0,76 (95% IC: -1,59 a 0,08; P = 0,08; I² = 0%; n = 169). El análisis estadístico en el subgrupo de individuos caucásicos reveló una DM estadísticamente no significativa de disminución del %MG de -0,76 (95% IC: -2,22 a 0,70; P = 0,31; I² = 36%; n = 93). El análisis del efecto total, reveló una DM estadísticamente significativa de disminución del %MG de -0,76 (95% IC: -1,44 a -0,09; P = 0,03; I² = 0%; n = 260).

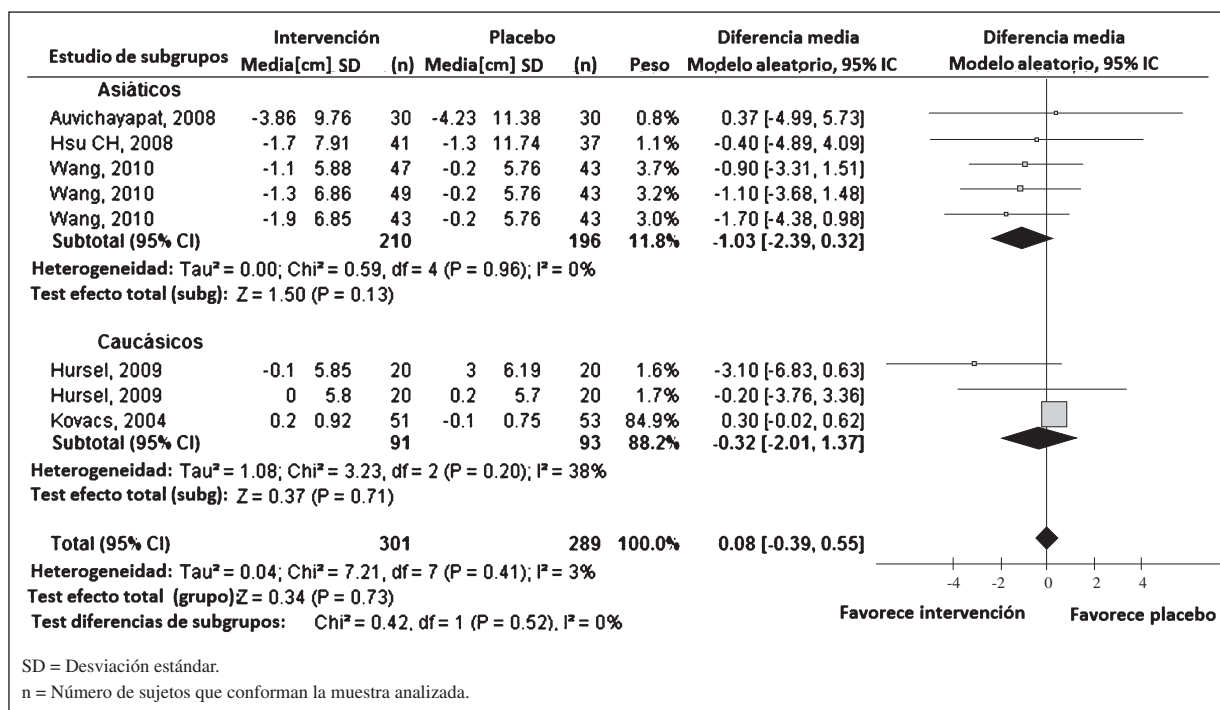


Fig. 6.—Efecto del consumo de té verde en el perímetro de cintura (cm); subgrupos individuos asiáticos e individuos caucásicos.

Efecto del té verde en el perímetro de la cintura (fig. 6): 5 estudios evaluaron la relación entre la ingesta de té verde y su efecto en el perímetro de cintura (n = 301), 3 estudios en individuos asiáticos (n = 210) y 2 estudios en individuos caucásicos (n = 91). El análisis estadístico en el subgrupo de individuos asiáticos reveló una diferencia media (DM) estadísticamente no significativa de disminución del perímetro de cintura de -1,03 cm (95% IC: -2,39 a 0,32; P = 0,13; I² = 0%; n = 210). El análisis estadístico en el subgrupo de individuos caucásicos reveló una DM estadísticamente no significativa de disminución del perímetro de cintura de -0,32 cm (95% IC: -2,01 a 1,37; P = 0,71; I² = 38%; n = 91). El análisis del efecto total, no reveló ningún efecto en la variación del perímetro de cintura de 0,08 cm (95% IC: -0,39 a 0,55; P = 0,73; I² = 3%; n = 301).

Efecto del té verde en el perímetro de la cadera (fig. 7): 3 estudios evaluaron la relación entre la ingesta de té verde y su efecto en el perímetro de cintura en individuos asiáticos (n = 210). El análisis estadístico reveló una diferencia media (DM) estadísticamente no significativa de disminución del perímetro de cadera de -0,10 cm (95% IC: -1,14 a 0,93; P = 0,85; I² = 0%; n = 210).

Discusión

El metaanálisis reveló que la ingesta de té verde o de sus extractos no se asocia a efectos estadísticamente significativos sobre la disminución del peso corporal, del IMC, del porcentaje de grasa corporal, del perí-

metro de cintura y de la cadera en adultos asiáticos o individuos caucásicos. El único resultado estadísticamente significativo fue para el efecto del té verde en el porcentaje de masa grasa cuando se evaluó el tamaño del efecto total (sin tener en cuenta los subgrupos), obteniéndose una disminución del 0,76% en la estimación de la masa grasa. La magnitud del efecto, pese a ser estadísticamente significativa, no es clínicamente relevante.

En comparación con el metaanálisis Hursel R et al. 2009²¹, los autores del presente metaanálisis decidieron eliminar el estudio de Kozuma K et al. 2005⁴⁵ porque el grupo intervención no recibía una bebida con cafeína. También se eliminaron el estudio de Nagao T et al. 2007⁴¹, el estudio de Tsuchida T et al. 2002⁴⁹, el estudio de Hase T et al. 2001⁵⁰, y el estudio de Nagao T et al. 2001⁵¹, porque el grupo control recibía una bebida con igual contenido en cafeína que el grupo intervención. El metaanálisis de Hursel R et al. 2009²¹ solamente evaluó el efecto del té verde sobre el peso corporal total, sin observar el efecto sobre la masa grasa u otros componentes que ofrezcan un valor de adiposidad. Al igual que el presente metaanálisis, el estudio de Hursel R et al. 2009²¹ evaluó por separado los subgrupos de individuos asiáticos e individuos caucásicos. Al contrario que el presente metaanálisis, dicho estudio encontró una diferencia estadísticamente significativa entre la ingesta de té verde y la disminución del peso corporal, aunque no detalló si dicha diferencia era clínicamente relevante.

El metaanálisis de Phung OJ et al. 2010²², realizó 3 comparaciones y las evaluó por separado: (a) catequinas

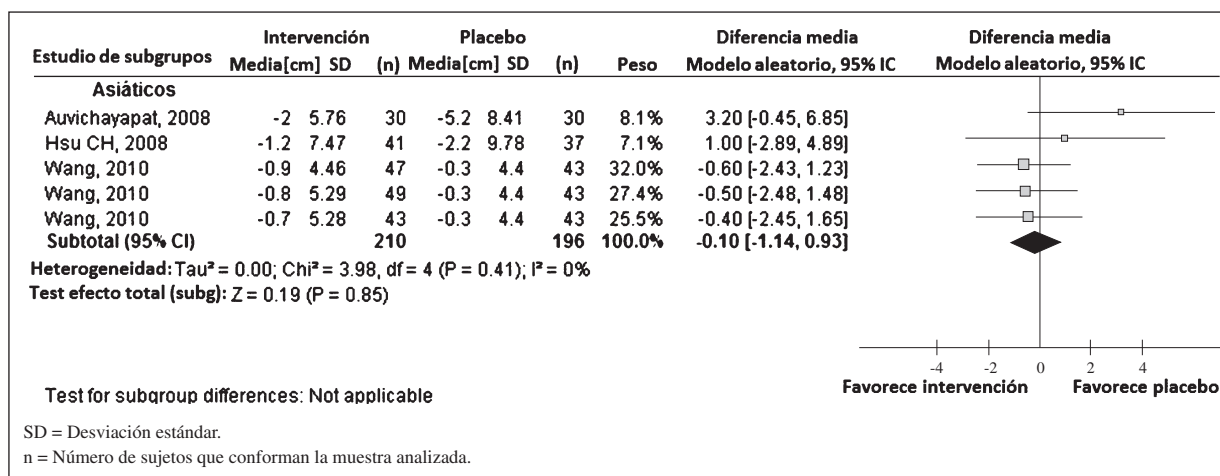


Fig. 7.—Efecto del consumo de té verde en el perímetro de cadera (cm).

y cafeína *versus* grupo control con cafeína (7 estudios); (b) catequinas y cafeína *versus* grupo control sin cafeína (6 estudios); y (c) catequinas *versus* control sin cafeína. De los 6 estudios de interés para el presente metaanálisis (comparación b), el de Chan CC et al. 2006⁴² fue eliminado porque no es un estudio doble ciego; el estudio de Fukino Y et al. 2005⁴³ porque no es un estudio doble ciego y porque los sujetos de la muestra padecían diabetes mellitus; y el estudio de Maron DJ et al. 2003⁴⁷ porque el grupo intervención recibía una bebida cuyo contenido en cafeína no estaba adecuadamente descrito. El metaanálisis de Phung OJ et al. no estableció diferentes subgrupos de población (individuos asiáticos y individuos caucásicos). Los resultados del análisis estadístico del grupo de comparación de interés para el presente estudio (comparación b), no mostraron resultados estadísticamente significativos.

Pese a no haber evaluado exhaustivamente los datos de Jurgens TM et al. 2012²³ debido a que en el momento de su publicación el presente metaanálisis ya estaba en fase de análisis de datos, las conclusiones y hallazgos del metaanálisis de la *Cochrane Collaboration* van en la misma dirección que los resultados del presente estudio: resultados estadísticamente no significativos o clínicamente irrelevantes.

Limitaciones del estudio

Asimismo, la explotación de una sola base de datos (PubMed/Medline), puede significar no haber incluido estudios publicados y de interés para la presente revisión. Sin embargo, al no existir estudios de solapamiento de bases de datos en materia de nutrición humana y dietética, se desconoce la relación entre el tiempo invertido en la búsqueda de estudios y la obtención de estudios relevantes derivados de la explotación de una o más bases de datos. Este punto debería ser estudiado con detenimiento para poder establecer las bases de datos mínimas que deben ser explotadas en materia de

nutrición humana y dietética para poder asegurar que se incluyen la mayor parte de los estudios publicados, optimizando el tiempo y los recursos invertidos en dicha tarea. En cualquier caso, la exhaustiva revisión de los estudios incluidos en dos revisiones sistemáticas y metaanálisis, minimiza el posible sesgo de selección.

Finalmente, no haber analizado de forma exhaustiva los estudios incluidos en el metaanálisis de Jurgens TM 2012 et al.²³, puede verse como una limitación más. Sin embargo, la obtención de resultados y conclusiones en la misma dirección y magnitud, hace pensar a los autores del presente metaanálisis que el riesgo de sesgo es mínimo.

Conclusiones de los autores

Los ensayos aleatorizados y controlados publicados entre los años 2000 y 2013 revelan que la ingesta de té verde o sus extractos (catequinas y cafeína) no tiene un efecto estadísticamente significativo o clínicamente relevante sobre el peso y la composición corporal de adultos de entre 18 y 60 años con sobrepeso u obesidad. Existe poca evidencia de alta calidad (ensayos controlados aleatorizados, doble ciego, de un mínimo de 12 semanas de duración) y con metodología homogénea. No se puede establecer, en base a la evidencia científica evaluada, una recomendación de consumo de té verde para la disminución o mantenimiento del peso corporal o la modificación de su composición corporal.

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Revisión

Consumo de fructosa y sus implicaciones para la salud; malabsorción de fructosa e hígado graso no alcohólico

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Resumen

La ingesta de fructosa se ha incrementado considerablemente en los últimos años, especialmente bajo la forma de jarabe de maíz alto en fructosa, debido a su gran poder edulcorante. Diversos estudios, han asociado su elevado consumo con alteraciones metabólicas, hígado graso no alcohólico y malabsorción de fructosa, entre otras patologías. Esta revisión tiene como objetivo actualizar acerca del efecto de la alta ingesta de fructosa en el hígado e intestino, asociada principalmente a alimentos procesados con fructosa agregada.

Métodos: Para la búsqueda bibliográfica se utilizaron las bases de datos de Pubmed, Scopus y Scielo, seleccionando aquellos artículos publicados después del año 2000 y resultantes de las palabras claves “fructose intake, high fructose corn syrup, nonalcoholic fatty liver and fructose, fructose malabsorption, fructose intolerance/metabolism”.

Resultados: La búsqueda arrojó 735 publicaciones de las cuales 78 cumplieron con los criterios de inclusión.

Conclusiones: El consumo de fructosa ha aumentado en las últimas décadas, especialmente a través de bebidas endulzadas y productos alimentarios con fructosa agregada. La alta ingesta de fructosa tiene un impacto a nivel intestinal y hepático, asociándose a patologías como hígado graso no alcohólico y malabsorción de fructosa.

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Palabras clave: *Ingesta de fructosa. Hígado graso no alcohólico y fructosa. Malabsorción de fructosa.*

FRUCTOSE CONSUMPTION AND ITS HEALTH IMPLICATIONS; FRUCTOSE MALABSORPTION AND NONALCOHOLIC FATTY LIVER DISEASE

Abstract

Fructose intake has increased considerably in recent years, especially in the form high fructose corn syrup, due its high sweetening power. Several studies have associated high intake of fructose to metabolic alterations, as nonalcoholic fatty liver disease and fructose malabsorption, among other pathologies. This review aims to update about the effect of high intake of fructose in the liver and intestine, mainly associated with processed foods with added fructose.

Methods: An updated literature search was conducted using databases (Pubmed, Scopus and SciELO), selecting articles published after the year 2000, resulting from the keywords “fructose intake, fructose intolerance, nonalcoholic fatty liver and fructose, fructose malabsorption”

Results: Of 735 articles initially retrieved, 78 met the inclusion criteria.

Conclusions: Fructose consumption has increased in recent decades, especially due to increased consumption of sweetened beverages and processed foods with added fructose. High fructose intake has been associated to pathologies as NAFLD and fructose malabsorption.

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Keywords: *Fructose intake. Nonalcoholic fatty liver and fructose. Fructose malabsorption.*

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Abreviaturas

- ACC: Acetyl-coa carboxylase.
ACL: ATP-citrate lyase.
AG: Ácidos grasos.
AGCC: Ácidos grasos de cadena corta.
ApoB: Apolipoproteína B.
ATP: Adenosin-5'-trifosfato.
BEAs: Bebidas endulzadas con azúcar.
cAMP: Adenosin-mono-fosfato cíclico (*del inglés: Cyclic adenosine monophosphate*).
ChREBP: Proteína de unión al elemento de respuesta a carbohidratos (*del inglés: Carbohydrate responsive element-binding protein*).
DHAP: Dihidroxiacetona fosfato (*del inglés: Dihydroxyacetone phosphate*).
EHNA: Esteatohepatitis no alcohólica.
ENS: Encuesta Nacional de Consumo Alimentario.
FAS: Fatty acid synthesis.
GA3P: Glycerol 3-phosphate.
HDL: Lipoproteína de alta densidad (*del inglés: High-density lipoprotein*).
HELENA-CSS: Healthy Lifestyle in European by Nutrition in Adolescence Cross-Sectional Study.
HFCS: Jarabe de maíz alto en fructosa (*del inglés: High Fructose corn syrup*).
HGNA: Hígado graso no alcohólico.
KHK: Ceto-hexoquinasa (*del inglés: Ketohexokinase*) o Fructoquinasa.
L-CPT I: Liver-type carnitine palmitoyltransferase 1.
LDL: Lipoproteína de baja densidad (*del inglés: Low-density lipoprotein*).
LDN: Lipogénesis de novo.
MAF: Mala absorción de fructosa.
MUFA: Ácidos grasos monoinsaturados (*del inglés: Monounsaturated fatty acid*).
NF-κB: Factor nuclear kappa B (*del inglés: Nuclear factor kappa-light-chain-enhancer of activated B cells*).
NHANES: National Health and Nutrition Examination Survey.
PPAR-α: Peroxisome proliferator-activated receptor alpha.
PP2A: Proteína fosfatasa-2 (*del inglés: Protein phosphatase 2*).
ppm: Partes por millón.
SCD1: Stearoyl-coa desaturase-1.
SFA: Ácidos grasos saturados (*del inglés: Saturated fatty acid*).
SREBP: Proteína de unión al elemento de respuesta a esteroides (*del inglés: Sterol regulatory element-binding protein*).
TAGs: Triacilglicéridos.
TCA: Ácido tricarbóxico.
THE: Test de Hidrógeno Espirado.
VLDL: Lipoproteína de muy baja densidad (*del inglés: Very low density lipoprotein*).
Xu-5-P: Xylulose 5-phosphate.

Introducción

La fructosa es un monosacárido presente en forma natural en frutas, verduras, miel y en forma agregada en alimentos etiquetados como diet o light, bebidas y néctares. La ingesta de este monosacárido se ha incrementado considerablemente en los últimos años, especialmente en la forma de “Jarabe de maíz alto en fructosa”, que entrega un gran poder edulcorante en una amplia gama de alimentos procesados. En los países desarrollados y en vías de desarrollo, el consumo de bebidas gaseosas ha aumentado significativamente en la población, lo que implica un elevado consumo de fructosa asociado a efectos en la salud.

La fructosa a pesar de tener una nomenclatura similar a la glucosa, presenta diferencias en su metabolismo, por ejemplo se absorbe más lentamente que la glucosa, aunque es captada y metabolizada de manera más rápida por el hígado, su efecto estimulante sobre la liberación de insulina es inferior al de la glucosa y su captación es independiente de ésta.

Literatura reciente, asocia el consumo de fructosa con diversas alteraciones metabólicas como: Intolerancia a la fructosa de causa genética, hígado graso, alteraciones en la sensibilidad a la insulina, diabetes mellitus tipo 2 y mala absorción de fructosa (MAF) causante de síntomas gastrointestinal. El objetivo de esta revisión es actualizar acerca del efecto de la alta ingesta de este monosacárido asociado a alimentos con fructosa agregada y sus efectos a nivel intestinal y hepático en seres humanos.

Metodología

La búsqueda de la literatura se realizó con las palabras claves: fructose intake, high fructose corn syrup, nonalcoholic fatty liver and fructose, fructose malabsorption, fructose intolerance/metabolism. La información fue recolectada en las bases de datos Pubmed, Scopus y Scielo, dentro de los criterios de selección de la información se priorizó artículos publicados posterior al año 2000 a excepción de 8 artículos con años de publicación inferiores al mencionado que fueron integrados por la relevancia de su contenido. Además, se citan páginas web de relevancia en el tema. Se priorizaron las publicaciones realizadas en revistas científicas del área de la nutrición y medicina, seguido por aquellas especializadas en salud pública y tecnología de alimentos. De dicha búsqueda se encontraron 78 artículos que cumplieron con los criterios de inclusión.

Resultados

Los resultados de la información recopilada serán presentados de la siguiente forma: 1. Consumo de Fructosa (15 publicaciones); 2. Absorción y metabolismo de la Fructosa (11 publicaciones); 3. Fructosa

e implicaciones en la salud (52 publicaciones). Este último aspecto se subdividirá en: 3.1. Efectos generales de la alta ingesta de fructosa (15 publicaciones). 3.2. Mala absorción de la Fructosa (12 publicaciones) y 3.3. Fructosa e Hígado graso no alcohólico (25 publicaciones).

1. Consumo de fructosa

La fructosa es un monosacárido de 6 carbonos que se encuentra de forma natural en alimentos como frutas, verduras y miel. Durante miles de años, los seres humanos consumieron alrededor de 15 a 24 g/día de fructosa (4-5% de las calorías totales en relación a 2.000 kcal/día promedio), provenientes principalmente de frutas y verduras. Estudios iniciales de consumo de fructosa, mostraron que la ingesta promedio diaria de sacarosa (disacárido compuesto por 50% de glucosa y 50% de fructosa) alcanzaba a 80 g/día (8% de fructosa en una dieta de 2.000 kcal/día)^{1,2,3}. Actualmente, la mayor cantidad de fructosa consumida en la dieta de países desarrollados y en vías de desarrollo proviene de la adición de “jarabe de maíz” o “jarabe de maíz alto en fructosa” (HFCS, del inglés High Fructose corn syrup) que se encuentra en bebidas gaseosas, néctares, alimentos de bajo contenido calórico y alimentos libres de gluten; principalmente como edulcorante en reemplazo de la sacarosa² y/o glucosa debido a su intenso sabor dulce y su bajo índice glicémico⁴. En los últimos años diversos países han experimentado un dramático y sostenido aumento en el consumo de bebidas endulzadas con azúcar (BEAs). Las BEAs incluyen una amplia gama de bebidas de fantasía (carbonatadas o no carbonatadas), néctares de frutas y jugos azucarados, compuestos por agua, CO₂, saborizantes, acidulantes, aditivos y edulcorantes calóricos de origen natural tales como sacarosa, jarabe de maíz alto en fructosa (que consiste en glucosa y 42, 55 o incluso 90% de fructosa) o jugo de fruta concentrados^{5,6,7}.

En el año 1970, el HFCS representaba < 1% de todos los edulcorantes calóricos disponibles para el consumo en los EE.UU, aumentando rápidamente a 42% en el año 2000⁸. De esta forma, el HFCS, es la fuente dietética más importante de fructosa, presente como monosacárido libre agregado a los alimentos. La sacarosa, disacárido compuesto por fructosa y glucosa, representaría una fuente secundaria de ingesta de fructosa. De esta forma, el incremento de 1.000% reportado para la fructosa durante los últimos 40 años, se atribuye principalmente a utilización de HFCS por la industria alimentaria^{6,9}.

Del mismo modo, diversos estudios estadounidenses y europeos muestran un incremento en el consumo de bebidas gaseosas y golosinas tanto en adultos como en niños. Solo en Estados Unidos se estima un consumo de fructosa cercano a los 54,7 g/día (10% de las calorías totales), siendo los adolescentes, el grupo etario con mayor consumo que corresponde a 73 g/día⁹.

Un estudio de cohorte realizado en el mismo país examinó la tendencia nacional en el consumo de bebidas azucaradas en la NHANES entre los años 1988-1994 y 1999-2004, con una muestra de 15.979 y 13.431 sujetos mayores de 20 años, respectivamente, arrojando un aumento en el consumo de bebidas gaseosas de 58% y 63% entre los dos períodos ($p < 0,001$)¹⁰. A pesar que el consumo de fructosa en algunos países de Europa es menor que en Estados Unidos^{10,11}, un estudio transversal HELENA-CSS, ejecutado en 8 países de la comunidad europea cuyo objetivo fue describir el volumen y energía consumido a través de bebidas gaseosas en 2741 adolescentes; arrojó un consumo per cápita de 227,7 ml/día y 116,8 kcal/día, siendo el segundo producto bebestible más consumido después del agua¹¹.

A nivel mundial, Chile es el tercer país con mayor consumo per cápita de bebidas refrescantes, luego de EE.UU y México, llegando durante el año 2011 a 2 mil 449 millones de litros, donde el 81,5% corresponde a las bebidas gaseosas¹². Las bebidas no alcohólicas son el tercer producto más importante en la canasta de alimentos de la familia chilena, con un consumo per cápita de 120 litros al año (consumo per cápita de 328 ml/día), sólo superado por bienes de consumo básico como la carne y el pan¹³. En relación con estos datos, la Encuesta Nacional de Consumo Alimentario, realizada en Chile a 5.120 personas mayores de 2 años de edad, mostró que más del 80% de la población consume grupos específicos de azúcares como golosinas, bebidas y refrescos¹⁴.

2. Absorción y metabolismo de la fructosa

En el intestino delgado, específicamente en la membrana apical del enterocito se produce la absorción de fructosa, donde se encuentra el transportador de glucosa 5 (GLUT5), único y específico para fructosa, que la transporta en forma pasiva desde el lumen a la sangre^{1,15}. Otro transportador de fructosa, de baja afinidad, es el GLUT2, que también es capaz de reconocer otros monosacáridos como la glucosa y galactosa^{1,16}. Después del transporte apical mediado por GLUT5 o GLUT2, la fructosa es transportada en la membrana basolateral por GLUT2¹, donde posteriormente desde la circulación portal es transportada al hígado a través de GLUT2 o GLUT5. La fructosa se absorbe más lentamente que la glucosa, aunque es captada y metabolizada de manera más rápida por el hígado. Su efecto estimulante sobre la liberación de insulina es inferior al de la glucosa y su captación es independiente de ésta¹⁷.

La distribución del GLUT-5 en el intestino es mayor en la zona proximal (duodeno y yeyuno proximal) en comparación con segmentos distales (yeyuno e íleon distal) y su expresión génica parece estar estrictamente regulada por factores como la nutrición, hormonas y ciclos circadianos^{1,18}. De esta forma, se ha observado que su expresión en ratas recién nacidas es baja y aumenta después de la lactancia. En adultos, tanto en ra-

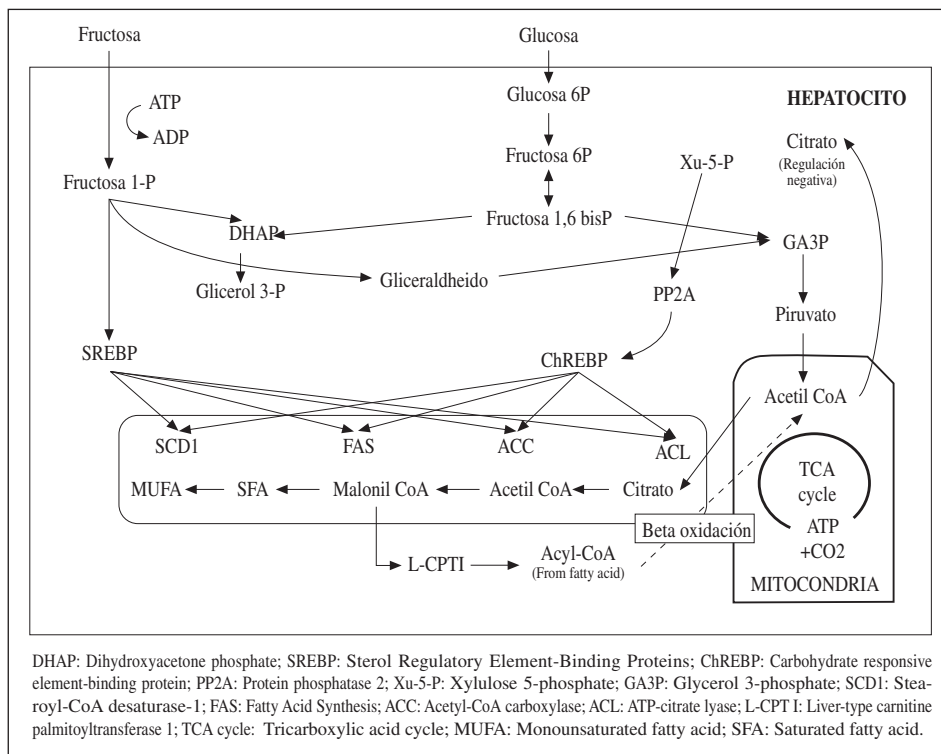


Fig. 1.—Metabolismo hepático de la fructosa. La fructosa es convertida a fructosa 1-fosfato por la fructoquinasa y posteriormente metabolizada a triosas fosfato, entrando a la vía glicolítica y sirviendo como una fuente no regulada de glicerol 3 fosfato y acetaldehído, favoreciendo el proceso de lipogénesis de novo (LDN).

tas como humanos, la expresión y actividad del GLUT-5 esta aumentada 5 veces en comparación a recién nacidos, además los niveles de expresión de mRNA de la proteína están aumentados en un 65% con una dieta alta en fructosa¹. Por lo tanto, la expresión y función de GLUT5 se ha visto incrementada por el consumo de dietas altas en fructosa y sería más eficiente a medida que avanza en edad. La expresión del gen *glut5*, se relaciona con los niveles de adenosin monofosfato cíclico (cAMP) tanto in vitro como in vivo cuando se expone a fructosa¹⁹, pero se desconocen las diferencias de los efectos del cAMP sobre la regulación transcripcional y post-transcripcional de GLUT-5 debido a la fructosa.

La absorción de fructosa aumenta en presencia de glucosa, galactosa y algunos aminoácidos¹⁹ y disminuye por la presencia de sorbitol. Si bien se desconoce cuál es el transportador del sorbitol, al parecer compartiría el transportador GLUT-5 con la fructosa²⁰.

La principal vía de metabolización de la fructosa es en el hígado, donde ocurre la conversión de fructosa en fructosa-1-fosfato por la fructoquinasa (KHK), enzima que tiene una acción 10 veces más rápida que la glucoquinasa y hexoquinasa²¹. La fructosa-1-fosfato es convertida por la aldolasa B en triosas fosfato, di-hidroxiacetona fosfato y gliceraldehído 3-fosfato, metabolitos intermediarios de la glicólisis. De esta forma, la fructosa sirve como fuente no regulada de glicerol 3-fosfato y acetil-CoA en las diversas vías metabólicas como glicólisis, gluconeogénesis y lipogénesis^{1,18,22,23,24} (fig. 1). En el caso de la glucosa, el metabolismo se regula por los niveles de citrato y de

adenosin-5'-trifosfato (ATP), que inhiben por retroalimentación a la fosfofructoquinasa, con la consecuente reducción de la conversión de la fructosa 6-fosfato en fructosa 1,6-bisfosfato^{5, 24}. Después de la ingesta de fructosa, las triosas fosfato son el principal precursor lipogénico, que pueden ser convertidas en piruvato, para posteriormente ser oxidado en el ciclo del ácido tricarboxílico (TCA) en la mitocondria a nivel hepático (fig. 1).

3. Fructosa y sus implicaciones para la salud

A nivel gastrointestinal, la ingesta elevada de fructosa, podría ocasionar síntomas asociados a una MAF, como distensión abdominal, meteorismo y diarrea. Existe una relación directa entre la aparición de sintomatología gastrointestinal y el aumento en la ingesta de fructosa²⁵. Al parecer, la fructosa tiene una absorción limitada en el intestino delgado; se ha estimado que al ingerir altas cantidades, la mitad de la población no podría absorber una carga mayor a 25 g. Las consecuencias fisiológicas de la MAF, incluyen un aumento de la carga osmótica luminal, ser sustrato de rápida fermentación para bacterias en el colon, alterar la motilidad gastrointestinal y generar un cambio en la flora intestinal²⁶.

Por otra parte, el consumo de bebidas gaseosas con HFCS, ha demostrado estar asociado al desarrollo de insulinorresistencia (IR)²⁷, hígado graso no alcohólico^{14,28}, diabetes mellitus^{6,11,29}, obesidad^{6,29} y enfermedades cardiovasculares³⁰.

3.1. Mala absorción de fructosa

Existen alteraciones en el metabolismo de la fructosa, producidas por defectos enzimáticos, que ocasionan la patogenia de Intolerancia a la fructosa. Estas alteraciones se producen por 3 defectos enzimáticos. 1.- Por deficiencia de fructoquinasa, la que no genera síntomas clínicos y por tanto no requiere tratamiento. 2.- La deficiencia de la aldolasa B, que ocasiona la Intolerancia Hereditaria a la Fructosa, e impide la transformación de la fructosa-1-fosfato en fructosa 1,6 difosfato, y 3.- Deficiencia de fructosa-1,6-difosfatasa que transforma glucosa a partir de sustratos neoglucogénicos como lactato, glicerol, alanina y también la fructosa (fig. 1)³¹.

Por otra parte, existe una absorción ineficiente de fructosa, llamada MAF, que puede o no generar síntomas gastrointestinales como diarrea, distensión y dolor abdominal. En la actualidad, se conoce que los efectos de la fructosa en el intestino son dosis dependientes³², sin embargo aún no se conoce la capacidad normal de absorción de fructosa, lo que contribuye a que sea un cuadro clínico poco entendido. De esta manera, no se ha definido si los síntomas gastrointestinales se deben a una sobrecarga de fructosa o por defectos en el transportador de fructosa a nivel intestinal.

La frecuencia de la mala absorción de fructosa se ha reportado en algunos estudios con un bajo tamaño muestral³³; similar a otros problemas relacionados a la absorción otros hidratos de carbono, como la lactosa³⁴. El Test de Hidrógeno Espirado (THE) es una técnica sencilla, útil y de bajo costo, utilizado para el diagnóstico de la mala absorción de fructosa. El fundamento de esta técnica se basa en la producción de hidrógeno generado por el metabolismo de las bacterias intestinales luego de la degradación de los hidratos de carbono. Si frente a una carga determinada de fructosa oral, se obtienen resultados en el THE superiores a 20 ppm, es indicador de MAF. A pesar que no existe una dosis clara para detectar malabsorción clínica de fructosa, actualmente se usan cargas de 25 a 50 g³⁵.

Lo anterior concuerda con estudios iniciales en personas sanas, donde se concluye que la capacidad de absorción de fructosa, oscila en un amplio rango establecido entre 5-50 g^{36,37}. Un estudio randomizado, doble ciego que utilizó dosis de 15 g, 25 g y 50 g en personas adultas sanas determinó que la capacidad normal máxima de absorción es de 25 g (en solución al 10%), y sobre ese umbral se puede pesquisar MAF³⁸, ya que se ha demostrado que dosis mayores a 50 g de fructosa serían inapropiadas para la caracterización clínica de la MAF³³. En este sentido, estudios en personas sanas reportaron que un 37,5% y 71% de los sujetos mal absorbían al administrar una carga de 50 g de fructosa en una solución al 10% y al 20%, respectivamente³⁹.

En base a lo anteriormente expuesto, la sintomatología en personas con MAF es variada, siendo los más frecuentes dolor abdominal y diarrea, que desaparecen luego de eliminar la fructosa de la dieta. Reportes de

MAF en individuos australianos, estadounidenses y tailandeses, muestran que la frecuencia de mala absorción es de 39%, 10% y 14,2%, respectivamente, con cargas de 25 g a 35 g^{35, 37-40}.

Según la literatura, la MAF se asocia a una menor expresión y/o actividad del GLUT-5 y GLUT-2^{26,32,36,41,42}. Junto con esto, no se han encontrado mutaciones en el gen *glut5* que expliquen la mala absorción.

La capacidad de provocar síntomas secundario a la MAF puede depender de varios factores: 1) la cantidad y calidad de los hidratos de carbono ingeridos, 2) el tiempo dedicado al consumo y la naturaleza de las comidas, 3) la velocidad del vaciamiento gástrico, 4) respuesta del intestino delgado a una carga osmótica, 5) la motilidad intestinal, 6) la capacidad metabólica de la microflora bacteriana del colon; y 7) la capacidad de compensación del colon para reabsorber agua y ácidos grasos de cadena corta (AGCC)^{42,43}.

No está claro si la ausencia de síntomas, después de la MAF da alguna señal de su rol en la génesis de los síntomas; sin embargo, se ha demostrado que en pacientes con alteraciones funcionales del intestino, los síntomas como distensión mejoran al restringir la fructosa de la dieta⁴⁴.

3.2. Fructosa e hígado graso no alcohólico

La enfermedad de Hígado graso no alcohólico (HGNA) se refiere a un amplio espectro de daño hepático, que consiste desde una forma benigna de esteatosis simple (definida por la presencia de triacilglicéridos (TAGs) en los hepatocitos en el examen histopatológico) el que puede progresar a una condición más severa como inflamación o esteatohepatitis (EHNA), que pueden resultar en cirrosis y falla hepática⁴⁵. Actualmente, el HGNA ha emergido como la causa más importante de enfermedad hepática en el mundo, tanto en niños como adultos^{46,47}. Junto con esto, la prevalencia y severidad de HGNA ha sido relacionada al aumento en la incidencia de obesidad y diabetes mellitus tipo 2 en la población, estableciéndose mecanismos asociados entre estas patologías y el HGNA^{45,48}. Las implicaciones clínicas de la enfermedad derivan de la ocurrencia en la población y su potencial de progresar a cirrosis y falla hepática⁴⁹.

El HGNA es considerado como la manifestación hepática del síndrome metabólico, su prevalencia en la población norteamericana adulta es de 34%, pero en pacientes con esteatosis hepática es de 53% y en pacientes con EHNA alcanza un 88%⁵⁰. Estudios realizados a autopsias han identificado lípidos intrahepáticos en 36% de los adultos normopeso y en 72% de los adultos obesos⁵¹ versus 5% en niños normopeso, 16% en niños sobrepeso y en 38% en niños obesos⁴⁶.

De acuerdo con la teoría conocida como “two-hit theory” (teoría de los dos sucesos)⁵²: i) la primera anomalía metabólica es la esteatosis hepática que involucra una respuesta lipotóxica con un componen-

te de estrés oxidativo e incluye factores nutricionales y alteraciones en el metabolismo lipídico del hígado, esto es resultado principalmente de la IR, ii) el segundo suceso es la inflamación hepática^{45,53,54}, asociado a estrés oxidativo⁴⁵.

La esteatosis hepática es una condición benigna, potencialmente reversible y no necesariamente lleva a injuria hepática irreversible. Desde un punto de vista temporal, la esteatosis hepática se desarrolla cuando la captación y síntesis de novo exceden la oxidación y exportación de TAGs por las lipoproteínas^{55,56}.

Actualmente, existe gran controversia acerca de los efectos metabólicos de elevadas ingestas de fructosa dietaria a nivel hepático. Principalmente, estos efectos han sido asociados a un balance energético positivo. Sin embargo, estudios en modelos animales y humanos muestran que ingestas elevadas de fructosa con dietas ad libitum e isoenergéticas, generarían daño hepático^{57, 58}.

Específicamente, se ha observado que las dietas con alto contenido de fructosa aumentan la concentración de triglicéridos en el plasma y estimula la lipogénesis de novo (LDN) a nivel hepático. Al aumentar la LDN se incrementa la síntesis de apolipoproteína B (Apo B) que antecede el aumento de la síntesis de VLDL (del inglés: very low density lipoprotein), lo que podría provocar el aumento de las lipoproteínas transportadoras de TAGs plasmáticos⁴⁴. Se han descrito cambios en otras lipoproteínas como las HDL (del inglés: high density lipoprotein) y las LDL (del inglés low density lipoprotein) pequeñas y densas, que podrían relacionarse con el desarrollo de aterosclerosis en sujetos que consumen fructosa en comparación a aquellos que ingieren glucosa⁴³. Igualmente, en otro estudio se observó que los niveles plasmáticos en ayuna de colesterol total, LDL, apoB y LDL oxidado fueron significativamente mayores en aquellos individuos que consumen bebidas endulzadas con fructosa, pero no en aquellos sujetos que consumieron bebidas endulzadas con glucosa^{38,39}.

Evidencia reciente en modelos animales ha mostrado que el consumo a largo plazo de fructosa libre, glucosa y sacarosa inducen síndrome metabólico, acumulación intrahepática de TAGs y ácido úrico, ganancia de peso, hiperglicemia, intolerancia a la glucosa e hipertensión^{59,60}. Asimismo, en ratas alimentadas con una dieta alta en fructosa durante 8 semanas se observó una reducción en la expresión de PPAR- α (del inglés peroxisome proliferator-activated receptor alpha) y de las enzimas lipo-oxidativas; en contraste a un aumento en la expresión de SREBP-1c y de las enzimas lipogénicas (fig. 1)⁶¹. Por lo demás, al suministrarle una solución de fructosa al 10% (peso/vol) durante dos semanas a ratas, se redujo la actividad de PPAR- α con la consecuente reducción en la oxidación de AG en el hígado y aumento de la actividad de NF- κ B (del inglés nuclear factor kappa-light-chain-enhancer of activated B cells), cambios que no se observaron en el grupo de ratas a las que se les suministró glucosa al 10% (peso/vol)⁶². Alteraciones similares se han observado en animales alimentados con

fructosa a corto plazo⁶³⁻⁶⁶. La activación de NF- κ B en hámsteres insulinoresistentes alimentados con fructosa suprimió la sobreproducción hepática de apoB100, revelando una asociación entre la respuesta inflamatoria y la secreción de lipoproteínas apoB100, factor involucrado en la presencia de esteatosis hepática⁶⁷, esto concuerda con las alteraciones en la síntesis y/o secreción de lipoproteínas mencionada previamente en estudios en humanos con HGNA^{68, 69}.

En seres humanos, la evidencia apunta a que el consumo de fructosa se asocia a un aumento en los marcadores de riesgo cardio-metabólico debido a un incremento de la grasa visceral⁷⁰. Al comparar los efectos de una ingesta de fructosa o glucosa que representa el 25% de las calorías totales durante un período de 10 semanas en un grupo de adultos, ambos grupos presentaron aumento significativo del peso corporal y masa grasa, sin embargo los sujetos que consumieron fructosa presentaron adicionalmente, aumento en la adiposidad visceral, alteraciones en el perfil lipídico e IR, variables que no se alteraron en el grupo que consumió glucosa⁷¹. En concordancia con estos resultados, un estudio reciente realizado en primates, mostró que dietas altas en fructosa con ingesta calórica ad libitum generó esteatosis hepática *versus* dietas isocalóricas altas en fructosa que no mostraron esteatosis hepática pero sí un estado inflamatorio en el hígado⁵⁸.

Asimismo, un estudio en 427 sujetos demostró que la ingesta de fructosa es dos a tres veces más alta en pacientes con HGNA en comparación a sujetos controles normalizado por IMC y que se asoció con estados avanzados de fibrosis en HGNA diagnosticado mediante biopsia^{28,72}. Estos estudios confirman que la alta ingesta de fructosa genera un efecto metabólico que no había sido advertido hasta el momento.

Discusión

El consumo de fructosa se ha masificado y aumentado principalmente a través de la ingesta de BEAs en todos los estratos sociales a nivel mundial. En EEUU, el aumento de la ingesta de fructosa ha sido de 32% entre los años 1977-2004, principalmente debido al incremento en el uso de HFCS⁷³. Chile es el tercer mayor consumidor de BEAs en el mundo, siendo el tercer producto más importante en la canasta familiar, especialmente en el nivel socioeconómico bajo.

La ingesta de alimentos que contienen fructosa en forma natural (frutas y miel) en una dieta saludable, aportan aproximadamente un 5% de las calorías totales en relación a 2.000 kcal/día promedio; en contraste con una dieta occidental caracterizada por alto aporte de energía y alimentos procesados como néctares, bebidas endulzadas y snacks, los cuales aportan altas dosis de fructosa principalmente en forma de HFCS. En consecuencia, actualmente estamos expuestos a altas ingestas de fructosa a través de alimentos procesados con fructosa agregada, siendo el principal contribu-

yente las BEAs. Al parecer, el impacto de la ingesta calórica, no se relacionaría a los efectos generados por la fructosa en sí, más bien es el exceso de carga que sobrepasa el umbral de tolerancia fisiológica.

Es importante mencionar que el consumo de alimentos que contienen fructosa de forma natural, como frutas, verduras y miel, tienen una baja ingesta en la población general, a pesar de promover su consumo a nivel de salud pública por ser un factor protector en el desarrollo de obesidad y enfermedades cardiovasculares^{6,29}. Por este motivo, estos alimentos no son la causa principal de un consumo excesivo de fructosa.

Las consecuencias de la alta ingesta de fructosa se han asociado a la aparición de síntomas gastrointestinales en relación a una alteración de su capacidad de absorción. Al parecer, existe una respuesta dosis dependiente entre la fructosa y síntomas gastrointestinales, que podría generar a largo plazo una adaptación intestinal a la fructosa dietaria, como se ha visto en modelos animales⁷⁴. Hasta el momento, no se conoce la capacidad de absorción normal para la fructosa en sujetos sanos, lo cual limita el uso de la metodología del THE como método de diagnóstico para la MAF. Sin embargo, no se debe desconocer que estamos frente a un problema real de sintomatología gastrointestinal frente a altas ingestas de fructosa en la población general. Al parecer, su tratamiento sería restringir la fructosa de la dieta, principalmente de alimentos procesados con fructosa agregada, debido a su alto aporte de este monosacárido.

El HGNA es la enfermedad crónica hepática más frecuente en adultos y niños. Ciertos azúcares en la dieta, y en particular la fructosa, contribuyen al desarrollo de alteraciones hepáticas, siendo esto proporcional a la cantidad y tiempo de exposición a la fructosa consumida demostrado en modelos animales. Sin embargo, sigue siendo controversial, si la ingesta de fructosa por sí sola puede causar HGNA o si solo contribuye cuando se consume en exceso al producir balance energético positivo y resistencia a la insulina⁷⁵.

En Chile, la ley de etiquetado nutricional no obliga al productor a informar la cantidad de fructosa agregada, siendo incluido su aporte calórico a la clasificación en "azúcares añadidos", sin diferenciarla con la sacarosa utilizada en la industria alimentaria. No existe una metodología que permita determinar la cantidad de fructosa agregada o aquella incluida en su forma natural (ej. Néctar de frutas), por lo tanto, se dificulta la fiscalización de la adición de éste monosacárido.

Junto a lo anterior y debido a los cambios en los patrones de consumo alimentario, los organismos internacionales sugieren que los azúcares libres deben limitarse a menos del 10% del total de la energía diaria; dando preferencias a bebidas sin azúcar agregada y restringir los azúcares añadidos, azúcares de la miel, jarabes y jugos de fruta con azúcar agregada⁷⁶⁻⁷⁸.

Finalmente, es necesario reglamentar en base a la evidencia, la cantidad de fructosa agregada a los productos alimentarios procesados, de manera tal de evi-

tar la aparición de alteraciones hepáticas y gastrointestinales.

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Revisión Executive functions in anorexia nervosa

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Abstract

Introduction: The pathophysiologic mechanisms that account for the development and persistence of anorexia nervosa (AN) remain unclear. With respect to the neuropsychological functioning, the executive functions have been reported to be altered, especially cognitive flexibility and decision-making processes.

Objectives: The aim of this study was to review the current state of the neuropsychological studies focused on anorexia nervosa, especially those highlighting the executive functions.

Methods: This was done by means of a searching process covering three relevant electronic databases, as well as an additional search on references included in the analysed papers. Eventually we have to mention other published reviews and a hand-search.

Results and discussion: Comparing AN patients and healthy controls the results remain controversial and so remains the comparison of different eating disorders with respect to the neuropsychological dysfunction. The role of variables such as depression, anxiety and obsessiveness needs to be clarified. There seems to be some base to state that some commonalities exist in the so-called extreme weight conditions (anorexia, obesity). The link between neuropsychological dysfunction in AN and biomarkers remains unclear. The role of neuropsychological deficits in AN, as initial factors or simply as mere consequences, remains unclear too. The link between the body image disturbances and the neuropsychological dysfunction needs to be clarified. The similarities between the AN neuropsychological dysfunction and that found in other mental disorders may be considered up to date as a mere approach. The same applies to the relationship between the AN patients' neuropsychological performance and personality or gender.

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FUNCIONES EJECUTIVAS EN LA ANOREXIA NERVIOSA

Resumen

Introducción: Los mecanismos fisiopatológicos que explican el desarrollo y la persistencia de la anorexia nervosa (AN) siguen sin estar claros. Con respecto al funcionamiento neuropsicológico, se han señalado alteraciones en las funciones ejecutivas, especialmente en la flexibilidad cognitiva y en los procesos de toma de decisiones.

Objetivos: El objetivo de este trabajo fue revisar el estado actual de los estudios neuropsicológicos sobre anorexia nervosa, especialmente los centrados en las funciones ejecutivas.

Métodos: Se realizó un proceso de búsqueda con tres relevantes bases de datos electrónicas, así como una búsqueda adicional con las referencias incluidas en los documentos analizados. Finalmente hay que mencionar otras revisiones ya publicadas y una búsqueda manual de otras fuentes.

Resultados y discusión: Los datos de comparación de pacientes y controles sanos siguen siendo controvertidos, así como la comparación entre los diferentes trastornos de la alimentación con respecto a la disfunción neuropsicológica. El papel de variables como depresión, ansiedad y obsesividad necesita ser aclarado. Parece que hay alguna base para afirmar que existen algunos puntos en común entre los llamados trastornos de peso extremo (anorexia, obesidad). El vínculo entre la disfunción neuropsicológica en AN y biomarcadores aún no está claro. El papel de los déficits neuropsicológicos en la AN, como factores iniciales o simplemente como meras consecuencias, tampoco está aclarado. La relación entre los trastornos de imagen corporal y la disfunción neuropsicológica debe asimismo aclararse. Los datos sobre las similitudes, en cuanto a la disfunción neuropsicológica, entre AN y otros trastornos mentales pueden ser considerados, hasta la fecha, como una mera aproximación. Lo mismo ocurre con la relación entre el rendimiento neuropsicológico de los pacientes con AN y la personalidad o el género.

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Palabras clave: Anorexia nervosa. Neuropsicología. Rendimiento cognitivo. Flexibilidad cognitiva. Set shifting. Toma de decisiones. Planificación.

List of abbreviations

AN-p: Anorexia Nervosa-purging type.
AN-r: Anorexia Nervosa-restrictive type.
AN: Anorexia Nervosa.
BMI: Body Mass Index.
BN: Bulimia Nervosa.
CNS: Central Nervous System.
ED: Eating Disorders.
EDNOS: Eating Disorders Not Otherwise Specified.
EWC: Extreme Weight Conditions.

Introduction

Anorexia nervosa (AN) is a severe mental pathology being characterized by a pathological concern with body shape and weight above all. The possibility that there is a dysfunction of the Central Nervous System (CNS) in patients with AN has been explored in several ways, including neuropsychological studies. Thus, several studies assessing the relationship between cognitive processing and certain eating behaviours have been conducted, aiming to achieve a better understanding of the pathophysiology of AN.^{1,2}

The specific pathophysiology of AN is not completely known, taking into account that different factors seem to be involved.² Up to the date AN has been described on the basis of clinical phenotypes (for example restrictive- vs. purging-type). As far as the aetiology is concerned that description seems to be not effective enough.³ As a consequence, new ways of study seem to be necessary.⁴ In this regard, some authors have suggested these potential new focuses, thus mentioning the study of endophenotypes, the disease-associated traits more useful to determine the relationship with underlying genes and neuropsychological functions.^{3,5} It has been said that neuropsychology might lead to an explanatory model of AN.⁶

Neuropsychological studies in AN have supported the hypothesis of a disturbance on the inhibitory control–emotional regulation–executive function circuit.⁷ In AN, a relevant cognitive trait appears to be executive dysfunction, which includes three specific neurocognitive elements: decision-making, response inhibition and cognitive flexibility.^{8–11} Thus, AN has been consistently associated to alterations on attentional and executive functioning (mainly set shifting and decision-making).¹ In addition some facets of executive functioning, such as cognitive flexibility, have been considered as a risk indicator and are believed to be a possible endophenotype in AN.¹²

Alterations in decision-making, response inhibition and cognitive flexibility in AN highlight the importance of an adequate executive functioning to maintain an proper control of eating behaviour.⁷ Executive functions have a biological base (prefrontal brain circuits), which involves different cortical areas such as dorsolateral prefrontal, anterior cingulate and orbitofron-

tal.¹³ A question raised is if differences in these areas could imply different degree of vulnerability.

May be that the most important question is if the neuropsychological findings reported in AN are reversible with an appropriate treatment, so are cognitive deficits an expression of traits or a mere consequence emerged during the course of the disorders?¹ Besides some studies, which have reported that cognitive deficits diminish after weight restoration,^{14–17} others^{18–20} have not observed such an improvement. As a consequence, a repeated question emerges: What do neuropsychological deficits represent in AN? Are there state-related deficits and trait-related deficits?

The aim of this study was to review the current state of the neuropsychological studies focused on the executive functions in AN.

Methods

Searching process

The searching process covered three relevant electronic databases (Medline, EMBASE and PsycINFO). The general strategy included terms related to anorexia nervosa and neuropsychology. Then some key words and the Medical Subjects Headings were used as well as the Boolean operators AND/OR. The shared terms were (“Anorexia nervosa”[Mesh]) AND (“Decision making”[Mesh]) OR (“Response inhibition”) OR (“Cognitive flexibility”) OR (“Executive function”[Mesh]) OR (“Planning”) OR (“Working memory”[Mesh]).

Additional search was carried out on references included in the papers, published reviews and via hand searching. Literature search was not limited to particular years.

Studies meeting the following criteria were included in the review: (1) studies focused on anorexia nervosa and executive functions; (2) controlled trials and randomized controlled trials as well as cross-sectional studies. Applied exclusion criteria included: (1) case reports; (2) interventions targeting populations with other eating disorders; (3) participants with severe comorbidities; (4) neuroimaging- and neurophysiology-based studies; (5) not available full text. Reviews and meta-analysis were considered as other source of articles, which fitted the inclusion criteria.

The initial search yielded 189 references. These were combined in an EndNote 9 library and screened on the basis of title and abstract; those clearly not meeting the review criteria were excluded as well as duplicates. Thereafter, selected references were screened based on full text. Reasons for exclusion were applied and seventy studies were finally included.

Procedure

Taking into account the most used neuropsychological tests focused on the explored functions, those stud-

ies including the Wisconsin Card Sorting Test (planning, cognitive flexibility, ability of shifting among stimuli and control of impulsive responses not aimed at achieving and objective), the Stroop Colour and Word Test (inhibition and switching skills) and the Iowa Gambling Task (decision making, risk and reward and punishment value) were specially considered.

A thematic analysis was used to analyse the papers. The six-step framework of Braun and Clarke²¹ were followed for this proposal: becoming familiar with the data; creating initial codes; searching for themes; reviewing themes; defining and naming themes and producing the report. Fragments of data that identify a significant feature of such data were acknowledged and grouped together into related themes.^{21,22} As a result, the following different topics were obtained: a) Cognitive deficits in AN: Are they generally confirmed? ; b) Are there any differences between the cognitive deficits in AN and those found out in other ED? ; c) Variables usually associated to cognitive deficits in AN; d) Is there any support for the continuum spectrum of ED based on the findings of cognitive disturbances-related studies?; e) Biological bases of cognitive alterations in AN; f) Do cognitive deficits precede the onset of AN or are they a mere consequence (e.g. of starvation)?; g) Is there any relationship between cognitive deficits and body image disturbances in AN?; h) Are cognitive deficits in AN similar to those found out in other mental disorders?; i) Personality and gender.

Results

Cognitive deficits in AN: Are they generally confirmed?

Despite cognitive functions such as decision-making have been reported to be reduced in ED, some authors²³ have found out no significant differences in the Iowa Gambling Test when compared ED patients (including AN, n = 49) and healthy controls. These authors suggest that previous reported alterations could be related to other clinical characteristics. It must be noted that patients included in this study were euthymic and free of psychotropic medication. Similarly, Kingston et al. did not find differences between AN patients and controls by means of cognitive flexibility tasks.¹⁹

Other studies have found out that AN patients perform worse than healthy controls, for example in set-shifting tasks,^{24,25} visuospatial memory and central coherence,²⁶ visual constructional ability²⁷ and ability to master a conflict situation over time.²⁸

Are there any differences between the cognitive deficits in AN and those found out in other ED?

In the case of bulimia nervosa (BN), decision-making abnormalities and executive reductions can be

demonstrated and might be neuropsychological correlates of the patients' dysfunctional everyday-life decision-making behaviour.²⁹ By means of the Iowa Gambling Test, AN patients, BN patients and obese patients have shown significant impairment comparing to healthy controls, the three groups not being significant different from each other.³⁰ Recently, by means of the concept of "extreme weight conditions" (EWC) executive functions have been explored with the Iowa Gambling Test, the Wisconsin Card Sorting Test and the Stroop and Word Test. As a result, authors conclude that EWC (AN and obesity) have similar dysfunctional executive profile.⁷ In a recent review, both AN patients and BN patients are reported to show cognitive deficits. Nevertheless it seems that cognitive rigidity is more frequent in AN patients and alterations in decision-making or central coherence are more often found out in BN.³¹ Within the group of patients with AN, the cognitive profiles of restrictive (AN-r) and purging (AN-p) types seem to be different. By means of the Block Design and Object Assembly, AN-r perform significantly worse than AN-p. In addition no differences were found between AN-p and healthy controls. Exploring set shifting there were not differences among the three groups.³² Including AN-r, AN-p, BN and healthy controls, cognitive flexibility and motor inhibition have been shown to be unaltered in BN patient while AN patients showed a deficient motor inhibition compared to healthy controls.³³ Others, studying four groups of patients (AN-r, AN-p, BN and Eating Disorders Not Otherwise Specified -EDNOS-), have not observed differences in executive functions among them.³⁴ It must be noted that only 30% of the patients showed impaired performance in executive functions.

Variables usually associated to cognitive deficits in AN

Different variables have shown to be associated to cognitive rigidity and decision-making impairments in AN patients. In this regard, illness duration is associated to the score on the Hayling Sentence Completion Task. It seems to be a partial effect of years of education and body mass index (BMI) on neuropsychological performance as a whole (including Trail Making Test, Wisconsin Card Sorting Test, Iowa Gambling Test and the Hayling Sentence Completion Task). In addition, response inhibition processes and verbal fluency impairment were not associated to BMI and years of education but were associated to depression severity.³⁵ With respect to the depression symptoms, Giel et al. have found out that set-shifting ability was intact in AN patients without comorbid depression. On the contrary, patients with depression performed significantly poorer in the three tasks (Trail Making Test, Wisconsin Card Sorting Test and a Parametric Go/No-Go Test). The authors concluded that impairments of set-shifting ability in AN patients may partly be due

to comorbid depression disorders.³⁶ Another variable to consider, which have shown to be associated to the impairment in executive functions, is state anxiety.³⁴ In the study of Wilsdon et al., three groups were examined (AN patients, women who were high in obsessiveness and women who were low in obsessiveness) with no significant differences among the groups in executive functions (as measured with the Wisconsin Card Sorting Test). When controlling for depression and obsessiveness, AN patients and the high-obsessional group showed significantly more perseverations. Depression appeared to suppress variance that was irrelevant to the prediction of perseverance thus enhancing the importance of group membership.³⁷ Finally, the concept of metacognition has been related to the neuropsychological basis of insight into illness in AN patients, suggesting that metacognition might be an important mediator between basic cognitive deficits and poor insight.³⁸

Is there any support for the continuum spectrum of ED based on the findings of cognitive disturbances-related studies?

A continuum model has been proposed for ED, this model comprising of from anorexia nervosa to stable obesity. In this continuum the different subtypes of eating disorders are included, so AN-r, AN-p and BN along with obesity frame the continuum spectrum. According with this theory, all patients included in the spectrum may share certain neuropsychological features, for example those relate to executive functions. In this regard it has been shown that different ED patients have reduced ability on tasks such as the Rey-Osterrieth Complex Figure or the Tower of London Task.²⁷ In the case of BN and obesity, decision-making disturbances and executive reductions have also been demonstrated.^{29,30} Cserjési reported a common deficit in attention capacity in both AN and obesity, specifically when considered shifting capacity and mental rigidity (associated to frontal lobe based executive functions).³⁹ The recent study of Fagundo et al. highlights a similar dysfunctional executive profile with respect to the extreme weight conditions (AN and obesity).⁷ Despite considering similarities, the review of Idini et al. concludes that cognitive rigidity would be more frequent in AN while alterations in decision-making or central coherence are more often found out in BN.⁴⁰

Biological bases of cognitive alterations in AN

A sort of meeting point has been established between overeating and under eating, which would be the dopamine brain reward system. To sum up, impairments on decision-making, response inhibition and cognitive flexibility lead to unsatisfactory control of eating behaviour.⁷ In this regard, different studies have

reported some biological bases of the neuropsychological impairment thus leading to a research of biomarkers. In this field of study, Dmitrzak-Weglarz et al. have found out significant correlations between neurotrophin factor 4 and glial cell line-derived neurotrophic factor serum levels and executive function as measured by the Wisconsin Card Sorting Test.⁴¹ Seeking those biomarkers, the effect of a functional polymorphism (Val158Met) in the catechol-O-methyltransferase gene on the set-shifting abilities in AN have been explored. In this regard, only in the underweight AN patients that polymorphism affected cognitive performance. Moreover underweight AN patients who were Met homozygotes had significantly higher levels of perseveration.⁴²

The suggested substantial genetic influence for AN are based on works with results mainly inconsistent. Trying to investigate the neurocognitive endophenotypes approach of AN, Galimberti et al. analysed functions such as decision-making, set-shifting and planning in AN patients. Impaired performance on the Iowa Gambling Test and the Wisconsin Card Sorting Test were found out in AN patients and their relatives. Nevertheless planning kept preserved. Applying a heritability index, the results suggest a genetic effect influencing the performance in the case of the Iowa Gambling Test but not in the case of the Wisconsin test. The authors concluded the presence of a shared dysfunctional executive profile in AN patients and their unaffected relatives. This dysfunction is shown by way of deficient decision-making and set-shifting, suggesting that these impairments might constitute biological markers for AN.⁴³

The link between neuropsychological dysfunction in AN and biomarkers remains unclear. Considering that animal studies have established that glutamatergic pathways in the prefrontal cortex play an important role in set-shifting ability, Nakazato et al. tried to determine whether serum concentrations of glutamatergic neurotransmission-related amino acids were associated to set-shifting ability in both acute and recovered AN patients. As a result the authors did not find correlation between serum glutamine concentration and set-shifting performance.⁴⁴ In other study, Nakazato et al. measured serum brain-derived neurotrophic factor and set-shifting again in both current and recovered AN patients. In the same line, there was no significant correlation between serum brain-derived neurotrophic factor concentrations and performance on the Wisconsin Card Sorting Test.⁴⁵

Do cognitive deficits precede the onset of AN or are they a mere consequence (e.g. of starvation)?

There are studies, which have reported that as a result of treatment patients did not improve their cognitive performance.¹⁸ Other studies have reported the impaired cognitive functions to be improved but with an absence of association between cognitive and clinical rectifications, leading the authors to suggest the

existence of mediating factors.²⁴ In the same line that improvement seems not to be associated with changes in BMI.⁴⁶ In other cases a persistence of some altered cognitive functions has been observed after weight restoration.⁴⁷ With respect to set-shifting tasks in AN, Tchanturia et al.⁴⁸ have concluded that difficulties in these tasks did not show any improvement follow re-testing after weight recovery.

Recent studies try to direct the attention to the neuropsychological impairments as predisposing factors and/or specific eating disorder-related findings. An example of these efforts to search endophenotypes of ED is the several articles of Lopez et al. about the concept of central coherence.⁴⁹⁻⁵¹ Nevertheless, the potential confounding factors, comorbid pathologies, use of different medications, etc. make difficult to ascertain conclusions.²³

Aimed to summarize these controversial results, Duchesne et al. conclude that some cognitive dysfunction tend to disappear after treatment, thus supporting the hypothesis that these are functional deficits. Nevertheless, other deficits tend to persist, so they might precede the development of ED or even contribute to their development or to a worse prognosis.² In this line, the study of Favaro et al. shows that starvation affects dopamine release in the prefrontal cortex of AN patients with different effects on executive functions according to the catechol-O-methyltransferase genotype.⁴² Respecting set-shifting performance, some findings suggest that this function may be a consequence of AN.⁵² On the contrary, Tchanturia et al. suggest that impaired executive function in terms of set-shifting tasks could represent a vulnerability factor.⁵³ Similarly, Tencioni et al. did not find any differences among long-term recovered individuals, weight restored AN patients and those in acute phase with respect to set-shifting tasks with poor performance in the three groups. The authors suggest that set-shifting and central coherence seem to be promising cognitive endophenotypes of AN.⁵⁴ In the follow-up study of Gillberg et al. AN seems to be associated to a range of neuropsychological alterations that remain present long after the AN per se is no longer an important feature.¹⁷ Another longitudinal study showed that ten years after the AN onset, patients had poor results on the Object Assembly Test, thus indicating weak central coherence with a tendency to focus on details at the expense of configural information.⁵⁵ With respect to planning, it has been shown that this function remains impaired even after full recovery from AN.⁴⁰

On the contrary Hatch et al. concluded that cognitive impairments in AN patients appear to normalize with refeeding and weight gain.⁵⁶

Is there any relationship between cognitive deficits and body image disturbances in AN?

There is a shortage of studies based on the relationship between neurocognitive deficits and neurological bases of body image disturbances. Studying the body

schema, it has been reported that AN patients may have subtle cognitive dysfunctions which could interact with processing of body-schema-related information. In addition it is suggested that body image distortion may not be secondary to bottom-up perceptual disturbances.⁵⁷

Body image disturbances in AN patients have been shown to be related to frontal alterations, specifically these disturbances might be linked to the alterations of abstraction and critical abilities and with an obsessive frontal functioning. Pathological preoccupation with body shape would lead to intensive focus on the body and the search of perfection, which is typical of rigid personalities.⁵⁸

Are cognitive deficits in AN similar to those found out in other mental disorders?

Gillberg et al. studied a group of AN patients in which there was a subgroup of participants with autism spectrum disorders. In that subgroup there were cases with test profiles similar to those observed in autism and Asperger syndrome.⁵⁵ The study of Oldershaw et al. adds similar data. In this case, by means of Wisconsin Card Sorting Task to assess executive function, cognitive profiles of the two groups (AN patients and published data about autism spectrum disorders) were similar with respect to executive functions.⁵⁹ Considering AN-r, it has been reported that these patients have several common features (shifting capacity, mental rigidity) with anxiety disorders.³⁹ The deficient motor inhibition found out in AN patients has been considered to be similar to the cognitive profile of obsessive-compulsive spectrum disorders.³³

Personality and gender

Pignatti et al. have indicated that there exists a relationship between cognitive rigidity and fixed psychological traits in AN patients. Specifically perfectionist stable traits support this idea as excessive cognitive control can either improve or damage set-shifting and decision-making procedures.⁶⁰

As far as we know, the study of Tchanturia et al. is the only one devoted to clarify the role of gender in this field of study. Concretely they studied decision-making by means of the Iowa Gambling Test and they found out that both male and female AN patients performed significantly worse than healthy controls. Despite male had higher impulsive scores, that impulsivity did not predict poor decision-making performance. The authors concluded that both males and females had a similar decision-making performance.⁶¹

Discussion

Many studies have reported deficits in executive functions in AN patients^{37,58,60-64} generally related to

fronto striatal systems. In two previous reviews, it has been shown that the most repeated results about these deficits seem to involve the dorsolateral prefrontal cortex and the orbitofrontal cortex.^{35,65}

Despite being lots the studies in this regard, the fact of finding different results between AN patients and healthy controls remains not to be completely agreed.²³ Patients' characteristics have been an explanation for those who do not find out a worse performance in AN patients. In fact, it has been said that serotonergic drugs might influence the cognitive performances and in many cases patients enrolled in different studies were taking such a type of drugs.

Comorbidity is another factor potentially capable to lead to different results. It is known that depressive symptoms can affect decision-making performance⁶⁶ and in many cases this variable has not been taken into account. Moreover there are authors who consider that depressive symptoms do not influence executive functions such as decision-making.⁶⁷ Do depressive symptoms affect the decision-making process in AN patients or the eating-related symptomatology? That point seems to remain unclear.

Based of the above-mentioned results it is difficult to catch a general idea about the specificity of the executive dysfunction in AN when comparing with other ED. As a result of the studies of several authors, ED could share a general deficit in executive functions^{7,29,30,34} while for others it would have some differences among subgroups of ED.^{33,40} Finally, it must be noted that some findings point out that both similar dysfunctions and different dysfunctions might be observed in AN patients compared to other ED.³² One more time another point in this field of study is not completely consensual.

With respect to the possible variables associated to the cognitive deficits, medications, depressive symptoms, anxiety trait or obsessionality have been involved in the results of different studies. Not always the studies have controlled for these variables adequately^{6,62} or these variables have not been considered simultaneously.³⁴ May be that the main controversial factor to analyse is the one referred to the role of starvation in the cognitive performance. Some authors have found out a correlation between decision-making skills and BMI while others did not report that correlation.^{23,68} In this regard, Hatch et al. conclude that cognitive impairments AN patients appear to normalize with refeeding and weight gain.⁵⁶ In view of the controversial results in this topic, we agree with Duchesne et al. considering that it might be concluded that some cognitive dysfunctions tend to disappear after treatment while other deficits tend to persist, so they might precede the development of ED or even contribute to their development or to a worse prognosis.²

The continuum spectrum of ED is a theory which remain as object of debate. It is not something new. In fact, the notion of a common psychopathology in ED was established in 1982.⁶⁹ The concept of extreme weight

conditions adds a new element to support that to some extent all ED share psychological, psychopathological and neuropsychological features. In this regard, the study of Fagundo et al.⁷ represents a summary about this topic. This study hypothesizes with the idea that cognitive deficits observed in AN and obese patients might partially be an expression of their incapacity to successfully regulate reward and punishment which might be affect the planning every day functioning. Their cognitive performance and their eating behaviour seem to have similarities. Seeking for biomarkers, perhaps the cognitive mechanism underlying the decision-making process in different ED would be different. Impulsivity (obesity) and rigidity (AN) could be the two extremes in which would be possible to place all ED. Summarizing, individuals with either excessive food intake or food restriction show a similar dysfunctional executive profile. Nevertheless, the need to find specific biomarkers has not been followed by successful findings up to date despite having obtained some promising results.^{41,42}

Being a core of the AN symptomatology, the shortage of studies focuses on the relationship between neuropsychological functioning and body image disturbances may be the most relevant conclusion. Body image disturbances in AN patients have been related to frontal alterations (abstraction and critical abilities) and with an obsessive frontal functioning. In this regard, morbid concerns about body shape would lead to intensive focus on the body and the search of perfection. It must be noted that a linear correlation has been found out between body image disturbances and the greater rigidity of frontal functioning.⁵⁸

With respect to the neuropsychological findings in AN, several studies have reported similarities with other pathologies such as autism,^{55,59} anxiety disorders³⁹ and obsessive-compulsive disorders.³³ In other cases, the cognitive alterations observed in AN have been related to different levels of depression and anxiety^{34,56} as well as to obsessive traits.³⁵ Considering the obsessive-compulsive spectrum, Cavedani et al. and Liao et al. have suggested that obsessive-compulsive symptomatology would be behind of the Iowa Gambling Test performances while in another study of Cavedani et al. this was not confirmed.^{6,62,68} As a result of these finding it might be said that there are some similar findings in other mental disorders, thus is very difficult to state that the neuropsychological findings in AN are strictly specific of this disorder.

The neuropsychological functions in AN have been accompanied by studies based on neuroimaging and neurophysiology in order to correlate structural and functional brain changes with neuropsychological findings.^{65,70} Having the enormous amount of involved variables (weight, duration of illness, medications, etc.) in mind, it has been strongly difficult to demonstrate the correlation between brain changes and functional changes. In order to establish a cause-effect relation it would be necessary to develop longitudinal neuroimaging studies as well as more neuropsychological lon-

itudinal designs. Studies about the cognitive function in AN not only are relevant in order to seek biomarkers, biological traits laying the clinical expression, but just to implement new forms of treatment to specifically focus on the neuropsychological impairment of these patients.¹ The proposed dysfunction in prefrontal circuitry that mediates executive functions, reward and behavioural regulation (not only in AN but also in obesity) could be a starting point to be considered in future treatments.⁷

Conclusions

Different neuropsychological alterations have been described in AN. Nevertheless there are many inconsistencies among studies mainly due to methodological biases. Comparing AN patients and healthy controls the results remain controversial. Bearing in mind different ED, some authors consider several common disturbances while others have reported some differences among them. The role of different variables such as depression, anxiety, obsessionality, etc. needs to be more clarified. There seems to be some base to state that some commonalities exist in the so-called extreme weight conditions (from AN to obesity). With respect to the biological basis of executive functioning alterations, the link between neuropsychological dysfunction and biomarkers remains unclear. The role of neuropsychological deficits in AN, as initial factors or simply as mere consequences, remains unclear too. Another topic, which needs to be clearly improved, is that which refer to the link between the body image disturbances in AN and the neuropsychological dysfunction. The similarities between the neuropsychological dysfunction in AN and that found in other mental disorders may be considered up to date as a mere approach. The same applies to the relationship between the AN patients' neuropsychological performance and personality or gender.

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Original / *Obesidad*

Efecto del bypass gástrico sobre el riesgo cardiovascular y la calidad de vida en pacientes con obesidad mórbida

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Resumen

Objetivos: Determinar la prevalencia de las principales comorbilidades asociadas a la obesidad mórbida y evaluar el efecto del bypass gástrico sobre el estado ponderal, riesgo cardiovascular y calidad de vida en estos pacientes.

Métodos: Estudio descriptivo con medidas del cambio intrasujeto (antes-después) en una muestra de 162 pacientes de los resultados del bypass gástrico sobre la evolución ponderal, comorbilidades asociadas, riesgo cardiovascular a 10 años (estimado mediante las tablas de Framingham) y calidad de vida mediante el test BAROS (Bariatric Analysis and Reporting Outcome System).

Resultados: El índice de masa corporal (IMC) se redujo de $51,12 \pm 7,22$ kg/m² a $29,94 \pm 4,86$ kg/m² (72,85% de sobrepeso perdido) y se resuelven la hipertensión arterial (HTA), la dislipemia y la diabetes mellitus tipo 2 (DMT2) en el 71,93%, 91,38% y 82,93% respectivamente ($p < 0,001$). El riesgo cardiovascular mayor del 10% se reduce del 25,91% al 4,32% ($p < 0,001$). Según la escala BAROS, el resultado de la cirugía fue favorable en el 95% de los casos.

Conclusiones: La cirugía bariátrica mediante bypass gástrico demuestra ser muy efectiva para la reducción ponderal y comorbilidades asociadas, mejorando notablemente la calidad de vida.

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Palabras clave: *Obesidad mórbida. Bypass gástrico. Riesgo cardiovascular. Calidad de vida.*

Introducción

La obesidad es una enfermedad crónica multifactorial fruto de la interacción entre genotipo y ambiente, asociada a importantes complicaciones físicas y psi-

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EFFECT OF GASTRIC BYPASS ON THE CARDIOVASCULAR RISK AND QUALITY OF LIFE IN MORBID OBESE PATIENTS

Abstract

Objectives: To determine the prevalence of major comorbidities of morbidity obese patients and to evaluate the gastric bypass effect on the weight status, cardiovascular risk and quality of life in these patients.

Methods: The evolution of weight, comorbidity, 10-year follow-up of cardiovascular risk (estimated by the Framingham risk score) and quality of life using the test BAROS (Bariatric Analysis and Reporting Outcome System) was analyzed in 162 patients with morbid obesity before and 2 years after gastric bypass.

Results: Body mass index (BMI) was reduced from 51.12 ± 7.22 to 29.94 ± 4.86 kg/m² (72.85% loss of excess weight). Hypertension (HT), dyslipidemia and type 2 diabetes mellitus (T2DM) were resolved in 71.93%, 91.38% and 82.93% respectively ($p < 0.001$). Cardiovascular risk greater than 10% was reduced from 25.91% to 4.32% ($p < 0.001$). According to BAROS scale, surgery was positive in 95% of cases.

Conclusions: Gastric bypass is very effective in weight loss; benefits in comorbidities, cardiovascular risk and quality of life.

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cológicas que contribuyen a deteriorar la calidad y esperanza de vida de los pacientes que la padecen. Supone un importante impacto socio-sanitario por su alta frecuencia, las complicaciones derivadas y su elevada mortalidad. Se estima que el 54.7% de la población adulta española presenta exceso ponderal¹ y su prevalencia ha aumentado de forma alarmante en nuestra sociedad adquiriendo proporciones epidémicas².

El abordaje terapéutico de la obesidad está dirigido a mejorar o eliminar las comorbilidades asociadas y disminuir el impacto de las futuras complicaciones relacionadas con el exceso de peso. Se basa, fundamentalmente, en cambios en el estilo de vida (ali-

mentación, ejercicio y modificación de hábitos de conducta) y, ocasionalmente, farmacoterapia. Sin embargo, en muchos casos, estas herramientas no son suficientes para alcanzar una pérdida ponderal significativa y mantenerla a largo plazo. En pacientes con obesidad mórbida refractaria al tratamiento médico, la cirugía bariátrica, aunque no exenta de riesgos, se postula como un tratamiento eficaz en la consecución de una importante pérdida ponderal, y en la remisión o reducción de la mayor parte de las comorbilidades asociadas³. Actualmente, las indicaciones según las directrices del Nacional Institute of Health (NIH) quedan limitadas a sujetos con IMC > 40 kg/m² o IMC > 35 kg/m² en presencia de comorbilidades mayores, asumiendo la estabilidad psicológica y el compromiso para el seguimiento por parte del paciente para garantizar el éxito a largo plazo⁴.

Objetivos

Determinar la prevalencia de las principales comorbilidades asociadas a la obesidad mórbida y evaluar el efecto del bypass gástrico sobre el estado ponderal, riesgo cardiovascular estimado a los 10 años y calidad de vida de estos pacientes.

Métodos

Estudio descriptivo con medidas del cambio intra-sujeto (antes-después) en una muestra de 162 sujetos con IMC > 40 kg/m² o IMC > 35 kg/m² en presencia de comorbilidades mayores, a los que se les practicó un bypass gástrico en el Hospital Universitario Puerta del Mar de Cádiz desde enero de 2005 a diciembre de 2010. Se excluyeron aquellos pacientes intervenidos mediante otras técnicas de cirugía bariátrica y se analizaron variables demográficas, parámetros antropométricos y presencia de factores de riesgo cardiovascular clásicos basales y a los 2 años de la intervención.

Se definieron las alteraciones del metabolismo hidrocarbonado según los criterios propuestos por la American Diabetes Association (ADA)⁵ e hipertensión arterial (HTA) cuando los valores de presión arterial excedían de 140/90 mmHg o los pacientes tenían prescrito tratamiento hipotensor. Se identificó como pacientes dislipémicos a aquellos que presentaban cifras de colesterol total > 200 mg/dl ó cLDL > 160 mg/dl ó triglicéridos > 150 mg/dl ó cHDL < 40 mg/dl o cuando recibían tratamiento hipolipemiante.

La estimación del riesgo de enfermedad cardiovascular a los 10 años se determinó de acuerdo con las tablas de Framingham⁶, que incluyen los siguientes factores de riesgo: edad, sexo, colesterol total, cHDL, tensión arterial sistólica, tratamiento hipotensor, diabetes mellitus y tabaquismo, y con la adaptación de REGICOR⁷ para la población mediterránea. En función de los resultados, fueron clasificados en 3 cate-

gorías: riesgo bajo (< 10%), intermedio (10-20%) y alto (> 20%).

Las complicaciones derivadas de la intervención quirúrgica se clasificaron en precoces (cuando aparecieron en el primer mes) y tardías (detectadas después del primer mes). En las precoces se incluyen infección de herida operatoria, absceso intraabdominal, dehiscencia de la sutura, oclusión intestinal, hemorragia digestiva, rotura de bazo, neumonía, infección urinaria, fístula, embolismo pulmonar y defunción. En las tardías: estenosis de la anastomosis, comunicación gastro-gástrica, úlcera de la boca anastomótica, coledocistitis, eventración, vómitos, diarreas, síndrome de Dumping, malabsorción y desnutrición.

La calidad de vida se midió mediante el test BAROS⁸, que además de medir la repercusión sobre la autoestima, actividad física, social, laboral y las relaciones sexuales mediante una escala cualitativa, evalúa la evolución de las comorbilidades mayores (DMT2, HTA, dislipemia, SAOS u artropatía), de la siguiente forma: a) "actualmente presente", b) "mejoría" de la comorbilidad, pero que aún necesita tratamiento y c) "resuelta", en la que el paciente ha normalizado o remitido completamente su patología asociada. Como criterios de remisión se establecieron: tensión arterial < 140/90 mmHg sin tratamiento antihipertensivo y glucemia < 126 mg/dl con hemoglobina glicosilada (HbA1c) < 6% sin tratamiento farmacológico

La codificación y el análisis de los datos se realizaron mediante el programa estadístico SPSS versión 15.0 para Windows. Las variables cuantitativas que se ajustan a la normalidad se expresaron mediante media y desviación estándar, y las que no siguen una distribución normal mediante mediana y rango. La normalidad de las variables continuas se estudió mediante la prueba de Kolmogorov-Smirnov, aplicándose para las comparaciones entre grupos la prueba de la t de Student para muestras relacionadas o la prueba de Wilcoxon para el contraste no paramétrico. Las variables cualitativas se expresaron mediante porcentajes y se compararon mediante la prueba de la Chi cuadrado. La significación estadística se consideró en todos los casos para valores de $p < 0,05$.

Resultados

Se incluyeron 162 pacientes, 121 (74,3%) mujeres, con una edad media al momento de la intervención de $38,87 \pm 10,11$ años. A todos los pacientes se les practicó un bypass gástrico: en Y de Roux distal (con asa común de 50 a 100 cm) en 107 pacientes (66,1%), proximal (o derivación gastro-yeyunal) en 34 (21%) y de una anastomosis (BAGUA) en 21 (13%). La cirugía fue abierta en 132 casos (81,48%) y por vía laparoscópica en 30 (18,51%). El 14,9% de los pacientes presentaron complicaciones precoces, siendo la infección de herida quirúrgica (9,5%) la complicación más frecuente. Hubo un caso de defunción (0,7%). El 27,2% desa-

Tabla I

Evolución de los parámetros antropométricos, analíticos, comorbilidades y del riesgo cardiovascular estimado a los 10 años

Parámetros	Previo a la cirugía	2 años tras la cirugía	Reducción (%)	Significación estadística
<i>Parámetros antropométricos</i>				
Peso (kg)	136,55 ± 20,95	79,17 ± 14,02	57,38 (42,02)	p < 0,001
IMC (kg/m ²)	51,12 ± 7,22	29,94 ± 4,86	21,18 (41,43)	p < 0,001
<i>Parámetros analíticos</i>				
Glucemia (mg/dl)	113,82 (67-239)	88,31 (63-185)	25,51 (22,41)	p < 0,001
Colesterol total (mg/dl)	198,59 ± 39,84	142,27 ± 32,36	56,32 (28,36)	p < 0,001
C-LDL (mg/dl)	125,75 ± 33,81	73,30 ± 28,00	52,45 (41,70)	p < 0,001
C-HDL (mg/dl)	44,71 ± 10,33	50,89 ± 12,76	-6,18 (13,82)	p < 0,005
Triglicéridos (mg/dl)	155,88 ± 87,23	88,59 ± 42,09	67,29 (43,16)	p < 0,001
Ácido úrico (mg/dl)	6,10 ± 1,73	4,42 ± 1,55	1,66 (27,30)	p < 0,001
<i>Comorbilidades asociadas a la obesidad</i>				
Hipertensión [n (%)]	57 (35,4)	16 (10,1)	41 (71,93)	p < 0,001
Dislipemia [n (%)]	58 (36,0)	5 (3,2)	53 (91,37)	p < 0,001
Diabetes tipo 2 [n (%)]	41 (25,5)	7 (4,4)	34 (82,92)	p < 0,001
Hiperuricemia [n (%)]	42 (28,6)	7 (4,7)	32 (83,33)	p < 0,001
<i>Estimación del riesgo cardiovascular (Framingham)</i>				
Riesgo bajo (< 10%)	120 (74,07)	155 (95,6)	-35 (29,16)	p < 0,001
Riesgo intermedio (10-20%)	26 (16,04)	7 (4,32)	19 (73,07)	p < 0,001
Riesgo alto (≥ 20%)	16 (9,87)	0 (0)	16 (100)	p < 0,001

rollaron complicaciones tardías, siendo la eventración (12,2%) la más frecuente seguida de la desnutrición calórico-proteica grave (6,8%).

Previo a la cirugía, los pacientes presentaban un IMC medio de 51,12 ± 7,22 kg/m² y a los dos años de la intervención el porcentaje de sobrepeso perdido fue del 72,85%, siendo el IMC medio 29,94 ± 4,86 kg/m² (porcentaje de reducción del IMC del 41,27 ± 9,07%). La evolución de los parámetros antropométricos y analíticos se presenta en la tabla I.

Al inicio, 57 pacientes (35,4%) presentaban HTA, 58 (36%) dislipemia, 41 (25,5%) DMT2 y 42 (28,6%) hiperuricemia. De los 41 pacientes con DMT2, en tan sólo 11 (26,82%) persistía el diagnóstico a los 4 meses de la intervención. En la mayoría de los casos la duración de la diabetes era menor de 10 años, 34 de ellos (82,92%) se encontraba bajo tratamiento con agentes orales y el resto con tratamiento dietético, y no presentaban complicaciones crónicas conocidas. La media de HbA1c previa a la cirugía fue 7,55 ± 1,18% y 5,33 ± 0,59% (p < 0,005) a los dos años. En cuanto a la resolución de la HTA, la dislipemia y la DM2 a los dos años, tuvo lugar en el 71,93%, 91,38% y 82,93% de los casos, respectivamente (p < 0,001).

Según la escala BAROS realizada a los 2 años de la intervención, el resultado de la cirugía fue excelente en 56

pacientes (36,8%), muy bueno en 56 (36,8%) y bueno en 32 (21,1%). Respecto a la calidad de vida, en los aspectos evaluados por el test, la mayor ganancia fue en bienestar físico (“mucho mejor” en 146 pacientes, 90,12%) y la menor en la normalización de la actividad sexual (“mucho mejor” en 120 pacientes, 74,07%) (fig. 1).

Según las tablas de riesgo cardiovascular de Framingham, en 42 (25,92%) de los pacientes se categorizó un nivel de riesgo cardiovascular > 10% en el momento de la cirugía y en, su conjunto, el riesgo cardiovascular medio estimado disminuyó de forma significativa desde un 5,82 ± 7,4% al inicio del estudio hasta un 2,21 ± 2,02% (p < 0,001) a los dos años tras la cirugía (p < 0,001). En el subgrupo de pacientes con DMT2, esta reducción es aún más marcada, desde el 15,84 ± 9,32% previo a la intervención hasta el 4,32 ± 2,81% a los dos años (p < 0,001). Según el método REGICOR, el riesgo cardiovascular medio estimado previo a la cirugía fue del 3,36 ± 3,01 y a los dos años del 1,61 ± 0,98% (p < 0,001) (tabla I).

Discusión

La prevalencia de la obesidad mórbida en nuestro país se ha multiplicado por 3 en los últimos 15 años²,

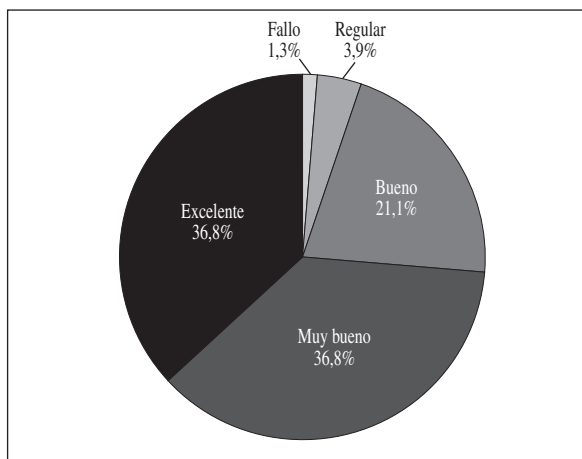


Fig. 1.—Test BAROS.

con el gran impacto que ello supone para la mayor parte de las enfermedades crónicas, como las cardiovasculares, la DMT2, la artrosis o la salud mental. La cirugía bariátrica es el tratamiento más efectivo a largo plazo en el tratamiento de la obesidad mórbida, permitiendo mantener la pérdida ponderal en el tiempo, y mejorar o resolver las comorbilidades asociadas. En España, como en el resto de países desarrollados, el número de intervenciones de cirugía bariátrica ha aumentado exponencialmente en los últimos años por el aumento progresivo de la prevalencia de obesidad mórbida, el fracaso de los tratamientos médicos y el desarrollo de la cirugía laparoscópica, que ha reducido la morbimortalidad.

En nuestro estudio, los sujetos intervenidos presentan un IMC muy elevado y se obtiene un porcentaje de sobrepeso perdido (72,85%) aún mayor que el descrito en otras series⁹, probablemente en relación con la frecuente realización de bypass gástrico distal con un mayor componente malabsortivo, cercano al obtenido con la derivación biliopancreática. La prevalencia de los factores de riesgo cardiovascular asociados a la obesidad, como la DMT2, HTA o dislipemia, presentan tasas similares a las descritas por otros autores^{4,10}.

Recientemente se han publicado dos nuevos ensayos clínicos aleatorizados y controlados que proporcionan una prueba más de que la cirugía puede ser más eficaz que el tratamiento médico estándar o intensivo^{11,12}. Estos datos de remisión, superiores a los de cualquier abordaje terapéutico intentado hasta la actualidad, plantean la posibilidad de considerar la cirugía como alternativa terapéutica en pacientes con DMT2 y un IMC inferior al considerado hasta el momento¹³.

En la evaluación inicial, en el 26% de pacientes se detectó un riesgo de presentar un evento cardiovascular en los próximos 10 años mayor del 10%, reduciéndose a menos del 5% a los 2 años de la intervención, similar a lo detectado en otras series^{14,15}. La mayoría de estudios publicados al respecto hacen referencia al método de estimación de riesgo cardiovascular de

Framingham; si asumimos que el modelo de REGICOR es el que mejor se adapta a nuestra población sin sobreestimar el riesgo, utilizándolo en nuestra serie se observa que el riesgo cardiovascular se reduce a la mitad.

En cuanto al análisis del cuestionario BAROS, los resultados son mejores que los publicados por algunos autores^{16,17}, aunque algo inferiores a lo reportado por otros¹⁸.

Las tasas de complicaciones son similares a lo publicado en otras series, con una tasa de mortalidad < 1%. Por el contrario, la incidencia de complicaciones es relativamente inferior en las series en las que predominan las técnicas por vía laparoscópica¹⁹.

Entre las limitaciones de nuestro estudio destaca el diseño observacional, llevado a cabo en un único centro, con un limitado tamaño muestral. Al incluir solo pacientes intervenidos mediante bypass gástrico, no podemos extrapolar los resultados al resto de técnicas quirúrgicas.

En conclusión, en nuestro medio el bypass gástrico se muestra muy eficaz en la pérdida de peso a corto y medio plazo en pacientes con obesidad mórbida, con una franca mejoría en su calidad de vida. Además, reduce notablemente el riesgo cardiovascular estimado, observándose de forma muy precoz los efectos beneficiosos sobre las alteraciones metabólicas.

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Original / *Obesidad*

Effectiveness of prediction equations in estimating energy expenditure sample of Brazilian and Spanish women with excess body weight

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Abstract

Objective: To assess the adequacy of predictive equations for estimation of energy expenditure (EE), compared with the EE using indirect calorimetry in a sample of Brazilian and Spanish women with excess body weight

Methods: It is a cross-sectional study with 92 obese adult women [26 Brazilian —G1— and 66 Spanish —G2— (aged 20-50)]. Weight and height were evaluated during fasting for the calculation of body mass index and predictive equations. EE was evaluated using the open-circuit indirect calorimetry with respiratory hood.

Results: In G1 and G2, it was found that the estimates obtained by Harris-Benedict, Shofield, FAO/WHO/ONU and Henry & Rees did not differ from EE using indirect calorimetry, which presented higher values than the equations proposed by Owen, Mifflin-St Jeor and Oxford. For G1 and G2 the predictive equation closest to the value obtained by the indirect calorimetry was the FAO/WHO/ONU (7.9% and 0.46% underestimation, respectively), followed by Harris-Benedict (8.6% and 1.5% underestimation, respectively).

Conclusion: The equations proposed by FAO/WHO/ONU, Harris-Benedict, Shofield and Henry & Rees were adequate to estimate the EE in a sample of Brazilian and Spanish women with excess body weight. The other equations underestimated the EE.

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EFICACIA DE LAS ECUACIONES DE PREDICCIÓN PARA LA ESTIMACIÓN DEL GASTO ENERGÉTICO EN UNA MUESTRA DE MUJERES BRASILEÑAS Y ESPAÑOLAS CON EXCESO DE PESO CORPORAL

Resumen

Objetivo: Evaluar la adecuación de las ecuaciones de predicción para la estimación del gasto energético (GE), en comparación con el GE medido por calorimetría indirecta en una muestra de mujeres brasileñas y españolas con exceso de peso corporal.

Métodos: Se trata de un estudio transversal con 92 mujeres adultas obesas [26 brasileñas —G1— y 66 españolas —G2— (20-50 años)]. Se evaluó el peso y la talla durante el ayuno para el cálculo del índice de masa corporal y las ecuaciones de predicción. Se evaluó el GE usando la calorimetría indirecta de circuito abierto con campana respiratoria.

Resultados: En G1 y G2, se encontró que las estimaciones obtenidas por Harris-Benedict, Shofield, FAO/OMS/ONU y Henry y Rees no difirieron del GE estimado por calorimetría indirecta, la cual presentó valores más altos que las ecuaciones propuestas por Owen Mifflin -St Jeor y Oxford. Para G1 y G2 la ecuación predictiva que presentó valores más cercanos al valor obtenido por la calorimetría indirecta fue la FAO/OMS/ONU (7,9% y 0,46% subestimación, respectivamente), seguido por Harris-Benedict (8,6% y 1,5% subestimación, respectivamente).

Conclusión: Las ecuaciones propuestas por la FAO/OMS/ONU, Harris-Benedict, Shofield y Henry & Rees fueron adecuadas para estimar el GE en una muestra de mujeres brasileñas y españolas con exceso de peso corporal. Las otras ecuaciones subestimaron el GE.

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Palabras clave: *Gasto energético. Ecuaciones de predicción. Calorimetría indirecta. Obesidad.*

Introduction

Obesity is a multifactorial disease characterized by excessive deposition of fat in adipose tissue, which may be due to excessive energy intake, and or changes in body energy expenditure, resulting in positive energy balance.¹

Ahmadi et al.² demonstrated that obese people had higher total energy expenditure (TEE), compared with normal weight. However, this increase may be due to increased basal metabolic rate (BMR) due to higher fat-free mass (FFM) and energy demand during physical activity. Mela and Rogers,³ found higher TEE in obese compared with normal weight, but the BMR that corresponds to the energy expenditure per kilogram of body weight at a given time, is lower in obese individuals.

The low metabolic rate (MR), expressed relative to FFM seems to be a risk factor for weight gain.⁴ In a prospective study in Pima Indians, Ravussin et al.⁵ showed that both the low resting metabolic rate (RMR) and low TEE increased risk of weight gain. The basal energy expenditure (BEE) and resting (REE) can be obtained through BMR and RMR, respectively, multiplied by 24 hours (1,440 minutes).

There are several methods for the assessment of EE with different levels of precision, including indirect calorimetry, which measures the MR by the determination of oxygen consumption (O₂) (with a spirometer), the production of carbon dioxide (CO₂) and excretion of urinary nitrogen, for a given period of time.⁶ This technique relies on the fact that all the O₂ consumed and CO₂ produced is due to the oxidation of the three major energy substrates, which are lipids, carbohydrates and proteins.⁷ In practice, an estimated value is used for the production of CO₂, measuring only the entrance of O₂.^{8,9}

Recognizing the need to estimate energy expenditure in institutions that have no indirect calorimetry, researchers have proposed the use of specific equations, developed from calorimetry studies in groups of individuals with similar clinical characteristics.¹⁰ Although the estimate of EE is the most common method, the predictive equations might generate errors.¹¹ Shetty¹² considers that the equations used to estimate the BEE in normal weight adults have reasonable precision (coefficient of variation 8%). By using predictive equation is important to know whether it predicts the spending baseline, resting or total, the population from which the equation was obtained and the factors that affect the predictive capability.¹³

In clinical practice it is impracticable to measure the calorimetric methods for EE, so the international use of the equations was recommended, modified from a compilation of data carried out by Schofield.¹⁴ Studies conducted in different ethnic groups found that these equations provide high BEE estimates, particularly for residents in the tropics.^{15,16,17} Wahrlich and Angels¹⁷ confer these differences to the fact that equations have been developed mostly from population samples of

North America and Europe which show differences in body composition, and live in different environmental conditions.

It is known that in populations with severe obesity is actually more difficult to fit the equations, because there is the difficulty in choosing the weight to be applied in the equation, which may influence a lot the results.¹⁸ The use of current weight leads to the overestimation of the results independent of the equation to be applied, and the use of ideal or adjusted weight can result in the underestimation of energy needs.¹⁹

This present study proposes to assess the adequacy of predictive equations for estimation of EE, using actual weight, based on the estimate of EE using indirect calorimetry in a sample of Brazilian and Spanish women with excess body weight.

It is expected that the equations obtained in tropical populations^{20,21} are more appropriate to estimate the EE of Brazilian women, and the equations proposed by FAO/WHO/ONU²² and Schofield¹⁴ are more appropriate for the estimation of EE in Spanish women. It is suggested that the prediction equations overestimate the EE, in a greater proportion among the women with overweight, compared with normal weight women.

Methods

Methodological course

All utilized data (indirect calorimetry and anthropometry) were obtained from two studies entitled: "Study of body composition and energy metabolism in normal weight, overweight and obese post-stable women" and "Effect of the association of diet with the polymorphism of genes PPAR γ 2 and beta2-adrenergic receptor in energy metabolism and body composition in obese women." These studies were approved by the Ethics Committee on human research at the Federal University of Viçosa (UFV) (No 059/2008) and University of Navarra (N^o 24 (2)/2004), respectively.

All women signed a formal informed consent. The data were supplemented by estimates of the EE calculations based on the equations of Harris Benedict,²³ Schofield,¹⁴ FAO/WHO/ONU,²² Henry and Rees,²⁰ Mifflin-St Jeor,²⁴ Owen²⁵ and Oxford.²¹

It is a cross-sectional study with 92 obese adult (aged between 20 and 50 years) women, counting 26 Brazilian (G1) and 66 Spanish (G2).

Casuistic

The data presented are derived from two studies. In the first study, 26 overweight women were selecting [body mass index (BMI) > 25 kg/m²], at the Health Division of the Federal University of Viçosa (UFV). In the second study, 66 overweight women were selecting (BMI > 25 kg/m²) in the Physiology and Nutrition

Department of the Faculty of Pharmacy and in the University Clinic of Navarra's University, Spain.

In both studies, the eligibility criteria were: absence of weight loss over 3 kg in the last 3 months, absence of chronic diseases (diabetes mellitus type 2, cardiovascular disease, kidney disease, thyroid disorders or cancer), nonsmoking, without using prescription drugs and not menopausal. Women who did not meet the above criteria or who did not meet the protocol provided were excluded.

In the selection, to prove the healthiness of the volunteers laboratory evaluations were held (blood count, fasting glucose, urinary nitrogen balance, urea, creatinine, total proteins and fractions, total cholesterol and its fractions and triglycerides) and urine (creatinine, albumin and total proteins) in specialized laboratories.

Anthropometric evaluation

Weight and height were the parameters evaluated, during fasting, for the calculation of BMI.²⁶ The women were weighed using electronic microdigital scale (Seca®) with the capacity of 150 kg and 100 g precision, wearing a lightweight fabric aprons. Height was determined using milimetric vertical anthropometer graph attached to scale, with 0.5 cm range.²⁷ The women remained upright, firm, with arms relaxed and head in the horizontal plane.

Evaluation of energy expenditure by indirect calorimetry

The women presented themselves at the metabolic unit by 07:00 o'clock, after fasting for 12 hours without performing strenuous physical activity in the last 24 hours and with minimal effort. The evaluation was performed using the open-circuit indirect calorimetry with respiratory hood (Metabolic Monitor Delta-trac-R3D).⁶

For the calculation of EE, it was used the values of the following volumes; inspired O₂ (VO₂), expired CO₂ (VCO₂) (ml/min) and urinary nitrogen.^{6,28} obtained by the calorimeter.

Evaluation of energy expenditure using prediction equations

The equations for predicting EE (kcal/24 hours) used in the study were the following:

- Harris & Benedict (1919): $BEE = 655.0955 + (9.5634 \times BM, \text{ kg}) + (1.8496 \times H, \text{ cm}) - (4.6756 \times \text{age, years})$.
- Schofield (1985): $BEE = [(0.062 \times BM, \text{ kg}) + 2.036] \times 239$ (18-30 years) $[(0.034 \times BM, \text{ kg}) + 3.538] \times 239$ (30-60 years).

- FAO/WHO/ONU (1985): $BEE = (14.7 \times BM, \text{ kg}) + 496$ (18-30 years) $(8.7 \times BM, \text{ kg}) + 829$ (30-60 years).
- Owen (1986): $BEE = 795 + (7.18 \times BM, \text{ kg})$.
- Mifflin-St Jeor (1990): $BEE = (9.99 \times BM, \text{ kg}) + (6.25 \times H, \text{ cm}) - (4.92 \times \text{age, years}) - 161$.
- Henry & Rees (1991): $BEE = [(0.048 \times BM, \text{ kg}) + 2.562] \times 239$ (18-30), $RMR = [(0.048 \times BM, \text{ kg}) + 2.448] \times 239$ (30-60 years).
- Oxford (Henry, 2005): $BEE = (10.4 \times BM, \text{ kg}) + (615 \times H, \text{ m}) - 282$ (18-30 years) $BEE = (8.18 \times BM, \text{ kg}) + (502 \times H, \text{ m}) - 11.6$ (30-60 years).

Note: BEE: Basal energy expenditure, BM: body mass (kg), H: height (m).

Statistical analysis

The data were evaluated as an average and standard deviation. To check the distribution of continuous variables was conducted adherence test of Kolmogorov-Smirnov.

For parametric variables, it was used the ANOVA test and Tukey test for comparison of the measured metabolic data with those obtained by each prediction equation. The unpaired test was used to compare metabolic and anthropometric data between groups.

It was used the computer program SPSS version 16.0, considering $p < 0.05$.

Results

The women's age in G1 and G2 was 36.62 ± 7.76 and 34.59 ± 7.56 years, respectively. These women's BMI was 31.16 ± 3.18 and 37.66 ± 6.24 kg/m², respectively. The age and BMI of the two groups G1 and G2 did not differ ($p > 0.05$). Of the total of 92 women with excess body weight, 17% were overweight, 39% grade 1 obesity, 25% were grade 2 obese and 19% grade 3 obesity. G1 were composed predominantly of overweight and obesity grade 1, while G2 were composed predominantly of obesities grade 1 and 2.

The REE obtained by indirect calorimetry (REE_{cal}) was higher in G2. Differences were found between the groups as proposed by the equations: Harris-Benedict, Shofield, FAO/WHO/ONU, Owen, Mifflin-St Jeor and Henry & Rees, being all the higher EE values in G2 (table I).

In G1, it was found that the estimates obtained by Harris-Benedict, Shofield, FAO/WHO/ONU and Henry & Rees did not differ from REE_{cal} , which presented higher values than the equations proposed by Owen, Mifflin-St Jeor and Oxford (table II).

In G2, only the equations proposed by Owen, Mifflin-St Jeor and Oxford presented EE lower than the indirect calorimetry, while the other equations did not differ from the indirect calorimetry (table II).

Table I
Comparison of energy expenditure by indirect calorimetry and prediction equations between groups

Variables	G1 (n = 26)		G2 (n = 66)		p-value
	Mean	SD	Mean	SD	
GER _{cal} (kcal.)	1680	139	1730	253	< 0,01
Harris-Benedict (kcal.)	1535	103	1705	161	< 0,01
Schofield (kcal.)	1524	113	1687	195	< 0,01
FAO/WHO/ONU (kcal.)	1547	108	1722	199	< 0,01
Owen (kcal.)	1363	61	1483	116	< 0,01
Mifflin-St Jeor (kcal.)	1445	131	1626	181	< 0,01
Henry & Rees (kcal.)	1498	99	1691	186	< 0,01
Oxford (kcal.)	1392	301	1606	166	< 0,01

G1: Brazilian obese; G2: Spanish obese.
SD: Standard deviation.

For G1 the prediction equation that was closest to the value obtained by the indirect calorimetry was the FAO/WHO/ONU (7.9% underestimation), followed by Harris-Benedict (8.6% underestimation), Shofield (9.2% underestimation) and Henry & Rees (10,8% underestimation), respectively.

For G2, the equation of the FAO/WHO/ONU (0.46% underestimation) also showed the most similar values to the calorimetry, then by order of approximation Harris-Benedict (1.5% underestimation), Henry & Rees (2.3% underestimation) and Schofield (2.5% underestimation).

For both G1 and G2 for the best equations were FAO/WHO/ONU, Harris-Benedict, Shofield and Henry & Rees.

Discussion

Indirect calorimetry is considered a standard method, after validation by comparison with the direct calorimetry,²⁹ however, its use is restricted to research due to the demanding cost and time for its conclusion,¹⁷ requiring the use of prediction equations in clinical practice.

The present study has shown that some equations were able to estimate the EE from a sample of overweight women in Brazil and Spain. In obese individuals, the accuracy of all prediction equations was reduced compared with non-obese individuals and the range of individual errors increases.¹¹

G2 showed greater REE_{cal} compared with G1, which is expected, since Spanish women had higher total body mass and fat-free mass. The standardization of REE, as suggested by Cercato et al.,³⁰ divides the population according to quintiles of weight, demonstrating that the higher the body weight, the higher is the REE.

Weg et al.¹⁹ state that the degree of overweight is a major factor influencing the result of the predictive

Table II
Comparison of the energy expenditure prediction equations in relation to indirect calorimetry, for group

Variables	G1 (n = 26)		G2 (n = 66)	
	Mean	SD	Mean	SD
REE _{cal}	1680	139	1730	253
Harris-Benedict	1535	103	1705	161
Schofield	1524	113	1687	195
FAO/WHO/ONU	1547	108	1722	199
Owen	1363 ^a	61	1483 ^a	116
Mifflin-St Jeor	1445 ^a	131	1626 ^a	181
Henry & Rees	1498	99	1691	186
Oxford	1392 ^a	301	1606 ^a	166

G1: Brazilian obese; G2: Spanish obese; REE_{cal}: resting energy expenditure for calorimetry indirect; SD: Standard deviation.

^ap < 0,005 vs calorimetry.

equations, however, most of the equations used was applied to normal weight individuals, which makes it very difficult to choose the most appropriate equation to determine the BEE of these individuals.

According to Rodrigues et al.,¹⁸ the Harris-Benedict equation tends to overestimate the values of BEE (around 7%) in obese Brazilian women. This overestimation may result in 20% less of the body weight loss than estimated value per month. Studies report that this equation when used in obese patients for evaluation of the BEE has mixed results, reaching 33% of variation.^{31,32} Wahrlich & Angels,³³ studying 60 women (20 to 40 years old) in Porto Alegre-Brasil, with a BMI of 21.7 ± 2.7 kg/m², observed that the equations of Harris & Benedict, FAO/WHO/ONU (only weight), Schofield and Henry & Rees, were not adequate to estimate the BEE, overestimating the results obtained by measurement in calorimetry.

However, the results of this study do not confirm these findings, as the Harris-Benedict equation did not differ from the calorimetry, both in the Brazilian (Viçosa-MG), and in the Spanish samples (Pamplona-Navarra). Both in G1 and G2 the equation with the highest percentage of adequacy was the FAO/WHO/ONU with underestimation related to the EE measured of 7.9% and 0.46% respectively.

Our results were similar to the study of Fett et al.,³⁴ which examined 28 sedentary women, from the state of São Paulo, with a BMI ranging between normality and obesity. There was an underestimation of up to 16% of the EE from these ones when compared with the measured by indirect calorimetry. The equations more appropriate were also FAO/WHO/ONU and Harris-Benedict, presenting, respectively, 4% and 3% of underestimation.

The main difference between REE and BEE is that REE is measured after the individual dislocation to the exam site. However, it is needed a prior resting period of 30 minutes to neutralize the effects of the physical activity performed.³⁵ Thus the result of the EE obtained by indirect calorimetry (REE) can be effectively compared with those estimated by the prediction equations in this study, which evaluated the BEE.

However, studies claim that REE is 10-15% higher than the BEE, which might explain the lower values of EE in some predictive equations when compared with indirect calorimetry.³⁶

This study presented limitations as specific sample of women from two regions, and small numbers of participants. The comparative evaluation between studies was also limited by the deficiency in the methodological description of them and the fact sides consider the BEE and REE as being equal.

Conclusion

Regardless the women nationality the equations proposed by FAO/WHO/ONU, Harris-Benedict, Schofield and Henry & Rees were adequate to estimate the EE in a sample of Brazilian and Spanish women with excess body weight. The equations of Owen, Mifflin-St Jeor and Oxford underestimated the EE of obese Brazilian and Spanish women.

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Original / *Obesidad*

Mixed dietary pattern is associated with a slower decline of body weight change during postpartum in a cohort of Brazilian women

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Abstract

Objective: The aim was to assess the effect of dietary patterns on postpartum body weight change (BWC).

Methods: A Food Frequency Questionnaire (FFQ) with 81 items was applied in 278 women having the first six months after delivery as the time frame. Body weight (BW) was measured at 15 days (baseline) and at 2.6 and 9 months postpartum. Principal components analysis was used to extract the dietary patterns. Linear mixed models were performed having BWC as the outcome and the dietary patterns as independent variables.

Results: Two major dietary patterns were identified: healthy and mixed. Energy intake was 2,838 kcal (DP = 624) and 2,233 kcal (DP = 455), for women classified in the highest quartiles of mixed and healthy dietary patterns, respectively. Mean BWC declined -0.151 kg/month (SE = 0.02) independently of the dietary pattern. Predicted values of BWC among women that have adhered to mixed dietary pattern indicated a lower BWC of 0.830 kg/month (SE = 0.24; $p < 0.001$) at 6 months and 0.938 kg/month (SE = 0.24; $p < 0.001$) at 9 months postpartum.

Conclusion: The mixed dietary pattern was associated with a slower rate of BWC during postpartum, compared the healthy dietary pattern.

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Keywords: *Dietary pattern. Postpartum. Body weight change. Cohort studies.*

UN PATRÓN DIETÉTICO MIXTO SE ASOCIA CON UN MENOR DECLIVE EN EL CAMBIO DEL PESO CORPORAL DURANTE EL PUERPERIO EN UNA COHORTE DE MUJERES BRASILEÑAS

Resumen

Objetivo: El propósito de este estudio fue evaluar el efecto del patrón dietético sobre el cambio de peso corporal (CPC) en el puerperio.

Métodos: Se aplicó una Cuestionario de frecuencia de alimentos (CFA) con 81 ítemes a 278 mujeres en el marco temporal de los siguientes 6 meses después del parto. El peso corporal (PC) se midió a los 15 días (basal) y a los 2,6 y 9 meses posparto. Se utilizó el análisis de los componentes principales para extraer los patrones dietéticos. Se realizaron modelos lineales mixtos, siendo el CPC el resultado y los patrones dietéticos las variables independientes.

Resultados: Se identificaron dos patrones dietéticos principales: saludable y mixto. El consumo de energía fue de 2.838 kcal (DP = 624) y 2.233 kcal (DP = 455), para las mujeres clasificadas en los cuartiles más altos de los patrones dietéticos mixto y saludable, respectivamente. El decremento promedio del CPC fue de -0,151 kg/mes (EE = 0,02) independientemente del patrón dietético. Los valores predictivos del CPC en las mujeres con un patrón dietético mixto indicaron un menor CPC de 0,830 kg/mes (EE = 0,24; $p < 0,001$) a los 6 meses y de 0,938 kg/mes (EE = 0,24; $p < 0,001$) a los 9 meses posparto.

Conclusión: El patrón dietético mixto se asoció con un ritmo de pérdida de peso más lento durante el puerperio en comparación con el patrón dietético saludable.

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Palabras clave: *Patrón dietético. Puerperio. Cambio en el peso corporal. Estudios de cohortes.*

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Introduction

The dietary pattern, energy intake and the large intra-individuals dietary intake variation during pregnancy may increase gestational weight gain (GWG).¹⁻³ Excessive GWG has been identified as a critical determinant of postpartum weight retention,⁴⁻⁵ which is the main expression of maternal obesity and may affect up to 20% of the women.⁶

Factor analysis considers the complex nature of dietary intake and has been used in epidemiologic studies to test the association of dietary patterns with health outcomes.⁷⁻⁸ This approach is considered an important tool and has been used to assess the effect of dietary pattern on body weight composition and obesity.⁹⁻¹²

Perceived role of the food and selection of a safe dietary pattern to ensure fetus health and improve breastfeeding are common concern among women during the reproductive period.¹³ These concerns may increase the number of food items consumed, and consequently total energy intake.¹⁴ The eating habit includes the diet quality and quantity and is modulated by many factors such as socio-economic variables.¹⁵⁻¹⁶

The literature regarding dietary pattern during postpartum is scarce and most studies have been performed during pregnancy.^{1,17-18} The few studies concerning dietary changes during the reproductive cycle are still inconclusive.¹⁹⁻²⁰ Castro et al. (2006)²¹ reported a decreased intake of carbohydrates, cereals, fruits, milk and dairy products during postpartum, when compared to pregnancy in Brazilian women. These authors have observed that an increase in protein intake during postpartum facilitated body weight loss.²²

The aim of this study was to describe dietary patterns in a cohort of Brazilian women and to examine the effect of these patterns on body weight change (BWC) over nine months of postpartum follow-up.

Materials and methods

Study design and participants

Data for the present study was collected using a prospective cohort design conducted from May 1999 to April 2001 at the Marcolino Candau Municipal Health Center and from the main maternity hospital in the study catchment area, in Rio de Janeiro municipality, Brazil. Participants were recruited at prenatal routine care and during the newborn routine immunization, and immediately after birth in the maternity hospital.

The study design involved 15 months of recruitment and nine months of follow-up after delivery, in which data was collected approximately at 15 days, 2, 6 and 9 months postpartum. A Food Frequency Questionnaire (FFQ) was applied at 6 months postpartum and was used to analyze the effect of dietary pattern on BWC during the first nine months postpartum. Information was based on 278 (65%) women aged 18-45

years of 430 (100%) that were recruited at baseline. Previous analyses have shown non-random losses of follow-up.⁶ We have demonstrated that the losses of follow-up were random with respect to all variables.²²⁻²³ Body weight at baseline ($P = 0.30$) and pre-pregnancy weight ($P = 0.27$) were not different between those who were followed and those who dropped out. Final model were adjusted for age women, because except to this variable, younger women have dropped out from the study. Analysis showed a random pattern of losses of dietary intake.

The ethic committee from the Institutional Review Board of the Institute for Studies in Collective Health (IESC) at the Federal University of Rio de Janeiro (UFRJ) approved the study. All the study's stages were announced to the participants, which provided written informed consent prior to participation in the study. Details of the study design and participation rates were presented elsewhere.²²⁻²³

Anthropometric assessment

Body weight (BW) was collected at baseline (15 days after delivery) and on 3 waves of follow-up (2, 6, and 9 months postpartum). Women were weighted without shoes and wearing light clothes on a digital scale, with a capacity of 150 kg and a precision of 0.1 kg (PL 150 Model, Filizzola Ltda., São Paulo, Brazil). The assessment of the anthropometric variables was performed in accordance with Lohman's protocol.²⁴ Body mass index (BMI) was calculated using weight measured at baseline. Pre-pregnancy BMI (PPBMI) was calculated using self-reported pre-pregnancy weight (PPW) or BW registered until the 13th gestational week; stature was measured using a stadiometer with precision of 0.1 cm (Holtain-Harpeden, UK). Percent of body fat (%BF) was calculated using an electrical impedance technique with equations provided by RJL Inc (RJL, USA). Other methodological details were previously described.⁶

Body weight change

BWC was considered the outcome. This variable was obtained taking into account body weight (kg) measured at baseline (15 days after delivery) and in the three follow-up visits: 2, 6, and 9 months postpartum. Negative BWC refers to a body weight loss during follow up and positive BWC refers to a body weight gain during postpartum. The outcome was defined as a time dependent variable because assumes different values in each point of observation.

Assessment of dietary intake

Usual dietary intake was obtained through a FFQ, that was administered by nutritionist at 6 mo postpartum

Table I
Factor loading of rotated factor matrix for major dietary patterns for woman at 6 months postpartum.
Rio de Janeiro, Brazil (1999-2001)

Food items	Dietary pattern*		Pryor communality Estimates
	Mixed	Healthy	
Rice	0.41426	-0.12478	0.57042714
Beans	0.42550	-0.02192	0.60614407
Breads	0.65657	-0.07005	0.61415965
Pasta and wheat	0.31926	0.07747	0.62629893
Eggs	0.25629	0.13733	0.79610512
Sausages	0.32738	0.21164	0.80643141
High-fat products	0.51255	0.10439	0.59599470
Fruit juices and soda	0.33729	0.21859	0.63169993
Cake and biscuits	0.19987	0.05757	0.65326564
Sugar and suits	0.37545	0.06228	0.62579956
Coffee and tea	0.18739	0.07582	0.47363270
Fruits	0.14372	0.59588	0.67459767
Green leafy vegetables	-0.13465	0.52131	0.55826530
Legumes/other vegetables	-0.01646	0.57011	0.59313859
Potato, roots and corn	0.19401	0.30700	0.66827487
Meat and poultry	0.06848	0.23962	0.60507685
Fish	0.04122	0.30957	0.67487103
Milk and dairy products	0.09510	0.27600	0.63928841

Standardized Cronbach's alpha coefficient was 0.64 from Mixed and 0.57 from Healthy dietary pattern.

and has the first six months after delivery as the time frame. FFQ was composed by 81 food and beverage items and 8 answer options (never or almost never; 1-3 times/month, 1 time/week, 2-4 times/weeks, 5-6 times/weeks, 1 time/day, 2-3 times/day, or more than 3 times/day). The FFQ was developed and previously validated by Sichieri & Everharth (1998).²⁵ Standard portions sizes were given from each food item.²⁶ Estimates of total energy intake and gramature of nutrients, foods and foods groups were calculated with a program previously developed using Statistical Analyses System (SAS) 8.2.²⁷ This program considered the food composition database created by the Escola Paulista de Medicina.²⁸ Foods compositions that were not included in this database were assessed from a national family-budget study.²⁹

To identify the dietary patterns, the 81 items listed in the FFQ were grouped into eighteen food groups, based on their nutritional characteristics: 1) Rice; 2) Beans; 3) Breads; 4) Cake and biscuits; 5) Meat and poultry; 6) Eggs; 7) Fish; 8) Green leafy vegetables; 9) Legumes and other vegetables; 10) Fruits; 11) Pasta and wheat; 12) Potato, roots and corn; 13) Sweetened beverages (Fruit juices and soda); 14) Sugar and suits (sugar, sweets and desserts); 15) Milk and dairy products; 16) High-fat products (processed meat, pizza, snacks, chips fries, butter, bacon and maiones); 17) Sausages (sausages, hamburger, viscous and ham); and 18) Coffee and tea.

Dietary patterns were extracted using principal component analysis (PCA). Firstly, Kaiser-Meyer-Olkin (KMO) was used to measure sampling adequacy. Two commonly applied criteria were used to identify the number of patterns to be retained: (a) the eigenvalues > 1.50 and (b) the Cattell's scree test plot. Factor loading of 0.25 was used as criteria to limit low inter-correlations between dietary variables in a factor.³⁰ Orthogonal varimax rotation of the factors was applied to improve the interpretation. Cronbach's alpha coefficient was used to evaluate internal consistency for each component retained. After all, the dietary patterns were named according to the nature of the food groups and the factors load (table I).

Assessment of co-variables

Breastfeeding, smoking and socio-demographic variables were investigated from structured questionnaires that were applied at the baseline, the first and second waves of follow-up. Family income (dollar), parity (number of children), age (years), schooling (years) and breastfeeding (days of predominant breastfeeding)³¹ were treated as continuous variables. Skin color was categorized in white and non-white (black or brown), and marital status was classified as single or married/living with a partner.

Table II
High dietary pattern quartile score by selected variables
for Brazilian women at 6 months postpartum.
Rio de Janeiro, Brazil (1999-2001)

Variables	Dietary pattern		p-value ¹
	Mixed	Healthy	
Mean (SD)			
<i>Intake:</i>			
Energy (kcal)	2,838 (624)	2,233 (455)	< 0.001
<i>Anthropometric:</i>			
Body weight	62.7 (14.9)	60.6 (9.6)	0.398
BMI	24.5 (5.6)	23.8 (3.6)	0.454
BMI Pre-Pregnancy	22.7 (5.0)	22.5 (2.7)	0.756
Body fat (%)	29.4 (7.9)	29.6 (5.2)	0.779
Retention	3.2 (5.6)	2.8 (4.4)	0.679
<i>Socio-demographic:</i>			
Age (years)	25.0 (6.2)	27.0 (5.3)	0.080
Income (dollars)	255 (146)	450 (341)	< 0.001
Schooling (years)	6.8 (3.1)	8.5 (3.1)	0.006
Parity	2.2 (1.36)	1.9 (1.2)	0.333
Breastfeeding (days)	103 (57.7)	102 (60.7)	0.940
N (%)			
<i>Socio-demographic:</i>			
Skin color			
White	18 (26.1)	15 (33.3)	0.404
No White	51 (73.9)	30 (66.7)	
Marital Status			
Married	51 (73.9)	40 (88.9)	0.051
Single	18 (26.1)	05 (11.1)	

¹P-value refers to ANOVA for continuous variables and chi-square for proportions.

Statistics

To verify the mother's characteristics at higher score pattern adherence, energy intake, anthropometric and socio-demographic characteristics were evaluated across the forth quartile of mixed and healthy dietary patterns (table II) using means and standard deviations (SD) and prevalence (%). Women with high score on quartiles of both mixed and healthy were kept at first dietary pattern (factor 1). Analysis of variance was used for the comparison of continuous variables between higher quartiles of mixed and healthy dietary patterns, and chi-square test was used for categorical variables.

The effect of dietary patterns on BWC among 278 women was evaluated with linear mixed effect models.³² The factor loading were standardized (mean equal to 0 and SD equal to 1) in order to make the multiple linear regression models comparables. Energy intake, family income and schooling that were associated were considered confounders ($p \leq 0.05$) as were associated with quartiles of both dietary patterns and with the outcome. %BF, age, skin color and marital status were also considered as potential confounding factors as were related with one of the

dietary quartiles ($p \leq 0.05$). A final model was also adjusted for PPW.

Linear mixed effect models were fitted in four steps. The outcome and postpartum time elapsed since delivery was considered as random effects and all other variables as fixed effects. First, the unconditional growth model that included time variable was fitted and named model A. Then, the unadjusted model B was fitted and included the interaction between time and the predictor variables (score of mixed and healthy patterns). Adjusted conditional models were fitted including the following co-variables: energy intake, %BF, age, family income, schooling, skin color and marital status (model C) and model D (all variables from model C plus PPW). All models were nested from an unconditional mean model that describes partition of the outcome variation (table III). Analyses were performed using SAS version 9.1.

Results

Two different dietary patterns were identified and were named mixed and healthy. The eigenvalues were 2.73 and 1.96, respectively. The cumulative variance was 26.1%. The mixed pattern explained 15.2% of the total variance and was composed of rice (0.41426), beans (0.42550), breads (0.65657), pasta and wheat (0.31926), eggs (0.25629), sausages (0.32738), high-fat products (0.51255), fruit juices and soda (0.33729), and sugar and suits (0.37545). The healthy pattern explained 10.9% of the variance and was composed of fruits (0.59588), green leafy vegetables (0.52131), legumes and other vegetables (0.57011), potato, roots and corn (0.30700), fish (0.30957), and milk and dairy products (0.27600). Standardized Cronbach's alpha coefficient was 0.64 for mixed and 0.57 for healthy dietary pattern. The pryor communality estimates and the lower communality were 0.47363 for coffee and tea (table I).

Energy intake was statistically ($p < 0.001$) different among highest quartiles of the mixed and healthy patterns (table II). Women situated on the highest quartile of the healthy dietary pattern had higher family income (255 versus 450 dollars, $p = 0.001$) and higher schooling (8.5 versus 6.8 years, $p = 0.006$) than women that had adhered to the highest quartile of mixed dietary pattern. Results showed that higher proportion of married's women adhered to the highest quartile of healthy dietary pattern (88.9 versus 73.9 years, $p = 0.051$).

According to Model A, BWC declined -0.151 kg/month (SE = 0.02), independently of the dietary pattern. Unadjusted mean BWC (model B) was -0.534 kg/month (SE = 0.20; $p < 0.01$) at 2 months; -1.101 kg/month (SE = 0.20; $p < 0.001$) at 6 months and -1.420 kg/month (SE = 0.21; $p < 0.001$) at 9 months postpartum. Adjusted mean BWC was -1.409 kg/month (SE = 0.21; $p < 0.01$) at 9 months (model C) and -1.597 kg/month (SE = 0.20; $p < 0.001$) in model D.

Table III
Regression coefficients estimates for postpartum predicting body weight change (2, 6, and 9 months) according to women's dietary pattern at six months postpartum. Rio de Janeiro, Brazil (1999-2001)

Parameter	Model A [‡] β (SE)	Model B ^{‡‡} β (SE)	Model C ^{‡‡} β (SE)	Model D ^{‡‡} β (SE)
<i>Fixed effects</i>				
<i>Intercept</i>				
Weight	63.1(0.76)**	63.2 (0.77)*	59.9 (1.58)**	62.5 (0.795)*
Mixed Pattern	–	-0.122 (0.92)	-0.281 (0.95)	0.378 (0.50)
Healthy Pattern	–	0.356 (0.95)	-0.409 (0.70)	0.562 (0.38)
<i>Rate of change</i>				
Months	-0.151 (0.02)**	–	–	–
Weight* 2 months	–	-0.534 (0.20)*	-0.534 (0.20)*	-0.593 (0.19)*
Weight* 6 months	–	1.101 (0.20)**	-1.101 (0.20)**	-1.297 (0.20)**
Weight* 9 months	–	-1.420 (0.21)**	-1.409 (0.21)**	-1.597 (0.20)**
<i>Mixed pattern</i>				
Weight* 2 months	–	0.269 (0.24)	0.269 (0.24)	0.235 (0.23)
Weight* 6 months	–	0.933 (0.24)**	0.933 (0.24)**	0.830 (0.24)**
Weight* 9 months	–	1.043 (0.25)**	1.403 (0.25)**	0.938 (0.24)**
<i>Healthy pattern</i>				
Weight* 2 months	–	0.055 (0.25)	0.055 (0.25)	0.043 (0.24)
Weight* 6 months	–	0.221 (0.25)	0.221 (0.25)	0.056 (0.25)
Weight* 9 months	–	0.086 (0.25)	0.080 (0.25)	-0.091 (0.25)
<i>Variance components</i>				
Level 1 (Within)	5.74 (0.29)**	5.59 (0.28)**	5.59 (0.28)**	5.01 (0.26)**
Level 2 (Between)	156.7 (13.4)**	157.6 (13.6)**	47.3 (4.21)**	10.6 (1.05)**
<i>Goodness-of-fit</i>				
-2 Res Log Likelihood	6,277.4	6,250.5	5,951.5	5,232.2
AIC**	6,281.4	6,254.5	5,955.5	5,236.2

[‡]Unadjusted model.

^{‡‡}Adjusted model.

*p ≤ 0.01; **p ≤ 0.001; ***Akayke Information Criterion. Models were fitted using a random intercept. Model A was the unconditional growth model that included time variable. Model B added the interaction between linear time and predictor variable (score of Mixed and Healthy). Model C is a conditional model with the controlled effect of the predictor variable adjusted by energy intake, percent of body fat, age, schooling, family income, skin color and marital status. Model D is a conditional model with the controlled effect of the predictor variable adjusted by energy intake, percent of body fat, age, schooling, family income, skin color, marital status and pre-pregnancy body weight.

Model D showed that women that adhered to healthy dietary pattern had a non-significant higher increase in mean BWC (higher body weight loss) of -0.091 kg/month (SE = 0.25) at 9 months postpartum. On the other hand, the final multivariate model (model D) pointed a significant decreased on mean BWC (lower body weight loss) of 0.830 kg/month (SE = 0.24; p < 0.001) at 6 months and 0.938 kg/month (SE = 0.24; p < 0.001) at 9 months postpartum (table III).

Discussion

The main findings of this study showed that the dietary patterns among Brazilian women during postpartum were classified as mixed and healthy. The mixed pattern was composed mainly of breads, high fat products, rice and beans, while the healthy pattern was composed of fruits, legumes and vegetables, roots and fish. BW has decreased approximately 1.6 kg over a nine months period independently of the dietary pattern. However, women with mixed dietary pattern presented a slower BWC during the first nine months postpartum when

compared with women that adhered to a healthy dietary pattern. BWC was categorized on time intervals and it was observed that women with mixed dietary pattern lost 0.830 kg less at 6 and 0.938 kg at 9 months postpartum compared with women that have adhered to healthy dietary pattern. To our knowledge, this is the first study that have investigated an association between dietary patterns and BWC during postpartum in the Brazilian population. Only one longitudinal study have comprised the whole reproductive cycle, however has analyzed the association of dietary patterns with lifestyle but not with BWC over time, as ours study did.¹⁹

Uusitalo et al. (2009)¹ has investigated the association of dietary patterns and GWG rate among 3,360 Finish women. The authors identified seven distinct dietary patterns: healthy, fast food, traditional bread, traditional meat, low fat, coffee and alcohol and butter. The results revealed a positive association between fast-food pattern and higher gestational GWG (kg/week). Other studies have evaluated the relationship between dietary patterns and obesity or body weight change (BWC), but were based only on cross-sectional or baseline data.³³⁻³⁴ The two avail-

able longitudinal studies did not include postpartum women.^{14,35} Schulze et al. (2006)³⁵ examined the association between dietary pattern and BWC among 57,670 North-Americans female nurses and observed that those who increased their western pattern score over time presented a greater weight gain from 1991 to 1999. Murtaugh et al. (2007)¹¹ found a positive association between western pattern and higher prevalence of excess of BW, in a cross-sectional dietary analysis, from a case-control study of breast cancer with 2,470 North-American women. On the other hand a prudent or healthy dietary pattern seemed to be associated with a lower risk of overweight or obesity.¹⁰⁻¹¹ Newby et al. (2006)¹⁰ studied 33,840 women from the Swedish Mammography Cohort and showed that obese women who increase the score for the healthy dietary pattern, presented larger decreases in BMI over 9 years of follow-up.

In Brazil, results from a survey conducted in 1996 in Rio de Janeiro, Brazil with a probabilistic sample of 2,040 households described the effect of a traditional diet comprised of rice and bean, and a lower risk of overweight.⁹ Sichieri et al. (2003)³⁶ based on food intake of 5,121 adults aged 20 to 50 years, from the Northeast and Southeast geographical regions, have shown a positive association between a pattern labeled mixed and higher BMI. The mixed pattern was comprised by industrialized foods such as sugar, cake, biscuits and dairy products.

Beyond the scarce scientific literature about dietary patterns in the postpartum period, there is a lack of evidence to understand how social and cultural factors could determine food intake change. Arija et al. (2004)³⁷ have verified a slight change in food consumption from pre-pregnancy to postpartum period between 80 recruited Spanish women and an increase in energy intake at 6 weeks postpartum coinciding with lactation. The study performed by Cucó et al. (2006)¹⁹ with 80 healthy women volunteers planning to get pregnant, described two stable dietary patterns over the reproductive cycle named sweetened beverages and sugars and vegetables and meat. In the same line, Crozier et al. (2009),²⁰ have shown two stable dietary patterns labeled prudent and high-energy with 2,270 United Kingdom pregnant women.

In the present study, only two patterns were retained based on the eigenvalues and the Cattell's scree plot test, the two adopted criteria. It seems that women tend to include different kinds of foods to improve dietary intake during reproductive cycle.

Appropriate nutrition is an important toll of public health nutrition that aims guarantee health for women during reproductive cycle and to prevent excessive GWG.³⁵ Excessive GWG may represent in the future greater postpartum weight retention and obesity.^{6,38} A diet that includes safe food during pregnancy or lactation that assures the health of both mother and child, and helps the breastfeeding process is a concern of most women. Arija et al. (2004)³⁷ has shown that

women tend to increase consumption of fruits, vegetables and milk, and decrease the intake of sugar and alcoholic drinks during pregnancy.

During postpartum, it is important to assure that a healthy diet is followed with an increase on portion size. Some studies have shown that an adherence to exclusive breastfeeding could be associated with a higher energy intake³⁹⁻⁴⁰ and, consequently, lower body weight loss. Chou et al. (1999)³⁹ have verified that although energy expenditure was similar between lactating mothers and the non-lactating group, the daily energy intake and fat consumption were higher among lactating women. Durham et al. (2011)⁴⁰ investigated 450 overweight and obese women between 6 and 9 weeks postpartum and compared food consumption according to breastfeeding status (exclusive or mixed/only formula feeding). Women that fully breastfeed their children had higher energy intake and consumed snacks more frequently than the others.⁴⁰

It is important to highlight the women's abilities to improve their diet during pregnancy and postpartum. Improvements need to be qualitative. Crozier et al. (2009)²⁰ have observed a small decrease in the prudent diet from pre-pregnancy and a small increase in high-energy score of dietary pattern in late pregnancy. Women should not restrict food intake during pregnancy, but during postpartum, after lactation has been established, it is acceptable that a prudent and moderate body weight loss attained through a caloric restriction helping to return to pre-pregnancy BW.^{22,41} An increase on the intake of safe foods like vegetables, legumes, fruits, low-fat dairy, beans and whole grains and a decreased of soda and sweetened beverages, fast-food, high sugar, fat foods and desserts, would prevent a higher weight gain during pregnancy and a lower postpartum weight retention.

In conclusion, authors signalize that dietary investigations about BWC during postpartum should consider lifestyle and socio-demographics factors in order to propose effective nutritional guidelines to prevent non-expected alterations on postpartum body weight. Was observed that women that have adhered to a mixed dietary pattern had a greater intake of energy, fat and industrialized products beyond beans and rice, and presented a slower rate of BWC during postpartum, compared to those with a healthy dietary pattern. The results presented here and in others studies should be accounted in this way.

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Original / *Obesidad*

Weight and body composition variations in overweight women along outpatient nutritional treatment

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Abstract

Introduction: To evaluate the treatment of obesity it is necessary to understand the weight changes, to improve intervention strategies.

Objective: To assess the progression of weight and body parameters in overweight women along a diet therapy.

Methods: 163 women participated in this study. They were evaluated for weight, circumferences (waist and hip), and body composition (lean mass and body fat) along the three treatment phases.

Results and Discussion: The weight loss percentage was higher in the first treatment phase than in the second one ($-6.8 \pm 4.8\%$ vs. $-4.0 \pm 2.7\%$, $p < 0.0001$). In the two first phases the circumferences and the lean mass decreased among women with weight loss. Body fat reduction occurred (-2.6%) during the first phase only.

Conclusion: Weight loss and reduction in body parameters occurred mainly in the first treatment phase, showing that it is necessary to rethink intervention strategies.

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Keywords: *Body weight changes. Weight loss. Obesity. Body composition.*

EVOLUCIÓN DEL PESO Y DE LA COMPOSICIÓN CORPORAL EN MUJERES CON EXCESO DE PESO EN TRATAMIENTO NUTRICIONAL EN AMBULATORIO

Resumen

Introducción: Para evaluar el tratamiento de la obesidad es necesario entender el curso de los cambios del peso para mejorar las estrategias de intervención.

Objetivo: Evaluar el peso y las medidas corporales de mujeres con exceso de peso durante un tratamiento nutricional.

Métodos: Fueron evaluadas 163 mujeres, con medición del peso, de las circunferencias (cintura y cadera) y de la composición corporal (masa magra y grasa corporal) en tres fases del tratamiento.

Resultados y discusión: El porcentaje de la pérdida de peso fue mayor en la primera que en la segunda fase del tratamiento ($-6,8 \pm 4,8\%$ vs $-4,0 \pm 2,7\%$, $p < 0,0001$). En las dos primeras fases hubo disminución de las circunferencias y de la masa corporal magra entre las mujeres que perdieron peso. La reducción de la grasa corporal ($-2,6\%$) se produjo sólo en la primera fase.

Conclusión: La reducción del peso y de las medidas corporales ocurren principalmente en la primera fase del tratamiento, alertando para la necesidad de una revisión de las estrategias de intervención.

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Palabras clave: *Cambios en el peso corporal. Pérdida de peso. Obesidad. Composición corporal.*

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Abbreviations

BMI: Body Mass Index.
C1: First visit.
WC: Waist Circumference.
HC: Hip Circumference.
C5: Fifth visit.
C10: Tenth visit.
C15: Fifteenth visit.
WHO: World Health Organization.
BEI: Bioelectrical Impedance.
C1-C5: Participants who attended at least five visits.
C6-C10: Participants who attended at least ten visits.
C11-C15: Participants who attended at least fifteen visits.
Subgroup WL: Participants that lost weight.
Subgroup WG: Participants that gained weight.
BF: Body Fat.

Introduction

The high prevalence of obesity and the adverse effects of excess weight call for treatments that take the specificities of the assisted group into account.¹ The female population is the most affected by excess weight and obesity;² in women, these conditions culminate in gender-specific complications such as higher incidence of cervical, endometrial, ovarian, and breast neoplasms; higher prevalence of amenorrhea and infertility; and complications during pregnancy.³

Weight loss improves the patient's metabolic profile and the aforementioned comorbidities. From a clinical standpoint, between 5.0 and 10.0% weight loss at the beginning of the treatment provides positive results.¹ However, patients undergoing the treatment usually wish to achieve much larger weight loss.⁴ Apart from losing weight, maintaining the weight loss is a common difficulty among obese patients, because this requires permanent changes in their eating habits and lifestyle. Studies have shown that 50.0% of the patients regain the lost weight within the first post-treatment year. After three to five years, approximately 85.0% of the subjects return to or even exceed the weight they had at the start of the treatment.⁵

Maintaining the eating habits acquired along diet therapy requires continuous motivation, which many times is difficult to sustain due to intrinsic and extrinsic factors. Short-term goals, like allowing patients to consume sweets and other food, may overlap with long-term aims, such as weight loss.⁶

The strategies that bring about essential behavioral changes to achieve successful weight loss are not necessarily the same strategies that are crucial to maintaining weight loss. To obtain sustained weight loss, it is vital to promote the following conditions: reduced food intake due to emotional reasons and flexible, non-conflicting self-control of food intake associated with intrinsic motivation for practising physical activities.⁷

Literature studies have highlighted the health benefits arising from weight loss; they have also discussed the difficulty that patients have in maintaining weight loss in the long term, which many times results in return to the initial weight.^{1,5} However, little has been said about patients' progression, weight loss milestones along the diet therapy, and the way in which these milestones could help develop strategies that translate into more effective weight loss and maintenance. In this context, the present study aims to evaluate how the weight and body composition of overweight women assisted at an outpatient clinic vary during the weight loss and maintenance phases of a diet therapy.

Materials and methods

This study evaluated 163 women admitted to an outpatient clinic between September 2005 and October 2009 and who underwent diet therapy to lose weight. The clinic specialized in obesity among women of reproductive age. All the participants were overweight or obese (Body Mass Index-BMI ≥ 25 kg/m²).

The nutritional treatment directed to reduce energy intake while preserving the recommended macronutrient composition for a "balanced diet".⁸

On the first visit (C1), the participants had their height, weight, waist circumference (WC), and hip circumference (HC) measured; their body composition (body fat and lean mass) was also evaluated. According to the protocol followed at the clinic, patients were re-evaluated every five visits (C1, C5, C10, and C15); all the measurements, except height, were repeated. The mean time between the visits varied between one and two months.

Body weight (kg) and height (m) were recorded on a Filizola digital scale (Personal Line) with a capacity of 150 kg and sensitivity of 0.1 kg, coupled to a stadiometer. The BMI was classified according to the cutoff points advocated by the World Health Organization (WHO)¹. WC and HC were measured using previously standardized techniques.⁹ Body composition (lean mass, in kg, and body fat, in %) was assessed by bioelectrical impedance (BEI) conducted on the equipment Biodynamics model 450.

To analyze the data, the women were divided into groups according to the number of visits. Participants who attended at least five, ten, and fifteen visits were included in groups C1-C5, C6-C10, and C11-15 (first, second, and third phases), respectively. Therefore, data analysis included 75, 20, and 6 women in phases 1, 2, and 3, respectively.

Within each group, participants were subdivided into subjects that lost weight (subgroup WL) and subjects that gained weight (subgroup WG). Weight loss and gain corresponded to a negative and positive variation higher than 0.5 kg, respectively.

The project was approved by the Research Ethics Committee of Hospital das Clínicas da Faculdade de

Table I
Weight and body composition changes in overweight women that lost (WL) and gained (WG) weight along the diet therapy. Ribeirão Preto (SP), Brazil, 2005-2009

	WL		WG	
	C1-C5 (n = 51)	C6-C10 (n = 13)	C1-C5 (n = 16)	C6-C10 (n = 7)
Weight (kg)	-6.8 ± 5.3*	-3.5 ± 2.5*	2.4 ± 1.9*	5.7 ± 5.1*
Weight (%)	-6.8 ± 4.8*	-4.0 ± 2.7*	2.4 ± 1.6*	5.6 ± 5.5*
WC (cm)	-7.8 ± 7.1*	-6.6 ± 11.1*	-0.7 ± 6.4	0.9 ± 3.4
HC (cm)	-6.1 ± 5.5*	-4.8 ± 5.2*	-0.7 ± 3.2	-0.4 ± 3.7*
BF (%)	-2.6 ± 8.9*	1.1 ± 3.0*	4.3 ± 6.4*	4.3 ± 9.3*
LM (kg)	-4.2 ± 9.4	-1.0 ± 5.2	0.6 ± 1.9	-0.1 ± 3.6

Data presented as the mean ± standard deviation.

Note. C-C: Time between visits; WC: Waist circumference; HC: Hip circumference; BF: Body fat percentage; LM: Lean mass.

* $p < 0.05$.

Medicina de Ribeirão Preto-University of São Paulo, Brazil (protocol number 10137/ 2010).

The data were processed and analyzed in a descriptive way (mean values-A and standard deviation-SD) and in percentage. To analyze and compare the mean weight, circumferences, and body weight values among the groups, the nonparametric Wilcoxon test was used for paired samples. To analyze and compare the mean lean mass among groups, the ANOVA method followed by the Kruskal-Wallis test was employed. The significance level was set at 95% ($p < 0.05$).

Results

The age of the participants varied between 19 and 54 years ($A = 30.2$ years, $SD = 6.6$ years); the BMI ranged from 25.4 to 57.3 kg/m^2 ($A = 37.5$ kg/m^2 , $SD = 6.1$ kg/m^2). The patients had other conditions associated with excess weight or obesity: polycystic ovary syndrome, insulin resistance, diabetes mellitus, infertility, endometriosis, dyslipidemia, arterial hypertension, and metabolic syndrome.

The mean weight loss was 6.8 (SD 4.8%), within the first five treatment months among the patients included in the subgroup WL; weight loss decreased gradually thereafter. In this subgroup, weight loss was significantly higher ($p = 0.0105$) in the first phase as compared with the second phase. The women who continued the treatment and maintained weight loss after the first visit achieved a mean weight loss of 4.0 (SD 2.7%), between C6 and C10 (table I) and 3.6 (SD 4.9%), between C11 and C15, without significant differences.

As for the subgroup WG, the mean weight gain was 2.4 (SD 1.6%), in the initial phase. Among the women who continued the treatment, the mean weight gain was 5.6 (SD 5.5%). Considering the initial weight, the weight gain was significant both in the first ($p = 0.0012$) and second ($p = 0.0008$) treatment phases.

Concerning body measurements, the patients belonging to the subgroup WL had significantly lower WC and

HC in both the first ($p < 0.0001$) and second treatment phases (WC: $p = 0.01$ and HC: $p < 0.001$). The body fat percentage also varied significantly in both phases (C1-C5: $p < 0.0001$ and C6-C10: $p = 0.0004$), but the amount of lean mass did not change significantly.

Of the total number of patients, 8.6, 73.4, and 70.0% ($n = 14, 88, \text{ and } 55$) quit between visits C1 and C2, C6 and C10, and C11 and C15, respectively. Nevertheless, in all the phases the percentage of patients that lost weight was higher (C1-C5: 68.0%, C6-C10: 65.0%, and C11-C15: 66.7%) than the percentage of patients that gained weight (C1-C5: 21.3%, C6-C10: 35.0%, and C11-C15: 33.3%). On average, the WC, HC, and body fat (BF) values decreased progressively along the first ten visits.

Only six women reached the third treatment phase. The mean weight and BMI varied from 109.3 kg ($SD = 31.0$ kg), and 43.7 kg/m^2 ($SD = 9.2$ kg/m^2), at the start of the treatment (C1) to 95.8 kg ($SD = 23.6$ kg), and 36.5 kg/m^2 ($SD = 6.2$ kg/m^2), at the fifteenth visit (C15), respectively. In the third phase, four women presented weight loss ($A = 3.6$ kg, $SD = 4.9\%$), whereas two women gained weight ($A = 1.4$ kg, $SD = 0.2\%$) (table II).

Table II
Weight and body parameters recorded for the patients assisted at the clinic on visits number 1, 5, and 10. Ribeirão Preto (SP), Brazil, 2005-2009

	C1 (n = 163)	C5 (n = 75)	C10 (n = 20)
Weight (kg)	97.3 ± 18.7	92.5 ± 17.8	94.2 ± 23.3
BMI (kg/m^2)	37.5 ± 6.1	35.9 ± 5.9	31.0 ± 13.4
WC (cm)	113.8 ± 14.5	109.2 ± 13.6	104.8 ± 14.4
HC (cm)	121.1 ± 13.1	118.0 ± 11.5	114.5 ± 9.3
BF (%)	40.9 ± 4.1	40.3 ± 5.0	39.0 ± 3.7
LM (kg)	57.3 ± 8.3	54.9 ± 9.4	54.3 ± 6.0

Data presented as the mean ± standard deviation.

Note. C1: First visit; C5: Fifth visit; C10: Tenth visit; BMI: Body Mass Index; WC: Waist circumference; HC: Hip circumference; BF: Body fat percentage; LM: Lean mass.

Discussion

Results revealed larger weight loss during the first treatment phase (first five visits), which corresponded to the first seven months of diet therapy on average. Thereafter, patients' weight stabilized, but some patients even returned to their initial weight. High and progressive dropout rates along the treatment was yet another finding of the present study.

The aforementioned results stem from the difficulty that overweight patients have in maintaining food restrictions—these individuals can tolerate restrictions in the short and medium term, but not in the long term. Therefore, these patients require social support to maintain the new eating habits and ensure long-term changes in the pattern of food intake.¹⁰ Another point to consider is the patient's expectations with respect to weight loss. Obese female patients start the treatment wishing to lose a large amount of weight,⁴ preferably over a short period. When the patients begin to encounter difficulty in achieving the weight loss they consider satisfactory, they become frustrated. The feeling that their effort is not being paid off diminishes their motivation to comply with the treatment.

The high dropout rates attested to the situation described above. Even the patients that continued attending the visits often presented reduced weight loss or gained the weight they lost, because they did not have the same motivation or did not make the same effort as compared with their commitment at the beginning of the treatment. A study investigating a group of patients under diet therapy reported a dropout rate of 50.0% during a 10-week follow-up.¹¹ West et al.¹² described that although many individuals were highly motivated at the start of the treatment, this motivation diminished along time. This finding might justify why two practices—rewarding for compliance with the diet or physical activity plan and remembering the reason why it is necessary to control weight—are associated with maintenance of weight loss and not with the loss itself.

Cooper & Fairburn¹³ proposed that when obese patients feel frustrated about not reaching the desired weight, they do not maintain the behavior they had while they were attempting to lose weight; i.e., they stop consuming food with low fat content, practising physical activities regularly, and monitoring weight constantly. The patients also neglect the need to use strategies to maintain weight. Consequently, they return to their previous eating habits and gain the weight they had lost.

Various psychological factors seem to be involved in regaining weight, such as inability to reach goals, dissatisfaction with the amount of lost weight, self-consciousness about body weight and physical shape, low self-esteem, lack of surveillance of weight control, dichotomous thinking, and tendency to use food as a way to compensate for mood swings and adversities.¹⁴

Bearing in mind possible explanations for the change in the pace of weight loss and the reasons for

patient dropout, it is necessary to adopt strategies that prevent treatment cessation and lack of motivation, to maintain compliance with the new eating habits. The WC, HC, and body fat percentage values decreased along the treatment, showing that the adoption of new patterns of food intake improved health.

Nevertheless, except for weight loss, many patients disregard the positive changes arising from the treatment of obesity. Many women are dissatisfied with the weight loss rate and underestimate the meaning of the weight loss they achieved. Patients that gain the lost weight usually express dissatisfaction.^{4,14} Therefore, it is important to highlight that the treatment of obesity does not focus on weight loss only; it should also target improved eating habits and quality of life.

Patients that can maintain weight loss for two years reduce the risk of gaining weight by 50.0%.¹⁵ Some strategies that help maintain effective weight loss in the long term exist: engaging in high-level physical activity, maintaining constant eating habits that include food with low fat and energy content, having breakfast on a daily basis, and self-monitoring the body weight.¹⁵ However, it is necessary to analyze how these strategies should be adopted along the treatment. Assessing weight progression is a necessary task if one wishes to implement intervention strategies at each therapeutic stage, mainly after the first six months of diet therapy, so that treatment becomes more effective in terms of improved eating habits, weight loss, and weight maintenance in the long term. During exploratory qualitative studies, it might be necessary to know the difficulties patients encounter in these stages; it might also be crucial to investigate what triggers weight gain after the start of the treatment.

Conclusion

Weight loss occurs mainly during the first months of diet therapy treatment. Therefore, it is necessary to implement periodic assessments and to change strategies along the treatment, because the process of weight loss is long and demands constant motivation. Modifications made to the eating habits and lifestyle may be difficult to maintain along the treatment. New diagnostic studies on the problems and difficulties related to diet therapy must be conducted, to improve our understanding of the treatment phases and to implement more effective strategies toward weight loss and maintenance.

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Original / *Pediatría*

Higher levels of C-reactive protein associated with higher adiposity in Mexican schoolchildren

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Abstract

Introduction: The development of chronic-degenerative diseases secondary to obesity in early infancy has alerted health providers to the importance of identifying the risk factors for obesity and assessing preventive treatment to reduce risks. Studies performed on a pediatric population have examined the role of inflammatory biomarkers (specifically CRP and TNF- α) and adiposity with inconsistent results.

Objective: To assess the relationship between the serum levels of C-reactive protein and tumor necrosis factor- α with adiposity measured by bioimpedance analysis in schoolchildren.

Methods: Cross sectional design. Data were collected from 74 schoolchildren randomly selected in a local primary school in the city of Colima, Mexico. The mean age was 9.4 years (1.5, SD); 33 (44.6%) were girls. The adiposity (percentage of fat mass) was measured using bioimpedance analysis and anthropometric measurements. Serum C-reactive protein and tumor necrosis factor alpha were determined with enzyme-linked immunosorbent assay. The association between adiposity and serum inflammatory biomarkers was assessed with non parametric tests (Mann Whitney and Kruskal Wallis tests), and parametric tests (Pearson's correlation).

Results: Children with obesity had a significantly higher level of C-reactive protein [2.90 mg/L (0.07-9.37)] compared with children with a normal percentage of fat mass [0.71 mg/L (0.07-5.75)] ($p < 0.001$). No differences between groups were identified regarding serum levels of tumor necrosis factor- α . Modest correlations were identified between serum levels of C-reactive protein, adiposity determined by bioimpedance analysis ($r = 0.453$, $p < 0.001$); body mass index ($r = 0.398$, $p = 0.001$); triceps skinfold ($r = 0.369$, $p = 0.002$); and subscapular skinfold ($r = 0.405$, $p < 0.001$). No correlation was found between adiposity and serum tumor necrosis factor- α .

Conclusion: Subclinical inflammation manifested by higher serum levels of C-reactive protein was identified in schoolchildren with higher percentage of fat mass as determined by bioimpedance analysis and other anthropometric measurements.

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LOS NIVELES ELEVADOS DE PROTEÍNA C REACTIVA SE ASOCIAN A UNA MAYOR ADIPOSIDAD EN ESCOLARES MEXICANOS

Resumen

Introducción: Las enfermedades crónico-degenerativas, secundarias a la obesidad en niños, ha alertado a los profesionales de la salud sobre la importancia de identificar los factores de riesgo asociados a obesidad y establecer un enfoque preventivo para reducir el riesgo de complicaciones. Algunos estudios realizados en población pediátrica han estudiado el papel de los biomarcadores inflamatorios [específicamente proteína C-reactiva (PCR) y factor de necrosis tumoral alfa (TNF- α)] asociado a adiposidad con resultados inconsistentes.

Objetivo: Evaluar la relación entre los niveles séricos de PCR y TNF- α con adiposidad determinada mediante impedancia bioeléctrica en niños en edad escolar.

Métodos: Diseño transversal analítico. Se recopilaron los datos de 74 alumnos seleccionados al azar en una escuela primaria local en la ciudad de Colima, México. La edad media fue de 9,4 años (1,5 DE), treinta y tres (44,6%) fueron niñas. La adiposidad (porcentaje de grasa) se midió mediante impedancia bioeléctrica y antropometría. La PCR y TNF- α séricos se determinaron con el ensayo por inmunoadsorción ligado a enzimas (ELISA). Las comparaciones de las variables entre los grupos se analizaron con pruebas no paramétricas (U de Mann Whitney y Kruskal Wallis) y la correlación de Pearson.

Resultados: Los niños con obesidad presentaron un nivel sérico [2,90 mg/L (0,07-9,37)] significativamente más alto de PCR en comparación con los niños con un porcentaje normal de grasa [0,71 mg/L (0,07-5,75)] ($p < 0,001$). Con respecto a los niveles séricos de TNF- α no se identificaron diferencias entre los grupos estudiados. Se obtuvieron correlaciones modestas entre los niveles séricos de PCR con la adiposidad determinado por impedancia bioeléctrica ($r = 0,453$, $p < 0,001$); índice de masa corporal ($r = 0,398$, $p = 0,001$); pliegue cutáneo tricipital ($r = 0,369$, $p = 0,002$), y pliegue cutáneo subescapular ($r = 0,405$, $p < 0,001$). No se encontró correlación entre la adiposidad y el nivel sérico de TNF- α .

Conclusión: La inflamación subclínica determinada por elevación de los niveles séricos de proteína C-reactiva fue identificada en niños en edad escolar con mayor porcentaje de grasa determinado por impedancia bioeléctrica y antropometría.

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Palabras clave: *Adiposidad en escolares. Adiposidad. Proteína C reactiva. Factor de necrosis tumoral alfa. Impedancia bioeléctrica.*

Abbreviations

BIA: Bioimpedance analysis.
BF: Body fat.
BMI: Body mass index.
CDD: Chronic-degenerative diseases.
CRP: C-reactive protein.
CVD: Cardiovascular disease.
NW: Normal weight.
SSF: Subscapular skin fold.
TNF- α : Tumor necrosis factor alpha.
TSF: Triceps skin fold.
OB: Obese.
OF: Overfat.
ST: Skinfold thickness.
STE: Slaughter equation.
UF: Underfat.
WC: Waist circumference.

Introduction

The development of chronic-degenerative diseases (CDD) such as type 2 diabetes mellitus, hypertension, dyslipidemia, and carotid-artery atherosclerosis secondary to obesity in early infancy has alerted health providers to the importance of identifying the risk factors for obesity and assessing preventive treatment to reduce cardiovascular disease (CVD). It has been reported that an obese adult who was an overweight or obese child, has an increased risk for developing CDD.¹ Also, several studies have described the association between low grade chronic inflammation manifested by the elevation of inflammatory biomarkers including c-reactive protein (CRP) or inflammatory cytokines such as interleukin-6 and tumor necrosis factor alpha (TNF- α) with obesity, insulin resistance, and CVD.²⁻⁸

Studies performed on a pediatric population have examined the role of inflammatory biomarkers (specifically CRP and TNF- α) and adiposity with inconsistent results. Some of them have identified an association between higher serum concentrations of inflammatory biomarkers with higher measures of adiposity, but others have identified higher concentrations in children with a normal nutritional status compared with those that are obese.^{2,4,7-11} In other respects, these studies have measured adiposity mainly by body mass index (BMI) or waist circumference (WC) and there are only a few that have measured adiposity with direct methods.^{2,5}

The primary aim of this study was to assess the relationship between the serum levels of CRP and TNF- α with adiposity measured by bioimpedance analysis (BIA) in schoolchildren. The secondary aim was to correlate the percentage of fat by BIA, BMI, WC, triceps skin fold (TSF), and subscapular skin fold (SSF) with the serum concentrations of CRP and TNF- α .

Materials and methods

Patients and study design

Seventy-four schoolchildren randomly selected in a local primary school in Colima, Mexico were recruited in the study between november 2011-march 2012. The mean age was 9.4 years (1.5, SD); thirty-three (44.6%) were girls. A cross-sectional design was used in the study. Children with genetic, chronic, and systemic diseases, or current or recent infection were excluded. The dependent variables were serum concentrations of CRP and TNF- α and the independent variable was the adiposity determined by BIA.

Anthropometric assessment

Standardization: Before the data were collected, the main author and two collaborators performed an anthropometrical standardization trial evaluating consistency (intra-group individual measurements) and validity (inter-group comparison with a gold standard) through Pearson's bivariate correlations; when the "r" was below 0.8, the anthropometrical technique was reviewed and corrected until the desired intra and inter-group correlations were achieved.^{12,13}

Weight: Study subjects were weighed on a balance beam scale, without shoes and a minimum of clothing. Weight was recorded to the nearest 100 g.^{14,15}

Height: Height was measured and recorded to the nearest 0.1 cm using a standimeter with a movable block. The subjects were measured while standing, without shoes, heels together, back as straight as possible, and arms hanging freely; the head was positioned in the Frankfort horizontal plane and the movable block was brought down until touching the head.^{14,15}

Body mass index (BMI). Was calculated as weight (kg) divided by height squared (m^2).¹²

Triceps skinfold (TSF). The right arm was previously positioned bent at the elbow at a 90° angle, with the upper arm held parallel to the side of the body. The distance between the acromion and the olecranon was measured with a fiberglass tape and the midpoint between these two points was marked. The TSF was measured with a Lange skinfold caliper at the previously marked midpoint with the arm hanging loosely at the side of the body. The examiner grasped a vertical pinch of skin and subcutaneous fat between the thumb and forefinger about 1 cm above the previously marked midpoint, gently pulling the skin away from the underlying muscle. The skinfold caliper was placed at the marked midpoint while maintaining the skinfold grasp. Readings were taken in millimeters as soon as the caliper came in contact with the skin and the dial reading stabilized. The average of the three readings was recorded in mm.¹⁵

Subscapular skinfold (SSF). The SSF was lifted on a diagonal and inclined infero-laterally approximately

45 degrees to the horizontal plane of the natural cleavage lines of the skin. The site was just below the inferior angle of the scapula. The subject stood comfortably erect with the hands relaxed at the sides of the body. The examiner palpated the subject's scapula to locate the inferior border of the scapula, grasping a horizontal pinch of skinfold at about 1 cm below the inferior angle of the right scapula. The jaws of the caliper were applied 1 cm infero-lateral to the thumb and finger lifting the skinfold, and three readings were taken. The average of the three readings was recorded in mm.¹⁵

Waist circumference (WC). The WC was measured using a fiberglass tape above the uppermost lateral border of the right ilium, at the end of a normal expiration, and was recorded at the nearest millimeter. The measurement was made while the subject stood upright, with feet together and arms hanging freely at the sides. The WC was classified in the percentiles according to the pattern published by Fernandez, et al. in Mexican-American children.¹⁷

Bioimpedance analysis

All subjects that underwent BIA were asked not to eat, drink, or exercise 8 hrs before testing. The subjects were placed in the supine position with arms and legs abducted from the body. Shoes, socks, belts and other metallic pieces were removed and the areas where the electrodes were placed were previously cleaned with alcohol. Source electrodes were placed proximal to the phalangeal-metacarpal joint on the dorsal surface of the right hand and distal to the transverse arch on the superior surface of the right foot. Sensor electrodes were placed at the midpoint between the distal prominence of the radius and ulna of the right wrist and between the medial and lateral malleoli of the right ankle.^{18,19} The BIA was performed using the QuadScand 4000 (Bodystat Limited, Great Britain); resistance and reactance values were provided by BIA and the percentage of fat mass was derived using the available BIA software.

The results of the percentage of fat were classified in four groups (underweight, normal, overweight, and obese) based on the body fat curves published by McCarthy et al.²⁰

Measurement of CRP and TNF- α

Five milliliters of venous blood samples were collected in tubes without additives after fasting (8 h). The samples were stored on wet ice and the serum was separated by centrifugation. The separated serum was kept frozen at -75° C until assayed for biomarkers of inflammation.

An ultra-sensitive enzyme-linked immunosorbent assay (ELISA) kit was used to determine TNF- α serum concentrations (*Invitrogen Corporation, Califor-*

nia USA) with standards assayed in duplicate. The cytokine determination sensitivity limit was 0.09 pg/mL. For the analysis of CRP, an ELISA kit was used (*Cell Biolabs Inc. California USA*) with a sensitivity limit of 1 ng/mL.

The serum levels of CRP were classified in the cut-points of low risk (< 1.0 mg/L), average risk (1.0-3.0 mg/L) and high risk (> 3 mg/L).²¹ The cases with serum levels of CRP > 10 mg/L were excluded.

Statistical analysis

The data were analyzed with the SPSS version 20. The variables studied were described as frequencies, percentages and median (interquartile range); inferential statistics were performed with non parametric tests (Mann Whitney and Kruskal Wallis tests), and parametric tests (Pearson's correlation). Statistical significance was set at a p value < 0.05.

Ethics

The study protocol was approved by the local ethics committee of the University of Colima, Mexico and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Signed informed consent was obtained from the parents or guardians before the children were enrolled in the study.

Results

The percentage of fat determined by BIA and based on body fat curves was classified into underweight (5.3%), normal (44.6%), overweight (13.5%), and obese (36.5%).

The anthropometric parameters (weight, height, BMI, WC, TSF, SSF) according to the percentage of fat mass determined by BIA are described in table I.

The serum levels of CRP and TNF- α are presented in table II. Children with obesity had a significantly higher level of CRP compared with children with a normal percentage of fat (p < 0.001). However, no differences were identified between groups regarding serum levels of TNF- α (p > 0.05).

The levels of CRP were in the low risk range (CRP < 1 mg/L) in 41.9 % of the children, in the average risk (1-3 mg/L) in 28.4% and in the high risk (> 3 mg/L) in 29.7%. Higher levels of CRP were associated with higher percentage of fat by BIA, BMI, WC, TSF, SSF (table III).

The median levels of CRP and TNF- α in girls were 1.4 mg/L (0.15-8.3 mg/L) and 4.1 mg/L (1-6-8.4 mg/L), respectively; in boys were 1.0 mg/L (0.07-9.4 mg/L) and 3.8 (0.58-12.0), respectively. No differences were found in the levels of CRP and TNF- α among girls and boys (p = 0.228 and p = 0.794).

Table I
Anthropometrical measures according to the percentage of fat mass determined by BIA. Data are reported as median and interquartile ranges

Anthropometrical measures	Underweight (n = 4)	Normal (n = 33)	Overweight (n = 10)	Obesity (n = 27)
Height (cm)	137.8 (128.0-153.0)	132.0 (107.0-157.0)	145.3 (130.5-155.0)	139.6 (120.5-169.0)
Weight (kg)	29.5 (23.3-40.8)	28.2 (17.1-58.7)	42.4 (26.2-63.1)	45.5 (28.2-80.2)
BMI [†] (kg/m ²)	15.6 (14.2-17.4)	15.9 (13.7-25.7)	20.2 (15.5-27.0)	23.9 (19.6-32.8)
WC [‡] (cm)	57.7 (54.5-63.5)	57.0 (46.0-85.0)	73.0 (60.5-88.0)	80.0 (65.0-101.0)
TSF [§] (mm)	10.3 (9.6-11.6)	13.6 (7.6-26.6)	21.2 (12.0-25.6)	24.3 (15.3-34.3)
SSF [¶] (mm)	8.3 (6.0-10.3)	10.0 (4.6-27.6)	21.0 (10.3-32.0)	27.0 (18.0-35.0)

[†]Body mass index; [‡]Waist circumference; [§]Triceps skinfold; [¶]SSF subscapular skinfold.

Table II
Biomarkers of inflammation according to the percentage of fat mass determined by BIA. Data are reported as median and interquartile range

Biomarkers of inflammation	Underweight (n = 4)	Normal (n = 33)	Overweight (n = 10)	Obesity (n = 27)
CRP [†] (mg/L)	0.31 (0.15-0.99)*	0.71 (0.07-5.75)**	1.11 (0.46-4.60)***	2.90 (0.07-9.37)
TNF α (pg/mL)	5.29 (2.80-6.44)	3.88 (0.64-12.0)	4.03 (0.98-6.00)	3.88 (0.58-6.74)

[†]C-reactive protein, [‡]tumor necrosis factor- α .

*p = 0.003 (underweight vs. obesity); **p = < 0.001 (normal vs. obesity); ***p = 0.046 (overweight vs. obesity) with Mann-Whitney U test.

Table III
Anthropometric data according to the classification of risk of CRP. Data are reported as median and interquartile range

Anthropometry	Low risk (n = 31)	Average risk (n = 21)	High risk (n = 22)	p*
% of fat by BIA [†]	20.6 (6.0-34.0)	30.4 (14.0-46.0)	33.8 (15.0-43.0)	< 0.001
BMI [‡] (kg/m ²)	16.5 (13.7-29.0)	20.3 (15.5-31.0)	23.2 (14.9-32.8)	< 0.001
WC [§] (cm)	58.3 (51.0-94.0)	70.5 (55.5-101.0)	76.9 (46.0-101.0)	0.001
TSF [¶] (mm)	13.5 (7.6-34.3)	21.0 (8.6-32.0)	21.5 (8.6-32.0)	0.001
SSF ^{**} (mm)	10.8 (4.6-28.3)	21.0 (6.0-33.3)	25.8 (5.0-35.0)	< 0.001

[†]Bioimpedance analysis BIA; [‡]BMI body mass index; [§]WC waist circumference; [¶]TSF triceps skinfold; ^{**}SSF subscapular skinfold.

*p determined by Kruskal-Wallis test.

Serum levels of CRP correlated with measures of adiposity (BMI, TSF, and SSF) (table IV) and with the percentage of fat mass determined by BIA (fig. 1).

The WC was not correlated positively with CRP, but when comparing the mean levels between the children with WC > percentile 90th vs. percentile 10-90th, the CRP levels were significantly higher in the group of children with WC > percentile 90th vs. percentile 10-90th (p = 0.001) (table V).

Discussion

In the present series, adiposity was determined by BIA since this method has shown a positive correlation between BMI and TSF.^{16,19} However, BMI is used to make a diagnosis based on the weight and size of individuals, but does not calculate an exact fat percentage. BIA allows

for the body fat percentage to be assessed and is relatively simple, quick, although requires technical skill. Some studies have reported the BIA as an alternative approach to dual-energy X ray-absorptiometry, the gold standard method for body composition assessment in children and adults.²²⁻²⁴ To the best of our knowledge, this is one of the few studies performed on children that determines body fat percentage with BIA and correlates the serum levels of inflammatory biomarkers.

No correlation was found between the percentage of fat mass and serum TNF- α concentration. This finding is similar to results reported in other published studies. In a study on 109 Mexican-American children, McFarlin et al.⁴ found no statistical difference in the levels of TNF- α and IL-6 in children presenting with normal nutritional status, overweight, and obesity. In Bulgaria, a study including 137 pre-puberal children that determined abdominal obesity by WC measurement did not

Table IV
Correlation of anthropometric variables with serum levels of TNF- α and CRP

Anthropometrical measures	Serum levels of TNF- α		Serum levels of CRP	
	r	p*	r	p*
Weight (kg)	-0.060	0.612	0.207	0.083
% fat mass (BIA) [†]	-0.014	0.904	0.453	< 0.001
BMI [‡] (kg/m ²)	-0.030	0.800	0.398	0.001
WC [§] (cm)	-0.025	0.833	0.313	0.008
TSF [¶] (mm)	0.038	0.748	0.369	0.002
SSF ^{**} (mm)	-0.074	0.529	0.405	< 0.001

[†]Bioimpedance analysis; [‡]BMI body mass index; [§]WC waist circumference; [¶]TSF triceps skinfold; ^{**}SSF subscapular skinfold.

*p determined by Pearson's correlation coefficient.

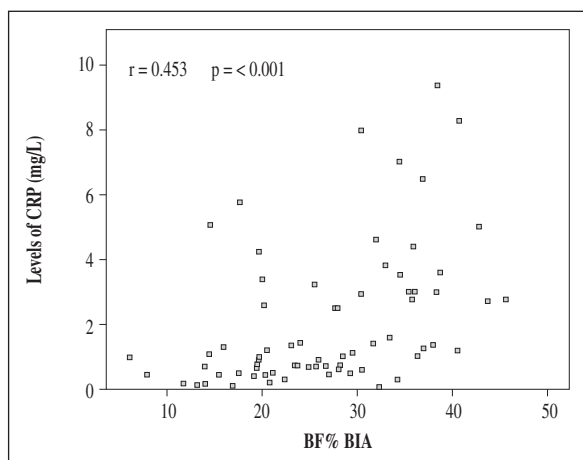


Fig. 1.—Correlation between serum levels of CRP (mg/L) and percentage of fat measured by bioimpedance analysis.

find cytokine elevation, including TNF- α , in the children that presented with abdominal obesity.⁷ A study published by Dixon et al.,¹¹ conducted on 112 Latino schoolchildren, found a higher circulating TNF- α level in thinner girls, and no differences for boys. These findings clearly differ from other authors that have identified significantly higher serum levels of TNF- α and IL-6 in obese children compared with non-obese children.^{2,8,9}

This discrepancy in the relationship between TNF- α concentrations and adiposity has been explained by differences in age, sex, body fat mass, mixed pubertal stages, mixed ethnic groups, and physical fitness level

Table V
Serum levels of CRP according to WC in percentiles

WC (percentiles)	Serum levels of CRP (mg/L)	
	Median	Interquartile range
Percentile < 10 th	0.69	(0.078-5.75)
Percentile 10-90 th	0.82	(0.122-7.99)
Percentile > 90 th	2.90	(0.070-9.37)

Comparing the levels between percentile > 90th vs. percentile 10-90th, p = 0.001 (Mann-Whitney U test).

among the studies.^{9,11,25-28} In the present study we asked the children not to exercise 8 hours before BIA body fat determination and venous blood extraction, and the children were at school when these were carried out; the ethnicities of the children were similar and they were school-aged children (less than 12 years old), although the Tanner-stage was not assessed.

Another important fact regarding TNF- α is the lack of a reference value in healthy children, which has already been reported by several authors.^{2,11}

Regarding CRP, the present study identified a modest correlation with the percentage of fat mass determined by BIA and levels of CRP. These results are consistent with other studies performed in pediatric populations. In 2007, McFarlin et al.⁴ determined the effect of weight on inflammatory biomarkers in Mexican-American children. They found significantly higher concentrations of plasma CRP in overweight children compared with children at risk for overweight (p = 0.003). In 2003, Wu, et al.¹⁰ evaluated the relationship of serum levels of CRP with anthropometrics in 835 children (12-16 years of age), and they found significantly higher concentrations of CRP in children with higher BMIs. In the study done by Galcheva⁷ on 137 pre-pubertal children (6-10 years of age), they reported that CRP concentrations increased in proportion to the degree of abdominal obesity. Retnakaran et al, also performed a study in 228 children in Canada, aged 10-19 years identifying higher levels of CRP in subjects with greater adiposity measured by BMI, WC and % of body fat.⁵ Other studies performed on children and adolescents have described relationships between inflammatory biomarkers with insulin resistance (measured by fasting insulin and the homeostasis model of insulin resistance), abnormal lipid profile (higher levels of LDL and lower levels of HDL), and hypertension and arterial changes.^{3,5-7,10,29} It is even thought to be a relatively moderate predictor of CVD risk in adults.³⁰ And although data regarding high CRP and obesity are correlated, there is currently no consensus that high serum levels of CRP can be regarded as a CVD risk marker in children and adolescents since there are not sufficient data linking increased CRP levels in childhood to adult disease outcomes.^{31,32}

Conclusion

Subclinical inflammation manifested by higher serum levels of C-reactive protein was identified in schoolchildren with higher percentage of fat mass determined by BIA and other anthropometric measurements. No relationship between the serum levels of TNF- α with adiposity measured by BIA and anthropometry was identified.

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Original / *Pediatría*

PRESENT; PRESCRIPTION of Enteral Nutrition in pediatric Crohn's disease in Spain

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Abstract

Objectives: Exclusive enteral nutrition (EEN) is one of the therapeutic strategies used to induce remission in pediatric Crohn's disease (CD). Although its use is recommended in clinical practice guidelines and consensus documents, the frequency of this practice in Spain is unknown.

Methods: A 70-item questionnaire (PRESENT; PRESCRIPTION of Enteral Nutrition in pediatric Crohn's disease in Spain) was drafted and distributed through the SEGHN (Spanish Society for Pediatric Gastroenterology, Hepatology and Nutrition) e-mail list.

Results: We received information from 51 Pediatric Gastroenterology Units. Of the 287 patients newly diagnosed with CD in 2011-2012 at these centres (139 in 2011, 148 in 2012), 182 (63%) received EEN (58% in 2011 and 68% in 2012). 26% of the patients who received EEN in the period studied (64/246) did so during relapses. All the physicians (100%) who responded to the questionnaire believe that EEN is effective in inducing clinical remission in mild to moderate CD. However, 24.5% of respondents never use EEN during relapses. The enteral formulas used most often used were polymeric formulas specific for CD (70.6%) and the preferred administration route was oral, with 60.8% using flavouring and 9.3% allowing a variable percentage of calories in the form of other foods. 65% use 5-ASA together with EEN, 69% use antibiotics and 95% immunomodulators (thiopurines). The duration of EEN tends to be 8 weeks (47.1%), and transition to regular diet was achieved sequentially over a variable period of time. Regarding barriers and limiting factors for the use of EEN, those most frequently reported include lack of acceptance by the patient and/or family (71%), lack of time and/or ancillary staff (69%) and difficulty in convincing the patient and/or family of the suitability of treatment (43%).

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PRESENT; PRESCRIPCIÓN DE NUTRICIÓN ENTERAL EN LA ENFERMEDAD DE CROHN PEDIÁTRICA EN ESPAÑA

Resumen

Objetivos: La nutrición enteral exclusiva (NEE) es una de las estrategias terapéuticas empleadas para inducir la remisión en niños con enfermedad de Crohn (EC). Pese a que la NEE se recomienda en las guías de práctica clínica y en los documentos de consenso, la frecuencia real de su empleo en España es desconocida.

Métodos: Encuesta compuesta por 70-items (PRESENT; PRESCRIPTION of Enteral Nutrition in pediatric Crohn's disease in Spain) que se distribuyó a través de la lista de distribución de Sociedad Española de Gastroenterología, Hepatología y Nutrición Pediátrica (SEGHN).

Resultados: Se recibieron los datos de 51 unidades de Gastroenterología Pediátrica del territorio español. De los 287 pacientes recién diagnosticados de EC durante los años 2011-12 en esos centros (139 en 2011 y 148 en 2012), 182 (63%) recibieron NEE (58% en 2011 y 68% en 2012). El 26% de los pacientes que recibieron NEE estaban en recaída. Todos los facultativos que respondieron pensaban que la NEE es efectiva para inducir la remisión clínica en los brotes leves-moderados. El 24,5% no emplean la NEE durante las recaídas. Las formulas enterales empleadas más frecuentemente fueron las específicas para EC (70,6%), la vía oral fue la más utilizada, el 60,8% utilizaron saborizantes y el 9,8% de las unidades permitían un porcentaje variable de calorías en forma de otros alimentos durante el periodo de NEE. El 65% emplearon 5-ASA junto con la NEE, el 69% antibióticos y hasta un 95% inmunomoduladores. La duración de la NEE fue de 8 semanas en el 47,1% de los casos, la transición hacia una dieta normal se realizó de forma secuencial. En relación a las barreras y factores limitantes encontrados por los respondedores para instaurar la NEE destacaban la falta de aceptación por el paciente y/o la familia (71%), falta de tiempo o de personal auxiliar (69%) y la dificultad para convencer al paciente o su familia de la idoneidad del tratamiento (43%).

Conclusiones: La frecuencia de empleo de la NEE en pacientes con EC es similar a la de otros cuestionarios europeos. Se precisan herramientas y recursos que faciliten

Conclusions: EEN use rates are similar to those of other European questionnaires. Tools that facilitate acceptance by the patient and family are needed. Increasing the time dedicated to this therapeutic modality is likewise important. Given the disparity of criteria for indicating treatment with EEN, it would be useful to have widely accepted clinical practice guidelines or protocols that facilitate the decision to use it.

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Keywords: *Exclusive enteral nutrition. Pediatric Chron's disease. Pediatric inflammatory bowel disease. Survey. Prescription.*

Introduction

Exclusive enteral nutrition (EEN) has been shown to be more effective than corticosteroids inducing mucosal healing in children with Crohn's disease (CD), without the side effects.¹⁻³ Although its use in pediatric CD is recommended in clinical practice guidelines⁴ and consensus documents, the frequency of this practice in Spain, where the incidence of inflammatory bowel disease (IBD) has been on the rise in recent years,⁵ is unknown. The aim of this study was to investigate the frequency and characteristics of the use of EEN in pediatric gastroenterology units in Spain through the use of a questionnaire prepared for this purpose.

Materials and methods

The questionnaire was based on other published⁶⁻⁹ studies, together with other previously unpublished items. The study was conducted by the IBD working group of the Spanish Society for Pediatric Gastroenterology, Hepatology and Nutrition (SEGHN) and supported by the SEGHN. All Pediatric Gastroenterology Units in Spain were contacted but participation was, of course, voluntary. Although not all Pediatric Gastroenterology Units have included their patients, all of the reference hospitals across Spain have participated.

The questionnaire (PRESENT: PRESCRIPTION of Enteral Nutrition in pediatric Crohn's disease in Spain) sent out consisted of 70 items that include general aspects of IBD and specific aspects of EEN for pediatric CD (Appendix II). The period for receiving the questionnaires was from May 2012 until January 2013. All questionnaires were reviewed and the authors were contacted personally if any errors were detected or if any items were not completed in order to request the pertinent clarifications.

Statistical analysis

The qualitative variables are expressed as a percentage. The chi-square test was used to contrast variables.

la aceptación por parte del paciente y de su familia así como disponer de más tiempo a dedicar para instaurar esta modalidad terapéutica. Dada la disparidad de criterios para la indicación de la EEN, sería útil disponer de guías de práctica clínica ampliamente aceptadas o protocolos que facilitan la decisión de utilizarla.

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Palabras clave: *Nutrición enteral exclusiva. Enfermedad de Crohn pediátrica. Enfermedad inflamatoria intestinal pediátrica. Encuesta. Prescripción.*

Values of $p < 0.05$ were considered to be statistically significant.

Ethical considerations

The study was approved by the Ethic's Committee of the first author's center, as representative of the rest of the hospitals. The authors do not have conflicts of interest.

Results

Data were received from 51 Pediatric Gastroenterology Units distributed across Spain. During the 2011-2012 period, 287 cases of CD were newly diagnosed (139 in 2011 and 148 in 2012) at these units; 246 received treatment with EEN in these two years, 182 (63.4%) patients as first-line therapy and 64 during relapses. All the patients who received EEN during relapses had responded previously to EEN at the onset of the disease. The frequency of EEN use as first-line therapy increased from 58% (81/139) in 2011 to 68% (101/148) in 2012 ($p = 0.08$).

Efficacy of EEN to induce remission

With regard to newly diagnosed CD, all those polled believe that EEN is effective in inducing clinical remission, having likewise verified such efficacy at some point. Ninety-six point one per cent (96.1%) maintained that it enables mucosal healing and 84.3%, histological remission. Of the 36 units that had performed endoscopy after EEN, 17 (47.2%) reported mucosal healing and 15 (41.6%) histological remission in some case. In response to whether EEN is effective in relapses, 83.4% contended that it induces clinical remission, 80.4% mucosal healing and 74.5% histological remission. Seventy-six point five per cent (76.5%) use or have used EEN in relapses, having confirmed clinical remission and endoscopic and histological remission in up to 69.2% and 36% of patients, respectively.

Table I
Indications for EEN according to disease characteristics

Newly diagnosed vs. exacerbations	76.5% only use EEN in newly diagnosed CD patients, not during relapses. 66.7% of those who use EEN in relapses only do so if the patient responded previously to EEN.
Behaviour [†]	43% indicate EEN only in cases of inflammatory phenotype (B1, non-stricturing, non-penetrating).
Location [†]	37.3% only use EEN when only the ileum (L1) or ileum and colon (L3) are affected. 62.7% use EEN regardless of disease location and 31.4% do not use EEN when upper gastrointestinal tract (L4a or L4b) is affected. 50% do not use it in cases with extraintestinal manifestations.
PCDAI [†]	6% only in mild disease, 41.1% in mild to moderate disease and 52.9% regardless of disease severity.
Perianal disease	70.6% use EEN to induce remission in cases of mild perianal manifestations (fissures or skin tags) or in cases of previously drained abscess.
Age	70.6% use it regardless of age and 16.7% do not use it in patients under the age of 3.
Other factors	62.7% only indicate EEN if the patient and their family are collaborative. 25.5% indicate it as the only therapeutic option. Delayed growth contributes to the prescription of EEN in 96.1% of subjects polled.

[†]According to Paris classification of IBD¹⁰.

[†]Pediatric Crohn's Disease Activity Index¹¹.

Indications for EEN

Table I shows the results for EEN indications.

Comparative analysis of the indications for EEN according to patient treated in units that providing follow-up to a high number of patients (> 50 patients/year) or a small number (< 50) revealed no significant differences.

Specific aspects of EEN

The most common response with regard to the duration of EEN was 8 weeks, chosen by 47.1% of the respondents, followed by 6-8 weeks (22.5%), 6 weeks (19.6%) and others (7.8%). None of those polled use it for periods under 6 weeks or greater than 12 weeks. The oral administration route was preferred in all cases, with nasogastric-feeding only being used when taking enteral formula by mouth was not possible. The response time to assess the efficacy of EEN was 2-3

weeks in 21.6%, 2-4 weeks in 18.4%, 3-4 weeks in 17.6% and 2 weeks in 15.7% of subjects polled.

Regarding which enteral formula was used, in 70.6% of the cases (36/51) polymeric formulas specific for IBD were used, enriched with TGF- β (Modulen IBD[®] or Resource IBD[®]); 29.4% indicated other formulas different from the specific ones (flavoured normal- or hypercaloric polymeric formulas or flavoured elemental formulas). The choice of formula was mainly influenced by factors such as taste, cost, availability, nutritional composition, evidence and experience. Table II shows that the most frequent reason for indicating specific formulas was their composition, with particular reference to TGF- β . In the group that used other formulas, 100% declared that there was no evidence that formulas made specifically for IBD were superior to standard polymeric formulas, and that the EEN itself is responsible for the patients' improvement; such effect cannot be specifically attributed to any of the ingredients.

Another aspect we wished to enquire about involved liquids, foods and amount of calories the pa-

Table II
Reasons for choosing the enteral formula

Reason(s)	IBD-specific enteral formulas (n = 36)	Other enteral formulas (n = 15)	p
Composition	58%	7%	0.0001
Availability	50%	0%	0.0001
Evidence	42%	100%	0.0001
Experience	28%	7%	0.079
Taste	17%	53%	0.012
Compliance	14%	53%	0.006
Specificity of the formula	8%	0%	0.234
Use of flavouring	6%	0%	0.336
Cost	3%	20%	0.046

Table III
Combination of EEN with pharmacological treatment

Drug	Always	Sometimes	Never	I don't know	No answered
Oral 5-ASA preparations	20%	45%	31%	2%	2%
Topical 5-ASA preparations	0%	27%	67%	4%	2%
Antibiotics	2%	67%	27%	2%	2%
Thiopurines	71%	24%	4%	0%	1%
Steroids	2%	18%	78%	0%	2%
anti-TNF	0%	35%	59%	4%	2%

tients were allowed to eat during the EEN treatment period; 90.2% answered only water and the remaining 9.8% indicated between 5-20% of all the calories estimated in the day. At all the centres, the physician in charge of the patient participates in the decision about the formula to be administered. Of subjects polled, 60.8% allow the use of flavouring; of these, 48.4% mention the flavouring provided by Nestlé Nutrition (with banana or strawberry flavour), 22.6% cocoa powder, 3.2% syrups of different flavours and 25.8% a variety of the aforementioned. Once the induction period has been completed, 94.2% progress to a normal diet in the following 2-4 weeks (7.6% follow their own protocol and the remaining 92.4% do not follow any protocols) and 5.8% change to a normal diet quickly, with no specific order when introducing the food groups.

After the induction period, 88.4% provides systematic enteral formula supplementation to all patients during a variable time period that depends on several factors (adherence, nutritional state, etc.). The majority of units opt to supplement with 20-30% of the total calories, which tend to range from 500-750 ml, depending on the patient. The remaining 11.6% only supplement if required for nutritional recovery.

Combination of EEN with pharmacological treatment

Regarding the drugs used concomitantly during the induction of remission with EEN, the results reported by respondents are found in table III.

Professionals involved in the administration of EEN and follow-up

The professionals involved in assessing and indicating therapeutic support via EEN vary according to centre (table IV).

The physician is solely responsible for the follow-up of these patients in 80.4% of the cases. In 9.8% the physician works with a dietician, in 5.8% with a nurse, in 2% with a nurse and psychologist and in the remaining 2% with a nurse, dietician and psychologist. Fol-

Table IV
Professionals involved in the indication of EEN

	Always	Sometimes	Never
Nurse	47%	22%	31%
Dietician	22%	16%	62%
Psychologist	4%	37%	59%
Physician	100%	0%	0%

low-up is primarily done via telephone and outpatient visits (74.6%) or exclusively by visits (25.4%). The frequency with which the patient is contacted during nutritional treatment is weekly in 56.3% of the centres, fortnightly in 33.3%, monthly in 6.3% and variable in the remaining 4.1%.

Assessment of response to EEN

The PCDAI was the most frequent index used (98%) followed by the wPCDAI.¹² Regarding the biochemical parameters to assess response after EEN, 100% use complete blood count (CBC) and albumin, 98% erythrocyte sedimentation rate (ESR), 78% faecal calprotectin, 35% C-reactive protein (CRP), 22% iron metabolism, and 8% fibrinogen and procalcitonin (PCT); 70.6% use endoscopy and 66.7% use radiological tests to assess the response to treatment.

Advantages and disadvantages of EEN

The results regarding advantages and disadvantages with EEN are shown in table V.

Difficulties

Multiple choice questions were used to explore the objections or difficulties reported by the professionals for establishing EEN; 14% of the respondents reported no difficulties, 36% only one difficulty, another 36% reported two difficulties and up to 14%, more than three difficulties (table VI).

Table V
Advantages and disadvantages of EEN

<i>Advantages</i>		<i>Disadvantages</i>	
Absence of side effects	80%	Maintenance and compliance difficulties. Motivation	80%
Clinical and histological remission (mucosal healing)	75%	Dietary considerations (monotonous, high volume to ingest, flavour)	30%
Improvement of nutritional parameters, growth and sexual maturity	61%	Requires closer follow-up than other treatments. Frequent check-ups	22%
Prevents the use of corticosteroids	29%	Slow improvement of symptoms	12%
Safety	10%	Altered quality of life (QoL)	12%
Outpatient setting	4%	Prolonged time period	10%
Update vaccination schedule	4%	Price	10%
Easy prescription	4%	Not useful in exclusively colonic or perianal disease	4%

Table VI
Difficulties found for establishing EEN

Lack of acceptance by the patient and/or family	71%
Lack of time and/or ancillary staff (dieticians, nutritionists, psychologists, etc.) to collaborate in the follow-up and support of these patients	69%
Difficulty convincing the patient and/or family of treatment suitability	43%
Budgetary limitations	10%
Difficulty using alternatives to the oral route at my centre (NG tube, gastrostomy)	8%
Difficulties in prescription and administration of the nutrition by the hospital (logistics)	2%
I do not believe in the benefits of mono-therapy EEN to induce remission	0%

Discussion

Although EEN has been proven to be beneficial in the treatment of pediatric CD, there are some questions that remain unanswered. We had access to data from different surveys regarding the use of this therapeutic modality in the United States, Canada, Europe, Israel and Australia,^{6-9,13} (table VII) but we did not know the real situation regarding EEN use in Spain.

The use of EEN is widespread in Spain, since all of the respondents confirm regular use of EEN, at a rate much higher than that published by other authors (table VII). Although the studies shown in table 7 have been published recently, much of the data were collected before a meta-analysis regarding the efficacy of EEN was published. Nevertheless, it is true that series with the greater number of patients and better design are subsequent to 2005, when the best evidence for EEN

in the treatment of CD was published. One of the possible reasons for this difference in use may be related to the fact that the Spanish National Healthcare System subsidizes enteral formulas for the treatment of CD. This is a key factor, since EEN has been shown to be superior to steroids in achieving mucosal healing,^{1,2,14} a situation that determines better prognosis in the following years, lower hospitalisation rate and less use of biological drugs.¹⁵

Despite the fact that the efficacy of EEN for controlling CD relapses is 50%,^{14,16} and even if there is not remission, there is a decrease in inflammatory activity and an improvement in nutritional state, only 24.5% use EEN in this scenario, which is likely conditioned by the difficulty for re-establishing and maintaining the EEN again for another 6-8 week period.

Initial studies revealed that EEN was less effective than steroids in exclusively colonic CD,¹⁷ although this

Table VII
Published surveys about use of EEN in CD

<i>Study</i>	<i>USA</i>	<i>Europe</i>	<i>Canada</i>	<i>Israel</i>	<i>Australia</i>	<i>Asia-Pacific</i>	<i>All data</i>
Levine et al ⁶	4.3%	61.8%	36%	19.2%	–	–	–
Steward et al ⁷	9%	–	32%	–	–	–	–
Gråfors et al ⁸	–	65% ^A	–	–	–	–	–
Whitten et al ^{9B}	100%	92%	–	–	–	75%	89%
Day et al ¹²	–	–	–	–	38%	–	–

^AOnly data from Sweden.

^BUSA 2 units; Asia-Pacific 8 units; UK 16 units; Europe 9 units.

was not corroborated by later studies.^{18,19} This is an important issue because 37.3% of the respondents do not use EEN in this clinical setting on the basis of their own previous experience. In our opinion, more studies along these lines are needed to clarify the real response according to disease extension.

Regarding the enteral formula used, there are two clearly differentiated groups: those who use specific formulas for IBD (Resource IBD[®] or Modulen IBD[®]) as it contains TGF- β and due to the motivating effect of taking a formula adapted to a specific disease, and another group that sustains, as made clear by the studies published, that there are no differences between formulas,²⁰⁻²³ attributing the improvement experienced by patients to the EEN and the administration conditions and not to any of their components. Another factor is compliance, which seems to be superior in the case of flavoured polymeric formulas. One reason for the 3% of survey respondents who used specific formulas for IBD patients was the price although the average price of a specific formula for IBD in Spain is 17 €/1,000 kcal, similar to non-specific pediatric normocaloric formulas; slightly more expensive than pediatric hypercaloric formulas (14,6 €/1,000 kcal) and more expensive than adults hypercaloric (9.3 €/1,000 kcal) and normocaloric (9,7 €/1,000 kcal) formulas.

The optimal method for introducing normal diet after EEN has not been established, and there is no data to suggest that progressing to a hypoallergenic diet, gradual or sudden introduction of diet following EEN influence the maintenance of remission.^{9,24}

The majority of respondents identified various difficulties in re-establishing diet, despite having no doubts about the efficacy of EEN. Almost three-quarters of those polled consider the lack of acceptance by the patient and/or family to be the main difficulty in establishing EEN. A more proactive attitude in the professional involved might have led to higher acceptance rates; not initially offering any other therapeutic option could also be considered a valid approach.

Added to this preliminary difficulty is the second most frequent barrier: lack of time and/or ancillary staff (dietitians, nutritionists, psychologists, etc.) to help in the follow-up and support of these patients. In our opinion, this greatly conditions prescription since, unlike steroids, EEN patients require a lot of motivation to achieve their goals and must be followed-up more frequently and closely.

Our study is the first of its kind to be conducted in Spain. The data were collected over a short period of time, at a time when the evidence regarding the beneficial effects of EEN is on the rise.

A limitation of all surveys is the fact that results reflect the opinions of a selected population, pediatric gastroenterologists, who usually use EEN, willing to participate in the study.

To summarize, 8 weeks of EEN is the most frequent therapeutic option in newly diagnosed CD children in Spain. Formulas made specifically for IBD are used

the most. The advantages of EEN compared to other therapeutic modalities are mucosal healing without side effects. The difficulties most frequently found were lack of acceptance by the patient and/or family and lack of time and/or ancillary staff to help in the follow-up and support of these patients.

Tools to facilitate acceptance by the patient and family are needed. Increasing the time dedicated to this therapeutic modality is likewise important. Given the disparity of criteria for indicating treatment with EEN, it would be useful to have widely accepted clinical practice guidelines or protocols that facilitate the decision to start with EEN.

Appendix I

The following investigators participated in the PRESENT study:

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Appendix II

Questionnaire on the use of exclusive enteral nutrition as treatment in Crohn's disease

A. General information about patients with IBD on follow-up in your Unit

1. How many patients with inflammatory bowel disease (IBD) do you currently have on follow-up in your unit?
2. How many of them are diagnosed with Crohn's disease (CD)?
3. How many were diagnosed in 2011?
4. How many of the patients with CD were treated in 2011 with EEN?
5. How many of these were recently diagnosed?

B. Exclusive Enteral Nutrition (EEN) in newly diagnosed CD patients

6. Do you **think** that EEN is effective in inducing **clinical** remission in CD patients?
7. Do you **think** that EEN is effective in inducing **endoscopic** remission in CD patients?
8. Do you **think** that EEN is effective in inducing **histological** remission in CD patients?
9. Do you **use** EEN in newly diagnosed CD patients?
10. Have you **verified** whether EEN is effective in inducing **clinical** remission in CD patients?
11. Have you **verified** whether EEN is effective in inducing **endoscopic** remission in CD patients?
12. Have you **verified** whether EEN is effective in inducing **histological** remission in CD patients?

C. Exclusive Enteral Nutrition (EEN) during CD relapses

13. Do you **think** that EEN is effective in inducing **clinical** remission in CD patients?
14. Do you **think** that EEN is effective in inducing **endoscopic** remission in CD patients?
15. Do you **think** that EEN is effective in inducing **histological** remission in CD patients?
16. Do you **use** EEN during relapses?
17. Have you **verified** whether EEN is effective in inducing **clinical** remission in CD patients?
18. Have you **verified** whether EEN is effective in inducing **endoscopic** remission in CD patients?
19. Have you **verified** whether EEN is effective in inducing **histological** remission in CD patients?

D. Indications and contraindications of EEN in CD

<i>Question</i>	<i>T</i>	<i>F</i>
20. I only use EEN in newly diagnosed patients, not in relapses		
21. I use EEN in relapses only if there was a previous response to EEN		
22. The location of the disease influences my indication for EEN.		
23. I only use it in cases when the ileum (L1) or ileum and colon (L3) are affected.		
24. I do not use EEN in exclusively colonic disease (L2).		
25. I do not use EEN if the upper digestive tract (duodenum, oesophagus) is affected (L4).		
26. I do not use EEN in perianal disease regardless of the perianal manifestations (fissures, fistulas, tags, abscesses, etc.).		
27. I do use EEN if the perianal disease is in the form of fissures or tags or if there is a correctly drained abscess		
28. I do not use EEN if the perianal disease is in the form of fistulas or abscesses even if correctly drained.		
29. I use EEN regardless of the phenotype (inflammatory, stricturing or penetrating)		
30. I only use EEN in inflammatory phenotypes		
31. I only use EEN in inflammatory and penetrating phenotypes		
32. I only use EEN in inflammatory and stricturing phenotypes		
33. I use the PCDAI to estimate the severity		
34. I use EEN in all CD patients, regardless of severity		

Appendix II (cont.)

Questionnaire on the use of exclusive enteral nutrition as treatment in Crohn's disease

<i>Question</i>	<i>T</i>	<i>F</i>
35. I only indicate EEN in mild disease		
36. I only indicate EEN in moderate disease		
37. I only indicate EEN in severe disease		
38. I only indicate EEN in mild to moderate disease		
39. I only indicate EEN in moderate to severe disease		
40. For severe disease, in addition to the PCDAI, I consider other factors when deciding whether or not to use EEN, such as: general status is affected, significant weight loss, prolonged symptoms, diagnostic delay, significant puberty delay, and also if there is upper digestive tract involvement.		
41. If the patient has a severe disease and presents one or several of the factors from the previous question I DO NOT indicate EEN.		
42. I consider age as a factor when indicating EEN.		
43. I use EEN regardless of patient age.		
44. I do not use EEN in children under the age of 2-3 years.		
45. I only use EEN starting at a determined age.		
46. I only use EEN if I observe that the patient and their family are collaborative.		
47. I indicate EEN and "make them" collaborative, providing no other options.		
48. I do not use EEN in cases of extraintestinal manifestation.		
49. Delay in weight or growth contributes to whether I indicate EEN.		

E. Specific aspects of EEN

50. What is the standard duration of EEN at your unit? (days, weeks, months)
51. Do you ever prolong EEN more than 12 weeks? Specify.
52. Which type of formula do you tend to use for EEN?
- a) Modulen IBD
 - b) Resource IBD
 - c) Other Polymeric Formula. Specify:
 - d) Semi-elemental Formula. Specify:
 - e) Elemental Formula. Specify:
53. What are your reasons for using this type of formula? (cost, taste, composition, availability, scientific evidence, etc.).
54. Does the physician participate in the decision on which formula to administer as EEN for Crohn's disease?
55. What is the most frequent route of administration? Rate as 1, 2 or 3, with 1 being the most frequent:
- | | | |
|------|---------|-------------|
| Oral | NG tube | Gastrostomy |
|------|---------|-------------|
56. What do you allow the patients to eat or drink during the EEN period? Specify the % of daily calories.
57. Do you use flavouring? Specify the type (cocoa powder, syrups, etc.)

F. EEN as maintenance therapy

58. How do you effect progression from EEN to normal diet? Do you follow any clinical practice guidelines or protocols?
59. Once the EEN period has been completed, do you prescribe the formula as a supplement? If so, how much do you prescribe and for how long? The quantity can be expressed in ml or in % of daily calories.

G. Drugs used during EEN in newly diagnosed CD patients

60. If you tend to use adjuvant therapy with EEN in newly diagnosed CD patients, specify which, and the frequency of use. Mark with an X

	<i>Always</i>	<i>Sometimes</i>	<i>Never</i>	<i>I don't know</i>
Oral 5-ASA				
Topical 5-ASA				
Steroids				
Antibiotics				
Immunomodulators				
Anti-TNF				

H. Professionals involved in the administration of EEN

61. Which of these healthcare professionals is routinely involved in the administration of EEN at your centre?

	<i>Always</i>	<i>Sometimes</i>	<i>Never</i>	<i>I don't know</i>
Nurse				
Dietician				
Psychologist				
Physician				

I. Follow-up protocol

62. Who performs the follow-up of these patients at your centre? (physician, nurse, dietician, other):
 63. Which method do you use for the follow-up of these patients? (telephone, email, visit to clinic, etc.)
 64. With what frequency do you contact the patient?

J. Assessment of response to treatment

65. How do you assess response to treatment?

	<i>Always</i>	<i>Sometimes</i>	<i>Never</i>	<i>I don't know</i>
Symptoms				
Lab tests				
Endoscopy				
Radiology				

- Symptoms: do you use any scores? Which?
- Tests: specify the parameters you use (CRP, PCT, Calprotectin, Lactoferrin, orosomucoid, others)
- Endoscopy
- Radiology (mark those that correspond)
 - Ultrasound
 - MR
 - Barium enema transit time

K. Advantages and disadvantages of EEN

66. Advantages	67. Disadvantages

L. Limiting factors for the use of EEN

68. Which of the following factors do you consider to be limiting at your Unit for an improved/greater use of EEN. Circle:
- a) Lack of time and/or ancillary staff (dietitians, nutritionists, psychologists, etc.) to help in the follow-up and support of these patients.
 - b) Difficulties in prescription and administration of the nutrition by the hospital (logistics).
 - c) Budgetary limitations.
 - d) Difficulty convincing the patient and/or family of the treatment suitability.
 - e) Lack of acceptance by the patient and/or family.
 - f) Difficulty using alternatives to the oral route at my centre (NG tube, gastrostomy).
 - g) I do not believe in the benefits of mono-therapy EEN to induce remission.
 - h) Others:

M. Greater use of EEN

69. What type of information or material would you like to have available in order to use EEN more regularly?

N. Comments (70)

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Original / *Síndrome metabólico; diabetes*

Glycemic control and lipid profile of children and adolescents undergoing two different dietetic treatments for type 1 diabetes mellitus

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Abstract

Objective: To compare the glycemic control and lipid profile of children and adolescents undergoing two different dietetic treatments for type 1 Diabetes Mellitus assisted at the Children and Adolescent's Diabetes Mellitus Health Center-UFRJ.

Methods: A retrospective longitudinal study conducted between 2002 and 2006. We evaluated the same subjects in two different periods: after 1 year in TD and subsequently after 1 year in CCHO. The evolution of the nutritional status during the dietary treatments was evaluated using Body Mass Index (BMI) for age. The lipid panel was evaluated according to the 1st Guideline for Prevention of Atherosclerosis in Childhood and Adolescence, used in Brazil, and the glycemic control was evaluated by measuring glycated hemoglobin (HbA1c).

Results: We evaluated 93 individuals, 38.7% children and 61.3% adolescents. The mean age at study entry was 11.1 (\pm 2.66) years and the mean disease duration was 6.1 (\pm 3.2) years. A significant difference in the percentage of adequacy of HbA1c ($p = 0.000$) and in the values of total plasma cholesterol ($p = 0.043$) was found after 1 year of CCHO diet, which did not happen during the observation time of TD. The evolution of anthropometric nutritional status showed no significant difference between the beginning and the end of both dietary treatments.

Conclusion: The results of this study suggest that a more flexible food orientation program can contribute to the improvement of blood glucose levels without causing deterioration of the lipid profile when compared to TD.

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CONTROL GLUCÉMICO Y PERFIL LIPÍDICO DE NIÑOS Y ADOLESCENTES SOMETIDOS A DOS TRATAMIENTOS DIETÉTICOS DISTINTOS PARA LA DIABETES MELLITUS TIPO 1

Resumen

Objetivo: Comparar el control glucémico y el perfil lipídico de niños y adolescentes sometidos a dos tratamientos dietéticos distintos para la diabetes mellitus tipo 1 atendidos en el Centro de Salud para Niños y Adolescentes con Diabetes Mellitus-UFRJ.

Métodos: Estudio longitudinal retrospectivo realizado entre 2002 y 2006. Evaluamos a los mismos individuos en dos momentos distintos: tras un año en tratamiento para diabetes (TD) y posteriormente tras un año con conteo de hidratos de carbono (CHC). La evolución del estado nutricional durante los tratamientos dietéticos se evaluó empleando el índice de masa corporal (IMC) para la edad. El panel de lípidos se evaluó de acuerdo con la 1ª Guía para la prevención de la aterosclerosis en la infancia y adolescencia, empleada en Brasil, y el control glucémico se evaluó midiendo la hemoglobina glucosilada (HbA1c).

Resultados: Evaluamos a 93 individuos, 38,7 % niños y 61,3 % adolescentes. La edad promedio en el momento de entrada en el estudio fue de 11,1 (\pm 2,66) años y la edad promedio de duración de la enfermedad fue de 6,1 (\pm 3,2) años. Se encontró una diferencia significativa en el porcentaje de adecuación de la HbA1c ($p = 0,000$) y en los valores del colesterol plasmático total ($p = 0,043$) tras un año de dieta con CHC, lo cual no ocurrió durante el periodo de observación de TD. La evolución del estado nutricional antropométrico no mostró diferencias significativas entre el inicio y el final de ninguno de los tratamientos dietéticos.

Conclusión: Los resultados de este estudio sugieren que un programa de orientación alimentaria más flexible puede contribuir a la mejora de la glucemia sin producir un deterioro del perfil lipídico en comparación con el TD.

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Palabras clave: Diabetes tipo 1. Dieta. Conteo de hidratos de carbono.

Introduction

Significant advances occurred in the recent decades^{1,2} to improve the treatment of Diabetes Mellitus (DM). The American Diabetes Association (ADA) recommends as its main objective for the Medical Nutrition Therapy (MNT) prevention of the development of chronic complications through an adequate nutrient intake and lifestyle modification.¹ The maintenance of a proper anthropometric nutritional status by the patient is necessary, as well as, knowledge about nutrition and healthy eating practices at any stage of the lifecycle.^{3,4}

The possibility of having food items limited in the daily diet is a great concern of the diabetic patient and their families. For this reason, the possibility of removing these prohibitions should be strongly considered even if some adjustments become necessary, such as an increased frequency of glucose monitoring and/or further intensification of insulin scheme.^{5,6}

During the 20th century, the recommended diet for DM patients underwent several changes, especially regarding the use of CHO. The first dietary recommendations advocated an increased consumption of CHO in order to replace the loss of sugar in the urine. Later, this practice changed and CHO started being avoided.⁷ In 1912, Frederick M. Allen, developed the “Therapeutic hunger Allen”, in which he offered 1,000 kcal/day and 10 g CHO/day, with the goal of keeping individuals alive until, supposedly, insulin began to be produced again. Thus, until the emergence of exogenous insulin in 1921, patients with DM were treated with diets very low in CHO and in a semistarvation state.⁸

In this sense, the carbohydrate count (CCHO), used since the mid-1920s, was one of the dietary planning strategies recommended by the *Diabetes Control and Complications Trial* (DCCT).⁹ Since ADA's report in 1994, CCHO started being recommended, aiming to optimize glycemic control avoiding even the smallest variations in postprandial glycemia.^{9,10}

Even after the advent of insulin therapy, scholars continued recommending a diet low in CHO and rich in lipids. However, over the decades, ADA's nutritional recommendations suffered some modifications due to new discovery in the scientific literature.¹¹ In the past, it was believed that the restriction of several food items would be the best form of treatment, as it would prevent glycemic elevation. Such procedure, however, caused severe malnutrition, leading individuals to early death. Recent published guidelines reflect a more flexible approach in relation to nutritional interventions and the carbohydrate content of the diet, allowing the patients to adjust their own insulin based on the content of nutrient intake. This is the basic principle of carbohydrate counting.¹²

Mehta et al.¹³ found that CCHO accuracy and appropriate glucose monitoring were associated with lower levels of HbA1c in studies with children and adolescents between 4 and 12 years old.

In the context of CCHO, modern therapies, including insulin pump and flexible insulin regimens, resulted in less restrictive diets.¹⁴ However, young patients with DM 1 should be advised about the importance of being totally conscious about the method being adopted and that the consumption of a healthy diet should also be an integral part of nutrition education in diabetes.^{14,15}

This study aims to compare the glycemic control and lipid profile of children and adolescents undergoing two different dietetic treatments for type 1 Diabetes Mellitus assisted at the Children and Adolescent's Diabetes Mellitus Health Center-Pediatrics Institute Martagão Gesteira (IPPMG), Federal University of Rio de Janeiro (UFRJ).

Materials and methods

This is a retrospective longitudinal study, based on database produced by a Reference Center in the treatment of juvenile diabetes, in its medical charts of patients attended from 2002 to 2006.

This Hospital is a reference in the treatment of type 1 diabetes in children and adolescents in Rio de Janeiro, and is characterized by the presence of a multidisciplinary team, which consists of doctors, nutritionists, psychologists and nurses.

This study evaluated the same subjects in two different periods: 1 year follow-up of traditional diet for diabetes (TD) and, subsequently, 1 year follow-up of CCHO diet.

We included in the study all the patients with DM1 who started dietary guidance for CCHO between the years 2003 and 2005 (n = 147), excluding those with less than 2 or more than 15 years of disease duration, and those with any other endocrine disease with possible effects on nutritional status and metabolic control. Thus, 54 patients were eliminated for not meeting the criteria for inclusion in the study. The final sample comprised 93 patients.

It was named in this study as TD the dietary counseling based on caloric distribution of food. TD was calculated based on the total energy value of the diet (VET) according to FAO/OMS¹⁶ recommendations, which was distributed into 5 to 6 daily meals. Patients received an individualized dietary plan and a list of food substitution which was based on food groups, with similar energy values. The exchanges allowed were only those among the same food group. Patients were also instructed to restrict the use of sweet food items.

This method of exchanging food items, divides food into groups in which each portion of food contains approximately 15 g of CHO, enabling the exchange between them. In the counting method used, the lists of substitutions were based on portions of the food pyramid and its main groups were defined as: cereal, pasta and vegetables; breads and crackers; fruit; salad vegetables; dairy products; meat and sweets. Groups could

Table I
Sample characteristics of baseline observation (TD0). Brazil, Rio de Janeiro

Variables	Children		Adolescents		Total	
	n	%	n	%	n	%
<i>Gender</i>						
Male	22	61.1	24	42.1	46	49.4
Female	14	38.9	33	57.9	47	50.6
Total	36	100.0	57	100.0	93	100.0
Variables	Mean	SD	Mean	SD	Mean	SD
Age (years)	7,4	2,47	14,8	2,86	11,1	2,66
Time of disease (years)	4,5	1,94	7,3	3,4	6,1	3,2

SD: Standard deviation.

be measured considering 15 grams of carbohydrate if they contained CHO, and the possibility of measuring this amount in kitchen utensils.¹⁷ It was defined as the beginning of this dietary method the observation period of 12 months prior to the beginning of CCHO (TD0) diet. From this baseline, patients were evaluated after 6 months (TD1) and after 12 months (TD2) following TD, when it was introduced CCHO (CCHO0) dietary counseling. Therefore, the period TD2 corresponds to the period CCHO0 (TD2 = CCHO0).

CCHO dietary treatment was calculated using VET and adding the daily requirement of carbohydrate (CHO). The patients received an individualized dietary plan which had its meals distributed as in TD and the amount of CHO was predetermined for each meal. The patient received a list of substitution, based on food groups, in which the exchange was allowed even between different groups, provided that the total amount of CHO was respected at every meal. There was no restriction of any food item. Once introduced to the CCHO dietary orientation, patients were evaluated after 6 months (CCHO1), and after 12 months (CCHO2).

Patients were classified as prepubertal (children) or pubescent (adolescent) according to the degree of sexual maturation, despite the chronological age. We considered prepubertal, girls and boys in stage 1 for breasts (M1) and genitals (G1), respectively, and pubertal those in stage 2 or more.^{18,19}

The classification of the anthropometric nutritional status was based on BMI/age, and classified according to the recommendation of the Health Ministry.²⁰ The collected data were cholesterol, LDL-C, HDL-C and triglyceride levels in TD0, TD2 and CCHO2. The lipid profile was evaluated according to the First Guideline for Prevention of Atherosclerosis in Childhood and Adolescence²¹, which considers as suitable values: total cholesterol < 150 mg/dl, LDL-C < 100 mg/dl, HDL-C ≥ 45 mg/dL, and triglycerides < 100 mg/dl.

Glycemic control was assessed by measuring glycated hemoglobin (HbA1c), which was classified as percentage of adequacy of laboratory reference val-

ues, according to age, alternative analysis endorsed by ADA.²² It was considered as suitable any value up to 30% of the maximum reference for the age group of 2-5 years old, up to 25% for those between 5 and 13 years old, and < 20% for patients over 13 years old. The level of HbA1c was measured using high performance liquid chromatography (HPLC).

Statistical analysis was performed using the program *Statistical Package for the Social Sciences* (SPSS) version 17.0 for Windows.

The dependent variables average value was calculated at each time interval of observation. Once verified the normality of the data, analysis of variance (ANOVA) for repeated measures was applied to the mean values of the proportion of appropriate HbA1c and anthropometric indices in 3 different times (start, 6 and 12 months) for each dietary method, and changes in lipid profile in 2 different times (start and 12 months). The Bonferroni test was used for statistical comparison between the mean values obtained.

For the analysis of categorical variables we used the chi-square and Fisher's exact test. It was considered statistically significant values of $p < 0.05$.

This project was approved by the Research Ethics Committee-IPPMG/UFRJ, under the registration number 21/06.

Results

The final sample consisted of 93 children and adolescents, 50.5% male (n = 47) and 49.5% female (n = 46). Time of diabetes diagnosis was of 6.18 ± 3.22 years, and most of them were attending elementary school (100%, n = 89) (table I). According to the anthropometric nutritional status classification, 76.7% (n = 56) were categorized as normal weight, 6.8% (n = 5) as underweight and 16.4% (n = 12) as overweight before CCHO. There was an increase in the percentage of children with overweight in the first period of observation during CCHO, which was reduced during the second period of observation. Such a change was not significant (table II).

Table II
Nutritional status at different timepoints. Brazil, Rio de Janeiro

Timepoints	Children						Adolescents					
	Normal weight		Low weight risk		Overweight risk		Normal weight		Low weight risk		Overweight risk	
	n	%	n	%	n	%	n	%	n	%	n	%
TD ₀	27	69.2	4	10.3	8	20.5	44	9.8	0	0.0	5	10.2
TD ₁	28	71.8	3	7.7	8	20.5	44	9.8	1	2.0	4	8.2
TD ₂ = CCHO ₀	31	79.5	4	10.3	4	10.3	43	6.0	1	2.0	6	12.0
CCHO ₁	13	3.3 ^a	3	7.7	23	59.0 ^b	46	8.5	1	1.9	5	9.6
CCHO ₂	30	76.9 ^c	2	5.1	7	17.9 ^d	45	8.2	1	2.0	5	9.8

TD₀: Traditional diet initial observation; TD₁: 6 months observation of traditional diet; TD₂: 1 year observation of traditional diet; CCHO₀: Carbohydrates counting diet (CCHO) initial observation; CCHO₁: 6 months observation of CCHO diet; CCHO₂: 1 year observation of CCHO diet.

^aPercentage lower than CCHO₀ (p < 0.05); ^bPercentage higher than CCHO₀ (p < 0.05); ^cPercentage higher than CCHO₁ (p < 0.05); ^dPercentage lower than CCHO₁ (p < 0.05).

The comparison of the differences between BMI was not significant in any observation period, and there were also no differences between gender.

It was observed an adequacy of HbA1c in 63.3% of patients on TD₀, 59.4% on TD₁, 62.5% on TD₂, 72.6% on CCHO₁ and 75.9% on CCHO₂. Mean values of HbA1c adequacy underwent significant reduction during the first semester of CCHO observation (p = 0,007) and during the whole year of the study (p = 0,000), not observing any significant change during TD. There was significant reduction in these averages for both pubertal stages at the end of the first year of CCHO observation (p = 0.004 for children and p = 0.015 for adolescents).

Inadequate levels of total cholesterol and LDL-C were found respectively in 64.9% and 41.9% of patients on TD₀, 62.8% and 41% on TD₂ and 58% 36.4% on CCHO₂. When analyzing the influence of the dietary method on the adequacy of lipoproteins, there were no significant differences at the end of 1 year of nutritional counseling, as well as no differences according to the different sexual maturation stages.

Table III shows the comparison between the mean values of the variables related to glycemic control and lipid profile. Regarding insulin dose, there was no

significant change in the mean values of insulin/kg in both study periods (TD and CCHO).

Discussion

Due to the fact that nutritional therapy is a key component in maintaining adequate metabolic control, it has been discussed over and over, aiming a better adherence to this therapy and consequent reduction in the onset and severity of acute and chronic disease complications.²³ Studies show that compliance with the prescribed nutrition plan improves the level of HbA1c in adults²⁴ and has been correlated with better blood glucose control in children.^{25,26} The adequacy of the dietary guidance to the lifestyle of each patient should be considered at the time of prescribing each individualized eating plan and it should also be able to follow the changes that occur throughout life.

High glycated hemoglobin is associated with the development of microvascular and macrovascular complications of the disease. Thus, maintaining satisfactory levels of HbA1c throughout the patient's life should be one of the treatments goals. The improvement of the HbA1c adequacy means of

Table III
Biochemical variables mean values at all observation periods of patient treated at the Diabetes Mellitus Center - IPPMG-UFRJ. Brazil, Rio de Janeiro

Variable	TD ₀	TD ₁	TD ₂ (= CCHO ₀)	CCHO ₁	CCHO ₂
HbA1c (Adequacy %)	122.09 ± 26.24	123.20 ± 28.74	123.02 ± 30.99	113.83 ± 23.51 ^a	108.55 ± 22.05 ^{ab}
Colesterol (mg/dl)	172.59 ± 40.42	–	170.05 ± 44.64	–	163.72 ± 40.48 ^a
Tryglicerides (mg/dl)	66.72 ± 28.25	–	74.31 ± 38.01 ^d	–	66.10 ± 32.24
HDLc (mg/dl)	53.46 ± 14.41	–	55.55 ± 15.92	–	54.57 ± 11.68
LDLc (mg/dl)	103.60 ± 37.32	–	96.40 ± 34.82	–	95.01 ± 37.52

TD₀: Traditional diet initial observation; TD₁: 6 months observation of traditional diet; TD₂: 1 year observation of traditional diet; CCHO₀: Carbohydrates counting diet (CCHO) initial observation; CCHO₁: 6 months observation of CCHO diet; CCHO₂: 1 year observation of CCHO diet.

HbA1c: Glycated hemoglobin; HDLc: High density lipoprotein; LDLc: Low density lipoprotein.

^aMean value lower than CCHO₀ (p < 0.05); ^bMean value lower than CCHO₁ (p < 0.05); ^cMean value higher than CCHO₀ (p < 0.05); ^dMean value higher than TD₀ (p < 0.05).

the CCHO diet demonstrated in this study is consistent with the results of the *Diabetes Control and Complications Trial*.¹⁵ A study conducted in São Paulo, involving adolescents with DM1, in which it was evaluated the effect of CCHO technique in a single meal for 4 months, showed a significant reduction in HbA1c, accompanied by maintenance of total cholesterol and triglycerides.²⁷ These results point to the possibility of a more flexible dietary therapy that promotes a much better quality of life, since it has been demonstrated that 1% reduction in HbA1c levels, corresponds to a 44% reduction in the risk of chronic complications of the disease.⁹

Although we found among our patients a high prevalence of dyslipidemia in comparison to other studies, we can observe that the average values of LDLc described in our study were much lower than the values found in the scientific literature.²⁸⁻³⁰ Such differences can be attributable to the use of different reference values. It should be noted that the cutoff values used in this study were based on new guidelines for children and adolescents,¹⁷ in which most of the normal values for total cholesterol and LDLc suffered significant reduction compared to previous existing guidelines.^{31,32}

Clinical practice experience has shown that, in childhood, treatment of the disease is directly related to the levels of understanding and adherence by the children's parents/guardians. Dietary and behavioral changes in children only become viable if there are changes in the family's eating habits and lifestyle.³³ When the disease appears during adolescence, essential attitudes to control the disease may be overlooked by the young patients. At this life stage, the need of the so called "diabetes education", together with the establishment of more flexible routines, are essential for an adequate adherence to the treatment.

The weight deviation found in children during the first half of the CCHO period may have occurred because of the greater variety of food allowed. The initial adaptation to a more flexible nutritional plan containing a variety of food choices can initially lead to an increased energy consumption. These findings highlight the importance of a close attention and monitoring of the nutritional status of diabetic patients, with the aim of detecting very early any possible nutritional problems to implement a necessary diet plan intervention. Patton et al.³⁴ emphasizes that dietary planning should not only prioritize CCHO.

The successful implementation of flexible schemes requires the ability to count carbohydrates and calculate the insulin dose correctly. Measures to assess adherence to the diabetes treatment have been developed, but they do not assess knowledge and ability to implement a plan, which are prerequisites for the therapy adhesion.^{35,36}

In this context, diabetes education is crucial to allow individuals to effectively control diabetes. Moreover, there is also the need for a continuous assessment of the patient's disease and treatment knowledge.³⁷

In this study there was no difference in weight gain at the end of the monitoring period on CCHO diet. This fact can be explained by the presence of an individualized guidance suitable for each stage of development and nutritional continuous monitoring throughout the treatment of the disease.

All the patients received proportional doses of insulin throughout the observation period of the study, regardless of the dietary method adopted. This finding demonstrates that despite the relationship between CHO intake and insulin dose administered on CCHO diet, it is possible to administrate insulin doses according to the recommendations for each age group. It must be noted that apart from the fear that an eating plan with greater freedom of choice may compromise the metabolic control of diabetes, resistance to a more flexible feeding behavior is due to a concern about the risk of excessive weight gain, which would associate in turn, the greater insulin need. The observed results do not justify such concern and suggest that the CCHO diet is a positive alternative nutritional intervention for children and adolescents with diabetes.

This study indicates that CCHO diet contributed to a significant improvement on glycemic control without promoting significant changes on other biochemical parameters. In addition, it highlights the importance of a clinical-nutrition monitoring, strengthening the necessity of a multidisciplinary team approach in treating diabetic children and adolescents.

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Original / Síndrome metabólico; diabetes

Effect of different protein types on second meal postprandial glycaemia in normal weight and normoglycemic subjects

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Abstract

Background: Diabetes mellitus is a global epidemic affecting 346 million people in the world. The glycemic control is the key for diabetes prevention and management. Some proteins can stimulate insulin release and modulate glycemic response.

Objectives: To assess the effect of the consumption of different types of protein (whey protein, soy protein and egg white) on a second meal postprandial glycaemia in normal weight and normoglycemic subjects.

Methodology: Randomized crossover clinical trial. After an overnight fast of 12-hours, ten subjects attended the laboratory to drink one of the protein shakes (whey, soy or egg white) or the control drink. Thirty minutes later, the subjects consumed a glucose solution (25 g glucose). Glycemic response was monitored at times 0 (before glucose solution) and 15, 30, 45, 60, 90 and 120 min (after glucose solution consumption). Incremental area under the glycemic curve (iAUC) was calculated by the trapezoidal method. Furthermore, glycemic response was assessed by a new method using iG equation.

Results: Compared with control, whey and soy protein drinks reduced postprandial iAUC in 56.5% ($p = 0.004$) and 44.4% ($p = 0.029$), respectively. Whey protein was the only protein capable of avoiding great fluctuations and a peak in postprandial glycaemia. The assessment of glycemic response by iG equation showed positive correlation with iAUC (Pearson 0.985, $p < 0.05$).

Conclusion: The consumption of whey and soy protein 30 minutes before a glucose load resulted in lower iAUC compared with control drink. Whey protein maintained postprandial glycaemia more stable.

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Keywords: Glucose metabolism. Type 2 diabetes mellitus. Dietary protein. Food and beverages.

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EFECTO DE DIFERENTES TIPOS DE PROTEÍNA EN LA GLICEMIA POSTPRANDIAL DE LA SEGUNDA COMIDA EN INDIVIDUOS DE PESO NORMAL Y NORMOGLICÉMICOS

Resumen

Introducción: La diabetes mellitus es una enfermedad epidémica que afecta a 346 millones de personas en el mundo. El control glicémico es la clave para la prevención y el control de la diabetes. Algunas proteínas pueden estimular la liberación de insulina y modular la respuesta glicémica.

Objetivos: Evaluar el efecto del consumo de diferentes tipos de proteínas (proteína de suero de leche, proteína de soja y la clara de huevo) de la glicemia postprandial en una segunda comida en individuos de peso normal y normoglicémicos.

Metodología: Este fue un ensayo clínico aleatorizado cruzado. Después de un ayuno nocturno de 12 horas, diez individuos asistieron al laboratorio para beber uno de los batidos de proteínas (suero de leche, soja o clara de huevo) o la bebida control. Treinta minutos más tarde, los individuos consumieron una solución de glucosa (25 g de glucosa). La respuesta glicémica fue monitorizada en los tiempos 0 (antes de solución de glucosa) y 15, 30, 45, 60, 90 y 120 min (después del consumo de la solución de glucosa). El área incrementada bajo la curva de glicemia (iAUC) fue calculada por el método trapezoidal. Por otra parte, la respuesta glicémica se evaluó mediante un nuevo método que utiliza la ecuación de iG.

Resultados: En comparación con el control, las bebidas de suero de leche y de proteína de soja reducen iAUC postprandial en 56,5% ($p = 0,004$) y 44,4% ($p = 0,029$), respectivamente. La proteína de suero es la única proteína capaz de evitar grandes fluctuaciones y un pico de glicemia postprandial. La evaluación de la respuesta glicémica por la ecuación iG mostró correlación positiva con iAUC (Pearson 0,985, $p < 0,05$).

Conclusión: El consumo de suero de leche y proteína de soja 30 minutos antes de una carga de glucosa resultó en menor iAUC en comparación con la bebida control. La proteína del suero mantiene la glucemia postprandial más estable.

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Palabras clave: Metabolismo de glucosa. Diabetes mellitus tipo 2. Proteínas alimentarias. Alimentos y bebidas.

Abbreviations

- β: Beta.
BMI: Body mass index.
CCK: Cholecystokinin.
DPP-4: Dipeptidyl-peptidase 4.
FAO: Food and Agriculture Organization of United Nations.
GIP: Glucose-dependent insulintropic polypeptide.
GLP-1: Glucagon like peptide-1.
iAUC: Incremental area under the curve.
iG: Equation of incremental glycemia.
IPA: Peptide sequence Ile-Pro-Ala, called β-lactosin A.
T2DM: Type 2 diabetes mellitus.

Introduction

Diabetes mellitus is one of most worldwide epidemic morbidity. It affects 346 million of people in the world.¹ The key for type 2 diabetes (T2DM) prevention and management is glycemic control,² which in turn can prevent microvascular complications related to the disease.³ Beside that, great variabilities in pre and postprandial glycemia increase oxidative stress leading to deleterious effects on health.⁴ Therefore, it is recommended the consumption of foods capable to reduce great glycemic fluctuations.⁵

Protein present in foods can stimulate insulin secretion.⁶ However, not all protein types are capable to stimulate enough insulin secretion to decrease glycemic response.⁷ Proteins are constituted by amino acids and it has been shown that the serum level of isoleucine, leucine, valine and lysine have a strong correlation with insulinemic response.⁸ This effect has been linked to an increase in incretins release,⁸⁻¹¹ such as GIP (glucose-dependent insulintropic polypeptide) and GLP-1 (glucagon like peptide-1).^{9,10} In addition, the rate of protein digestion alters GIP levels, which is an insulintropic peptide.¹¹ Thereby, the effects of proteins on glycemia depends on its source, amino acids profile and digestion rate.¹²

Whey protein it is rapidly digested and contains high amounts of isoleucine, leucine, valine and lysine, which are potential modulators of glycemia.^{6,13-15} Apparently, whey protein exerts a greater effect on glycemia than do other protein derived from animal or plant sources.

Even though the effect of protein on immediate postprandial glycemia has been well investigated, its impact on glycemia after the consumption of a subsequent meal is not clear.⁶ Hence, the aim of the present study was assess the effect of the consumption of different types of protein (whey protein, soy protein and egg white) on a second meal postprandial glycaemia in normal weight and normoglycemic subjects.

Methods

Subjects

Eligibility criteria included normal body weight (Body Mass Index 18,5-24,9 kg/m²),¹⁶ and normal fasting glucose (glycemia: 70-99 mg/dL). Smokers, pregnant women, people with diabetes, impaired glucose, family history of diabetes and lactose malabsorption, besides the ones using drugs that affects metabolism were excluded from the study. Volunteers were recruited by advertising on university *campus*. During recruitment subjects filled out a form containing personal information, data related to inclusion criteria, life style, familiar and individual medical history. Sample size was calculated¹⁷ considering the incremental area under the curve of glycemic response¹⁴ (iAUC). A statistical power of 90% and an expected difference of 10% in the baseline values were adopted.

The protocol of the study was in agreement with Declaration of Helsinki and approved by the Human Ethical Committee in Scientific Research (protocol number 067/2012) of Universidade Federal de Viçosa, Brazil. All participants were informed about benefits of the study and signed the informed consent before testing began.

Protocol

This is a crossover study in which after a 12 h overnight fasting, subjects reported to the laboratory to participate of four experimental sessions in a random order. In each session, one of the protein drinks or the control drink was consumed within 15 minutes. There was a wash out period of at least one day between sessions. Thirty minutes after consuming one of the previously mentioned drinks, the subjects consumed a 25 g of anhydrous glucose solution and stayed in the laboratory for the next 2 hours for postprandial glycemic response assessment. At the end of experimental session all subjects received a standardized meal and then dismissed to do their daily activities. The experimental design of our study is illustrated in figure 1.

Anthropometric data and Body Composition Assessment

Height and weight were respectively measured¹⁶ using a stadiometer fixed to the wall (SECA 206®, graduation of 0.1 cm) and a platform digital scale (Toledo Brasil 2096PP®, graduation of 50 g). Body composition was assessed by skinfold thickness¹⁸ using a Lange skinfold caliper (accuracy of 0.1 cm). The sum of bicipital, tricipital, subscapular and suprailiac skinfolds was used to estimate body fat percentages.¹⁹

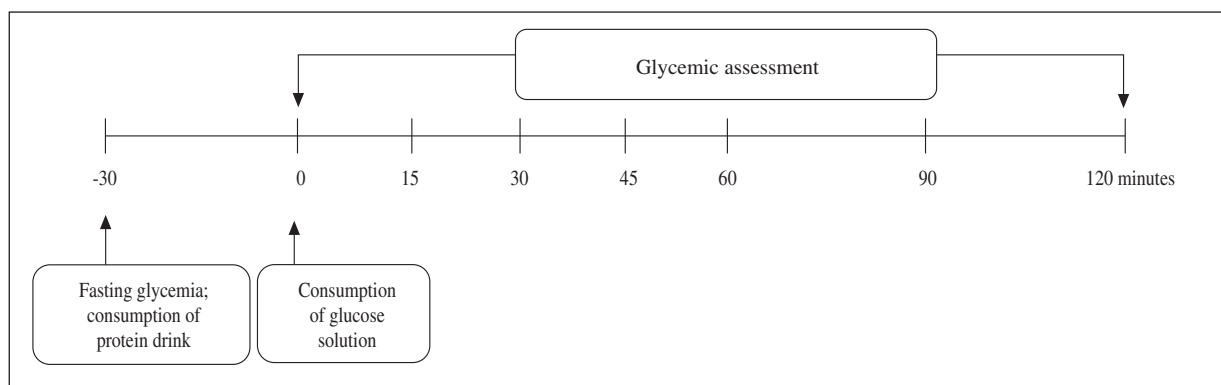


Fig. 1.—Experimental design of the study. After a 12 h overnight fasting subjects consumed the control or one of the protein drinks (whey protein, egg white or soy protein). Thirty minutes later subjects consumed a glucose solution (25 g of glucose). Finger-stick blood samples were collected in the fasting state (0 min), and 15, 30, 45, 60, 90, 120 min. after the start of glucose solution.

Table I
Energy content, macronutrient composition and amino acids profile of protein concentrates (100 g of product) tested in the study

	Whey protein	Egg white	Soy protein
Energy (kJ)	1,548.09	1,464.24	1,464.41
Carbohydrate (g)	3.0	9.37	0
Fat (g)	0.87	0	0
Protein (g)	88.5	78.12	90
<i>Amino acids profile (g/100 g)</i>			
Ala	5.3	4.6	4.2
Arg	2.2	4.4	8.0
Asp	11.9	8.2	12.1
Cys	2.7	2.1	1.4
Glu	18.9	1.0	20.4
Gly	1.7	2.8	4.2
His	2.1	1.8	2.7
Ile	7.2	4.5	4.3
Leu	11.2	6.8	7.8
Lys	8.8	5.4	6.5
Met	2.2	2.7	1.4
Phe	3.1	4.7	5.4
Pro	7.8	3.1	5.3
Ser	5.3	5.5	5.7
Thr	8.0	3.6	3.6
Trp	1.9	1.0	1.0
Tyr	3.2	3.1	4.1
Val	6.3	5.1	4.5

Test drinks

The test drinks were a glucose solution, control drink and three protein drinks. The glucose solution was prepared diluting 25 g of anhydrous glucose (Vetec/Rio de Janeiro) into 200 mL of spring water. Control drink was prepared blending 200 mL of spring water, 2 g of calories-free blackberry powder juice (Clight®). Protein drinks were prepared by adding one of the following protein concentrates (0.5 g·kg⁻¹ of subject body weight) to control drink: whey protein (Diacom®, Belo Horizonte), egg white (Nutryclin®, Viçosa) or soy pro-

tein (Nutrysoy®, Paraná). The nutritional composition of the drinks is presented in table I.

Postprandial glycemia assessment

Capillary finger-stick blood samples were taken in the fasting state (0 min) and at 15, 30, 45, 60, 90 and 120 min after the consumption of the glucose solution. Glucose levels were measured using a glucometer (One Touch Ultra II®, LifeScan Inc., Milpitas, CA). The incremental area under the glycemic response curve (iAUC) was calculated by the trapezoidal method²⁰ using the software SlideWrite 7.0®.

Glycemic response was also assessed by the mean incremental glycemia using the equation $iG = \Sigma \text{increment of postprandial glycemia (0-2 h)}/n$, in which n is the number of subjects.

Statistical analysis

Statistical analyses were conducted using SPSS 17 for Windows (SPSS, Inc., Chicago, IL, USA). Data are expressed as mean and standard error of mean (SEM). Data normality and homoscedasticity were assessed by Kolmogorov-Smirnov and Levene tests, respectively. One-Way ANOVA was used to assess significant differences in iAUC and iG. Two-Way Repeated Measures ANOVA was applied to verify the interaction of time and treatment factors, followed by post hoc comparisons using Tukey's tests when necessary. The criterion for statistical significance was $p < 0.05$ (α level of 5%). The association between iAUC and iG was assessed by Pearson's correlation.

Results

A total of ten subjects (4 men and 6 women), mean fasting glycemia 4.78 ± 0.05 mmol/L, BMI 22.0 ± 0.82 kg/m², and $25.6 \pm 1.86\%$ body fat participated in the study (table II).

Table II
Mean \pm SE characteristics presented by subjects
at baseline (n = 10)

	Means	SEM
Age (years)	24.9	0.58
Weight (kg)	61.35	3.05
Height (m)	1.7	0.02
BMI (kg/m ²)	22.0	0.82
Body fat (%)	25.6	1.86
Fasting Glucose (mmol/L)	4.78	0.05

BMI: Body Mass Index.

Fasting glycemia did not differ between study sessions ($p < 0.05$). There was an effect of time ($p < 0.001$) and treatments ($p < 0.004$), and an interaction of time and treatment ($p < 0.001$) in postprandial glycemia. Glycemia thirty minutes after the consumption of the protein drinks or the control drink (0 min) did not differ (fig. 2A). However, whey protein drink resulted in lower glycemic response compared with soy and egg white drinks at 15 minutes ($p = 0.007$). At 30 minutes, whey protein led to lower glycemic values than soy, control and egg white ($p = 0.001$) drinks. Lower glycemic values for whey protein was also observed at 45 minutes compared with control ($p < 0.001$) and egg white ($p = 0.02$) drinks. Whey and soy protein drinks resulted in lower glycemic response ($p = 0.02$ and $p = 0.001$, respectively) than the control, at 60 minutes. No differences were detected at times 90 and 120 minutes ($p > 0.05$) (fig. 2A). Whey protein resulted in a more stable response during the 120 min in which glycemia was assessed (fig. 2A).

Whey and soy protein drinks reduced postprandial iAUC in 56.5% ($p = 0.004$) and 44.4% ($p = 0.029$) respectively, compared with control. However, postprandial iAUC did not differ between the protein drinks (whey, soy and egg white) ($p > 0.05$) (fig. 2B).

There was a positive correlation between the glycemic response assessed by the iG equation and by the iAUC (0.985, $p < 0.05$). Furthermore, whey (3.97 mmol/L) and soy (5.52 mmol/L) proteins mean incremental glycemia were significant lower ($p < 0.04$) than the ones obtained for egg white (5.89 mmol/L) and control (9.85 mmol/L).

Discussion

Glycemic control is the main objectives of nutritional intervention in diabetics and pre diabetics. Therefore, glycemia should be as close as possible to normal levels to avoid the manifestation of diabetes in predisposed subjects and the development of comorbidities related to T2DM.²¹ Thus, it has been recommended the adoption of therapeutic strategies capable to prevent the occurrence of glycemic peaks.⁵

In the present study, the protein drinks and control drink was consumed 30 minutes before assessing the glycemic response to the glucose solution. This procedure is necessary to ensure that the observed response reflects the production and release of insulin stimulated by protein load.¹⁰ Monitoring glycemic response in shorter time period (less than 30 minutes) would reflect the effect of stimulus of previous meal, not of the protein load.²²

The impact of consuming 50 g of protein (whey protein, tuna, turkey or egg white) for 12 weeks 30 minutes before two daily main meals on postprandial glycemia and insulinemia was assessed in 22 healthy men.¹⁵ Whey protein decreased iAUC compared to turkey and egg white, and increased insulinemic response compared with all the other protein tested.¹⁵ It has been proposed that the reduction of glycemia is due to increase of insulin releasing and of incretins production and also a reduction in gastric emptying rate.^{6,7,12,14}

Amino acids exert different stimulus on postprandial insulinemia.^{23,24} Leucine, isoleucine, lysine and valine are in high concentrations in whey protein. Due to their insulinotropic properties, these amino acids can increase insulinic release and sensitivity, contributing to reduce glycemic response.²⁴ We observed that whey protein has approximately 62% more of those amino acids than soy protein and egg white, and may have favored our results. However, in our study, we did not monitor the postprandial insulinemic responses.

The stimulus for insulin release mediated by whey protein is complex. Its mechanisms may reflect a synergistic effect of amino acids (such leucine, isoleucine, lysine and valine and threonine) and also the activation of incretins (ex: GIP) effect on pancreatic β -cells.^{12,25}

It has been proposed that whey protein stimulates incretins release due to the presence of Ile-Pro-Ala a peptide sequence, called β -lactosin A, identified from hydrolyzed of β -lactoglobulin²⁶. The results of studies have shown the inhibitory role of IPA over dipeptidyl-peptidase 4 (DPP-4) activity, an enzyme responsible of GIP and GLP-1 degradation, extending the half-life of these incretins in the bloodstream.^{8,26} Moreover, GIP level in the blood could increase concomitantly with an increase in insulin levels, after consuming meals containing whey protein.^{7,8,12} Whey protein intake can slow gastric emptying rate, reducing glycemic response of the next meals. This effect increases the postprandial release of cholecystokinin (CCK), GLP-1 and GIP¹².

The mean incremental glycemia (iG) we used showed to be a good method to assess the glycemic response because it presented a good correlation with the traditional method recommended by FAO.²⁰ The assessment of the effect of each protein shake on glycemia by iG was easier and faster than the traditional methodology and it does not require the use of specific software.

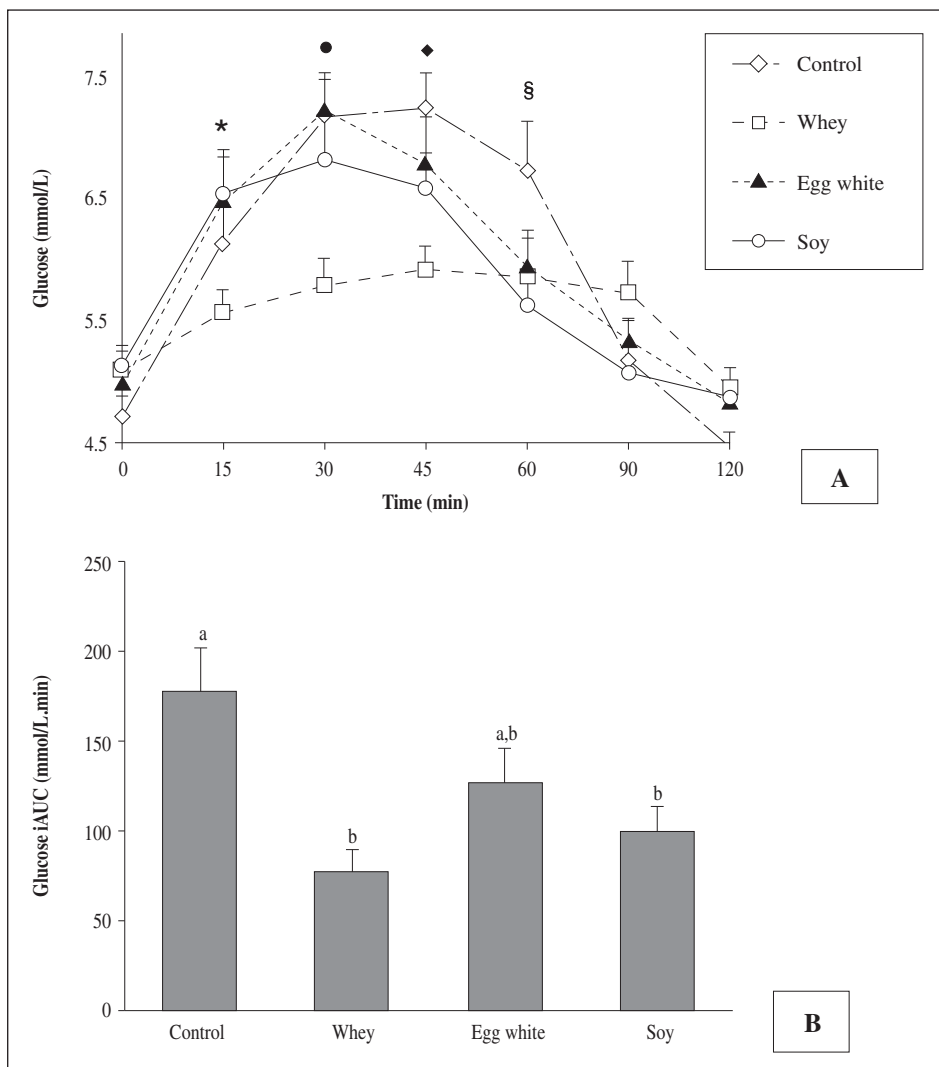


Fig. 2.—Mean \pm SE postprandial glucose response (0-120 min.) (A), and postprandial incremental area under the glycemic response curve (iAUC) (0-120 min.) (B) in response to the consumption of control and of three different types of protein drinks (whey protein, egg white and soy). *Whey protein drink mean values are significantly lower ($p = 0.007$) than the ones obtained for egg white and soy protein drink. •Whey protein drink mean values are significantly lower ($p = 0.001$) than control, egg white and soy. •Whey protein drink mean values are significantly lower ($p \leq 0.02$) than control and egg white protein drinks. §Soy and whey protein drink mean values are significantly lower than control ($p = 0.001$ and $p = 0.02$, respectively) (A). Bars followed by different letters differ significantly from each other (B).

Conclusion

The consumption of whey and soy protein 30 minutes before a glucose load resulted in lower iAUC compared with control drink. Furthermore, whey protein maintained postprandial glycemia more constant. The effects of whey protein chronic consumption on T2DM prevention and management of T2DM should be assessed in long-term feeding trials.

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Original / *Nutrición enteral*

A safe “cut, tie and thread-pull” method for percutaneous endoscopic gastrostomy tube removal in children with congenital craniofacial anomalies and pharyngeal stenosis

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Abstract

Percutaneous endoscopic gastrostomy (PEG) is a widely used method for tube feeding with enteral nutrition. Both PEG's insertion and PEG's removal are usually easy and uncomplicated. The latter can be, however, of substantial difficulty in children with distorted anatomy, such as pharyngeal stenosis or endured craniofacial trauma, when regular endoscopy is contraindicated. The aim of the study was to assess the very simple, but rarely used method for percutaneous removal of the tube by pulling the thread. Four children (4 males, mean age 4.1 year) were analyzed. In all of them the procedure was successful, quick and uncomplicated. To conclude, the thread method should be recommend in case the endoscopic removal is impossible.

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Keywords: PEG. Pull technique. Craniofacial anomalies.

UN MÉTODO SEGURO PARA “CORTAR, ATAR Y TIRAR DEL HILO” PARA RETIRADA DE SONDA MEDIANTE GASTROSTOMÍA ENDOSCÓPICA PERCUTÁNEA EN NIÑOS CON ANOMALÍAS CRANEOFACIALES Y ESTENOSIS FARÍNGEA CONGÉNITAS

Resumen

La gastrostomía endoscópica percutánea (GEP) es un método muy utilizado para alimentación por sonda con nutrición enteral. Habitualmente tanto la inserción como la retirada de la sonda mediante GEP es fácil y sin complicaciones. Sin embargo, la segunda puede ser sustancialmente difícil en niños con una anatomía alterada como la estenosis faríngea o que haya sufrido un traumatismo craneofacial, en donde la endoscopia rutinaria está contraindicada. El propósito de este estudio fue evaluar un método muy sencillo pero rara vez usado como es la retirada percutánea de la sonda con el hilo. Se analizaron 4 niños (4 varones, edad media 4,1 años). En todos ellos el procedimiento fue exitoso, rápido y sin complicaciones. Para concluir, el método del hilo debería recomendarse en el caso de que la retirada endoscópica no sea posible.

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Palabras clave: GEP. Técnica de tirar. Anomalías craneofaciales.

Introduction

Percutaneous endoscopic gastrostomy (PEG) is a widely used method for insertion of a gastrostomy tube in patients who are unable to swallow and who require the administration of enteral nutrition.¹ The procedure is safe, the incidence of complications related to PEG

and further enteral nutrition is low, while the surgical gastrostomy is usually associated with a higher rate of complications.^{1,2}

The PEG's removal represent rarely discussed procedure as it poses no difficulties in most of patients. It can be, however, of substantial difficulty in children with distorted anatomy, such as pharyngeal stenosis or endured craniofacial trauma, when regular endoscopy is contraindicated.

In those patients, the surgical procedure under general anesthesia is usually required, which increases the risk and number of possible complications. It would be useful to develop a new method, less invasive and safer.

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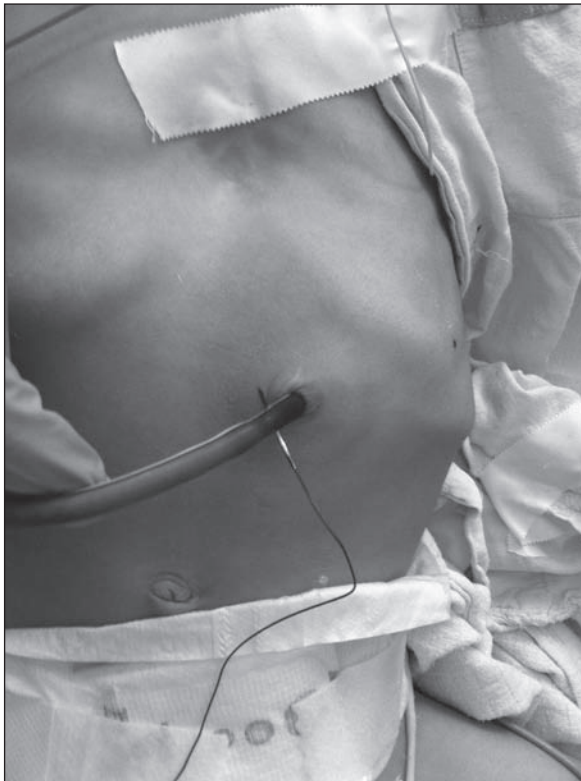


Fig. 1.—Placement of the thread through the stump.

The aim of the study was to assess the very simple, but rarely used method, which was the percutaneous removal with the thread.

Method

Four children (4 males, mean age 4.1 year) were analyzed. The indication was the tube blockage and unsuccessful provision of nutrients. The underlying diseases were as follow: Pierre-Robin syndrome in one, malformation syndrome in three of them.

PEG removal's necessity was due to the inability to infuse feeding solution through the tube-blockage (n = 2) and peritubular leakage (n = 2). In one patient in addition to aforementioned symptoms inability to push in and rotate the tube was noticed - the buried bumper syndrome was diagnosed. Mean time before tube removal was 8 months (range 5-21 months). PEG devices were 10 Ch to 16 Ch.

In all cases it was impossible to insert a regular endoscope with a channel for the loop, it was only possible to insert an infant tool with a probe channel. Mean number of preceding endoscopic attempts was 2/child.

Informed consent was obtained in all patients. The method was approved by a local ethical committee.

The PEG removal procedure was performed under general anesthesia. The prophylactic antibiotic



Fig. 2.—Cutting off the PEG.

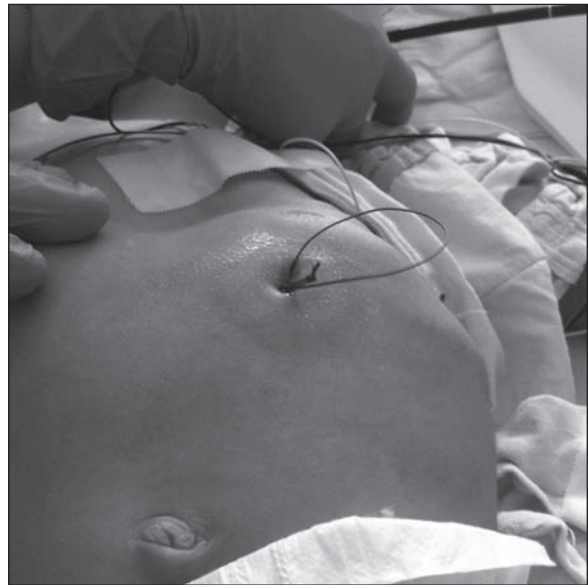


Fig. 3.—PEG's insertion in the stomach.

shot was administered. At first the cutting needle was passed through the external end of the PEG tube, and the integrity of the tube was checked with a traction. The PEG tube was cut approximately 2,5 cm above skin level, and a needle was passed 1 cm over the skin through the PEG tube and tied afterwards (figs. 1, 2). The distal end of the thick, nonabsorbable suture was inserted into the stomach along with the shortened PEG stump (fig. 3). The thread was then grabbed with an endoscopic forceps inside the stomach after lubrication with gel (fig. 4). The thread and the endoscope was brought out through the mouth. The surgeon was able to remove shortened PEG stump orally by pulling the thread (figs. 5, 6). In one case PEG stump was blocked in the proximal pharynx, and Magill's forceps were used to extract it.

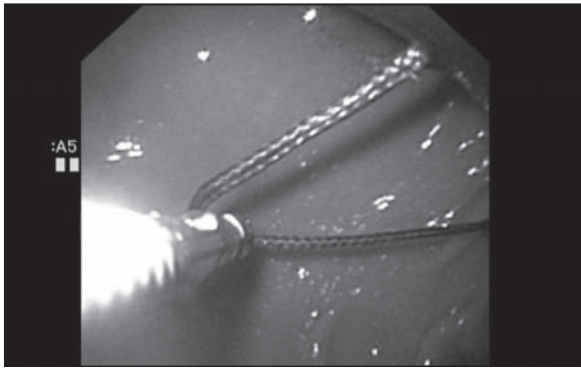


Fig. 4.—Intraluminal view.



Fig. 5.—Insertion of the endoscope.

Results

In all of four patients the procedure was successful. There were not any postoperative complications. Mean duration of the procedure was 6.6 minutes (range: 4.5-11.2 min.)

After the removal, the enteral feeding via nasogastric tube was performed for 4-5 weeks and another PEG was reinserted subsequently.

Discussion

Several methods of PEG removal are described in the literature, e.g. the “cut-and-push” technique for PEG removal was described in 1991. The “cut-and-push” technique is cutting the tube at the skin level and allowing the tube and internal flange to pass spontaneously.⁹ This technique is used in patients who are thought to have no risk of distal adhesions or strictures – so patients with previous abdominal surgery should be excluded for this type of PEG removal.^{9,10} Still the

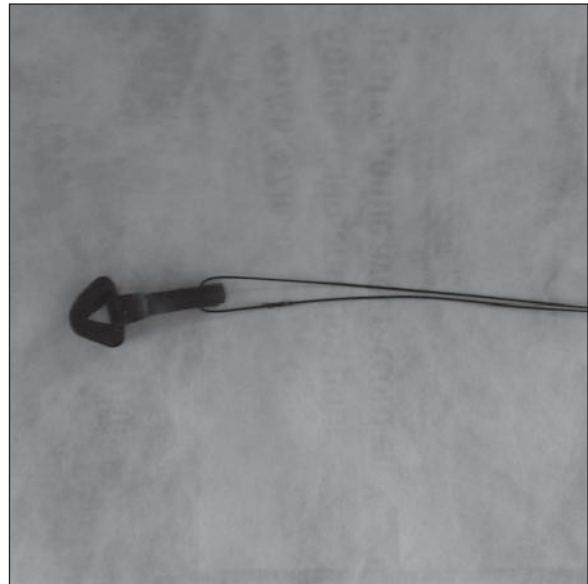


Fig. 6.—Removed PEG's stump.

remnant can become blocked in the bowel, and result in perforation and even a death of the patient.^{9,10,11} The PEG flange may be retrieved endoscopically but this may become technically challenging in children with pharyngeal stenosis, for example with Pierre-Robin Syndrome, with innate craniofacial anomalies, gothic palate or acquired pharyngeal stenosis e.g. after trauma, as was the case in our patients. External traction causes tissue disruption, the patients do not tolerate the procedure well, and retrieval of the PEG is often unsuccessful. The grasp with endoscopic forceps is often not so assured and the cut PEG fragment can be blocked in the esophagus.

In case the infusion of feeding solution via the tube due to its blockage and peritubular leakage, there are indications for the PEG removal. When aforementioned symptoms are accompanied by the inability to push in and out and to rotate the tube and abdominal pain - buried bumper syndrome should be considered.⁵ Klein et al first described the latter in 1990.¹² Usually patient is referred for emergency endoscopy or surgical removal of the bumper. In some cases removing the PEG tube is achievable by external traction, without an abdominal incision, especially in cases in whom retrieval-type PEG tubes have been used.¹³ The only migrated bumper we had was removed using an open surgical technique (minilaparotomy) after the endoscopic attempt of the retrieval failed, and a new tube was placed. Although some authors advocate leaving the internal bumper in situ as a relatively safe treatment option,¹⁴ it is in our opinion risky, because it may result in serious complications including gastrointestinal bleeding, perforation of the stomach, peritonitis and death.¹⁵

To conclude, it should be emphasized that the cut, tie and pull method is safe and quick and not technically challenging in children with congenital or acquired

pharyngeal stenosis. It can reduce the mean time of the PEG tube removal and moreover can be performed by a single endoscopist.

Statement of authorship

All authors state that they have made substantial contributions to the study and that they give their approval to the final version of the manuscript.

Acknowledgements

Adam Hermanowicz was a main researcher and the coordinator of the study. He was responsible for the conception and contributed to the experimental design, data interpretation and writing of the manuscript. All authors contributed to the data collection and writing of the manuscript. Stanislaw Klek critically revised the intellectual content of the study and contributed to its creation.

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Original / *Nutrición enteral*

Enteral nutrition in critical patients; should the administration be continuous or intermittent?

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Abstract

Enteral nutrition therapy (ENT) is an essential part in the management of critically ill patients, having a significant impact on these patients' clinical results. It can be administered on a continuous or intermittent basis using an infusion pump. There is a discussion on which of these techniques has the best performance, involving a number of factors such as nausea, diarrhea, and particularly the relationship between diet volume and the ratio of programmed calories to calories effectively supplied to the critical patients.

Objectives: To compare the forms of continuous or intermittent infusion of enteral nutrition, using as primary outcome the level of estimated caloric needs daily supplied.

Methods: Observational prospective randomized clinical study carried out in an intensive care unit on 41 patients divided into two groups, of intermittent (ENT during 18 hours with a 6-hour nocturnal pause), or continuous (ENT during 24 hours continuously) administration. The secondary outcome variables measured in this study were bowel evacuation, distension, emesis, with the primary outcome variable being the relationship between infusion volume and the estimated-to-supplied ratio of caloric needs. The rejection index of the null hypothesis was established at 5% for all the tests.

Results: Most of the patients received more than 60% infusion of enteral diet over the 5 days of study ($p = 1,0$), with no difference regarding the provision of caloric needs. No statistically significant difference between groups was found in the variables vomiting, abdominal distension or diarrhea.

Conclusion: The administration modalities of continuous or intermittent enteral nutrition are similar in which regards the comparison of the variables included in this study.

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NUTRICIÓN ENTERAL EN PACIENTES CRÍTICOS; ¿SU ADMINISTRACIÓN DEBERÍA SER CONTINUA O INTERMITENTE?

Resumen

La terapia con nutrición enteral (TNE), una parte esencial del manejo de los pacientes críticos, tiene un impacto significativo en los resultados clínicos de estos pacientes. La TNE puede administrarse de forma continua o intermitente utilizando una bomba de infusión. Existe una discusión sobre cuál de estas dos técnicas tiene un mejor rendimiento, lo que implica una serie de factores como náuseas, diarrea y especialmente la relación entre el volumen de la dieta y la proporción entre calorías que se programan y las que realmente se proporcionan efectivamente a los pacientes críticos.

Objetivos: Comparar las formas continua e intermitente de infusión de nutrición enteral, utilizando un nivel de necesidades calóricas estimadas suministradas diariamente como resultado principal.

Métodos: Estudio clínico prospectivo y observacional, de distribución aleatoria, de 41 pacientes en una unidad de cuidados intensivos (UCI), divididos en dos grupos, intermitente (TNE durante 18 horas con una pausa nocturna de 6 horas) o continua (TNE durante 24 horas de forma continua). Evaluamos como variables secundarias de resultados la evacuación, distensión, emesis y como variable principal de resultado la relación entre el volumen de infusión y el cociente entre necesidades calóricas estimadas a suministradas. Se estableció el índice de rechazo de la hipótesis nula en el 5% para todos los tests.

Resultados: La mayoría de los pacientes recibieron > 60% de la infusión de la dieta enteral a lo largo de los 5 días del estudio ($p = 1,0$), sin observarse diferencias en la provisión de las necesidades calóricas. No se observaron diferencias estadísticamente significativas entre los grupos con respecto a las variables vómitos, distensión abdominal o diarrea.

Conclusión: Las modalidades intermitente o continua de administración de la nutrición enteral son similares en lo que respecta a la comparación de las variables de este estudio.

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Palabras clave: *Nutrición enteral. Administración continua e intermitente.*

Introduction

Nutrition therapy is essential among the health care practices for critically ill patients. It is an adjuvant therapy which main objective is to attenuate the development of malnourishment.¹ Its efficiency depends on a number of factors, such as metabolic status of the patient and his/her response and behavior during the treatment.

Enteral nutrition therapy (ENT) has presented good results for a critically ill patient, therefore this is generally preferred to a total parenteral nutrition whenever the patient's gastrointestinal tract allows for it.² The use of enteral nutritional support is linked to reduced infective complications, maintenance of intestinal mucosal barrier integrity, and reduced bacterial translocation.¹

However, the clinical behavior of this group of patients may interfere with ENT, thus affecting its administration and, as a consequence, its efficiency. This clinical characteristic may be directly linked to severity of the disease or to its treatment, with the requirement for sedatives, mechanical ventilation and therapy with antibiotics or vasoactive drugs.

The clinical manifestations of these alterations generally occur through the presence of intercurrent disorders such as abdominal distension, vomiting, and diarrhea.^{3,4} Pulmonary infection caused by bronchial aspiration due to the increased volume of gastric residue between feeding steps, which has high morbidity and mortality, is one of the most feared complications.^{5,6} Such complications may interfere with one of the basic concepts of the objective of this therapy, which is to supply calories to the patient; additionally, they may determine a decrease in the total caloric infusion goal prescribed to the patient.

Therefore, the modality of ENT infusion, either continuous or intermittent, may influence such complications.

However, few studies can be found in the literature with conclusive results on this subject, mainly in critical patients. The purpose of this study is to compare two methods of ENT infusion (continuous or intermittent), and the way in which they can contribute toward complications which impair the efficacy of the therapy.

Methods

Observational, prospective, randomized clinical study, carried out on patients under clinical treatment, over 18 years of age, of both genders, candidates to receive enteral nutrition therapy exclusively. The nasoenteral feeding tube was placed in gastric location and data were collected during the first five days in hospital. Patients with diabetes, hypothyroidism or any surgery in the upper gastrointestinal tract were excluded. The project was approved by the Research Ethical Committee of Julio Muller University Hospital (CEP 637/09).

On admission to the ICU, patients were randomly assigned to Group I-intermittent (ENT for 18 hours, with one 6-hour nocturnal pause), or Group II-continuous (ENT for 24 hours uninterruptedly). In both groups enteral nutrition therapy was delivered through an infusion pump.

In addition, on admission to the ICU patients had their nutritional status assessed using the Global Subjective Evaluation-GSE; severity of their condition and metabolic stress was assessed using APACHE II (acute physiology and chronic health evaluation) score (< 10 indicates mild disease). Caloric and protein needs were estimated by the following rules: a) 25-30 calories/kg of body weight, and b) 1.5 g of protein/kg of body weight. The estimated caloric needs were gradually delivered during the first three days of hospital stay (30%, 60% and 100%, respectively). A commercially available processed enteral formula (Peptamen®), nutritionally complete, was used for both groups, containing 100% whey protein, with 1.5 cal/ml caloric density.

Patients underwent bedside gastric residue volume assessment by manual aspiration performed before installation of any new step of enteral diet. The cutpoint level of 250 ml was established to continue or suspend ENT administration, which is in agreement with the protocol followed in our medical service.

The level of caloric needs was determined by observing the quantity of ENT infusion collected by the nursery report and annotations made on the fluid balance form, continuously monitored during 24 hours. Inherent complications due to the use of ENT were also monitored, with the following study variables being chosen: incidence of diarrhea, bowel constipation, distension and vomit.

Sample calculation was based on the variable gastric residue; considering an 80% beta error (type II) the sufficient number of patients was calculated to be 16. The Chi-square and Fisher's Exact tests were used to compare categorical data and to test the association between independent variables. Student's *t* or Mann Whitney's tests were used to compare two continuous variables. Comparison between variables was made using Relative Risk (RR) with a 95% Confidence Interval. The rejection index of the null hypothesis was established at 0.05 or 5% ($\alpha = 5\%$).

Results

After randomization 41 patients were included in the study, 18 (44%) in Group I (intermittent) and 23 (56%) in Group II (continuous).

Demographics and clinical data are displayed in table I, where no difference between the groups could be identified.

The percentage of nutritional intake received along the study days was described. During the five study days it could be noticed that 17 patients (74%) in

Table I
Demographics and clinical data of the study sample

Variable	G1 (18 h)		G2 (24 h)		p
	Mean	SD	Mean	SD	
Estimated weight (kg)	70.2	± 15.2	60.5	± 14.7	0.08*
Height (cm)	1.7	± 0.2	1.6	± 0.1	0.66*
Age (years)	68.9	± 19.4	61.3	± 20.8	0.23*
BMI (kg/m ²)	24.6	± 5.0	22.3	± 4.3	0.13*
Gender (M/F)					0.76**
Male	10		14		
Female	08		09		
ASG (n%)					0.59***
A	01 (06)		03 (13)		
B	11 (61)		11 (48)		
C	06 (33)		09 (39)		
Apache	20.7	4.95	22.4	6.05	0.33****

*Student t – Data as mean + SD.

**Fisher's Exact Test.

***Chi-square Test.

****Mann Whitney's Test.

ASG Avaliação Subjetiva Global.

Table II
Achievement of caloric needs along the study days

Day when CN* was achieved	G1 (18 h)			G2 (24 h)			p**
	Freq	%	% Acum	Freq	%	% Acum	
Did not achieve	08	44	–	06	26	–	–
Day in-hospital		0	0	01	04	04	1.00
First day	01	06	06	01	04	09	1.00
Second day	04	22	28	07	30	39	0.52
Third day	03	17	44	06	26	65	0.22
Fourth day		0	44	01	04	70	0.12
Fifth day	02	11	56	01	04	74	0.32
Overall total	18	100	–	23	100	–	–

*CN: Caloric needs.

**Fisher's Exact Test.

Group II, but only 10 patients (56%) in Group I received adequate caloric intake. Although the needs in Group II were achieved more quickly and in a higher percentage, no statistically significant difference could be found in this study ($p = 0.32$), as shown in table II.

Complementing table II, figure 1 demonstrates the gradual increase of ENT acceptance as length of hospital stay advanced.

The study patients were evaluated according to the complications they showed along the days of data collection. Table III displays the results obtained after exploring the variables bowel evacuation, distension, and emesis. Both groups were similar in this regard, with no statistically significant difference ($p < 0.05$ for the three items above described).

At the end of data collection only 3 (7%) patients died, and 38 (93%) patients who remained in the study until the fifth day were considered as being discharged from the project. There was no significant difference between the two groups ($p = 0.57$).

Discussion

A mandatory discussion when using ENT relates to what administration method is chosen, whether intermittent or continuous.

A global analysis of our data demonstrated that both study groups had similar results, with no significant differences relating to the method of ENT administration to the critical patients.

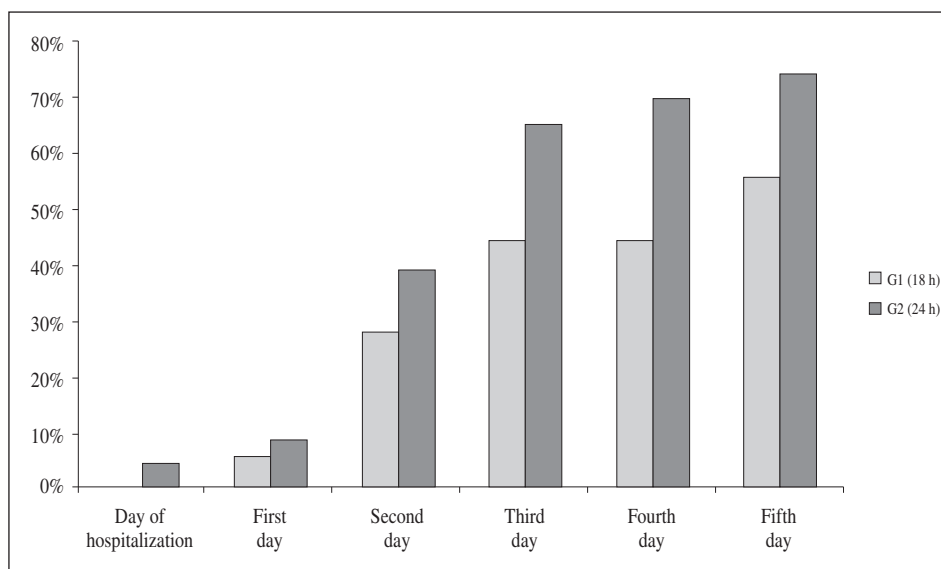


Fig. 1.—Days of hospitalization to achieve the caloric needs.

Evacuation	G1 (18 h)	G2 (24 h)	<i>p</i>
Normal	10 (56%)	10 (44%)	
Diarrhea	05 (28%)	06 (26%)	0.57*
Constipated	03 (17%)	07 (30%)	
Distension			
No	06 (33%)	09 (39%)	
Yes	12 (67%)	14 (61%)	0.70*
Emesis			
No	14 (78%)	16 (70%)	
Yes	04 (22%)	07 (30%)	0.72**

*Chi-square Test.
**Fisher's Exact Test.

Intermittent infusion resembles more the usual, regular feeding process, which follows the physiological cycles. Interruption of the administration is programmed, thus allowing for a temporary rest from the nutrition therapy of the patient.

Continuous infusion has the typical feature of providing a constant and slow flow, as required by patients who do not tolerate any type of more rapid or voluminous infusion.⁵

In this study we consider that the regularity of infusion was maintained in both forms of administration by programming the pump drip, the only difference laying in the planned drip interruption in the intermittent form.

After determining the amount of caloric needs, we observed during the five days of the study that neither group achieved the supply of total estimated caloric needs, according to table II.

Patients in Group II achieved the prescribed caloric needs more rapidly, especially during the first 48 to 72

hours. This difference was maintained until the fifth day, yet no statistically significant difference was seen in the comparison with Group I. A study showing results similar to ours found that a high percentage of critical patients received less than 50% of the initially prescribed caloric needs during the first days of ENT.⁶

A study conducted at the Julio Muller University Hospital of UFMT involving critical patients in the intensive care unit showed that 75.6% of patients using ENT took up to six days to fulfill their nutritional needs.⁷ Their data are similar to the ones in this study. It is worth noticing that an early achievement of the programmed target of nutritional needs in fact interferes positively with the critical patient's treatment.

Both methods presented advantages and disadvantages, since the differences they showed may interfere with several physiological processes, consequently with clinical processes as well.

As an example of such advantages, Vanessa Fujino et al.⁸ suggest, in a revision of the literature, that a nocturnal interruption of six hours should be programmed aiming to reduce the intragastric bacterial population. During the nocturnal pause the gastric pH that was not blocked by the diet falls down to a bactericidal level in the stomach, thus decreasing the gastrointestinal tract bacterial population. This in turn will favor the decrease in levels of nosocomial pneumonia due to bacterial increase.

The variables we chose to represent complications of using ENT in the study patients are often commented in studies about this subject.^{3,4,9} One of the most discussed complications in this setting is the presence of diarrhea, which often may become a factor to determine suspension of ENT in critical patients.

In a prospective study comparing the continuous and intermittent methods of infusion, a higher incidence of diarrhea, tube displacement and aspiration pneumonia was evidenced by the intermittent method

of administration without the use of infusion pump. In the group receiving continuous ENT there was greater occurrence of pump obstruction, however they had as advantage a higher percentage of infusion of the daily prescribed diet.⁹

Ciocon et al.¹⁰ showed results where diarrhea was significantly more frequent in the intermittent than in the continuous group.

In our study the variables diarrhea and constipation were equally frequent in both groups. After analyzing the variables, no statistically significant difference was found, thus asserting the groups parity.

Decrease in the incidence of this complication in the ICU is considered a positive aspect, in addition to the fact that in both surveys it was not a cause for interruption of ENT administration.^{3,9-11} It may be associated to medications or infections rather than ENT. Additionally, diarrhea may adversely affect absorption of nutrients and the nutritional status itself. These factors lead to additional stress for the patient and to increased healthcare costs.^{3,12}

Whenever the patient presents with diarrhea, ENT administration modality in critical patients is also a very important point, which should be analyzed along with the type of formula employed. Evidence exists that the continuous use through infusion pump is a strong ally in the treatment of diarrhea, since a decrease to small doses of the volume infused may enhance the patient's tolerance to the enteral formula.^{5,9}

In relation to the variable constipation, although the comparison of the groups yielded no significant difference in our results, there is still controversy in the literature on constipation in critical patients, so that no specific definitions are available on this matter. Some studies suggest that there is an association between the critical status of a patient, who usually takes many drugs, and the incidence of bowel constipation.¹²⁻¹⁴

The variables abdominal distension and emesis were evaluated as well, however results were equivoque between the two groups, showing no statistically significant difference.

Even if we consider the difficulties of collecting data in critical patients, some remarks must be made to our study. The reduced number of study days made it impossible to evaluate the patients over longer periods, which might likely yield different results.

Based on the present results, besides a mere adoption of ENT administration protocols for critical patients, we believe we can give a contribution to the clinical practices followed nowadays in the ICU. The scientific demonstration that no difference exists in results of using continuous or intermittent administra-

tion enables us to choose more freely which ENT form of delivery will best fit the clinical status of the patient and the procedures adopted at any given moment regarding its *propaedeutics* and therapeutic options.

Therefore, if needed, we can decide to submit the patient to a programmed pause in his diet (intermittent infusion). During this period a number of activities can be scheduled which interfere with the infusion, especially for the ICU routine procedures, with no damage to the enteral nutrition therapy.

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Original / *Nutrición enteral*

Physicochemical and nutritional characteristics of handmade enteral diets

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Abstract

Introduction: There is an increasing use of enteral therapy at home, which reduces costs and improves patients' quality of life. Homemade food diets are being commonly used in the households of undeveloped countries, but those diets vary in composition and characteristics depending on the ingredients and preparation procedures adopted in its preparation, which influences the quality of the diet to satisfy the nutritional needs of patients.

Objective: This study aimed to formulate and determine the quality of homemade enteral diets.

Methods: An enteral diet plan was prepared by using conventional food, consisting of 6 meals, totalizing 2 liters per day, and it was adopted a proportion of 25% of solid food. The diets were analyzed for stability, viscosity, flow, pH, chemical and nutritional composition.

Results and discussion: The enteral diet plan was adequate in its physical-chemical aspects, however, it presented low percentages of adequacy, 20-53%, between the estimated and real content of macronutrients in the soup, formula used for lunch and dinner, which impaired the nutritional quality of the enteral diet plan.

Conclusions: The results showed the difficulty of establishing the nutritional content of these diets, especially when made of meat and vegetables. Therefore, it is suggested a mixed enteral therapy by using commercial diets to achieve part of the nutritional needs of the patient together with enteral diets of homemade food to supplement it and also to redeem the psychosocial values of the feeding process.

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Keywords: *Enteral nutrition. Enteral formula. Food quality. Food analysis.*

CARACTERÍSTICAS FÍSICO-QUÍMICAS Y NUTRICIONALES DE LAS DIETAS ENTERALES CASERAS

Resumen

Introducción: Existe un creciente uso de la terapia enteral domiciliar, lo que reduce los costes y mejora la calidad de vida para los pacientes. Las dietas elaboradas con alimentos caseros están siendo usadas comúnmente en los domicilios de los países subdesarrollados, pero estos varían en composición y características dependiendo de los ingredientes y procedimientos adoptados en su preparación, lo que influye la calidad de estas dietas para satisfacer las necesidades nutricionales de los pacientes.

Objetivo: Desarrollar y determinar la calidad de las dietas enterales caseras.

Métodos: Se elaboró un plan de dieta enteral casera, con alimentos naturales, consistente en 6 comidas, con un total de 2 litros por día, utilizando una proporción de 25% de sólidos. Las dietas se analizaron para determinar la estabilidad de su composición, viscosidad, flujo, pH, composición química y nutricional.

Resultados y discusión: Las dietas eran adecuadas en sus aspectos físico-químicos, sin embargo, presentaron bajos porcentajes de adecuación, 20 a 53%, entre el contenido estimado y real de macronutrientes en la sopa, fórmula usada en el almuerzo y la cena, que afectó a la calidad nutricional del plan de dieta enteral.

Conclusiones: Los resultados muestran las dificultades de establecer el contenido nutricional de estas dietas, sobre todo cuando son a base de carne y verduras. Por lo tanto, se sugiere una mezcla de terapia enteral casera e industrial, mediante el uso de dietas comerciales para lograr parte de las necesidades nutricionales del paciente, junto con dietas caseras para complementar y compensar también los valores psicosociales del proceso de alimentación.

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Introduction

The enteral nutritional therapy aims to maintain or restore the nutritional status of individuals who fail to maintain a sufficient oral intake, although having a gastrointestinal tract fully or partially functioning. Its administration is related to the reduction of infectious complications and maintenance of the integrity of intestinal flora.^{1,2} Lesions of jaw and central nervous system, anorexia, cancer, and hypermetabolic conditions such as burns and severe infections are examples for nutrition enteral indication.^{1,3}

As feeding is not exclusively related to the physiological aspects, but also to psychosocial needs, enteral nutrition, likewise, is surrounded by symbolisms. For patients on enteral feeding, food may lose its social aspect, as family integration and expression of affection, which is intensified in hospitalization.⁴ The practice of home enteral therapy, which is increasing in several countries,^{2,5,1} tends to rescue the psychosocial values of food, making possible a family life for the patient, in addition to prevent contamination and reduce hospital costs for the health system in general.^{3,4,5}

There are several industrialized enteral diets in the market, chemically defined in labels, safely storage during reasonable time.^{6,7,8} Such diets also have the advantage of reduced need for handling, which helps to preserve a higher hygienic quality, due to its process of production and packaging, as well as reduces the risk of complications from diet contamination itself.^{3,9} However, the industrialized formulas are expensive, so their continued use is basically impractical for low-income families and even by health institutions with reduced budget.^{3,9} This leads to the use of enteral food made formulas, also known as non-industrial or handmade diet prepared with food, mixed or not with industrial products and nutrient modules.^{10,11}

In North America and Europe the prevalence use of industrialized enteral diets is common.^{1,5,12} But in underdeveloped or developing countries, like Brazil, there has been a considerable prevalence on handmade diets in home therapy, and even in hospitals located in the poorest regions such as the Valle Jequitinhonha.^{3,9,13} The quality aspects that influence the effectiveness of treatment, such as pH, fluidity, stability and nutritional composition of handmade diets may vary depending on the ingredients that are used and the procedures which are adopted in its preparation and storage process.^{8,11,14} Another factor that limitates the quality of these diets is the indirect estimation of its nutritional composition, based on food composition tables, which also show great variability and scarcity of data.^{11,15} Besides, there is still little knowledge about the actual loss of nutrients during the preparation of handmade enteral diets, which also turns its nutritional quality questionable.^{13,14}

The Human Rights to Adequate Food is recognized in various international standards, such as in article 25 of the Universal Declaration of Human Rights and article 11 of the International Covenant on Economic,

Social and Cultural Rights.^{16,17} Since 2003 there have been many achievements towards the institutionalization of this right by Latin America countries, the Caribbean, including Argentina, Brazil, Guatemala, Ecuador and Venezuela, which has already established Food Safety Laws, based in the Human Rights to Adequate Food warranty.^{16,17} Nevertheless, individuals in enteral therapy with low purchasing power still have not guaranteed any access, availability or adequacy in this diet.^{8,9} For the use of enteral diets made of food is necessary to monitor their nutritional content, as well as their physical and chemical characteristics because of the direct influence they have on its fluidity, which is a determining factor for a correct passage through the catheter.^{11,18,19} Several studies have shown that handmade diets have reached ideals physicochemical parameters, however, most of the time, its nutritional quality was based only on the estimated calculation from food composition tables.^{3,7,20,21,22}

To provide subsidies that assist the prescriptions for handmade enteral formulas, in order to ensure food and nutritional safety for patients on enteral therapy, the present study aimed to formulate and determine the characteristics of physicochemical and nutritional quality of homemade enteral diets.

Methods

Raw material

To elaborate these enteral diets low-cost food was chosen: beef (lean meat with no fat or aponeurosis), carrot, soybean oil (Liza[®]), iodized salt (Swan[®]), maltodextrin (Lowçucar[®]), whole milk (Lide[®]), Mucilon Rice (Nestle[®]), banana (in stage 7 of ripening, yellow with brown areas), mango and orange (in stage C5 of maturation).²³ The ingredients were selected based on their nutritional value, according to food composition tables,²⁴ industrialized product labels, also osmolality and solubility characteristics previously tested by other authors.^{25,26}

Food plan

The diet plan was based on the nutritional needs of an adult²⁷ and had the purpose of adding the psychosocial aspects of food to the home nutritional enteral therapy, divided into 6 meals a day, whose preparation process were similar to the standard fare. The concepts of the meals were: fruit shakes for breakfast and afternoon snack; natural fruit juice for morning snack, soup for lunch and dinner; milk with Mucilon[®] for supper (table I). The proportion of solids consisted of 25% solute (w/v) established according to the osmolality parameters already tested in other studies.¹¹

The enteral feeding plan was characterized as normocaloric and normoproteic, according to the esti-

Table I
Enteral diet plan

<i>Meals and volume</i>	<i>Diets</i>	<i>Formulation of the diets</i>		
		<i>Ingredients</i>	<i>Weight/volume</i>	<i>Homemade measure</i>
Breakfast 350 mL	Banana Shake	Whole milk	200 mL	1 tea cup
		Banana	60 g	1 small unit
		Maltodextrin	27 g	3 tablespoons
		Water	–	Until complete volume
Morning snack 250 mL	Juice	Orange juice	250 mL	1 cup
Lunch and dinner 350 mL/each	Soup	Beef	75 g	4 tablespoons
		Carrot	24 g	2 tablespoons
		Whole milk	200 mL	1 tea cup
		Maltodextrin	36 g	4 tablespoons
		Soybean oil	8 mL	1 tablespoons
		Broth cooking	–	Until complete volume
Iodized salt	2 g	1 coffee spoon		
Afternoon snack 350 mL	Mango Shake	Whole milk	200 mL	1 tea cup
		Mango	60 g	Half unit
		Maltodextrin	27 g	3 tablespoons
		Water	–	Until complete volume
Supper 350 mL	Milk with Mucilon®	Whole milk	200 mL	1 tea cup
		Mucilon®	21 g	3 tablespoons
		Maltodextrin	27 g	3 tablespoons
		Water	–	Until complete volume

mated nutrients²⁴ in a volume of 2 liters per day. The percentage of caloric distribution among the macronutrients was established as: proteins, up to 20%, lipids 30-35%, 50-60% carbohydrates.^{11,19}

Formulas preparation process

The diets were developed in laboratory under similar conditions to home. For the soup preparation, carrots, previously cleaned, together with meat were cooked in small pieces, for 40 minutes in a pressure cooker (12psi, ch. 4.5 L, Colck®, Brazil) with 800 mL water. After cooking, the ingredients were liquefied (Britania®, Diamante, São Paulo, Brazil) with whole milk, iodized salt and maltodextrin. The contents were then sieved on nylon mesh with openings of 1 mm in diameter, until undissolved solids were retained. After sieving, soybean oil was added together with the broth left up to complete 350 ml and then homogenized for 2 minutes. For each feeding formula another one was identically performed without adding soybean oil in order to determinate the pH.

To prepare the shakes, the fruits were previously cleaned, peeled and cut into pieces, and then liquefied (Britania®, Diamante, São Paulo, Brazil) for 5 minutes with whole milk and maltodextrin. The formula was then screened following the procedure used for the soup, and added water up to reach 350 ml. The fruits were sanitized beforehand and the juice extracted with the aid of a manual orange juicer (Plasvale®,

Brazil). The suspension obtained was sieved on nylon mesh with opening of 1 mm in diameter. For supper, milk and Mucilon® were liquefied (Britania®, Diamante, São Paulo, Brazil) for 4 minutes and then also screened. The preparations were placed in sterile glass containers, sealed and left to stand for 3 hours at room temperature, approximately 22 ± 2° C for further analysis.

Physical chemistry quality analysis

To test the stability of the diets they were subjected to a visual inspection of phases separation process, after being homogenized and tightly packed, then rested for 3 hours.³ The viscosity of the formulas was considered adequate if it did not cause obstruction when administered through a 10-French catheter (1 French = 0.33 mm), by the gravitational method.²⁸ Fluidity evaluation was carried out by means of drip test, gravitational method, using 200 mL of the diet in plastic bottles (Darrow®) connected to the equip (B. Braun Laboratory®) to check the number of drops by minute.²⁰ To determine the pH we used 12 mL of non oil diets at room temperature by means of pH meter (Analyser®, São Paulo, Brazil), according to Menezes and Araújo protocol.²⁰

Nutritional quality analysis

The nutritional value of the enteral food plan was previously estimated by food composition tables²⁴

Table II
Nutritional quality and physical chemistry of the homemade enteral diets

Nutrients	Banana Shake	Juice	Soup	Mango Shake	Milk with Mucilon®
Solids (g/%)	18.79 ± 0.02	9.08 ± 0.01	11.59 ± 0.01	16.64 ± 0.02	17.91 ± 0.01
Ashes (g/%)	0.50 ± 0.01	0.03 ± 0.02	0.17 ± 0.01	0.40 ± 0.03	0.40 ± 0.01
Protein (g/%)	2.02 ± 0.13	0.60 ± 0.01	1.42 ± 0.01	2.03 ± 0.15	2.16 ± 0.23
Lipids (g/%)	1.90 ± 0.07	0.11 ± 0.06	3.06 ± 0.10	1.68 ± 0.38	1.83 ± 0.01
Carbohydrate*	14.36	8.33	6.93	12.53	14.41
Real caloric density [†]	0.83 kcal/mL	0.37 kcal/mL	0.61 kcal/mL	0.73 kcal/mL	0.83 kcal/mL
Estimated caloric density [‡]	0.82 kcal/mL	0.27 kcal/mL	1.32 kcal/mL	0.77 kcal/mL	0.87 kcal/mL
Drops per minute	97 a 103	118 a 120	95 a 102	95 a 103	75 a 80
pH	6.04 ± 0.0	5.5 ± 0.0	6.15 ± 0.0	6.32 ± 0.0	6.9 ± 0.0

*Calculated by difference: Carbohydrate = 100 - (protein + lipids + ashes).

[†]Values obtained by chemical analyzes.

[‡]Values estimated by food composition tables.

± Standard deviation.

and information on the labels of processed products. Sequentially, it was also analyzed the real nutritional content in the formulas.

Moisture was determined by drying process in hot-house,²⁹ ashes by incineration in a muffle furnace at 550° C²⁹ and total lipid content according to Blight and Dyer method.²⁸ Protein content was quantified through the determination of total nitrogen by Kjeldah method²⁹ using the 6.25 factor for total conversion of nitrogen in crude protein. Total carbohydrates were estimated by difference and the results were expressed in g/100 mL diet on a wet basis. Those analyzes were conducted in triplicates, the results presented in arithmetic mean and standard deviation. For the metabolizable energy calculation the Atwater Factors were applied, which determines 4 kcal per gram of carbohydrate and protein, and 9 kcal per gram of lipids.³⁰

To obtain the nutritional quality of the diets, the percentage of match between the nutritional content of estimated macronutrients and the results of chemical analyzes of composition was calculated. According to the 360 Resolution of December 23th of 2003,³¹ a difference up to 20% for more or for less is tolerated in the nutritional content information presented on feeding products. Based on this Reference,³¹ a range of at least 80% of match between the results obtained in laboratory tests and nutritional contents estimated was adopted as a quality parameter.

Results

On subjective analysis, all diets showed beige color, appearance and smell just fine. The stability test did not show phase separation after 3 hours after preparation when at rest and at room temperature. None of the formulas caused obstruction when administrated trough a 10-Frech catheter, by gravity method, which indicates the adequacy of their viscosity.²⁸ It was also expected,

since the formulas were sieved on a 1 mm nylon mesh, before been administrated trough the catheter.

In the aspect of fluidity, the formulations passed through the 10-French catheter without clogging, with dripping from 78 to 120 drops/minute (table II), not depending on the opening of the equip for retarding or accelerating its passage, which indicates that it is possible its administration by gravity method. The orange juice had a pH of 5.5 and the milk with Mucilon® diet recorded the highest pH-value of 6.9. The other diets ranged between 6.04 and 6.32 (table II) which suggests that they showed good physicochemical quality.

The results of the chemical analyzes, of the diets composition, as well as the estimated energy value by food composition tables²⁴ are shown in table II. The comparison between real and estimated nutritional content of the diets showed low percentages of adequacy for soup (table III). With the exception of the soup, the percentage of adequacy for the other preparations were adequate, 86-122%, however, the presence of the soup in both main meals (lunch and dinner) has limited the eating plan to achieve good nutritional quality, with low percentages of suitability for proteins and lipids (table III).

The chemical analyzes showed that the diet plan resulted in a low-fat diet, with a considerable decrease in the proportion of protein and total energy intake compared to estimated values for the distribution of macronutrients and total energy intake (fig. 1).

Discussion

As for physical and chemical characteristics, the results were similar to those found by other authors,^{11,20,26} who demonstrated that a concentration of 25% solids allows proper drainage through the equip. The registered times were similar to those at 120 drops/minute in pre-pyloric position and 60 to 120 drops per minute

Table III
Percentage adequacy of macronutrient diets

Diets	Protein (g)			Carbohydrate (g)			Lipids (g)		
	Real* (g)	Estimated [†] (g)	% [‡]	Real (g)	Estimated (g)	%	Real (g)	Estimated (g)	%
Banana Shake 350 mL	7.07	7.22	98	50.26	48.75	103	6.66	6.93	96
Juice 250 mL	1.21	1.40	86	16.66	15.20	109	0.22	0.20	110
Soup 350 mL	4.99	22.76	22**	24.25	45.51	53**	10.71	21.20	50**
Mango Shake 350 mL	7.08	6.91	102	43.84	44.92	122	5.90	6.77	88
Milk with Mucilon® 350 mL	7.55	7.99	94	50.45	52.99	95	6.41	6.77	95
Enteral diet plan 2,000 mL	32.88	69.04	44**	185.4	252.88	82	40.62	63.07	60**

*Values obtained by chemical analyzes.

[†]Values estimated by food composition tables.

[‡]Percentage of matching the real nutritional content and the estimated one.

**Values below the parameterized nutritional quality.

post-pyloric, as suggested by Baxter.³² Smaller calibers provide greater comfort to the patient, but they increase the chances of catheter obstruction.²⁸ For administration by gravity, which is generally used in households, it is recommended to use catheters with an internal diameter of 10-French or more.²⁸ Formulas with high viscosity can cause obstruction when administered through small catheters, but none of the formulas of this study caused obstruction in 10-French calibers.²⁸

Most diets made by food showed slightly acidic or neutral pH, which favors the growth of microorganisms, so that the person responsible for its preparation must be instructed about the proper hygiene practices to be followed in the handling, preparation, storage and administration of the diet.^{3,13,26} On the other hand, the pH found in the formulations promotes the gastric motility; since this can be reduced by using solutions with pH lower than 3.5. As well as in formulas with pH less than 4.6 this can cause obstruction in the catheters.^{3,19,25} All diets in this study had pH values greater than 4.6.

Regarding nutritional quality, unlike other formulations, the soup had adequacy percentages below 80% considering the soil nutrients found by chemical analyzes and those calculated by food composition tables.²⁴ The protein content showed the greatest discrepancy among these values, with only 22% in correlation to the soup, which led to an adequacy percentage of 44% of the total protein content of the diet plan. The soup was the only preparation with flesh meat content. During its screening an accumulation of meat fibers

was observed on the sieves, which were discarded by the inability to pass through the catheter. Low percentage of match between the levels of real and estimated nutrients, especially protein content, were also found in other studies^{8,9,11,13,18,33} being justified by the significant amount of waste disposed in sifting.

Felicio et al.¹³ has also found a low percentage of suitability, about 40% to the total caloric value of the food plan, consisting of 4 handmade enteral diets used in a hospital in Valle Jequitinhonha-MG, when comparing their chemical analyzes results with nutritional values estimated by the food composition tables.¹³

According to these authors,¹³ in order to be able to flow through the catheter it is necessary to perform a hiperdilution on non-industrialized diets, which difficult to reach the desired caloric density for the diet.

Mitne et al.³³ have analyzed the nutritional quality of non-industrial enteral diets in three Brazilian hospitals, and they found significant differences between the real and the estimated content in food composition tables. In a study conducted in a public hospital in João Pessoa city-Estate of Paraíba, values chemical analyzes were performed on four different non-industrialized enteral diets and they found that none of them reached the macronutrient and total energy estimated in the food composition tables.^{8,11}

Santos and Moraes⁹ also found similar results when they analyzed the adequacy percentage of macronutrients and total energy for non-industrial enteral formulas of soup type and milk-based preparations. In this

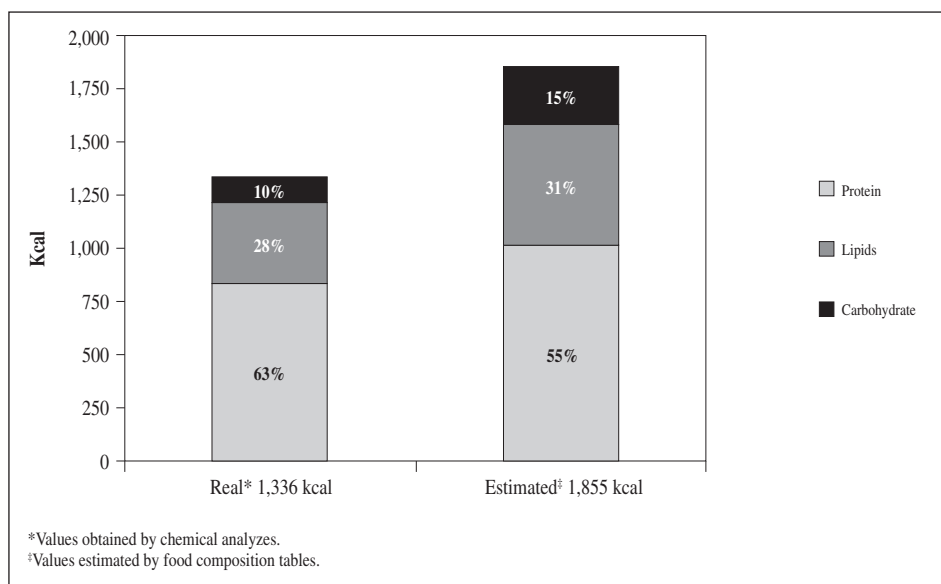


Fig. 1.—Real and estimated distribution of macronutrients of enteral diet plan.

study,⁹ the preparations on milk basis obtained about 70% of adequacy between macronutrient content and total energy, compared to the estimated values, and the soups reached percentage below than 50% for proteins, lipids and total energy. Of the macronutrients analyzed in food plan, the carbohydrates obtained the highest suitability content estimated, 82%, which can be explained by the high solubility of the maltodextrin, main source used in the diets.

The utilization of nutrients is also conditioned upon a proper distribution of macronutrients in the diet.⁸ The low correlation between the estimated and the real macronutrients in the soup impaired the nutritional balance of the diet plan, as shown in figure 1. The administration of a diet that does not reach the estimated energy value, as well as balance in the proportion of its macronutrients, may result in loss of lean body mass and adipose tissue, hindering the maintenance and/or recovery of the individual nutritional status, which directly reflects in the control of health-disease process.^{8,34}

The preparation of enteral diets with food of high physical, chemistry and nutritional qualities has as limiting factors: physical and chemistry instability of formulations, the difficulty of achieving an adequate flow in the catheter, the risk of contamination during handling and preparation processes, the inaccuracy of previous estimates for nutritional content and the relative loss of nutrients during the whole process of preparation, which also can lead to imbalance in the distribution of macronutrients in the diet.^{9,11,26}

Due to these obstacles, the exclusive use of enteral diets madden by food may hinder the achievement of the goal of enteral nutrition. Thus, a mixed enteral therapy that provides part of the patient's nutritional needs by handmade enteral diets, based on juices and fruit shakes, and complemented with industrialized enteral diets seems to be indicated as best alternative to avoid damages to the health of individuals in enteral nutrition.

The use of diets made with food, besides contributing to the nutritional support, tends to recover psychosocial values of feeding process, since the meals can be prepared by the family using conventional food.

Despite the higher cost of mixed enteral therapy due to the use of industrial diets, the Human Right to Adequate Food predicts the responsibility of the State to guarantee to all citizens permanent access to adequate food in quantity, health and nutrition quality, according to the special needs of each one.¹⁶ And thus, individuals who have this right violated, as in case of necessity and lack of access to industrialized enteral formulations, may require their provision to the State, in other words, they may seek for the enforceability of this right by public power.¹⁷ In this context, health professionals should have their actions aimed at ensuring rights of health and nutrition to the population, going beyond compliance and nutritional prescription, but promoting empowerment and awareness, guiding their patients about their guarantees of access to especial formulas.^{17,35}

The knowledge of the nutritional composition of enteral diets is critical to the effectiveness of enteral therapy.³ However, there is still a paucity of data regarding health and nutritional quality, based on chemical analysis, of handmade enteral diets. Thus, more studies are needed that seek to establish quality standards for nutritional analyzes in these diets, besides seeking for food formulas that meet those parameters.

Conclusions

The handmade enteral diets have good physicochemical quality. Regarding nutritional quality, the fruit shakes, fruit juices and milk mixtures with Mucilon® have good adequacy in its contents of estimated and analyzed macronutrients, reaching the expected quality. However, the soup presents significant losses in nutritional composition.

tion, possibly occurring during the screening, which leads to low percentages of adequacy, which is determining for a nutritional quality expected from the food plan.

Given to the difficulty of determining the nutritional composition in handmade enteral diets, especially the ones that have meats and vegetables, a mixed enteral therapy, using industrialized and handmade diets, is suggested to meet the nutritional needs of the patients and to add the psychosocial values to the treatment.

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Original / Alimentos funcionales

Restriction of dairy products; a reality in inflammatory bowel disease patients

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Abstract

Introduction: Calcium deficiency is considered a risk factor for the development of osteoporosis in inflammatory bowel disease (IBD) patients. Various dietary restrictions, including milk products are reported by these patients.

Objective: To evaluate dairy product and dietary calcium intake by IBD patients.

Methods: This cross-sectional study enrolled 65 outpatients with IBD recruited from one reference center for IBD. A semi-structured questionnaire (to collect demographic, socioeconomic and clinical data) and a quantitative food frequency questionnaire were administered. With regard to clinical data, we evaluated the anthropometric nutritional status, the disease classification, the disease activity index and the presence of gastrointestinal symptoms. Self-reported modifications in the use of dairy products were evaluated.

Results: The IBD patients' ages ranged from 20-75 years and 67.0% were diagnosed with ulcerative colitis. The majority (64.7%) reported restricting dairy products. The frequency of gastrointestinal symptoms was higher among the Crohn's disease patients who restricted dairy products than among those with no restrictions (100% vs 42.9%; $p = 0.013$); this result was not observed among the UC (ulcerative colitis) patients. Disease activity was also more frequent in the IBD patients who restricted dairy products than in those with no restrictions (23.8% vs 4.5%; $p = 0.031$), and among the UC patients, extensive disease was more common in the patients who restricted dairy products than in those with no restrictions (42.9% vs 20.0%; $p = 0.03$).

Conclusion: Restricting dairy products is common among IBD patients, possibly due to disease activity, the presence of gastrointestinal symptoms and the extension of the disease.

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Keywords: Inflammatory bowel disease. Ulcerative colitis. Crohn's disease. Dairy products. Dietary calcium.

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RESTRICCIÓN DE PRODUCTOS LÁCTEOS; UNA REALIDAD EN PACIENTES CON ENFERMEDAD INFLAMATORIA INTESTINAL

Resumen

Introducción: Se considera que la deficiencia de calcio es un factor de riesgo para el desarrollo de osteoporosis en pacientes con enfermedad inflamatoria intestinal (EII). En estos pacientes se han notificado diversas restricciones dietéticas.

Objetivo: Evaluar la ingesta de productos lácteos y calcio de la dieta en pacientes con EII.

Métodos: En este estudio cruzado se reclutaron 65 pacientes ambulatorios con EII procedentes de un centro de referencia para EII. Se administraron un cuestionario semi-estructurado (que recogía datos demográficos, socio-económicos y clínicos) y un cuestionario de frecuencia de consumo de alimento. Con respecto a los datos clínicos, evaluamos el estado nutricional antropométrico, la clasificación de la enfermedad, el índice de actividad de la enfermedad y la presencia de síntomas gastrointestinales. Se evaluaron las modificaciones auto-notificadas en el uso de los productos lácteos.

Resultados: Las edades de los pacientes con EII variaban entre los 20 y 75 años y el 67,0% fueron diagnosticados de colitis ulcerosa. La mayoría (64,7%) notificaban una restricción de los productos lácteos. La frecuencia de síntomas gastrointestinales fue mayor en los pacientes con enfermedad de Crohn que restringían los productos lácteos que en aquellos que no lo hacían (100% frente a 42,9%; $p = 0,013$); este resultado no se observó en los pacientes con colitis ulcerosa CU. La actividad de la enfermedad también fue más frecuente en los pacientes con EII que restringían los productos lácteos que en aquellos sin restricción (23,8% frente a 4,5%; $p = 0,031$) y, en los pacientes con CU, la enfermedad extensa fue más habitual en pacientes que restringían los productos lácteos que en aquellos que no lo hacían (42,9% frente a 20,0%; $p = 0,03$).

Conclusión: La restricción de productos lácteos es habitual en pacientes con EII, posiblemente debido a la actividad de la enfermedad, la presencia de síntomas gastrointestinales y la extensión de la enfermedad.

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Palabras clave: Enfermedad inflamatoria intestinal. Colitis ulcerosa. Enfermedad de Crohn. Productos lácteos. Calcio de la dieta.

Abbreviations

IBD: Inflammatory bowel disease.
CD: Crohn's disease.
UC: Ulcerative colitis.
BMI: Body Mass Index.
FFQ: food frequency questionnaire.

Introduction

Inflammatory bowel disease (IBD), mainly represented by Crohn's disease (CD) and ulcerative colitis (UC), is a chronic inflammatory disorder associated with gastrointestinal and systemic complications.¹ IBD has been a major gastroenterological problem in the Westernized world.²

Calcium deficiency, mainly as a result of steroid use, has been reported in both CD and UC patients.³ The development of osteoporosis and an increased risk of fractures are increasingly common in these patients.⁴ These problems become more severe when patients reduce the amount of calcium-rich foods they consume. This behavior is perpetuated by food beliefs in an attempt to control symptoms or to prevent the recurrence of the disease. Health professionals who advise restrictive diets also contribute to this deficiency.⁵

Between 1960 and 1970, some studies reported an improvement in symptoms and a lower likelihood of the recurrence of disease activity in UC patients who excluded dairy products from their diet. These results suggested that milk could be an important factor in the onset or exacerbation of UC,^{6,7} although the studies had methodological limitations.⁸

Considering the significant impact of calcium deficiency on bone health and patients' quality of life, the objective of this study was to evaluate the intake of dairy products and dietary calcium by inflammatory bowel disease patients.

Materials and methods

Patients

This is a cross-sectional study conducted between September 2011 and March 2012 in the outpatient Gastroenterology and Nutrition Unit at Professor Edgar Santos University Hospital, Salvador, Bahia, Brazil. Sixty-five consecutive patients were included in this study. Informed consent was obtained from all the patients, and the Ethics Committee and the Institutional Review Board of the Professor Edgar Santos University Hospital approved the protocol of this study.

Inclusion and exclusion criteria

Patients were invited to participate in the study according to the following inclusion criteria: age over 18

years and a UC or CD diagnosis according to clinical, endoscopic, radiological and/or pathological study findings.⁹ The exclusion criteria were pregnancy, intestinal resection, malignant diseases, celiac disease, lactose intolerance, chronic renal failure and severe liver disease.

Demographic, socioeconomic, clinical and dietary data

The demographic and socioeconomic data included gender, age and education level. With regard to clinical data, we evaluated anthropometric nutritional status, the disease classification, the disease activity index and the presence of gastrointestinal symptoms (abdominal pain, bloating, nausea, vomiting, diarrhea, bloating and bloody stools). The dietary data comprised self-reported information about changes in the current consumption of dairy products (cow's milk and derivatives) as well as the reasons for such changes.

For the CD patients, we applied the Harvey and Bradshaw index (1980),¹⁰ considering disease activity as a score ≥ 5 points. The Lichtiger index (1994)¹¹ was used for UC patients, and active disease was defined as an index value ≥ 10 points. We applied the Montreal Classification for both CD and UC patients.¹²

The Body Mass Index (BMI) was used to describe the patients' anthropometric nutritional status.^{13,14} The anthropometric measurements were taken by professionals who were experienced in taking these measurements. Body weight (kg) was measured twice with the patients wearing light clothes and no shoes. Weight was evaluated using a digital scale accurate to 100 g, and height (in centimeters) was measured with a stadiometer accurate to 0.5 cm.¹³

Evaluation of dietary data

The food frequency questionnaire (FFQ) was used in combination with a photo album for the assessment of the portions and average daily intake of dairy products and calcium (dietary calcium). This FFQ was validated for use in studies of interventions and/or prevention programs for chronic diseases.¹⁵

The consumption of dairy products was transformed into daily portions for the statistical analysis, and one serving or more per day was considered adequate intake.¹⁶ We analyzed information concerning the self-reported changes in the most recent consumption of dairy products (cow's milk and derivatives) as well as the justifications for these changes. The reduction or exclusion of cow's milk and derivatives or substitution with soy milk was considered dairy product restriction.

The average daily dietary calcium intake was calculated using the Personal Nutrition software (DietWin-Porto Alegre, Rio Grande do Sul, Brazil). Adequate calcium intake was defined as the equivalent of 800 mg per day

Table I
Description of the demographic, anthropometric and clinical characteristics of the Crohn's disease and ulcerative colitis patients

Variables	CD (n = 21)	UC (n = 44)
Age (years) (mean ± SD)	39.9 (9.9)	47.1 (14.4)
Gender [n (%)]		
Male	9 (42.9)	16 (36.4)
Female	12 (57.1)	28 (63.6)
Anthropometric status ¹ [n (%)]		
Underweight	3 (14.4)	4 (9.1)
Normal	9 (42.8)	28 (63.6)
Overweight	9 (42.8)	11 (25.0)
Disease duration (years) (mean ± SD)	6.8 (3.2)	7.5 (4.9)
Extension of ulcerative colitis (n (%))		
Distal	–	22 (50.0)
Left-sided	–	10 (22.7)
Extensive	–	12 (27.3)
Location of Crohn's disease [n (%)]		
Terminal ileum	4 (19.0)	–
Colon	9 (42.9)	–
Ileocolon	8 (38.1)	–
Upper GI	0 (0.0)	–
Behavior of Crohn's disease (n (%))		
Nonstricturing, nonpenetrating	13 (61.9)	–
Stricturing	3 (14.3)	–
Penetrating	3 (14.3)	–
Stricturing + perianal	1 (4.8)	–
Penetrating + perianal	2 (9.5)	–
Disease activity index [n (%)]		
Remission	17 (81.0)	41 (93.2)
Activity	4 (19.0)	3 (6.8)
Gastrointestinal symptoms [n (%)]		
No	8 (38.1)	28 (63.6)
Yes	13 (61.9)	16 (36.4)

CD: Crohn's disease; UC: ulcerative colitis.

¹n = 43 UC patients.

for individuals from 19 to 50 years old of both genders, 800 mg per day for males 51 to 70 years old and 1000 mg per day for female subjects 51 to 70 years old.¹⁷ The calcium present in beverages, nutritional supplements and medications was not recorded in this study.

Statistical analysis

For the descriptive analysis, we calculated the means with standard deviations (mean ± SD) and medians with ranges for the continuous variables; we calculated the absolute and relative frequencies for the categorical variables. The differences between CD and UC patients with regard to calcium and dairy product intake, the restriction of dairy products and disease duration were analyzed with the Mann-Whitney test. The chi-square test or Fisher's exact test was calculated to determine the strength of the association between two categorical variables. SPSS 15.0 software (SPSS, Chicago, IL,

United States) was used for the statistical analyses. $P < 0.05$ was considered statistically significant.

Results

The patients' mean age was 44.8 ± 13.5 years, and the mean disease duration was 7.2 ± 4.4 years. The age ranges of the men and the women were 20-61 years and 23-75 years, respectively. The majority were female (61.5%), and 72.0% had at least a high school education. Among the women, 45.0% were older than 50 years.

Of the IBD patients, 56.9% had adequate anthropometric nutritional status, and 30.8% were overweight. Of the patients evaluated, 89.2% were clinically in remission. Gastrointestinal symptoms were reported by 44.6% of the IBD patients. Bloating and bleeding were the main symptoms, reported by 20.5% (9/44) and 18.2% (8/44) of the UC patients, respectively. However, abdominal distension and abdominal pain were reported by 57.1% (12/21) and 33.3% (7/21) of the CD patients, respectively (data not shown). The demographic and medical characteristics of the Crohn's disease and ulcerative colitis patients are shown in table I.

Modifications to the consumption of dairy products

Regarding the patients' dietary characteristics, 52.3% of the patients reported some change in their consumption of dairy products after being diagnosed with IBD. The majority of the patients (64.7%) reported restricting cow's milk and its derivatives (reducing or excluding these foods and substituting soy milk). The most common reason for this behavior was the exacerbation or onset of symptoms (45.5%), followed by guidance by health professionals (36.4%). Approximately 80.0% of the CD patients had seen a nutritionist (table II).

Consumption of dairy products and dietary calcium

The majority of IBD patients had low dairy product intake (52.0%) and inadequate dietary calcium intake (90.8%) (table II). Only three patients reported taking calcium supplements (data not shown).

There was no statistically significant difference in the intake of dairy products or dietary calcium between the CD and UC patients ($P = 0.37$ and $P = 0.28$, respectively) (table II).

Consumption of dairy products and demographic, anthropometric and clinical characteristics

No association was observed between the reported restriction of dairy products and age, gender, anthro-

Table II
Frequency of modifications in dairy product and dietary calcium intake by inflammatory bowel disease patients

Variables	IBD (n = 65)	CD (n = 21)	UC (n = 44)
Modifying the consumption of dairy products [n (%)]			
No	31 (47.7)	11 (52.4)	20 (45.5)
Yes	34 (52.3)	10 (47.6)	24 (54.5)
Types of modifications [n (%)]			
Exclusion/Reduction	17 (50.0)	6 (28.6)	11 (25.0)
Substitution for nonfat milk	9 (26.5)	2 (9.5)	7 (15.9)
Substitution for soy milk	5 (14.7)	1 (4.8)	4 (9.1)
Increased intake	3 (8.8)	1 (4.8)	2 (4.5)
Justifications for restrictions ¹ [n (%)]			
Exacerbation or onset of symptoms	10 (45.5)	5 (23.8)	5 (11.4)
Advice for healthcare professionals	8 (36.4)	1 (4.8)	7 (15.9)
Fear of eating	1 (4.5)	0 (0.0)	1 (2.3)
Magazines/Brochures/Books	1 (4.5)	1 (4.8)	0 (0.0)
Others	2 (9.1)	0 (0.0)	2 (4.5)
Counseling with nutritionist ² [n (%)]	36 (55.4)	15 (78.9)	21 (48.8)
Steroid use (n (%))	6 (9.2)	2 (9.52)	4 (9.09)
Daily intake of dairy product (servings) [median (range)]	0.90 (0.0-5.9)	0.90 (0.0-4.8)	0.88 (0-5.9)
Daily intake of dietary calcium (mg) (mean ± SD)	564.7 ± 348.9	625.8 ± 361.2	535.5 ± 343.2
Inadequate dairy product intake [n (%)]	34 (52.0)	11 (52.4)	23 (52.3)
Inadequate dietary calcium intake [n (%)]	59 (90.8)	18 (85.7)	41 (93.2)

IBD: Inflammatory bowel disease; CD: Crohn's disease; UC: Ulcerative colitis.

¹n = 22 to IBD patients, n = 7 to CD patients, n = 15 to UC patients who reported reducing or excluding and substituting soy milk.

²n = 19 CD patients because of the absence of data.

pometric status, disease duration or counseling from a nutritionist ($P > 0.05$). Among the CD patients, no association was found between the restriction of dairy products and the location and behavior of Crohn's disease ($P > 0.05$). However, the frequency of gastrointestinal symptoms was higher among the CD patients who restricted dairy products compared with those with no restrictions (100% vs 42.9%; $P = 0.013$); the same result was not observed in UC patients (table III).

Disease activity was more frequent in the IBD patients who restricted dairy products than in those with no restrictions (23.8% vs 4.5%; $P = 0.031$). Among the UC patients, extensive disease was more frequent among the patients who restricted dairy products than among those with no restrictions (42.9% vs 20.0%; $P = 0.03$) (table III).

Discussion

In our study, the majority of IBD patients reported having changed their dairy product intake after being diagnosed with IBD, and the majority had low dairy product intake and inadequate dietary calcium intake. The restriction of dairy products seems to be associated with gastrointestinal symptoms and the activity and extension of the disease in these patients.

During active disease, the restriction of dairy products is common among IBD patients.¹⁸ Among the fac-

tors associated with the restriction of dairy products, the presence of gastrointestinal symptoms, the desire to relieve symptoms, food beliefs and dietary advice are most strongly related.^{5,18,19} However, in prospective studies, no association was found between dairy product intake and an increased frequency of disease relapse.^{5,20}

In this study, the extensive form of the disease in UC patients seems to be associated with the restriction of dairy products. However, Jowett and colleagues (2004) found the same association in a group of UC patients.⁵ One possible explanation for our findings is that gastrointestinal symptoms are related to active disease and the extensive form of the disease in UC patients. Thus, the restriction of dairy products could be attributable to the spread of information among patients and health professionals about the occurrence of lactose intolerance in IBD patients.

Although no association was found between dairy product restriction and counseling from a nutritionist, the recommendation of a health professional is another factor that has encouraged these individuals to restrict their dairy product intake.⁵ The fact that some IBD patients, most commonly CD patients, may develop lactose intolerance contributes to the prescription of this nutritional restriction. Some factors must be evaluated before the patient restricts dairy products, such as the fat present in these foods,^{21,22} the amount of lactose consumed, the residual activity of intestinal lactase,

Table III
Modifications in dairy product intake and the demographic, anthropometric and clinical characteristics of the inflammatory bowel disease patients

Variables	IBD (n = 65)		CD (n = 21)		UC (n = 44)	
	Restriction	No restriction	Restriction	No restriction	Restriction	No restriction
Age (years) (mean ± SD)	43.4 ± 12.9	45.4 ± 13.8	41.3 ± 7.7	39.3 ± 11.1	44.5 ± 15.1	48.3 ± 14.2
Sex [n (%)]						
Male	11 (52.4)	14 (31.8)	5 (71.4)	4 (28.6)	6 (42.9)	10 (33.3)
Female	10 (47.6)	30 (68.2)	2 (28.6)	10 (71.4)	8 (57.1)	20 (66.7)
Anthropometric status ¹ [n (%)]						
Underweight	2 (10.0)	5 (11.4)	1 (14.3)	2 (14.3)	1 (7.7)	3 (10.0)
Normal	13 (65.0)	24 (54.5)	3 (42.9)	6 (42.9)	10 (76.9)	18 (60.0)
Overweight	5 (25.0)	15 (34.1)	3 (42.9)	6 (42.9)	2 (15.4)	9 (30.0)
Disease duration (years) (mean ± SD)	8.0 ± 4.5	6.9 ± 4.4	8.3 ± 3.3	6.0 ± 3.0	7.3 ± 4.9	7.9 ± 5.1
Extension of ulcerative colitis [n (%)] ^a						
Distal					3 (21.4)	19 (63.3)
Left-sided					5 (35.7)	5 (16.7)
Extensive					6 (42.9)	6 (20.0)
Location of Crohn's disease [n (%)]						
Terminal ileum			2 (28.6)	2 (14.3)		
Colon			1 (14.3)	8 (57.1)		
Ileocolon			4 (57.1)	4 (28.6)		
Upper GI			0 (0.0)	0 (0.0)		
Behavior of Crohn's disease [n (%)]						
Nonstricturing, nonpenetrating						
Stricturing			0 (0.0)	2 (14.3)		
Penetrating			1 (14.3)	2 (14.3)		
Stricturing + perianal			5 (71.4)	8 (57.1)		
Penetrating + perianal			0 (0.0)	1 (7.1)		
Disease activity index [n (%)] ^a						
Remission	16 (76.2)	42 (95.5)	4 (57.1)	13 (92.9)	12 (85.7)	29 (96.7)
Activity	5 (23.8)	2 (4.5)	3 (42.9)	1 (7.1)	2 (14.3)	1 (3.3)
Gastrointestinal symptoms [n (%)] ^a						
No	7 (33.3)	29 (65.9)	0 (0.0)	8 (57.1)	7 (50.0)	21 (70.0)
Yes	14 (66.7)	15 (34.1)	7 (100)	6 (42.9)	7 (50.0)	9 (30.0)
Counseling with nutritionist ²						
No	7 (35.0)	19 (45.2)	1 (14.3)	3 (25.0)	6 (46.2)	16 (53.3)
Yes	13 (65.0)	23 (54.8)	6 (85.7)	9 (75.0)	7 (53.8)	14 (46.7)

IBD: Inflammatory bowel disease.

¹n = 43 UC patients.

²n = 19 CD patients because of the absence of data.

^aP < 0.05.

the ability of the colonic flora to ferment lactose and individual sensitivity to the products of lactose fermentation.²³

Some patients have replaced dairy products with soy milk. However, it is known that soy milk products are usually enriched with tricalcium phosphate. This fortificant has the best sensory characteristics, however, the calcium bioavailability is lower compared with cow's milk and other fortificants such as calcium carbonate.²⁴⁻²⁷ Therefore, soy milk does not seem to be a good option as a rich source of bioavailable calcium, and recommendations for the intake of foods rich in calcium need to be part of the treatment for IBD patients if dairy product restriction is recommended for some reason. In addition, dairy products are poor

sources of lactose and can be consumed by patients with lactose intolerance. They are not only rich sources of calcium but also sources of other micronutrients such as B complex vitamins.

Low dietary calcium intake is already common among the Brazilian population.²⁵ The mean daily dietary calcium intake among adults is 476.4 mg for females and 546.4 mg for males, and the prevalence of inadequacy among females and males is 90.7% and 83.8%, respectively.²⁸ The decrease in dietary calcium intake is clinically important in IBD patients, particularly those treated with steroids, postmenopausal women and the elderly because they have a higher risk of developing osteoporosis²⁹ and fractures.^{30,31} Adequate dietary calcium intake is one

of the preventive measures to reduce osteoporosis in IBD patients.³² The minimum recommended daily intake of calcium for the prevention of fractures in IBD patients is 1,000 mg and for postmenopausal women and men over the age of 55 years, the recommendation is 1,200 mg.³³

This study has some limitations, such as the sample size, the absence of a control group and the fact that patients who agree to participate in this type of study may have different eating habits. In addition, dietary restrictions could be associated with other medical conditions not evaluated in this study. Nevertheless, some of the results were similar to other studies, but prospective studies are still necessary to confirm the findings.

In summary, the restriction of dairy products and reduced dietary calcium intake are evident in IBD patients. These restrictions are mainly influenced by gastrointestinal symptoms and the activity and extension of the disease. Even in the absence of conclusive data on the frequency of lactose intolerance in these patients and the advancements in the knowledge about the absence of an association between diet and the exacerbation of symptoms or disease activity, restrictive diets are still a reality and may contribute to the compromised nutritional status of IBD patients. However, we must investigate other possible diagnoses that can cause gastrointestinal symptoms and address the complaints of the patients more thoroughly.

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Original / Alimentos funcionales

Effect of probiotics on human blood urea levels in patients with chronic renal failure

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Abstract

Introduction: Patients with chronic kidney disease (CKD) show an increase in bowel aerobic bacteria that produce uremic toxins and decreased anaerobic bacteria as bifidobacteria and lactobacillus. The latter can be used as probiotics. The probiotic with greater availability in Mexico, is the *lactobacillus casei shirota* (LcS), currently there is no known LcS specified dose that produces a benefit to the patient with CKD.

Objective: To determine the effectiveness of two different LcS doses in achieving a decrease in urea concentrations of at least 10% in patients with KDOQI stage 3 and stage 4 CKD.

Methodology: A simple randomized, controlled clinical trial. Outpatients treated at the National Institute of Medical Sciences and Nutrition Salvador Zubirán in México D.F. Patients were provided the LcS, as follows: Group A: 8×10^9 colony-forming units (CFU) and Group B: 16×10^9 CFU. Patients were followed-up for eight weeks, and baseline and final samples were obtained to calculate the basal and final concentrations, respectively, of blood urea and serum creatinine (CrS). During the follow-up, both groups consumed a diet of 30 kcal/kg/weight and 0.8 g/kg/weight of protein, and a food diary was made to assess both the adherence to the diet and LcS.

Results: Thirty patients with CKD were evaluated. When analyzing the percentage change between the different doses, a decrease > 10% was found in the blood urea concentrations for patients treated with the 16×10^9 dose, which was significant with respect to the baseline measurement.

Conclusion: There was a > 10% decrease in the serum urea concentrations with LcS in patients with stage 3 and 4 CRF.

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EFEECTO DE LACTOBACILLUS CASEI SHIROTA SOBRE CONCENTRACIONES DE UREA EN LA ENFERMEDAD RENAL CRÓNICA

Resumen

Introducción: Los pacientes con enfermedad renal crónica (ERC) muestran un aumento a nivel intestinal de bacterias aeróbicas que generan toxinas urémicas y disminución de bacterias anaeróbicas como bifidobacterias y lactobacilos. Estas últimas se pueden utilizar como probióticos. El probiótico con mayor disponibilidad en México, es el *lactobacillus casei shirota* (LcS), actualmente no se conoce que dosis de LcS puede generar un beneficio para el paciente con ERC.

Objetivo: Determinar el efecto de 2 dosis diferentes de LcS para disminuir al menos 10% las concentraciones de urea en pacientes con ERC estadios KDOQI 3 y 4.

Métodos: Ensayo clínico controlado con asignación aleatoria en el cual se incluyeron pacientes ambulatorios con ERC del Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán. Se asignó a los pacientes a uno de los dos grupos, grupo A: 8×10^9 unidades formadoras de colonias (UFC) y grupo B: 16×10^9 UFC. El seguimiento fue de ocho semanas, obteniéndose una muestra de sangre basal y otra final para conocer concentraciones de urea y creatinina. Ambos grupos consumieron una dieta de 30 kcal/kg/peso y 0,8 g/kg/peso de proteína, se realizó un diario de alimentación para evaluar el cumplimiento de la dieta y del tratamiento del LcS.

Resultados: Se evaluaron 30 pacientes. Al analizar el porcentaje de cambio entre las diferentes dosis se encontró una disminución mayor al 10% en urea sanguínea en pacientes con la dosis de 16×10^9 con respecto a su medición basal.

Conclusión: Existe una disminución > 10% de la concentración sérica de urea con el LcS en pacientes con ERC 3 y 4.

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Palabras clave: Urea. Toxinas urémicas. Dosis. Probióticos. *Lactobacillus casei Shirota*.

Introduction

Background

Currently, rising evidence exists that certain food can exert a beneficial effect on specific functions of humans in addition to their beneficial nutritional value. This benefit may lead to a positive impact on human health by preventing or treating diseases.¹ Thus, the concept of “functional food” has arisen, and it is defined as a product, modified food or nutritional ingredient that can exert beneficial health effects other than its traditional nutritional value.² Probiotics, prebiotics and symbiotics have obtained a relevant role in the field of functional foods.

The concept of probiotics was introduced at the beginning of XX century with Metchnikoff's studies.³ Now the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) define probiotics as “the living organisms that provide health benefits in the host when consumed in the appropriate quantity.”⁴

The attributed protective effect of probiotic microorganisms in improving the host resistance to pathogens.⁵⁻⁷

Various *in vitro* and *in vivo* studies of different pathological states suggest numerous health effects promoted by probiotics.^{5,7-13} For a beneficial effect in the host, it is necessary to ingest appropriate quantities of probiotic microorganisms or sufficient colony-forming units (CFU).¹⁶ This approach achieves a modification and equilibrium in the ecosystem of billions of microorganisms residing in the human gut, which reflects a good healthy state.

To understand the probiotics' effect on renal disease better, it is necessary to take into consideration that patients with renal disease usually have impaired intestinal microbiome. It is suggested that almost two thirds of individuals with uremia have abnormalities in the gastrointestinal mucosa and a disequilibrium in the intestinal ecosystem.¹⁷ The majority of these changes happen at the ileum level and in the colon, where the microbiome plays an important role. The increase in aerobic bacteria, such as *Escherichia coli*, results in an intestinal microbiome disequilibrium. These bacteria generate toxic substances, called uremic toxins, and decrease the anaerobic bacteria, such as bifidobacteria and lactobacillus.¹⁸

In chronic renal disease (CRD), there are higher urea concentrations and, consequently, increased ammonium. Thus, there is an increase in pH that promotes the growth of aerobic bacteria in the gastrointestinal tract and the subsequent production of uremic toxins. Conversely, bifidobacteria ferment carbohydrates and produce acetic and lactic acid to acidify the intestine. In that way, these bacteria prevent the growth of aerobic microorganisms and normalize the altered intestinal microbiome in CRF patients.¹⁹

Evidence exists that patients with uremia have a deteriorated intestinal barrier that is mainly due to the

disequilibrium of intestinal microbiome caused by the increase of pathogens.²⁰⁻²²

One of the requirements for the use of probiotics as adjuvants to remove urea or uremic toxins is the capacity of microorganisms to use metabolites as substrates. Thus, probiotics help intestinal microbiome decrease the bacteria producing uremic toxins. Urease is the enzyme responsible for hydrolyzing urea into ammonium and carbon dioxide, but only certain microorganisms can synthesize urease. In uremic patients, it has been shown that at high plasma urea concentrations, the fecal urease activity is increased. Thus, the increase in colon bacterial urease is considered a beneficial factor for uremic patients.²³ However, ammonium can be converted into nitrates by other microorganisms or return to the liver by diffusion, where it can be metabolized again into urea.

Probiotic dose in CRF

There have been several studies performed on CRF patients using different types of probiotics at different doses with the aim to reduce some uremic toxins. Simenhoff et al.²⁴ and Dunn et al.²⁵ have shown a decrease in dimethylamine (DMA) and nitrodimethylamine (NDMA) concentrations after using *L. acidophilus* in CRF patients with dialysis. Simenhoff's study was a double-blind trial with 30 patients on hemodialysis.²⁴ This researcher showed that 8 patients who were supplemented with *lactobacillus acidophilus* had lower dimethylamine and nitrodimethylamine concentrations, which are two of the uremic toxins produced in the small intestine. In the case of DMA, concentrations decreased from 224 ± 47 to 154 ± 47 $\mu\text{g/dL}$, while NDMA decreased approximately 31% ($p < 0.001$). Dunn et al. observed a significant decrease of 42% in the mean concentrations of DMA for patients supplemented with the probiotic ($p = 0.001$).²⁵

Among the most relevant clinical studies, which are used as background for the present work, are the studies by Takayama²⁶ and Taki.¹⁹ Both studies tested the probiotic *Bifidobacterium longum* in hemodialysis patients and reported a decrease in the toxin indoxyl sulfate. Takayama²⁶ observed a decrease in indoxyl sulfate from 4.9 mg/dL to 3.5 mg/dL ($p < 0.005$). Two years later, Taki et al.¹⁹ studied 27 patients over 12 weeks using different probiotic doses. From the first to the fourth week, these researchers supplemented a dose of 3×10^9 CFU, while from the fifth to the eighth week, a dose of 6×10^9 CFU was used, and from the ninth to the twelfth week, a 12×10^9 CFU dose was provided. These authors found that the most effective bifidobacteria dose was a 6×10^9 CFU dose and that these microorganisms were able to reduce the indoxyl sulfate concentrations from 164.4 ± 15 mmol/L to 149.6 ± 15.5 mmol/L ($p < 0.05$). These studies were performed in hemodialysis patients, which is a situa-

tion that could imply an important bias in the results, as it is unknown whether the decrease in uremic toxins was due to the dialysis process itself or due to the significant effect of the probiotics on the decreased urea.

Lactobacillus casei Shirota (LcS)

In the traditional classification system, *Lactobacillus casei* is a gram (+) bacteria, and it belongs to the subgenus *Streptobacterium*. This subgenus includes homofermentative organisms that can grow at 15° C and up to a maximum temperature of 41° C. This strain's guanine-cytosine content is 45-47%, and it produces L-lactic acid as its principal metabolic product from glucose, sucrose, lactose, fructose and maltose. In Mexico LsC is one of the probiotics with the greatest economic and material availability, and it is used for the production of fermented dairy products.

Human and animal studies have shown that administering LcS has beneficial effects, such as the following:

In humans:

- Beneficial modulation of intestinal flora;²⁷
- Improved fecal consistency;²⁷
- Infection protection;²⁷
- Immune activity modulation;²⁷
- Prophylactic effects on cancer development;²⁸
- Immunomodulatory effects;²⁹
- Salmonella typhimurium inhibition;³⁰
- Normal maintenance of ammonia concentrations and intestinal microbiome changes in patients with hepatocellular damage at stage Child-Pugh B, with or without ascites.³¹

In animals:

- Immune and cellular response modifications of type II collagen, thereby reducing arthritis development in rats;³²
- Decreased action of triglycerides and plasmatic cholesterol in rats;³³
- Growth inhibition of tumor cells in the thoracic cavity of mice.³⁴

Methods

The present study is a controlled, simple randomized clinical trial without blinding.

Participants

CRF patients were recruited through the external consultation of the Nephrology Department at the National Institute of Medical Sciences and Nutrition

Salvador Zubirán (Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán; INCMNSZ). Before the consultation, the records of the candidate patients were reviewed, and an invitation to participate in the study was made on the consultation day. To fulfill the study's objectives, CRF patients in stage 3 or stage 4, as reflected by the glomerular filtration rate (GFR) based on the MDRD (modification of diet in renal disease) formula, were considered. These patients were selected because stages 3 and 4 have more metabolic alterations without taking into account replacement therapy. Therefore, outpatients who fulfilled the inclusion criteria were invited to participate in this study.

Inclusion criteria

- Nephrology outpatients with stage 3 or 4 CRF (glomerular filtration rate from 59 to 15 mL/min/1.73 m² calculated by MDRD).
- Age between 18 and 65 years.
- Either sex.
- Literate patients.
- Mexico City residents.
- Signed informed consent.

Exclusion criteria

- Patients under replacement therapy.
- Patients with a diagnosis of diabetes mellitus.
- Patients with lupus erythematosus.
- Patients who had a renal transplant.
- Intolerance to whole milk and dairy products.

The evaluated interventions were two different doses of LcS that were included in a fermented dairy drink product. Two groups were formed as follows: group A received a fermented dairy drink in an 80-mL bottle with 8 x 10⁹ CFU of LcS, and group B received two 80-mL bottles of the fermented dairy drink for a total of 16 x 10⁹ CFU of LcS. The size, color, flavor and physical aspects of the bottles were the same for both groups. Patients visited INCMNSZ every 15 days to obtain 15 or 30 bottles of LcS (depending on the assigned group) during the two months.

Objectives

The objective was to determine the LcS dose needed to achieve a greater than 10% decrease in the blood urea concentration in stage 3 and stage 4 CRF patients. Therefore, the hypothesis was that the administration of a fermented dairy product containing 16 x 10⁹ CFU of LcS could decrease the blood urea concentrations by at least in 10% in stage 3 and stage 4 CRF patients.

Measurements

All patients were attended at the Metabolic Unit of INCMNSZ.

This study was conducted according to the principles of the Declaration of Helsinki of the World Medical Association and was approved by The Ethical Committee of the INCMNSZ.

All participants gave written informed consent. Once a potential patient was identified, the patient and a relative received an explanation of the nature and objectives of the present study. The patients had the opportunity to read the informed consent and resolve all of their doubts. A free decision to enter the study and the policy of no reprisal against the patient for a denial of participation were highlighted. Once agreeing to enter the study, the patient was asked to sign the informed consent. The informed consent was also signed by a responsible relative of the patient, by the researcher and by two witnesses. After the consent was received, the intervention, evaluation and biochemical measurement components of the study were started.

In the first visit, general information was obtained about the patient's underlying disease, comorbidities and type and dose of the medications taken. All patients gave a baseline blood sample in the fasting state for a determination of the serum creatinine and urea concentrations. After the blood draw, the patients were randomized to received a LcS dose. The subjects participated in a follow-up at two weeks to monitor their adherence to the diet and the consumption of the LcS dairy drink and the final evaluation after the two months of treatment. Blood samples were obtained at the end of the intervention period to determine the final blood creatinine and urea concentrations.

All patients followed an isocaloric (30 kcal/kg ideal weight) and isoproteic (0.8 g/kg ideal weight) diet during the two-month intervention. These diets were designed to ensure a good protein and energetic supply that would not directly affect the biochemical concentrations under study. A nutritionist specialized in renal disease calculated and explained these diets to each patient.

Each patient had previously received a daily food consumption diary to record food and lactobacillus (dairy drink) consumption during the 15 days before the follow-up visit. The dietary record aimed to monitor the adherence of each patient to the LcS and dietetic treatment. The specialized nutritionist trained each patient to correctly report the food and its quantity in the diary. The nutritionist explained how to record the day, the timetable of each meal, the dish name for each meal, the ingredients of each dish and the quantities to maintain a record that was as accurate as possible.

Nutripac 1.5[®] software was used to analyze the food diaries. The software assessed the quantity of the macronutrients consumed daily for each patient and calculated their mean during the 60 days of the LcS consumption. This approach allowed for the obtainment of

their mean energy, protein, carbohydrate and lipid consumption. Adherence was assessed by the percentage of overall adequacy. A good diet and LcS consumption adherence was considered when the percentage was not outside the $\pm 10\%$ (meaning between 90 and 110%) of the recommended diet for energy and each macronutrient in grams. Similarly, a low adherence to the fermented dairy drink was considered when the consumption of the total number of bottles was outside the $\pm 10\%$ of the recommended consumption (depending on the assigned dose).

Sample

Given that this was an exploratory study, the sample size was obtained at convenience. A total of 34 INCMNSZ outpatients who fulfilled the inclusion criteria were assessed.

A simple randomization was performed by using a table with random numbers and assigning even numbers to group A (8×10^9 CFU of LcS) and odd numbers to group B (16×10^9 CFU of LcS).

Statistical methods

Descriptive statistics based on the measurement levels of the variables was used, supporting the proportion measures, central tendency and dispersion. A paired t-test was used to compare dependent samples (baseline and final), and a t-test was used to compare independent samples (group A vs. group B). For categorical variables, a χ^2 test was used. A $p < 0.05$ was considered significant. The SPSS 16 statistical program was used to perform the data analysis.

Results

Participant flow diagram

A total of 36 patients were invited to participate in the study. Three of them did not fulfill the inclusion criteria, two of them refused to participate, one did not tolerate the fermented dairy product and one claimed personal reasons for not being able to attend the follow-up. A total of 32 patients were included and begun the protocol (fig. 1).

Baseline samples were obtained from a total of 30 patients, which included 14 women and 16 men. Table I shows the assessed variables. A medications registry was evaluated based on each drug's activity, thereby allowing the grouping of them into seven different types of medications, as follows: lipid lowering, in which only statins and fibrates were registered; antihypertensives (calcium channel blockers, beta-blockers and angiotensin-converting enzyme inhibitors were registered); diuretics; calcium carbonate; xanthines in-

hibitors; and supplements, among which only iron and complex B vitamin was registered. Table I also shows the number of patients who used these medications at baseline.

During the follow-up, the adherence to the lactobacillus supplementation and the nutritional plan provided to the patients was evaluated. Sixty nutrition diaries per patient were analyzed. The data were used to estimate the mean energy, protein, carbohydrate and lipid consumption for each patient. From these data, a population mean was obtained, and it was compared with the mean recommended by the nutritionist to obtain the percentage of adequacy. The differences between the recommended energy quantity and the consumed energy during the follow-up were $2,058 \pm 197.1$ kcal. vs $2,071 \pm 230.4$ kcal. respectively. No statistically significant differences were found, and an adequacy percentage of 101% was observed, reflecting a good adherence to the consumed calories.

When the macronutrient consumption during the follow-up was compared in all patients, no significant differences were found between the recommended quantities in grams and ingested grams. The adequacy percentage between the recommendation and the real consumption was 106% (56.3 g vs. 60.14 g, respectively), 102% and 100.1% for proteins, lipids and carbohydrates, respectively. Although these percentages are greater than the recommended values, they are within

the range of $\pm 10\%$ and are thereby considered to indicate good adherence.

No significant differences were found between groups A and B for energy and macronutrient consumption after an eight-week follow-up. Energy (kcal): $2,087 \pm 62.92$ vs $2,057 \pm 58.87$ grams of protein: 61.97 ± 6.29 vs 58.31 ± 4.38 grams of carbohydrates: 333.5 ± 8.03 vs 325.3 ± 8.31 and grams of lipids: 58.18 ± 2.52 vs 58.74 ± 1.74 , respectively.

The mean adherence to the LcS treatment was 97% for group A and 98% for group B with an overall adherence of 98%.

When the final data were obtained from all patients who fulfilled the eight-week follow-up, the baseline and final measurements for the variables under study were compared in the entire population. No significant differences were obtained with the exception of weight and BMI (body mass index) and blood urea (table II).

The effects of LcS on the urea concentrations (fig. 2) and on different variables (table III) were analyzed in groups A and B.

An analysis of the percentage change obtained during the eight-week follow-up was performed. Patients who consumed a dose of 16×10^9 CFU showed a greater percentage change when compared with those who consumed only a dose of 8×10^9 CFU, which was a difference of -10.98% vs. -3.37%, respectively ($p = 0.309$). Table IV shows the percentage change of the different studied variables.

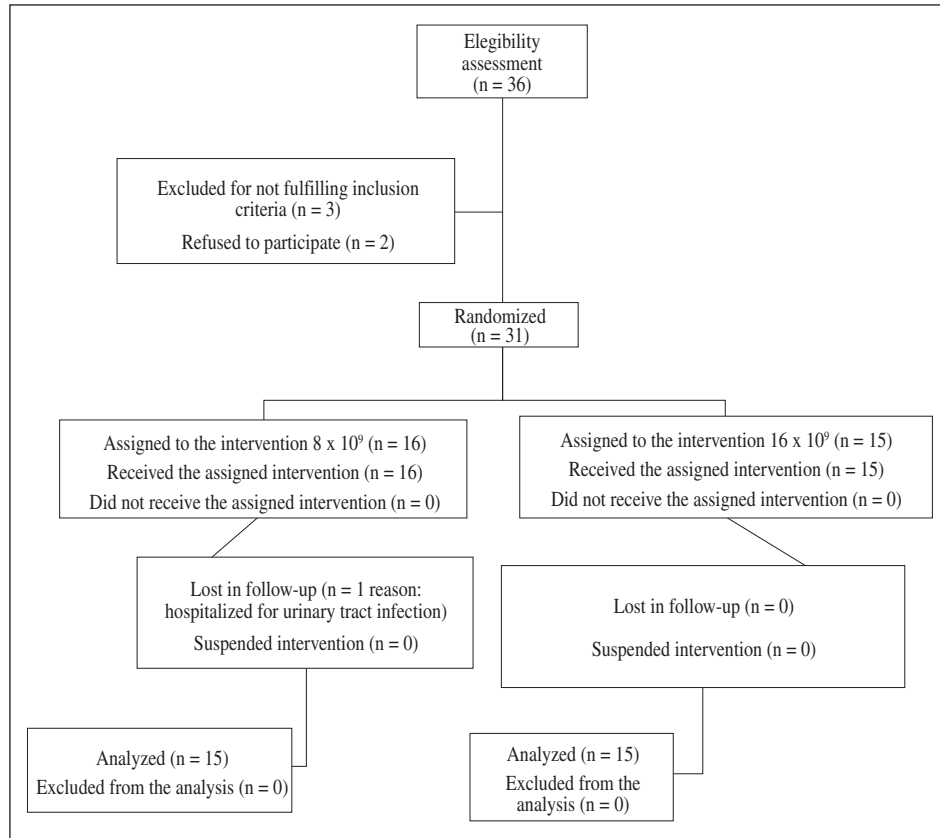


Fig. 1.—Subjects flow diagram through follow-up.

Table I
Baseline characteristics of the population according to the assigned dose

	Total sample n = 30 x ± SD	Group A dose 8 x 10 ⁹ CFU n = 15 x ± SD	Group B dose 16 x 10 ⁹ CFU n = 15 x ± SD	p
Age (years)	41.47 ± 15.35	43.8 ± 14.44	39.13 ± 16.36	n.s.
Weight (kg)	70.68 ± 12.11	69.66 ± 12.8	71.7 ± 12.39	n.s.
BMI (kg/m ²)	26.23 ± 3.36	25.52 ± 3.15	26.93 ± 3.51	n.s.
Height (cm)	163 ± 0.94	164 ± 0.99	162 ± 0.92	n.s.
Sex (F/M)	14/16	7/8	7/8	n.s.
Urea (mg/dL)	81.66 ± 26.39	82.13 ± 32.96	81.20 ± 18.86	n.s.
Creatinine (mg/dL)	2.48 ± 0.89	2.44 ± 0.79	2.52 ± 1.01	n.s.
GFR MDRD (mL/min/1.73 m ²)	30.7 ± 11.77	30.66 ± 12.18	30.74 ± 11.71	n.s.
Medications				n.s.
Statins n (%)	18 (60%)	8 (50%)	10 (71%)	n.s.
Fibrates n (%)	17 (56%)	9 (56%)	8 (57%)	n.s.
Antihypertensives n (%)	27 (90%)	15 (93%)	12 (85%)	n.s.
Diuretics n (%)	22 (73%)	10 (62%)	12 (85%)	n.s.
Calcium carbonate n (%)	12 (40%)	5 (33%)	7 (71%)	n.s.
Xanthines inhibitors n (%)	13 (43%)	7 (43%)	6 (42%)	n.s.
Vitamin and mineral supplements n (%)	19 (63%)	9 (56%)	10 (71%)	n.s.

Table II
Variables measured at baseline and at the end of the follow-up

Parameters	Baseline measurement n = 30 X ± SD	Final measurement n = 30 X ± SD	p
Weight (kg)	70.38 ± 12.11	69.81 ± 12.01	0.013
BMI (kg/m ²)	26.23 ± 3.36	25.90 ± 3.36	0.008
Sex (F/M)	14/16	14/16	n.s.
Urea (mg/dL)	81.66 ± 26.39	73.23 ± 19.49	0.031
Creatinine (mg/dL)	2.48 ± 0.89	2.47 ± 1.04	n.s.
GFR MDRD (mL/min/1.73 m ²)	30.7 ± 11.77	31.86 ± 12.34	n.s.

Discussion

It has been shown that patients with renal diseases have intestinal microbiome alterations. Approximately two thirds of uremic individuals show abnormalities in the gastrointestinal mucosa and a disequilibrium in the intestinal ecosystem.⁶ The majority of these changes occur at the level of the ileum and in the colon, where microbiome play an important role. An intestinal microbiome disequilibrium is due to an increase of aerobic bacteria, such as *Escherichia coli*. These bacteria are able to generate toxic substances, known as uremic toxins, that subsequently decrease anaerobic bacteria, such as bifidobacteria and lactobacillus.⁷ The majority of the produced fecal ammonium comes from urea hydrolysis by intestinal bacteria. In CRF, there are greater urea concentrations and, consequently, increased

ammonium. Thus, there is an increase in pH that promotes the growth of aerobic bacteria in the gastrointestinal tract and the subsequent production of uremic toxins. Bifidobacteria (used as probiotics) ferment carbohydrates and produce acetic and lactic acids to acidify the intestine. Hence, these bacteria prevent the growth of aerobic microorganisms, and they normalize the altered intestinal microbiome in CRF patients.^{15,35}

In the present study, an eight-week intervention with LcS was evaluated in 30 patients with stage 3 or 4 CRF. This study is one of the few in this new field of research concerning probiotics and their effect on renal diseases, specifically in patients without replacement therapy. The problem of previous studies,^{16,17,25,26} where dialysis also occurred, is the difficulty in evaluating the actual probiotic effect without the dialysis interference. However, the importance of this type of study in CRF patients lies in the benefits that could be obtained if symptoms promoted by the increase of uremic toxins were decreased. Notably, the present study is an exploratory study based on the previous studies by Simenhoff,²⁴ Taki,¹⁹ Takayama,²⁶ Dunn²⁵ and, specifically, Torre and Vargas.³¹ The latter study evaluated the effect of LcS on the ammonium concentrations in patients with chronic liver disease. These researchers demonstrated that LcS had a positive effect on decreasing ammonium levels in these patients because ammonium is a urea precursor for which intestinal bacteria are notably involved. LcS was chosen as a good probiotic to be tested in CRF patients with the main objective of establishing a recommended dose for these patients. In fact, only a few reports exist concerning an acceptable dose for each case. This

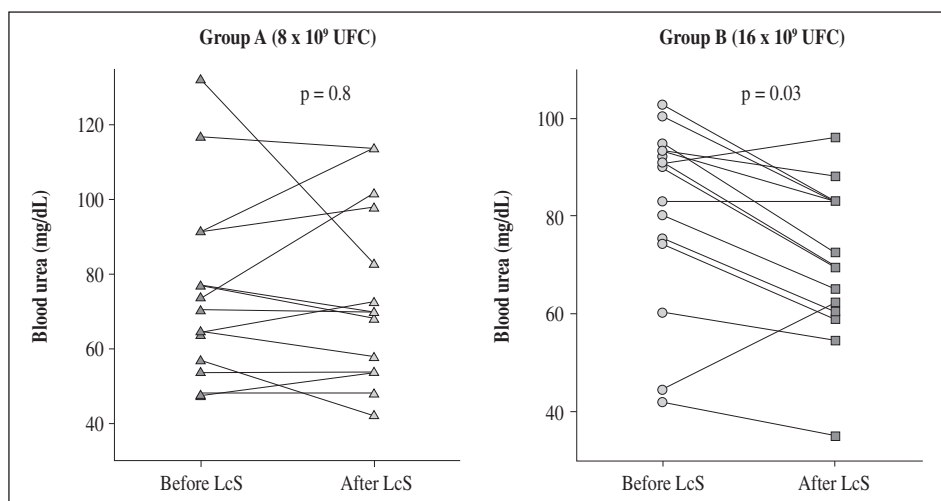


Fig. 2.—The effect of the LcS treatment on the serum urea concentrations.

Table III
Variables assessed at baseline and at the end of the intervention for each group

Parameters	Group A dose 8×10^9 CFU		p	Group B dose 16×10^9 CFU		p
	Baseline measurement n = 15 X ± SD	Final measurement n = 15 X ± SD		Baseline measurement n = 15 X ± SD	Final measurement n = 15 X ± SD	
Weight (kg)	69.6 ± 12.18	68.64 ± 12.44	0.038	71.7 ± 12.39	70.98 ± 12.51	n.s.
BMI (kg/m ²)	25.52 ± 3.15	25.13 ± 3.03	0.19	26.93 ± 3.52	26.66 ± 3.41	n.s.
Sex (F/M)	7/8	7/8		7/8	7/8	
Urea (mg/dL)	82.13 ± 32.96	75.52 ± 23.06	n.s.	81.20 ± 18.86	70.95 ± 15.62	0.003
Creatinine (mg/dL)	2.44 ± 0.79	2.40 ± 0.76	n.s.	2.52 ± 1.01	2.53 ± 1.29	n.s.
GFR MDRD (mL/min/1.73 m ²)	30.66 ± 12.18	31.22 ± 12.44	n.s.	30.74 ± 11.77	31.86 ± 12.34	n.s.

Table IV
Percentage change according to the assigned dose

Variables	Group A (8×10^9 CFU) (n = 15) X ± SD	Group B (16×10^9 CFU) (n = 15) X ± SD	p
Weight %	-1.53 ± 2.27	-1.04 ± 2.86	n.s.
BMI %	-1.51 ± 2.24	0.91 ± 2.76	n.s.
Urea %	-3.37 ± 22.43	-10.98 ± 16.45	n.s.
Creatinine %	0.51 ± 12.62	-2.05 ± 10.76	n.s.
GFR MDRD %	3.28 ± 15.90	4.34 ± 13.01	n.s.

scarcity is observed because the effects of these microorganisms still require further study. Additionally, each strain can function differently, which also hinders the research on dose determinations and the effects of probiotic bacteria.

In the present study, the evaluated doses were the following: 8×10^9 and 16×10^9 CFU. Although a dose of 24×10^9 CFU was used in the study performed by Torre and Vargas,¹⁷ it is important to consider that the results of the present study are the first part of future

studies where the effect of LcS on clinical and biochemical parameters and on different toxins will be assessed in CRF patients. The fermented dairy LcS product contains an important quantity of carbohydrates, and the majority of people with CRF also suffer from diabetes mellitus. For these reasons, it was suggested that larger doses could affect the patients' glycemic control. Moreover, the objective was to have a greater external validation in future studies. In the present study, patients with diabetes mellitus were not included. The study population was small, and patients with diabetes mellitus suffer from major comorbidities that could introduce possible confounders when evaluating the dose effect specifically on CRF patients.

When all the population under study was used to assess the LcS effect on the serum urea concentrations, the decrease in this toxin was confirmed. This result coincides with the one reported by Torre and Vargas,³¹ where a decrease in serum ammonium concentrations was observed in patients with hepatic cirrhosis. The main difference was the level of decrease. In the case of hepatic patients, the level of decrease was 45%, while the decrease for the renal patients was only 10.98%. This finding could be due to the dose used because, as

mentioned before, Torre and Vargas³¹ used a dose of 24×10^9 CFU in all patients.

The greatest decrease, of almost 11%, in the patients' serum urea concentrations was observed after the 16×10^9 dose. Comparing these results with other corresponding studies that used different types of probiotics, the present LcS results do not seem encouraging. In a study performed by Simenhoff,²⁴ *Lactobacillus acidophilus* was used, and a 67% decrease in the dimethylamine (DMA) concentrations and a 31% decrease in the nitrodimethylamine (NDMA) concentrations (toxins generated in CRF) was achieved for dialysis patients. Nevertheless, it is important to emphasize two points that are directly involved in the decrease of DMA and NDMA. First, both toxins are directly produced in the intestine in a way that the lactobacillus used can have a direct effect on the toxin. Urea is a toxin that comes not only from amino acid oxidation by intestinal bacteria but also from various reactions in the urea cycle where intestinal bacteria are not present. Second, hemodialysis patients receive an additional intervention for the elimination of toxins generated by the CRF. The present study evaluated only patients in stage 3 and 4 such that replacement therapy would not cause any confounding effect.

A tool that could provide a greater credibility to the effect of any probiotic microorganism under study in not only the present study but also in the previous studies is the intestinal bacteria count by fecal microbiology. In this way, the change in intestinal microbiome during the intervention could be assessed, verifying the bacterial overgrowth of the intervention microorganism. This approach could ensure that the effect corresponds to the concrete microorganism and not to another mechanism. This method could serve as a tool in future research.

In other studies, the reduction in uremic toxins with the use of probiotic bacteria was greater than the reduction observed in the present LcS study. These studies with lower doses have found a decrease percentage similar to the one observed by Simenhoff in dialysis patients.²⁴ Similar to Simenhoff, Dunn²⁵ used *Lactobacillus acidophilus* at a dose of 3×10^9 CFU and obtained a 42% decrease in the DMA toxin. Alternatively, Taki¹⁹ and Takayama²⁶ used *Bifidobacterium longum*, and they found a decrease in the indoxyl sulfate toxin, which has also the advantage of being produced directly in the intestine. Takayama²⁶ observed a 28% reduction using a dose of 3×10^9 CFU. Taki¹⁹ is the only investigator who obtained results similar to the ones obtained in this study with LcS. This researcher used three different doses over 12 weeks and observed that a dose of 6×10^9 CFU had a greater effect on indoxyl sulfate, achieving a reduction of 9.2%. The variance found in the doses used and the differences in the percentage decrease of toxins suggest the need for further investigation on the effects of probiotic bacteria, their adequate dose

and the time by which they must be used. To date, there has been little consistency among the studies with renal patients, which might suggest that each probiotic bacteria is different and specific.

Concerning the evaluated nutritional treatment, we observed a great adherence from all participants in our study, which positively influenced the results. A good diet adherence from all patients in both the 8×10^9 and 16×10^9 CFU groups permitted a greater homogeneity in variables that could influence the results, mainly including the serum urea concentration, which is significantly affected by protein consumption.

Adherence to the LcS treatment was high, reaching 98%. However, the applied methodology in the present clinical trial was not the best possible. For future studies, an intestinal bacteria quantification to verify the adherence to the probiotic consumption is recommended.

Based on the results obtained to date, it can be concluded that a further investigation on the effects and adequate doses is necessary to prevent and help minimize the production of uremic toxins in CRF patients. In the present study, the 16×10^9 CFU dose showed better results, reaching a decrease of almost 11% for the serum urea concentration. This decrease was significant with respect to the baseline value for the urea concentrations. However, it is necessary to assess larger doses to determine whether they have a greater effect on the reduction of urea. Additionally, it is necessary to assess different toxins to determine if a greater reduction could be obtained that could yield a positive impact on uremic symptoms and on complications caused by CRF-generated toxins. The study's sample size was also small, which could account for the lack of differences between the baseline and final values with the evaluated doses.

Conclusions

In patients with stage 3 and stage 4 CRF, there is a greater than 10% decrease in the serum urea concentrations after a conventional dietetic treatment with LcS. A LcS dose of 6×10^9 CFU resulted in a greater decrease of the blood urea level.

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Original / *Investigación animal*

Effect of conjugated linoleic acid mixtures and different edible oils on body composition and lipid regulation in mice

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Abstract

Introduction: Evidences suggest that commercial and natural conjugated linoleic acids (CLA) differentially affect nutritional status and lipid metabolism.

Objective: To investigate the differential effect of two types of CLA preparations supplemented to dietary fats containing different proportions of n-9, n-6 and n-3 fatty acids (FA) on body composition, triacylglycerol (TG) levels and lipid metabolism in mice.

Methods: Growing mice were fed diets containing olive, maize and rapeseed oils supplemented with an equimolecular mixture of CLA (mix-CLA) or a rumenic acid (RA)-rich oil for 30 days. Body weight gain, carcass composition, tissue weights, plasma and tissue TG levels, and lipid regulation parameters were evaluated.

Results: Independently of the dietary fats, mix-CLA decreased body weight gain and fat depots related to lower energy efficiency, hepatomegaly, increase of serum TG and decrease of muscle TG. Rapeseed oil prevented the hepatic steatosis observed with mix-CLA supplementation to olive and maize oils by increasing TG secretion. RA-rich oil supplementation decreased fat depots without hepatomegaly, hepatic steatosis and hypertriglyceridemia. Olive oil, by an equilibrium between FA uptake/oxidation, prevented the increase of muscle TG induced by the RA-rich oil supplementation to maize and rapeseed oils.

Discussion and conclusion: The proportions of dietary unsaturated FA modulated the different mix-CLA and RA-rich oil response to lipid metabolism in mice. Finally, rapeseed oil prevented the hepatic steatosis induced by mix-CLA, and the most beneficial effects of RA-rich oil were observed when supplemented to olive oil, due to the reduced lipid accretion without changes in TG levels.

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Keywords: *Conjugated linoleic acid. Rumenic acid. Nutritional status. Lipid metabolism.*

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EFFECTOS DE MEZCLAS DE CONJUGADOS DEL ÁCIDO LINOLÉICO Y DIFERENTES ACEITES COMESTIBLES SOBRE LA COMPOSICIÓN CORPORAL Y REGULACIÓN DE LÍPIDOS EN RATONES

Resumen

Introducción: Las evidencias sugieren que las mezclas de Ácido Linoleico Conjugado (ALC) de origen comercial o natural diferencialmente afectan diferencialmente al estado nutricional y al metabolismo lipídico.

Objetivo: Investigar el efecto de dos preparaciones de ALC como complemento de grasas dietarias con diferentes proporciones de ácidos grasos (AG) n-9, n-6 y n-3 sobre composición corporal, niveles de triacilglicéridos (TG) y metabolismo lipídico en ratones.

Métodos: Se alimentó a ratones en crecimiento con dietas con aceite de oliva, maíz y canola, o colza suplementadas con una mezcla equimolecular de ALC (mezcla-ALC) o aceites ricos en ácido ruménico (AR) por 30 días. Se evaluó: ganancia de peso, composición corporal, peso de tejidos, niveles de TG plasmáticos y séricos, y parámetros de regulación lipídica.

Resultados: Independientemente de las grasas dietarias, la mezcla-ALC redujo el peso corporal y depósitos grasos relacionados con hepatomegalia, incremento de TG séricos y descenso de TG musculares. El aceite de canola previno la esteatosis hepática producida por la mezcla-ALC a aceites de oliva y maíz por incremento de la secreción de TG. AR decreció los depósitos grasos sin hepatomegalia, esteatosis hepática e hipertrigliceridemia. Aceite de oliva previno el incremento de TG musculares inducidos por suplementación con AR al aceite de maíz y canola.

Discusión y conclusión: Las proporciones de AG insaturados dietarios modularon la respuesta de mezcla-ALC y AR al metabolismo lipídico en ratones. Finalmente, aceite de canola previno la esteatosis hepática inducida por mezcla-ALC, y los efectos benéficos más notorios fueron observados cuando aceite de oliva fue suplementado con AR, debido a la reducida acreción de lípidos sin cambios en los niveles de TG.

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Palabras clave: *Ácido linoléico conjugado. Ácido ruménico. Estado nutricional. Metabolismo de lípidos.*

Abbreviations

AIN: American Institute of Nutrition.
ALA: α -linolenic acid.
ALP: alkaline phosphatase.
ALT: alanine transaminase.
ARA: arachidonic acid.
AST: aspartate transaminase.
BW: body weight.
c9,t11: *cis-9,trans-11*.
CLA: conjugated linoleic acid.
CPT-I: carnitine palmitoyltransferase-I.
DHA: docosahexaenoic acid.
EE: energetic efficiency.
EI: energy intake.
EPA: eicosapentaenoic acid.
EWAT: epididymal white adipose tissue.
FA: fatty acids.
FAS: fatty acid synthase.
G6PDH: glucose-6-phosphate dehydrogenase.
LA: linoleic acid.
LPL: lipoprotein lipase.
M: maize.
ME: malic enzyme.
O: olive.
OA: oleic acid.
PPAR γ : peroxisomal proliferator activated receptor- γ .
PUFA: polyunsaturated fatty acid.
R: rapeseed.
RA: rumenic acid.
SREBP-1c: transcription factor sterol regulatory element binding protein-1c.
t10,c12: *trans-10,cis-12*.
TG: triacylglycerol.
TG-SR: triacylglycerol-secretion rate.
U: units.

Introduction

Conjugated linoleic acid (CLA) is a group of positional and geometrical isomers of linoleic acid (LA) that are interesting due to their functional properties^{1,2}. The major contribution of natural CLA is supplied by dairy products and meats where *cis-9,trans-11* (*c9,t11*)-CLA, known as rumenic acid (RA), represents 80-90% of total CLA. On the other hand, industrially synthesized commercial CLA mainly contains a mixture of equimolecular amounts of *c9,t11*-CLA and *t10,c12*-CLA (mix-CLA) (approximately 37-40% each).

Many investigations^{1,2} have shown that CLA may have beneficial effects on cancer, obesity, inflammatory response, atherosclerosis and glucose and lipid metabolism. However, controversial and detrimental health effects have also been reported^{2,4}. In addition, it has been demonstrated that RA has a mechanism of action on lipid metabolism different from *trans-10,cis-12* (*t10,c12*)-CLA (mix-CLA), resulting in dissimilar body fat accretion^{3,5}. The conflicting results may be related to

several factors such as comparison of humans with studies of experimental animals, species of animals, physiological conditions, type and level of CLA and dietary fat, and time of feeding. A number of studies have shown that α -linolenic acid (ALA)⁶, γ -linolenic acid⁷, docosahexaenoic acid (DHA)⁸ and arachidonic acid (ARA)⁹ rich oils might attenuate or prevent insulin resistance and fatty liver induced by *t10,c12*-CLA or mix-CLA in mice. These effects might be related to the incorporation of specific fatty acids (FA) into the biological membranes and eicosanoid production derived from the different FA. Therefore, we hypothesized that the extension and type of the beneficial or negative effects of oils containing different relative amounts of the individual CLA on lipid metabolism are related not only to the presence of certain FA, but also to the proportion of the n-9, n-6 and n-3 FA present in the diet. Specifically, at least to our knowledge, there are no systematic studies dealing with the effects on nutritional parameters and lipid metabolism of commercial and natural-like CLA added to diets containing different proportions of unsaturated FA. Thus, the aim of this work was to investigate the differential effect of mix-CLA and RA-rich oil supplemented to dietary fats containing different proportions of n-9, n-6 and n-3 FA on body composition, TG levels and some regulatory mechanisms involved lipid metabolism in mice.

Methods

Materials

Most nutrients were chemical grade or better, with the exception of olive (O) oil (Nucete, La Rioja, Argentina), maize (M) oil (Arcor, Córdoba, Argentina), rapeseed (R) oil (Krol, Entre Ríos, Argentina), sucrose, cellulose, and maize starch, which were obtained from local sources. Mix-CLA and RA-rich oils were kindly provided by Lipid Nutrition B.V. (Wormerveer, The Netherlands). Standard chow for the adaptation period of animals was from Grupo Pilar[®] (Pilar, Córdoba, Argentina). FA standards were purchased from Sigma Chemical Co. (St. Louis, MO, USA). All solvents and reagents used for the FA quantification were chromatography grade, and all the other chemicals used were at least ACS degree. Plasma TG, alanine transaminase (ALT), aspartate transaminase (AST) and alkaline phosphatase (ALP) kits were purchased from Wiener Co. (Rosario, Argentina).

Diets

The diet compositions (table I) were based on the American Institute of Nutrition *ad hoc* writing committee recommendation (AIN-93G diet)¹⁰. All diets were isoenergetic (16.5 MJ/kg), exceeded the essential FA recommendations, and differed either in 1) dietary

Table I
Composition of experimental diets (g/kg of dry diet)

Ingredient	O	O+RA	O+mix-CLA	M	M+RA	M+mix-CLA	R	R+RA	R+mix-CLA
Maize starch	529.5	529.5	529.5	529.5	529.5	529.5	529.5	529.5	529.5
Casein	200.0	200.0	200.0	200.0	200.0	200.0	200.0	200.0	200.0
Sucrose	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Olive oil	70.0	60.0	60.0	–	–	–	–	–	–
Maize oil	–	–	–	70.0	60.0	60.0	–	–	–
Rapeseed oil	–	–	–	–	–	–	70.0	60.0	60.0
RA-rich oil	–	10.0	–	–	10.0	–	–	10.0	–
Mix-CLA oil	–	–	10.0	–	–	10.0	–	–	10.0
Fibre	50.0	50.0	50.0	50.0	50.0	50.0	50.0	50.0	50.0
Mineral mixture*	35.0	35.0	35.0	35.0	35.0	35.0	35.0	35.0	35.0
Vitamin mixture*	10.0	10.0	10.0	10.0	10.0	10.0	10.0	10.0	10.0
L-cystine-L-metionine	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
Choline	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Total energy (MJ/kg)	16.5	16.5	16.5	16.5	16.5	16.5	16.5	16.5	16.5

*Vitamin and mineral mixtures were formulated according to Reeves et al.¹⁰

O, olive; RA, rumenic acid; mix-CLA, *c*9,*t*11-CLA and *t*10,*c*12-CLA in equimolecular amounts; CLA, conjugated linoleic acid; M, maize; R, rapeseed.

fat source: O, M or R oils, and 2) absence or presence of 1 g of mix-CLA or RA-rich oil/100 g diet. The combination of these 2 variables allowed us to create the following diets: O; O+RA; O+mix-CLA; M; M+RA; M+mix-CLA; R; R+RA and R+mix-CLA containing 7 g of total fat/100 g diet. The FA composition of dietary fats, as well as the OA/LA/ALA proportions are shown in table II. These FA compositions as methyl esters were determined by gas chromatography using the equipment and conditions previously reported¹¹.

Animals and treatments

The experimental procedures were approved by the Ethics Committee of our School of Biochemistry and compiled according to the Guide for the Care and Use of Laboratory Animals¹². Male CF1 mice were obtained at the age of three weeks from the facilities at our University. The mice were housed in animal quarters under controlled conditions (23 ± 2°C and 12 h light-dark cycle) in individual stainless steel metabolic cages. After two weeks of adaptation period, mice (~22 g)

Table II
Fatty acid composition of dietary fats*

Fatty acid	Olive oil	Maize oil	Rapeseed oil	RA-rich oil	mix-CLA oil
14:0	0.0	0.0	0.1	0.0	0.0
16:0	17.1	12.2	4.0	3.9	5.9
<i>c</i> 9-16:1	2.0	0.1	0.2	0.0	0.0
17:0	0.1	0.0	0.0	0.0	0.0
18:0	1.6	1.9	2.2	1.0	1.2
<i>c</i> 9-18:1	55.2	32.0	61.1	13.4	9.1
<i>c</i> 11-18:1	4.8	0.5	3.5	0.5	0.4
<i>c</i> 9, <i>c</i> 12-18:2	17.2	51.3	18.4	1.5	1.1
<i>c</i> 9, <i>t</i> 11-18:2	0.0	0.0	0.0	60.5	39.0
<i>t</i> 10, <i>c</i> 12-18:2	0.0	0.0	0.0	17.8	38.8
20:0	0.3	0.5	0.5	0.0	0.0
<i>c</i> 11-20:1	0.2	0.3	0.9	0.0	0.0
<i>c</i> 9, <i>c</i> 12, <i>c</i> 15-18:3	0.7	0.9	8.6	0.0	0.0
22:0	0.1	0.2	0.2	0.1	0.0
24:0	0.0	0.2	0.0	0.0	0.0
Others	0.7	0.0	0.2	1.2	4.7
OA/LA/ALA proportions	55.2/17.2/0.7	32.0/51.3/0.9	61.1/18.4/8.6		

* All values are means as weight percentages of total fatty acid methyl esters.

RA, rumenic acid; mix-CLA, *c*9,*t*11-CLA and *t*10,*c*-12-CLA in equimolecular amounts; CLA, conjugated linoleic acid; OA, oleic acid; LA, linoleic acid; ALA, α -linolenic acid.

were randomly divided into ten weight-matched groups (n=6 per group). One group was killed at the start of the experiment with the purpose of determining initial composition and energetic content of carcass. The remaining animals had free access to water and were fed *ad libitum* during 30 d with one of the following diets: O; O+RA; O+mix-CLA; M; M+RA; M+mix-CLA; R; R+RA or R+mix-CLA. Mice were weighed, food intakes were recorded, and total faeces were collected daily during the whole dietary treatment. On day 30 (9.00-11.00 AM), mice were anaesthetized with azepromazine (1 mg/kg) and ketamine (100 mg/kg), their bodies were shaved, the abdomens were cut open and following the removal of the visceral organs, carcasses were weighed, chopped and frozen at -20°C until the compositional evaluation. In other experiments with the nine experimental groups (n = 6 per group), at the end of the dietary treatments, animals were anaesthetized in order to collect blood samples by cardiac puncture and dissected tissues according to the assay proposed or to perform the *in vivo* hepatic TG secretion rate (TG-SR) test. Blood samples were centrifuged at 4°C, and serum was immediately used or stored at -80°C until analyzed. Liver, epididymal white adipose tissue (EWAT) and gastrocnemius muscle were frozen, weighed, and stored at -80°C until processed.

Laboratory analysis

– *Carcasses, faeces and food compositions.* The protein, water and total fat contents, in aliquots from the carcass homogenate, faeces, and diets were estimated by Official Methods of Analysis of AOAC International¹³.

– *Bioavailability indexes of fat and protein.* The apparent absorption of dietary fat and protein, as bioavailability indexes, were assessed as the percentages of ingested fat or protein that were not excreted in the faeces.

– *Carcass energy retention and energy efficiency.* Carcass energy content was estimated from protein and lipid levels¹⁴. Carcass energy retention was estimated from the final carcass energy content and the carcass energy content at the start of the experiment in the weight-matched animals killed on day 0. The energy intake (EI) was calculated by multiplying weight of food consumed daily by the number of kJ/g diet. Energetic efficiency (EE) was estimated as percentage of body energy gain (kJ/30 d) divided by EI (kJ/30 d).

– *Serum parameters.* TG concentrations and biomarker enzyme activities of liver damage (ALT, AST and ALP) were carried out in serum by spectrophotometric methods using commercially available test kits.

– *Liver and muscle TG content.* Aliquots of liver or gastrocnemius muscle were powdered and homogenized in a saline solution for TG content quantifica-

tion by the spectrophotometric method cited in different articles^{11,15}.

– *In vivo hepatic TG-SR.* Another set of animals submitted to the same dietary treatments was fasted overnight and anaesthetized, as indicated above. Then the *in vivo* hepatic TG-SR was assayed according to the method based on the inhibition of peripheral removal of TG-rich lipoproteins by Triton WR1339, adjusted by our group^{11,15}.

– *Total Lipoprotein Lipase (LPL) activities.* Homogenates of gastrocnemius muscles and acetone powders of EWAT were prepared according to the procedure previously reported¹¹, and the total LPL activities were measured through a fluorimetric method¹⁶. In the case of EWAT, the results were expressed as, U (units)/g EWAT and U/ whole pad EWAT (U/EWAT), while the total LPL activity of gastrocnemius muscle was expressed as U/g gastrocnemius, considering that 1 U = 1 nmol of fluoresceine/min.

– *Lipogenic enzyme activities.* In liver and EWAT homogenates, fatty acid synthase (FAS; EC 2.3.1.85), malic enzyme (ME; EC 1.1.1.40) and glucose-6-phosphate dehydrogenase (G6PDH; EC 1.1.1.49) activities were measured according to the methods described by Lynen (1969)¹⁷, Hsu and Lardy (1969)¹⁸ and Kuby and Noltmann (1966)¹⁹, respectively. In liver, enzyme activities were expressed either as nmol NADPH consumed (FAS) or produced (G6PDH and ME) /min/mg of protein (1 mU = 1 nmol NADPH/min). In the case of EWAT, the results were expressed as mU/g EWAT (1 U = 1 mmol of NADPH consumed or produced/min) or per whole EWAT (U/EWAT). Protein content was determined by the Lowry technique²⁰.

– *Carnitine palmitoyltransferase-I (CPT-I) activities.* CPT-Ia and CPT-Ib (EC 1.3.99.3) activities were assessed in the mitochondrial fraction of liver and muscle, respectively, by the method of Bieber et al.²¹ The CPT-I activities were expressed as mU/mg of protein (1 mU = 1 nmol CoA/min).

Statistical analysis

The statistical analysis was performed using SPSS, version 17.0 (SPSS Inc., Chicago, IL, USA). Data were expressed as means ± standard errors of mean values, and were statistically analyzed by 3×3 ANOVA. All post-hoc multiple comparisons were made using Tukey's critical range test. Significant differences were considered at P < 0.05.

Results

All diets were well accepted showing a similar energy intake, as well as fat and protein apparent absorption associated with a positive body weight gain (table III). Nevertheless, the body weight gain was altered by the source of dietary fats and by the CLA. Specifically, R oil-fed animals increased the body

Table III
Effect of experimental diets on nutritional and body composition parameters

	O	O+RA	O+mix-CLA	M	M+RA	M+mix-CLA	R	R+RA	R+mix-CLA	ANOVA
BW gain (g)	8.3 ± 0.5 ^a	8.6 ± 0.6 ^a	4.4 ± 0.5 ^b	8.5 ± 0.5 ^a	8.9 ± 0.6 ^a	7.0 ± 0.3 ^c	11.5 ± 0.5 ^d	7.8 ± 0.5 ^{ac}	6.7 ± 0.5 ^c	F, I, F × I
EI (kJ/d)	59.3 ± 4.0	61.6 ± 4.8	60.8 ± 7.1	58.9 ± 4.9	53.2 ± 2.3	56.0 ± 2.9	58.9 ± 3.6	58.8 ± 6.7	57.3 ± 4.2	NS
<i>Apparent absorption (%)</i>										
Fat	97.1 ± 0.6	97.9 ± 0.1	96.8 ± 0.8	95.0 ± 1.3	97.0 ± 0.2	97.0 ± 0.7	96.5 ± 0.4	97.9 ± 0.1	97.9 ± 0.1	NS
Protein	93.2 ± 0.4	93.7 ± 0.3	95.0 ± 0.3	92.8 ± 0.3	93.6 ± 0.5	93.9 ± 0.8	92.8 ± 0.5	93.9 ± 0.7	93.3 ± 0.5	NS
<i>Carcass energy retention (kJ/d)</i>										
Total	2.4 ± 0.2 ^a	1.9 ± 0.1 ^a	0.2 ± 0.1 ^b	2.0 ± 0.2 ^a	1.9 ± 0.1 ^a	1.0 ± 0.1 ^c	3.8 ± 0.1 ^d	2.2 ± 0.2 ^a	0.4 ± 0.1 ^{bc}	F, I, F × I
Fat	1.3 ± 0.2 ^a	0.6 ± 0.0 ^b	-0.7 ± 0.1 ^c	0.9 ± 0.1 ^{ab}	0.7 ± 0.1 ^b	-0.6 ± 0.1 ^c	2.5 ± 0.1 ^d	1.3 ± 0.2 ^a	-0.6 ± 0.0 ^c	F, I, F × I
Protein	1.2 ± 0.1 ^{abc}	1.4 ± 0.0 ^{ad}	0.8 ± 0.1 ^c	1.1 ± 0.1 ^{bc}	1.2 ± 0.1 ^{abc}	1.5 ± 0.0 ^d	1.3 ± 0.1 ^{ab}	1.0 ± 0.0 ^c	1.1 ± 0.1 ^{bc}	F, F × I
EE (%)	4.2 ± 0.2 ^a	3.5 ± 0.1 ^{ab}	0.3 ± 0.1 ^c	3.2 ± 0.2 ^b	3.6 ± 0.3 ^{ab}	1.7 ± 0.1 ^d	6.3 ± 0.1 ^e	3.7 ± 0.3 ^{ab}	0.8 ± 0.1 ^c	F, I, F × I
<i>Carcass composition (g/100g)</i>										
Fat	9.7 ± 1.2 ^a	8.0 ± 0.6 ^a	4.5 ± 0.4 ^b	9.3 ± 0.8 ^a	9.3 ± 0.6 ^a	3.9 ± 0.3 ^b	13.6 ± 0.6 ^c	10.4 ± 0.8 ^a	4.5 ± 0.2 ^b	F, I, F × I
Protein	24.9 ± 0.8	24.1 ± 0.1	25.3 ± 0.5	24.3 ± 0.4	25.1 ± 1.3	27.1 ± 1.0	23.1 ± 0.4	22.7 ± 0.6	24.2 ± 0.3	NS
Water	63.0 ± 1.0	64.5 ± 0.4	66.0 ± 0.3	63.2 ± 1.0	63.7 ± 0.3	67.0 ± 0.3	60.1 ± 0.7	63.2 ± 1.0	66.6 ± 0.3	NS
<i>Tissue weights</i>										
<i>Liver</i>										
g	2.2 ± 0.1 ^a	2.4 ± 0.1 ^a	3.0 ± 0.2 ^b	2.3 ± 0.2 ^a	2.4 ± 0.1 ^a	2.6 ± 0.2 ^{ab}	2.2 ± 0.1 ^a	2.1 ± 0.1 ^a	2.8 ± 0.1 ^b	I
g/100 g BW	6.7 ± 0.3 ^a	6.8 ± 0.2 ^a	8.8 ± 0.3 ^b	6.5 ± 0.3 ^a	7.1 ± 0.1 ^a	8.0 ± 0.2 ^b	6.7 ± 0.2 ^a	6.6 ± 0.2 ^a	8.3 ± 0.3 ^b	I
<i>EWAT</i>										
g	0.4 ± 0.0 ^b	0.3 ± 0.0 ^b	0.1 ± 0.0 ^c	0.5 ± 0.0 ^b	0.3 ± 0.0 ^b	0.1 ± 0.0 ^{bd}	0.7 ± 0.0 ^e	0.2 ± 0.0 ^{bd}	0.1 ± 0.0 ^c	F, I, F × I
g/100 g BW	1.3 ± 0.1 ^a	0.9 ± 0.1 ^b	0.4 ± 0.0 ^c	1.5 ± 0.1 ^{ac}	1.0 ± 0.1 ^b	0.4 ± 0.0 ^{bd}	1.8 ± 0.1 ^c	0.7 ± 0.1 ^{bd}	0.4 ± 0.1 ^c	I, F × I
<i>Gastrocnemius</i>										
g	0.3 ± 0.0	0.3 ± 0.0	0.3 ± 0.0	0.3 ± 0.0	0.3 ± 0.0	0.3 ± 0.0	0.3 ± 0.0	0.3 ± 0.0	0.3 ± 0.0	NS
g/100 g BW	0.8 ± 0.1	0.9 ± 0.0	0.9 ± 0.0	0.8 ± 0.0	0.9 ± 0.0	0.9 ± 0.1	0.8 ± 0.0	0.9 ± 0.0	0.9 ± 0.0	NS

The results are expressed as mean values with their standard errors for six animals per group.

^{abcd,e}Mean values within a row with dissimilar superscript letters were significantly different ($P < 0.05$) by Tukey's critical range test after ANOVA (3×3). F, effect of dietary fat source; I, effect of absence or presence of CLA isomers; NS, not significant.

O, olive; RA, ruminic acid; mix-CLA, c9,t11-CLA and t10,c12-CLA in equimolecular amounts; CLA, conjugated linoleic acid; M, maize; R, rapeseed; BW, body weight; EI, energy intake; EE, energy efficiency; EWAT, epididymal white adipose tissue.

weight gain, and the supplementation with mix-CLA in all groups and RA-rich oil in R-mice diminished this parameter.

The higher body weight of R oil-mice was associated with a higher fat retention in carcasses, as well as in EWAT pads. The reduced body weight gain by mix-CLA in all dietary sources was mainly associated with losses of fat in carcasses and in fat pads. A differential and slighter effect was produced by RA-rich oil, where only a significant reduction of body weight gain was observed in R+RA animals. In this group, the changes in body weight gain were also related to a reduction in the content of fat carcass and EWAT.

The liver weight was not altered by the dietary fat sources; however, mix-CLA supplementation to diets induced hepatomegaly and these alterations were not associated with changes in biomarkers of hepatic damage (table IV).

In the absence of CLA supplementation, the TG levels in serum, liver and gastrocnemius muscle were not modified by the dietary fat source, but were altered by the type of CLA (table IV). Serum TG were increased in all animals fed diets supplemented with mix-CLA and in those mice fed with the M+RA diet. Hepatic TG levels showed differential effects depending on the fat source considered in mix-CLA supplementation and did not show differences by RA-rich oil supplementation. In this regard, the increase by mix-CLA in hepatic TG content was O+mix-CLA > M+mix-CLA > R+mix-CLA. In this latter group, this increase is not statistically significant when compared with those animals without mix-CLA. The TG content in the gastrocnemius muscles of animals fed diets supplemented with mix-CLA was significantly reduced, while RA-rich oil supplementation increased the TG content in those animals fed with M and R oil diets.

In the absence of CLA, the hepatic TG-SR did not change by the dietary fat source; however, it was highly increased in R+mix-CLA mice and in all animals fed with RA-rich oil supplemented diets. The total LPL activity in EWAT was increased by RA-rich oil and in greater proportion by mix-CLA. However, when the EWAT size was considered, the contribution to the total TG removal by LPL in animals fed diets supplemented with mix-CLA was significantly reduced, as well as in M+AR and R+AR mice compared to their respective controls. The gastrocnemius muscle total LPL activity was increased in M+RA and R+RA mice, and did not change by mix-CLA supplementation independently of dietary fat source. Since no differences were found in gastrocnemius weight, the expression of total LPL activity/total muscle showed the same pattern that per g of muscle (data not shown).

In the absence of CLA, the three hepatic lipogenic enzymes (FAS, ME and G6PDH) activities measured did not show differences by dietary fat source (table V) and, with the exception of R+RA mice in the ME activity, the supplementation with mix-CLA or RA-rich oil to diets increased both FAS and ME activities

without changes in G6PDH activity. In EWAT, the activities of these three enzymes (expressed as mU/mg protein) did not change by dietary fat source and were increased by mix-CLA and RA-rich oil supplementation. However, when the contribution of these enzymes to the total lipogenesis in the EWAT is estimated, RA-rich oil supplementation increased the activities of the three enzymes in the animals fed with any fat source, with the exception of R+RA mice in which the observed increase in FAS activity did not reach statistical significance. On the other hand, under this expression, mix-CLA supplementation to fat diets did not modify any of the lipogenic enzyme activities evaluated in EWAT.

The main enzymes involved in the β -oxidation of liver and skeletal muscle are the CPT-Ia y CPT-Ib, respectively. This enzyme increased in the liver of animals fed R and M+RA diets. In the gastrocnemius, the CPT-Ib activity was higher in mice fed M or R vs O diets, as well as in those fed with the mix-CLA diet.

Discussion

Several studies have reported the benefits and disadvantages on the nutritional status and lipid metabolism of different types of CLA, as well as of different dietary fat sources. To the best of our knowledge, there are no nutritional investigations dealing with the combination of naturally or commercially obtained CLA and different sources of fats and its effects on parameters related to risk of non-communicable disorders. Therefore, the aim was to investigate the differential effect of two types of CLA preparations supplemented to dietary fats containing different proportions of n-9, n-6 and n-3 FA on body composition, TG levels and lipid metabolism in mice.

In comparison with RA-rich oil, mix-CLA supplementation showed a very high influence on body composition and lipid parameters. The present results confirmed, and also extended to different dietary fats, data reported by other authors^{3,22,23}, in which the mix-CLA decreased the body weight gain associated with a deep reduction in fat storage and hepatomegaly, while RA-rich oil has a lower but significant reduction of fat pads without negative impact on liver. The alterations observed by mix-CLA have been described in mice³ as a "lipoatropic syndrome", and is due to the *t10,c12*-CLA isomer. Different outcomes have been observed in other species; thus, weak or no effects have been reported in normal rats and other animal models, leading to the conclusion that the species and strain are determinant of the biological response of CLA^{24,25}. In vivo and in vitro studies^{3,4,26,27} have indicated that the putative mechanism of the *t10,c12*-CLA effect might include, reduction of the total LPL activity in adipose tissue, decreased preadipocyte differentiation and proliferation, inhibition of stearoyl coenzyme A desaturase activity, increased apoptosis of adipocytes induced by tumor necrosis factor- α and enhanced

Table IV
Effect of experimental diets on serum biomarker of hepatic damage, TG levels and parameters related to TG regulation

	O	O+RA	O+mix-CLA	M	M+RA	M+mix-CLA	R	R+RA	R+mix-CLA	ANOVA
Serum activities (U/L)										
ALT	19.7 ± 1.2 ^{abc}	12.8 ± 1.0 ^d	22.9 ± 1.5 ^b	20.6 ± 0.7 ^{abc}	15.2 ± 0.7 ^{ad}	22.0 ± 1.0 ^{bc}	18.0 ± 0.8 ^{abcd}	16.8 ± 2.0 ^{abd}	23.7 ± 1.9 ^b	I
AST	43.3 ± 5.2	39.3 ± 6.6	54.5 ± 5.7	56.5 ± 2.0	45.5 ± 12.1	64.0 ± 5.5	39.3 ± 4.9	31.5 ± 7.5	42.7 ± 0.7	F, I
ALP	159.4 ± 9.0 ^{ab}	176.7 ± 16.8 ^a	169.9 ± 8.4 ^a	126.8 ± 18.9 ^{ab}	149.3 ± 11.3 ^{ab}	104.0 ± 14.2 ^b	156.0 ± 7.8 ^{ab}	141.3 ± 21.3 ^{ab}	153.1 ± 10.2 ^{ab}	F
TG levels										
Serum (mmol/L)	0.7 ± 0.1 ^a	0.7 ± 0.1 ^a	1.3 ± 0.2 ^{bc}	0.8 ± 0.0 ^a	1.1 ± 0.0 ^b	1.5 ± 0.1 ^c	0.7 ± 0.0 ^a	0.8 ± 0.1 ^a	1.5 ± 0.1 ^c	F, I
Liver (µmol/g)	32.5 ± 1.6 ^a	37.1 ± 2.0 ^{ab}	55.5 ± 3.4 ^c	32.7 ± 2.2 ^a	31.0 ± 1.9 ^a	43.6 ± 2.7 ^b	34.0 ± 1.9 ^{ab}	31.6 ± 2.0 ^a	37.9 ± 2.2 ^{ab}	F, I, F × I
Muscle (µmol/g)	7.0 ± 1.4 ^a	7.2 ± 0.8 ^a	3.0 ± 0.5 ^b	7.3 ± 0.5 ^a	11.1 ± 1.7 ^c	4.2 ± 0.8 ^b	7.3 ± 0.8 ^a	10.4 ± 1.2 ^c	3.9 ± 0.6 ^b	I
Hepatic TG-SR (nmol/ml/min)										
	173.9 ± 14.8 ^a	331.5 ± 26.6 ^{bc}	208.8 ± 9.2 ^a	193.3 ± 13.6 ^a	295.0 ± 37.1 ^c	195.0 ± 14.3 ^a	209.7 ± 20.1 ^a	312.7 ± 34.2 ^c	417.8 ± 32.2 ^b	F, I, F × I
Total LPL activities										
U/g EWAT	0.9 ± 0.0 ^b	1.7 ± 0.2 ^b	2.3 ± 0.2 ^c	0.8 ± 0.1 ^b	1.8 ± 0.1 ^b	2.4 ± 0.0 ^c	1.1 ± 0.1 ^a	1.9 ± 0.1 ^{bc}	2.2 ± 0.1 ^{bc}	I
U/EWAT	0.5 ± 0.0 ^{ab}	0.5 ± 0.1 ^b	0.3 ± 0.0 ^c	0.6 ± 0.1 ^{ad}	0.5 ± 0.0 ^b	0.5 ± 0.0 ^b	0.8 ± 0.1 ^d	0.5 ± 0.1 ^{bc}	0.3 ± 0.0 ^c	F, I, F × I
U/g muscle	11.5 ± 0.7 ^{ab}	12.8 ± 0.7 ^b	12.2 ± 0.4 ^b	9.9 ± 0.6 ^a	12.6 ± 0.6 ^b	9.9 ± 0.5 ^a	10.0 ± 0.5 ^a	11.7 ± 0.5 ^b	10.2 ± 0.4 ^a	F, I

The results are expressed as mean values with their standard errors for six animals per group.

^{abcde}Mean values within a row with dissimilar superscript letters were significantly different ($P < 0.05$) by Tukey's critical range test after ANOVA (3×3). F, effect of dietary fat source; I, effect of absence or presence of CLA isomers; NS, not significant.

O, olive; RA, ruminic acid; mix-CLA, *c9,t11*-CLA and *t10,c12*-CLA in equimolecular amounts; CLA, conjugated linoleic acid; M, maize; R, rapeseed; ALT, alanine transaminase; AST, aspartate transaminase; ALP, alkaline phosphatase; TG, triacylglycerol; TG-SR, hepatic TG secretion rate; LPL, lipoprotein lipase; EWAT, epididymal white adipose tissue.

Table V
Effect of experimental diets on lipogenic and oxidative enzyme activities

	O	O+RA	O+mix-CLA	M	M+RA	M+mix-CLA	R	R+RA	R+mix-CLA	ANOVA
Lipogenic enzyme activities										
<i>Liver (mU/mg protein)</i>										
FAS	29.7 ± 5.5 ^a	59.5 ± 7.1 ^{bc}	82.5 ± 2.6 ^d	31.0 ± 4.2 ^a	72.9 ± 3.4 ^{cd}	50.3 ± 2.5 ^b	33.3 ± 3.8 ^a	49.3 ± 4.3 ^b	62.5 ± 5.7 ^{bc}	I, F × I
ME	88.5 ± 1.5 ^{ab}	197.3 ± 6.5 ^c	328.8 ± 5.6 ^d	67.9 ± 5.6 ^a	137.4 ± 13.3 ^c	180.4 ± 3.2 ^c	102.2 ± 7.0 ^{abc}	122.1 ± 8.4 ^{bc}	207.1 ± 12.6 ^c	F, I, F × I
G6PDH	12.6 ± 1.9	8.8 ± 2.2	10.0 ± 0.9	10.4 ± 1.3	8.2 ± 2.1	8.1 ± 1.6	9.4 ± 2.5	8.4 ± 1.6	6.7 ± 0.8	NS
<i>EWAT (mU/mg protein)</i>										
FAS	25.9 ± 2.1 ^a	65.0 ± 5.9 ^b	55.3 ± 1.6 ^b	25.6 ± 3.6 ^a	56.4 ± 6.1 ^b	51.7 ± 9.0 ^{bc}	28.2 ± 1.3 ^{bc}	60.4 ± 5.2 ^b	54.5 ± 6.3 ^b	I
ME	61.8 ± 3.8 ^a	248.6 ± 13.2 ^b	211.9 ± 14.0 ^{bc}	52.8 ± 4.7 ^a	199.6 ± 12.9 ^{bc}	165.3 ± 5.3 ^c	54.4 ± 6.3 ^a	231.9 ± 16.3 ^b	222.5 ± 12.2 ^b	F, I
G6PDH	182.3 ± 14.6 ^a	654.3 ± 11.1 ^b	625.1 ± 20.6 ^b	150.2 ± 12.6 ^a	506.9 ± 76.7 ^{bc}	427.3 ± 50.1 ^c	155.5 ± 18.9 ^a	577.3 ± 40.0 ^{bc}	598.1 ± 30.5 ^{bc}	F, I
<i>EWAT (U/EWAT)</i>										
FAS	0.2 ± 0.0 ^a	0.4 ± 0.0 ^b	0.1 ± 0.0 ^a	0.2 ± 0.0 ^b	0.4 ± 0.1 ^b	0.2 ± 0.0 ^b	0.3 ± 0.0 ^{ab}	0.4 ± 0.1 ^b	0.2 ± 0.0 ^a	I
ME	0.6 ± 0.1 ^{ab}	1.3 ± 0.1 ^c	0.5 ± 0.1 ^a	0.5 ± 0.1 ^a	1.2 ± 0.0 ^c	0.5 ± 0.0 ^a	0.5 ± 0.1 ^{ab}	1.3 ± 0.0 ^c	0.8 ± 0.0 ^b	F, I, F × I
G6PDH	1.3 ± 0.2 ^a	3.7 ± 0.3 ^b	1.2 ± 0.2 ^a	1.1 ± 0.1 ^a	3.2 ± 0.2 ^b	1.0 ± 0.1 ^a	1.3 ± 0.2 ^a	3.6 ± 0.4 ^b	1.2 ± 0.2 ^a	I
CPT-I activities (mU/mg protein)*										
Liver	4.2 ± 0.4 ^{ab}	4.4 ± 1.1 ^{abc}	5.7 ± 0.9 ^{bc}	3.3 ± 0.7 ^a	7.7 ± 0.7 ^c	3.3 ± 0.5 ^a	6.7 ± 0.2 ^c	7.6 ± 0.8 ^{bc}	6.8 ± 0.4 ^{bc}	F, I, F × I
Muscle	1.1 ± 0.1 ^a	2.0 ± 0.4 ^{ab}	5.5 ± 0.2 ^{cd}	2.9 ± 0.6 ^{bc}	3.5 ± 0.2 ^{bc}	6.6 ± 0.3 ^d	4.0 ± 0.2 ^{ce}	3.0 ± 0.7 ^{bc}	6.4 ± 0.3 ^d	F, I

The results are expressed as mean values with their standard errors for six animals per group.

^{abcde}Mean values within a row with dissimilar superscript letters were significantly different ($P < 0.05$) by Tukey's critical range test after ANOVA (3×3). F, effect of dietary fat source; I, effect of absence or presence of CLA isomers; NS, not significant.

O, olive; RA, ruminic acid; mix-CLA, *c9,t11*-CLA and *t10,c12*-CLA in equimolecular amounts; CLA, conjugated linoleic acid; M, maize; R, rapeseed; FAS, fatty acid synthase; ME, malic enzyme; G6PDH, glucose-6-phosphate dehydrogenase; EWAT, epididymal white adipose tissue; CPT-I, carnitine palmitoyltransferase-1.

*CPT-Ia in liver, CPT-Ib in muscle.

energy expenditure via the family of uncoupling proteins.

Different sources of dietary fats had a dissimilar impact on the body composition of the animals. Strikingly, mice fed the R diet, showed an increased body weight gain associated with an enhanced energy efficiency and fat accretion. Even though it is generally known that n-3 PUFA reduce adiposity, most of the beneficial effects of n-3 PUFA are attributed to EPA and DHA. However, there is not enough evidence supporting that ALA-rich oils provide the same physiological effects²⁸. Thus, in agreement with our results but not with other results from animals fed with ALA-rich diets, Sealls et al.²⁹ in mice fed diets containing lard (low in n-3 PUFA), rapeseed oil or DHA+EPA-rich oil showed a larger size of the EWAT in the rapeseed oil fed animals. These results were explained by the activation of both transcription factor sterol regulatory element binding protein-1c (SREBP-1c) and peroxisomal proliferator activated receptor- γ (PPAR γ) when ALA levels were high, raising the lipogenesis in adipose tissue. In the animals fed with the R diet, the RA-rich oil supplementation decreased body weight gain associated with lower fat depots. The magnitude of the lowering effect of RA-rich oil on body weight gain was significantly lower than that observed by mix-CLA supplementation, but interestingly no hepatomegaly or other adverse effects were present in RA-rich oil fed mice. Independently of the effect on body weight gain, a reduction of the EWAT was found in all animals fed diets supplemented with RA-rich oil. The results of individual RA (purity: 90%) on body and adipose tissue weight are controversial³⁰, and the biochemical mechanisms proposed are unclear. However, in our experimental conditions the fat reduction induced by RA-rich oil could be related to lower total LPL enzyme activities observed in M+RA and R+RA, but not in O+RA groups. Akahoshi et al.³¹ did not find changes in body weight gain of RA (purity: 80%) fed rats for 26 d; however, they found a differential response depending on the adipose tissue considered. In this regard, they showed a lower perirenal adipose tissue weight associated with a tendency of lower epididymal fat pads and a raised brown adipose tissue. Lopes et al.,³⁰ demonstrated that RA (purity: 90%) fed rats had larger adipocytes than those fed *t10,c12*-CLA (purity: 90%), without any differences in the final fat pad weights.

It is very well known that dietary fats, as well as CLA might differentially alter the lipid metabolism, changing the levels of TG in the plasma and tissues of animals^{15,23}. Besides, there is no systematic study dealing with dietary fats, representing different proportions of n-9, n-6 and n-3 FA, supplemented with diverse types or preparations of CLA on TG regulation. The serum TG levels are regulated, among other mechanisms, by the liver TG-SR and by the peripheral TG removal in the white adipose tissue and skeletal muscle. Mix-CLA increased the serum TG in animals

fed with different fat sources which could be explained by a lower adipose tissue total LPL activity and in the R+mix-CLA group, additionally, by a higher hepatic TG-SR. On the other hand, RA-rich oil increased the serum TG levels only in animals fed the M+RA diet and this effect could be due to the higher hepatic TG-SR associated with a lower adipose tissue total LPL enzyme activity. The same effect of RA-rich oil on liver TG-SR and total LPL activity was observed in animals fed the R+RA diet; however, no changes in plasma TG concentrations were demonstrated. At least to our knowledge, there is no study on the physiological mechanisms that could explain this regulatory state observed in the R+RA group, but it could be hypothesized that the composition of the TG-rich lipoprotein of the animals fed the M+RA diet might have a lower affinity for the LPL enzyme than for those lipoproteins of the animals fed the R+RA diet. This hypothesis does not preclude that other biological mechanisms could be implicated. Similar results on serum TG concentration have been observed by de Deckere et al.³² in hamsters fed with mix-CLA and with individual isomers: *t10,c12*-CLA and *c9,t11*-CLA. However, a different response was obtained in hamsters by other authors⁵. The lowering effect of mix-CLA has also been observed by our group¹⁵ in mice fed hyperlipidaemic diets. Therefore, there is controversial response of serum TG by CLA and this effect could be related to species, animal model, isomer and type of dietary fat, among other factors.

The increased hepatic TG induced by mix-CLA in O+mix-CLA and M+mix-CLA groups, were clearly related with an unbalance between lipogenesis/ β -oxidation that was not compensated with a higher hepatic TG-SR. Specifically, we observed a stimulation of hepatic lipogenic enzyme activities: FAS and ME without changes in CPT-Ia activities in all mix-CLA-fed animals. Surprisingly, we found a differential effect in the R+mix-CLA group, where the liver TG-SR was notoriously increased, leading to an enhanced TG output that prevented the hepatic steatosis. The supplementation with RA-rich oil to the three dietary fats also raised the FAS and ME, without changes in CPT-Ia activity; but in all these groups the increased hepatic TG-SR could counteract and avoid the TG accretion in liver. The hepatic steatosis observed in mice fed O+mix-CLA and M+mix-CLA diets have been discussed in different conditions by other authors^{3,15,23} mainly by the same biological mechanisms. In contrast, little information has been reported on hepatic TG levels in animals fed the *c9,t11*-CLA isomer but there is consensus on the absence of changes^{22,23} in liver TG content. According to Clément et al.²² hepatic steatosis induced by the pure *t10,c12*-CLA isomer, specifically in mice, is secondary to hyperinsulinemia, which causes an increased FA uptake and synthesis, while hepatic steatosis was not noted in pure *c9,t11*-CLA-fed mice, which remained normoin-

sulinemic. In addition, Degrace et al.²³ proposed that pure *t*10,*c*12-CLA enhanced the malonyl-CoA generation and thus inhibited the CPT-I and FA oxidation. This mechanism together with an increased lipoprotein uptake and lipogenesis could explain the hepatic steatosis of *t*10,*c*12-CLA fed mice not induced by *c*9,*t*11-CLA.

White adipose tissue and muscle are key regulatory tissues for lipid metabolism and mobilization. Our results of the decreased EWAT weight in mix-CLA-fed mice are in agreement with the reduction of total LPL activity (expressed per total EWAT), and also with the results of other authors³³. The lower availability of FA in adipose tissue could explain the increased lipogenic enzyme activities observed in this study and in others³⁴, attempting to compensate the lower TG depots. However, comparing with mix-CLA, RA-rich oil supplementation decreases the total LPL enzyme activity to a lower extent, which seems to be not compensated by the increased lipogenesis in the adipocytes leading to a minor reduction of EWAT weights. Interestingly, we could not discard the possibility that other mechanisms might explain the reduction of EWAT, because in the O+RA group the reduction in EWAT was present parallel to normal total LPL activity. The TG content in muscle were decreased by mix-CLA and, at least in part, could be associated with a high CPT-Ib activity and not with a lower uptake by muscle total LPL activity. The CPT-I enzyme plays a key role in the transport of FA across the mitochondrial membrane; thus, FA might be oxidized obtaining acetyl CoA and energy. These results support further evidence showing that mix-CLA supplementation increases the β -oxidation in skeletal muscle³⁵. A very different effect was observed by RA-rich oil and depended on the fat source. Thus, RA-rich oil supplementation increased the muscle TG depots in M+RA and R+RA, but not in O+RA groups, and this fat accretion correlated with a raised muscle total LPL activity, without changes in CPT-Ib activity. Further studies on the comparison between the supplementation of mix-CLA or RA-rich oil to dietary fats are needed to elucidate the biological mechanisms involved in muscle TG regulation.

In brief, CLA modified the TG metabolism having different effects depending on the composition of CLA preparation, proportions of dietary unsaturated FA and tissue. The magnitude of reduction of fat in carcass and EWAT was higher in the mix-CLA than in the RA-rich oil supplemented diets, independently of the proportions of n-9, n-6 and n-3 FA presented in dietary fats. However, RA-rich oil showed beneficial effects without hepatomegaly, steatosis, or hypertriglyceridaemia. As a consequence of interactions between CLA and dietary fats, it is highlighted that rapeseed oil prevented the hepatic steatosis observed in mice fed olive and maize oils supplemented with mix-CLA by increasing TG-SR; and olive oil, by an

equilibrium between FA uptake/oxidation prevented the increase of muscle TG induced by the RA-rich oil supplementation to maize and rapeseed oils. Thus, the proportions of dietary unsaturated FA modulated the different mix-CLA and RA-rich oil response to lipid metabolism in mice.

Even though the experimental results in animal models, and specifically in mice, cannot be directly extrapolated to humans, knowledge of the mechanisms involved in the beneficial effects of natural and commercial CLA when ingested with different edible oils might be useful for the development of functional foods effective to prevent some metabolic disorders observed in human non-communicable chronic diseases.

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Original / Ancianos

Identification of different nutritional status groups in institutionalized elderly people by cluster analysis

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Abstract

Objectives: To apply a cluster analysis to groups of individuals of similar characteristics in an attempt to identify undernutrition or the risk of undernutrition in this population.

Methods: Design: A cross-sectional study. Setting: Seven public nursing homes in the province of Murcia, on the Mediterranean coast of Spain. Participants: 205 subjects aged 65 and older (131 women and 74 men). Measurements: Dietary intake (energy and nutrients), anthropometric (body mass index, skinfold thickness, mid-arm muscle circumference, mid-arm muscle area, corrected arm muscle area, waist to hip ratio) and biochemical and haematological (serum albumin, transferrin, total cholesterol, total lymphocyte count). Variables were analyzed by cluster analysis.

Results: The results of the cluster analysis, including intake, anthropometric and analytical data showed that, of the 205 elderly subjects, 66 (32.2%) were overweight/obese, 72 (35.1%) had an adequate nutritional status and 67 (32.7%) were undernourished or at risk of undernutrition. The undernourished or at risk of undernutrition group showed the lowest values for dietary intake and the anthropometric and analytical parameters measured.

Conclusions: Our study shows that cluster analysis is a useful statistical method for assessing the nutritional status of institutionalized elderly populations. In contrast, use of the specific reference values frequently described in the literature might fail to detect real cases of undernourishment or those at risk of undernutrition.

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Keywords: *Undernutrition. Malnutrition. Elderly. Nursing-home. Cluster analysis.*

IDENTIFICACIÓN DE GRUPOS DE PERSONAS MAYORES INSTITUCIONALIZADAS CON DIFERENTE ESTADO NUTRICIONAL MEDIANTE UN ANÁLISIS DE CONGLOMERADOS

Resumen

Objetivos: Aplicar un análisis de conglomerados (cluster analysis) para grupos de individuos de características similares en un intento de identificar la desnutrición o el riesgo de desnutrición en esta población.

Métodos: Estudio transversal llevado a cabo en 205 sujetos de 65 años (131 mujeres y 74 hombres), residentes en siete centros públicos de la Región de Murcia, localizada en la costa mediterránea de España. Se valoró ingesta dietética (energía y nutrientes), medidas antropométricas (índice de masa corporal, pliegues cutáneos, circunferencia muscular del brazo, área muscular del brazo, área muscular del brazo corregida, relación cintura-cadera) y parámetros bioquímicos y hematológicos (albúmina, transferrina, colesterol total, recuento total de linfocitos). Las variables se analizaron mediante análisis de conglomerados.

Resultados: Los resultados del análisis de conglomerados, incluyendo la ingesta, datos antropométricos y analíticos mostraron que, de los 205 sujetos ancianos, 66 participantes (32,2%) presentaron sobrepeso/obesidad, 72 (35,1%) tenían un estado nutricional adecuado y 67 (32,7%) estaban desnutridos o en riesgo de desnutrición. El grupo con desnutrición o en riesgo de desnutrición mostró los valores más bajos de la ingesta dietética y los parámetros antropométricos y clínicos.

Conclusiones: El estudio muestra que el análisis de conglomerados es un método estadístico útil para evaluar el estado nutricional de las poblaciones de ancianos institucionalizados. Por el contrario, el uso de los valores de referencia específicos, descritos con frecuencia en la literatura, podría no detectar situaciones reales de desnutrición o en riesgo de desnutrición.

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Palabras clave: *Desnutrición. Malnutrición. Residencias públicas. Personas mayores. Análisis de conglomerados.*

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Abbreviations

BMI: body mass index.
CAMA: corrected-arm muscle area.
E: energy.
MAC: mid-arm circumference.
MAMA: mid-arm muscle area.
MAMC: mid-arm muscle circumference.
RDI: Recommended Dietary Intake.
TSF: Triceps skinfolds.
WHR: waist to hip ratio.

Introduction

Malnutrition is an overall term used for different deviations from the normal nutritional status. As such it can refer to subjects who are either over- or under-nourished. Undernutrition is the state produced by the intake of insufficient macronutrients or micronutrients: protein-energy malnutrition or vitamin and mineral deficiency¹. However, the causes of poor nutritional status in older people are complex, and may be a result of poor dietary intake or a secondary consequence of acute or chronic disease².

Malnutrition in the elderly is a frequent and multifactorial problem, more prevalent in hospitals and nursing homes where it is rarely recognised and treated. It is also associated with massive healthcare expenditure^{3,4}. The effects of malnutrition are especially dramatic in older people, who tend to be the most vulnerable, fragile and dependent⁵⁻⁷. However, several studies have shown that nutritional therapies can substantially improve the nutritional status of the elderly⁸⁻¹².

A suitable evaluation of the nutritional status of elderly people and its associated factors should help reduce the prevalence of undernutrition, improving the quality of life, reducing the number of hospitalized and institutionalized persons, and cutting the public expense of providing health and social care for this population group^{4,13}.

Undernutrition in most developed countries ranges between 5 and 20% for the free-living elderly, but may be more frequent in nursing home residents and hospital patients (19-65%)^{14,15}. However, although undernutrition is a common problem in the elderly, no gold standard exists for evaluating nutritional status.

Data from recent studies concerning the prevalence of undernutrition in the elderly population vary greatly between studies and depend on the characteristics of the subjects studied, as well as the nutritional screening tool and the cut-off values considered for identifying the disorder¹⁶⁻²⁰. In a study conducted by our group, we found that the prevalence of undernutrition in the same population studied varied between 2 and 57% according to the ten nutritional screening tools used¹⁸. In another recent study, Poulia et al. (2012)¹⁹ found that the prevalence of undernutrition in the elderly ranged

from 42.7 to 97.6%, depending on the six nutritional screening tools used.

In view of the variability in the nutritional screening tools used, and the different parameters and normal values considered in the literature to define the nutritional status of older people, the aim of the present study was to assess nutritional status by means of a cluster analysis in an institutionalized elderly population from seven public nursing-homes from the province of Murcia (southeast Spain), in an attempt to identify undernutrition or the risk of undernutrition in this population.

Experimental methods

Subjects

The present study was carried out in the province of Murcia (southeast Spain). The age of the subjects ranged from 65 to 96 years and all lived in seven public nursing homes from urban areas. The inclusion and exclusion criteria were previously described¹⁸. A total of 205 subjects (131 women and 74 men) participated in the present study. The mean age \pm standard deviation was 78.6 ± 7.5 years.

Study design

Dietary intake, and anthropometric and biochemical measurements were assessed in all the participants in a cross-sectional study. The survey was conducted in a 24-month period starting in May 2007.

Dietary intake

Food intake was assessed using a previously validated 4-day weighed-food record of all food and fluids consumed during each meal. All subjects were also asked about any food consumed other than in the dining-room of the nursing home. The mean daily intake of energy and nutrients was estimated using GRUNUMUR software²¹. Data were compared with the Recommended Dietary Intake (RDI) for the Spanish elderly population and the dietary balance (percentage of total energy from each macronutrient) was compared with Mediterranean diet recommendations²²⁻²⁵.

Anthropometric measurements

Weight and height measurements were previously described¹⁸. Body mass index (BMI) was calculated as weight (kg)/height (m)².

Skinfold thickness was measured on the left side of the body, in triplicate to the nearest 0.2 mm using a calliper (GPM, Zurich, Switzerland) with a constant pressure of 10 g/mm². Triceps (TSF) and biceps skinfolds (mm) were

pinched in the front and back part of the arm, midway between the tip of the acromion and the olecranon process. Subscapular skinfold (mm) was pinched at an angle of about 45° to the vertical. Suprailiac skinfold (mm) was pinched just above the iliac crest in the mid-axillary line. Abdominal skinfold (mm) was measured vertically at about 2 cm left of the umbilicus.

Circumferences were measured in triplicate using a flexible non-stretch tape measure calibrated in mm. The mid-arm circumference (MAC, cm) was measured on the left arm midway between the tip of the acromion and the olecranon process. The mid-arm muscle circumference (MAMC) was calculated according to the following formula²⁶: $MAMC (cm) = MAC (cm) - 0.1 \times \pi \times TSF (mm)$. The mid-arm muscle area (MAMA) was calculated from the formula²⁷: $MAMA (cm^2) = [MAC (cm) - 0.1 \times \pi \times TSF (mm)]^2 / 4\pi$. The corrected-arm muscle area (CAMA) was calculated according to the following equations²⁸:

$$CAMA = [(MAC - 0.1 \times \pi \times TSF)^2 / 4\pi] - 10 \quad (\text{men})$$
$$CAMA = [(MAC - 0.1 \times \pi \times TSF)^2 / 4\pi] - 6.5 \quad (\text{women})$$

The waist-circumference was obtained midway between the lower rib margin and the iliac crest, following gentle expiration. The hip-circumference was measured over the widest part of the great trochanter. The waist to hip ratio (WHR) was obtained by dividing the values of both circumferences.

The anthropometric parameters were compared with those of the Spanish elderly population²⁹⁻³⁰. BMI was compared with the normal range for elderly people (24-29 kg/m²)³¹. The WHR and waist circumference were compared with the normal values for adults^{32,33}.

Blood collection and biochemical measurements

Fasting blood samples were obtained from all subjects during the early morning. Serum concentrations of albumin, transferrin and total cholesterol were measured using commercial kits (Roche Diagnostic, Mannheim, Germany) on an automated sequential multiple analyser (Roche Diagnostics, Mannheim, Germany). Total lymphocyte counts were made with a Sysmex XE-2100L Model Automated Cell Counter (Roche Diagnostics, Mannheim, Germany). Cut-off criteria for normal values of serum albumin, transferrin, cholesterol concentrations and the total lymphocyte count (35-53 g/l, 200-385 mg/dl for men and 185-405 mg/dl for women, 150-230 mg/dl and $1-4 \times 10^9/l$, respectively) used in the present study were defined in accordance with the recommended laboratory values from the 'Virgen de la Arrixaca University Hospital' (Murcia, Spain).

Ethics

The study protocol was performed in accordance with The Helsinki Declaration of Human Studies and

approved by the Ethical Committee of the University of Murcia. All participants provided their written informed consent.

Statistical analysis

Data are presented as mean \pm standard deviation or as percentages of subjects. The Gaussian distribution of variables was confirmed by the Kolmogorov-Smirnov test and homogeneity of variances by the Levene test. For parametric data, the differences in variables between sexes were analyzed by Student's t-test, and differences in variables between the 3 groups were analyzed by one-way analysis of variance (ANOVA) and subsequent post hoc Bonferroni. For nonparametric data the Mann-Whitney test was used to analyze differences in variables between sexes, and the Kruskal-Wallis test was applied for testing the differences between the three groups. Further testing with Mann-Whitney U test was carried out when significant differences were found. Chi-squared analysis and the analysis of corrected residuals were used to test whether there were significant differences in the proportion of people between different groups. The level of significance was set at 5% for all analyses. The multivariate statistical technique of cluster analysis was used to identify groups within this population that showed similar patterns of nutritional status. Analytical and anthropometric parameters frequently used in the literature to assess nutritional status (BMI, CAMA, serum albumin, transferrin, total cholesterol and total lymphocyte count), and dietary intake data (daily energy and protein intake) were used in this analysis. If clustering variables have scales of very different ranges, the variables with larger values will overwhelm those with smaller values. To make the contribution of all variables to the distance measure more comparable, the variables included in the analysis were standardized. In this study, cluster analysis was performed using the K-means method, in which the number of clusters needs to be preselected. Since no information was available on the appropriate number of clusters in the data set, a series of steps was taken to select the most suitable number. Firstly, several cluster analysis runs were conducted with a varying number of clusters (from two to five). Secondly, the analysis of variance tables of each analysis and the F-statistics of the group variables were inspected to identify cluster solutions with well separated clusters. Thirdly, the size of the emerging clusters and the differences in the variables across individual clusters from each run were examined. With the variables used, all three cluster solutions produced reasonably sized and well separated clusters of different nutritional status, and were therefore selected. The reliability of the cluster solutions was tested by discriminate analysis using the stepwise method. All the data were analysed using SPSS for windows (version 19.0, SPSS Inc., Chicago, USA).

Results

Average dietary intakes of energy and protein fulfilled the Recommended Dietary Intake (RDI) for Spanish elderly subjects. The balance of the diet (percentage of energy from each macronutrient) was well equilibrated (14.5% from proteins, 31.3% from lipids and 53.3% from carbohydrates). The studied subjects showed deficient intakes for zinc, folate and vitamins A, D and E.

The gender-related values of the anthropometric and biochemical parameters recorded in the 205 subjects are shown in table I. In general, the mean values of the anthropometric parameters were considered acceptable for an elderly Spanish population. BMI was within the normal range for such a population. WHR was at the limit of cardiovascular risk in both men and women. Waist circumference was higher than the recommended value for younger adults. The mean values of the biochemical parameters were within the local normal ranges.

Three groups of elderly people (A, B and C) were identified by the cluster analysis. The level of agreement between group membership identified by cluster analysis and predicted group membership using discriminate analysis was 95.1%, indicating a good stability for the cluster solutions. Of the 205 elderly subjects, 66 (32.2%) were assigned to group A, 72 (35.1%) to group B, and 67 (32.7%) to group C, each group representing a different nutritional status. There were no statistical differences for the variable gender among groups.

Table II shows daily dietary intake, and table III shows age, anthropometric and biochemical data for the three cluster groups. There were significant differences among the three groups for the variables included in the cluster analysis and also for the rest of the studied variables that were not included, except for vitamin D intake, WHR and abdominal skinfold thickness.

Group A showed the highest intake of energy and other components of the diet, the energy intake in this case being greater than the RDI for Spanish elderly people. Group B showed adequate energy intake, while group C showed the lowest intake of energy, being below the RDI for Spanish elderly people. In the three groups, protein intake appeared to cover the RDI for Spanish elderly people. The balance of the diet (percentage of energy from each macronutrient) was adequate for the three groups and agreed with Mediterranean diet recommendations. Group C showed the lowest energy percentage from lipids and the highest from carbohydrates. Group C also showed deficiencies in vitamin B₆ intake, which was suitably covered in the other two groups. All three groups showed deficient intakes for zinc, folate, and vitamins D, A and E. Only group A fulfilled the magnesium RDI.

Age was significantly different among groups, group C being the oldest. Group A showed the highest anthropometric data, whereas group C showed the lowest. The percentages of subjects with TSF, MAMC, MAMA values below the 10th percentile and CAMA values of ≤ 21.4 and ≤ 21.6 cm², for men and women, respectively, are shown in figure 1. These percentages were significantly higher in group C.

Table I
*Anthropometric and biochemical data for the elderly population**

Parameters	Total (n = 205)	Men (n = 74)	Women (n = 131)	p‡
Age (y)	78.6 ± 7.5	75.4 ± 7.7	80.3 ± 6.9	0.001
Weight (kg)	68.1 ± 14.1	71.6 ± 13.5	66.0 ± 14.2	0.006
Height (cm)	154.3 ± 8.3	162.8 ± 6.5	149.4 ± 4.3	0.001
BMI (kg/m ²)	28.4 ± 5.9	26.9 ± 4.4	29.3 ± 6.4	0.003
MAC (cm)	30.0 ± 4.7	28.9 ± 3.9	30.6 ± 5.1	0.009
MAMC (cm)	24.1 ± 3.2	24.5 ± 2.9	23.9 ± 3.4	0.268
MAMA (cm ²)	47.2 ± 12.6	48.3 ± 11.1	46.5 ± 13.4	0.343
CAMA (cm ²)	39.4 ± 12.6	38.3 ± 11.1	40.0 ± 13.4	0.341
Waist (cm)	100.2 ± 13.4	100.2 ± 11.9	100.1 ± 14.3	0.983
Hip (cm)	104.7 ± 11.9	100.5 ± 9.4	107.6 ± 12.7	0.001
WHR	0.95 ± 0.14	1.00 ± 0.07	0.91 ± 0.16	0.001
Bicipital (mm)	10.9 ± 5.5	8.1 ± 3.5	12.5 ± 5.8	0.001
Tricipital (mm)	18.6 ± 7.1	14.1 ± 5.0	21.1 ± 6.8	0.001
Subscapular (mm)	19.6 ± 7.6	17.9 ± 5.6	20.7 ± 8.5	0.010
Suprailiac (mm)	19.3 ± 9.6	13.5 ± 6.9	23.0 ± 9.3	0.001
Abdominal (mm)	24.7 ± 12.3	15.8 ± 6.3	31.0 ± 11.6	0.001
Albumin (g/l)	39.9 ± 4.3	40.6 ± 4.1	39.5 ± 4.4	0.077
Transferrin (mg/dl)	246 ± 43	249 ± 43	244 ± 43	0.386
Cholesterol (mg/dl)	196 ± 42	189 ± 40	200 ± 43	0.082
Lymphocytes (× 10 ⁹ /l)	2.00 ± 0.71	1.98 ± 0.69	2.02 ± 0.73	0.882

*Data are presented as mean values ± standard deviation. BMI: body mass index; MAC: mid-arm circumference; MAMC: mid-arm muscle circumference; MAMA: mid-arm muscle area; CAMA: corrected-arm muscle area; WHR: waist to hip ratio. ‡Student's *t*-test or Mann-Whitney test were used to compare means between genders.

Table II
Dietary intake for the three cluster groups and differences among groups*

Intake/d	Group A (n = 66)	Group B (n = 72)	Group C (n = 67)	p‡
Energy (kJ)	9238 ± 1494 ^a	7782 ± 1230 ^b	6937 ± 1481 ^c	0.001
Proteins (%E)	15.2 ± 2.3 ^a	13.8 ± 2.1 ^b	14.5 ± 3.1 ^{ab}	0.003
Proteins (g)	83.6 ± 17.2 ^a	64.0 ± 12.6 ^b	60.1 ± 17.6 ^b	0.001
Lipids (%E)	31.9 ± 5.7 ^a	33.3 ± 5.0 ^a	28.5 ± 4.7 ^b	0.001
Lipids (g)	78.4 ± 19.5 ^a	68.9 ± 15.8 ^b	52.5 ± 14.4 ^c	0.001
Carbohydrates (%E)	52.2 ± 5.8 ^a	51.7 ± 5.7 ^a	56.1 ± 5.4 ^b	0.001
Carbohydrates (g)	288.8 ± 53.8 ^a	240.3 ± 45.7 ^b	232.7 ± 52.4 ^b	0.001
Fiber (g)	24.2 ± 8.0 ^a	17.7 ± 6.6 ^b	16.3 ± 6.2 ^b	0.001
Calcium (mg)	1031 ± 242 ^a	860 ± 267 ^b	919 ± 341 ^{ab}	0.002
Phosphorus (mg)	1644 ± 412 ^a	1244 ± 376 ^b	1281 ± 502 ^b	0.001
Iron (mg)	15.3 ± 3.7 ^a	11.7 ± 3.5 ^b	11.0 ± 3.5 ^b	0.001
Zinc (mg)	8.3 ± 2.6 ^a	6.3 ± 2.0 ^b	5.8 ± 2.5 ^b	0.001
Magnesium (mg)	347 ± 86 ^a	266 ± 71 ^b	259 ± 79 ^b	0.001
Vitamin B ₁ (mg)	1.74 ± 0.49 ^a	1.38 ± 0.42 ^b	1.34 ± 0.48 ^b	0.001
Vitamin B ₂ (mg)	1.78 ± 0.38 ^a	1.43 ± 0.39 ^b	1.47 ± 0.47 ^b	0.001
Niacin (mg)	23.67 ± 6.30 ^a	17.10 ± 5.23 ^b	16.52 ± 7.15 ^b	0.001
Vitamin B ₆ (mg)	2.14 ± 0.47 ^a	1.65 ± 0.41 ^b	1.56 ± 0.50 ^b	0.001
Folate (µg)	258 ± 73 ^a	195 ± 70 ^b	184 ± 74 ^b	0.001
Vitamin B ₁₂ (µg)	4.89 ± 3.34 ^a	3.86 ± 2.20 ^b	3.69 ± 1.90 ^b	0.011
Vitamin C (mg)	200 ± 72 ^a	147 ± 67 ^b	138 ± 58 ^b	0.001
Vitamin A (µg)	830 ± 296 ^a	688 ± 303 ^b	645 ± 282 ^b	0.001
Vitamin D (µg)	3.36 ± 2.13	2.83 ± 2.41	3.67 ± 2.90	0.125
Vitamin E (mg)	8.71 ± 3.42 ^a	6.89 ± 2.49 ^b	5.66 ± 2.31 ^c	0.001

*Data are presented as mean values ± standard deviation. E, energy.

‡ANOVA or Kruskal-Wallis test followed by a post hoc Bonferroni or Mann-Whitney *U* test, respectively, were used to compare means between groups. ^{a,b,c}Means with the same letter are not significantly different from each other.

Table III
Anthropometric and biochemical data for the three clusters groups and differences among groups*

Intake/d	Group A (n = 66)	Group B (n = 72)	Group C (n = 67)	p‡
Age (y)	76.5 ± 6.4 ^a	79.3 ± 8.2 ^{ab}	79.9 ± 7.4 ^b	0.020
Weight (kg)	80.5 ± 10.1 ^a	64.9 ± 10.8 ^b	59.1 ± 12.1 ^c	0.001
Height (cm)	157.5 ± 8.7 ^a	152.1 ± 6.7 ^b	153.5 ± 8.4 ^b	0.001
BMI (kg/m ²)	32.6 ± 4.8 ^a	28.1 ± 4.4 ^b	24.6 ± 5.5 ^c	0.001
MAC (cm)	33.9 ± 3.9 ^a	29.5 ± 3.4 ^b	26.5 ± 3.6 ^c	0.001
MAMC (cm)	27.2 ± 2.3 ^a	23.4 ± 2.4 ^b	21.9 ± 2.5 ^c	0.001
MAMA (cm ²)	59.2 ± 10.1 ^a	43.9 ± 9.2 ^b	38.8 ± 8.6 ^c	0.001
CAMA (cm ²)	51.1 ± 10.7 ^a	36.4 ± 9.1 ^b	31.1 ± 8.5 ^c	0.001
Waist (cm)	108.8 ± 12.0 ^a	97.8 ± 10.7 ^b	93.5 ± 13.1 ^b	0.001
Hip (cm)	112.4 ± 9.7 ^a	103.3 ± 10.8 ^b	96.2 ± 9.7 ^c	0.001
WHR	0.93 ± 0.20	0.96 ± 0.08	0.97 ± 0.08	0.960
Bicipital (mm)	14.1 ± 6.3 ^a	10.9 ± 4.2 ^b	7.8 ± 3.8 ^c	0.001
Tricipital (mm)	21.5 ± 7.6 ^a	19.5 ± 5.9 ^a	14.6 ± 5.8 ^b	0.001
Subscapular (mm)	23.2 ± 8.4 ^a	19.7 ± 6.6 ^b	15.6 ± 5.9 ^c	0.001
Suprailiac (mm)	22.5 ± 10.8 ^a	20.0 ± 8.6 ^a	15.3 ± 8.1 ^b	0.001
Abdominal (mm)	24.6 ± 13.0	27.4 ± 12.5	19.6 ± 9.5	0.062
Albumin (g/l)	40.2 ± 3.0 ^a	42.8 ± 3.3 ^b	36.5 ± 4.0 ^c	0.001
Transferrin (mg/dl)	242 ± 33 ^a	274 ± 42 ^b	219 ± 36 ^c	0.001
Cholesterol (mg/dl)	189 ± 40 ^a	221 ± 34 ^b	176 ± 38 ^a	0.001
Lymphocytes (× 10 ⁹ /l)	1.93 ± 0.60 ^a	2.39 ± 0.74 ^b	1.66 ± 0.59 ^c	0.001

*Data are presented as mean values ± standard deviation. BMI, body mass index; MAC, mid-arm circumference; MAMC, mid-arm muscle circumference; MAMA, mid-arm muscle area; CAMA, corrected-arm muscle area; WHR, waist to hip ratio.

‡ANOVA or Kruskal-Wallis test followed by a post hoc Bonferroni or Mann-Whitney *U* test, respectively, were used to compare means between groups. ^{a,b,c}Means with the same letter are not significantly different from each other.

Serum albumin, transferrin, total cholesterol concentrations and the total lymphocyte count were significantly lower in group C. The percentages of subjects in each group with values for these param-

eters below the normal range are shown in figure 2. Group C showed the highest percentage of subjects below the normal range for all the biochemical parameters.

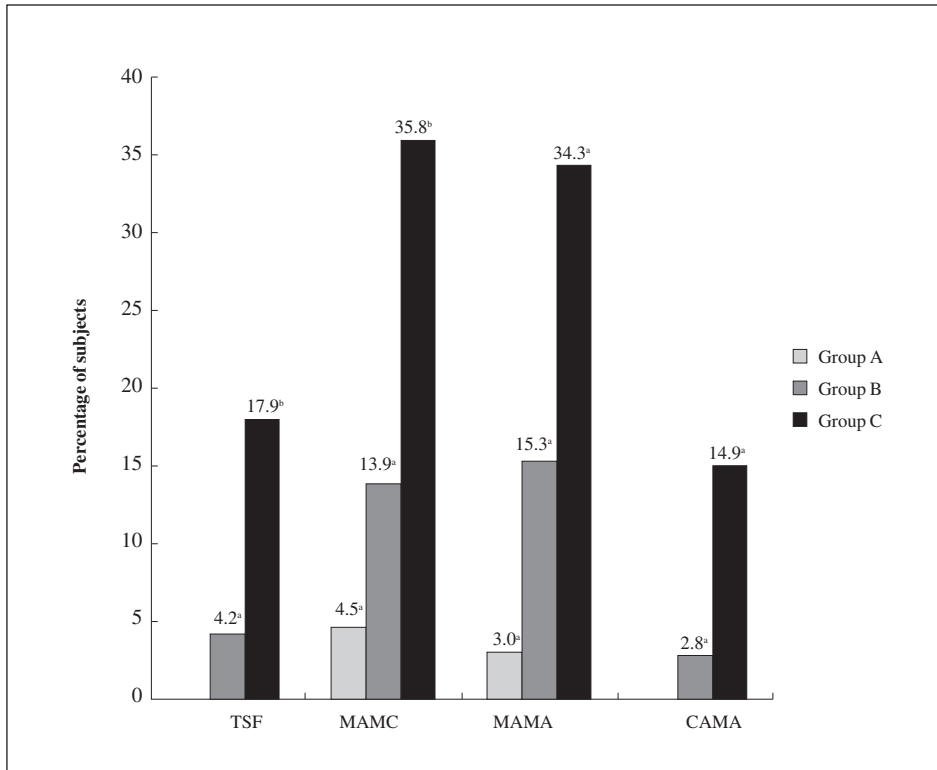


Fig. 1.—Percentage of subjects for the three clusters groups with triceps skinfold thickness (TSF), mid-arm muscle circumference (MAMC) and mid-arm muscle area (MAMA) under the percentile 10 of the Spanish elderly population and subjects with corrected-arm muscle area (CAMA) values of ≤ 21.4 and ≤ 21.6 cm², for men and women, respectively. ^{a,b,c}Percentages with the same letter are not significantly different from each other, determined by Chi-squared test and the analysis of corrected residuals. Group A: n = 66; Group B: n = 72; Group C: n = 67.

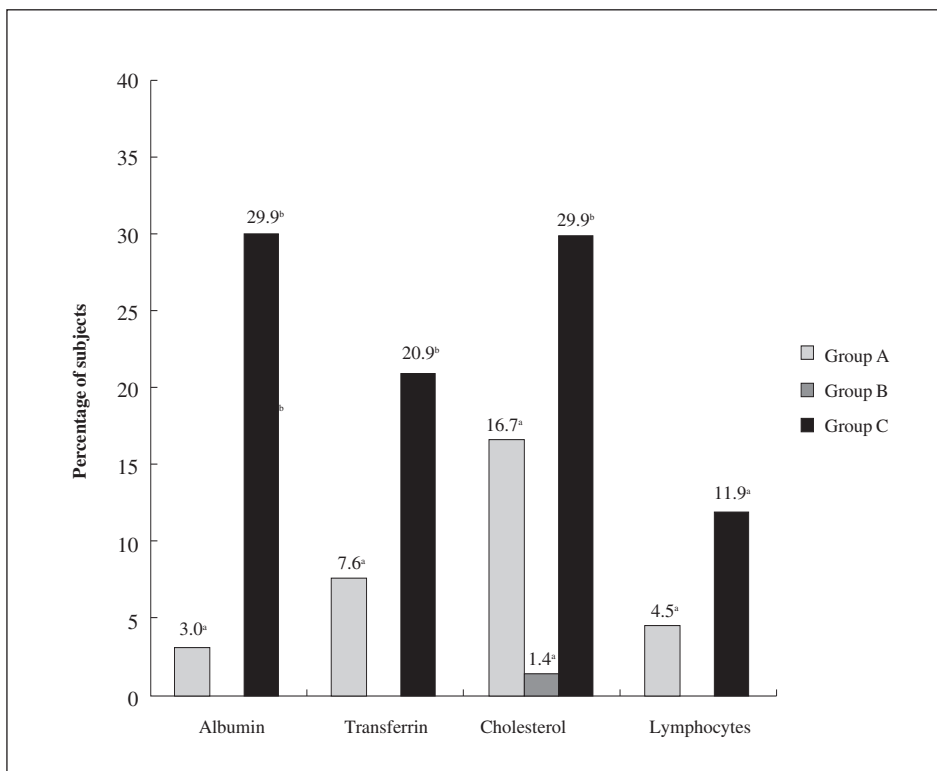


Fig. 2.—Percentage of subjects for the three clusters groups with serum albumin, transferrin, cholesterol concentration and total lymphocyte count values under the normal range in the three groups (Normal ranges: 35-53 g/l for albumin, 200-385 mg/dl for men and 185-405 mg/dl for women for transferrin, 150-230 mg/dl for cholesterol and $1-4 \times 10^9/l$ for total lymphocyte count). ^{a,b,c}Percentages with the same letter are not significantly different from each other, determined by Chi-squared test and the analysis of corrected residuals. Group A: n = 66; Group B: n = 72; Group C: n = 67.

Discussion

More than seventy tests or tools are currently available for detecting undernutrition all differing in their criteria, cut-off points, ease of use and acceptability^{34,35}. Since no single nutritional measurement or lower reference limit can be considered to diagnose undernutrition beyond doubt, a cluster analysis was used to identify undernourished subjects in the present study. Besides the anthropometric and biochemical parameters used frequently in other studies for the diagnosis of undernutrition, we also used dietary intake data, because dietary deficit intake is the primary cause of undernutrition³⁶.

Our results showed that the three groups had different nutritional statuses, differing significantly in dietary intake and anthropometric and biochemical variables.

Group A showed the highest energy intake, which was higher than the RDI. This excessive energy intake was accompanied by the highest anthropometric values. People in group A showed the greatest BMI ($32.6 \pm 4.8 \text{ kg/m}^2$), a value that was above than the normal range for elderly populations ($24\text{--}29 \text{ kg/m}^2$)³¹. The total population studied showed a higher than recommended waist circumference, indicating abdominal obesity, although, group A showed a higher value than groups B and C. Despite these high values, given the selective survival and the reduced risk of overweight in old age^{37,38}, it is not likely that this population is at great cardiovascular risk. The percentage of people in group A whose biochemical parameters were below the normal ranges may have been due to the presence of several illnesses but not to undernutrition. In view of these results, it might be said that group A was malnourished or at risk of malnutrition because of an excessive energy intake and overweight/obesity.

Group B could be considered as having an adequate nutritional status, an adequate energy intake, a BMI within the normal range for elderly populations and adequate values for the biochemical parameters.

Undernutrition is a dynamic process characterized by depletion of lean body mass, visceral proteins and body fat. It starts with inadequate nutrient intake, followed by a progressive series of metabolic, functional and body composition changes³⁹. The undernourished or at risk of undernutrition group (Group C) showed an energy intake below the RDI for Spanish elderly people, mainly because of a reduced lipid intake. This reduction in energy intake was also accompanied by a reduction in micronutrient intake. Consequently, muscle mass and fat deposits had the lowest values. Similar results have been described by other authors⁴⁰⁻⁴².

Values of TSF, MAMC and MAMA below the 5th or 10th percentiles have been used as indicators of undernutrition in elderly people⁴³. Friedman et al. (1985)⁴⁴ showed that CAMA values of ≤ 16.0 and $\leq 16.9 \text{ cm}^2$ for men and women, respectively, and even values close to

these (≤ 21.4 and $\leq 21.6 \text{ cm}^2$, for men and women, respectively) suggested nutritional risk. However, in the present study, a low percentage of people in group C showed values that might indicate nutritional risk for these CAMA values. A high percentage of undernourished people might not have been detected if a specific reference value had been used to diagnosis undernutrition.

Serum albumin, transferrin and total cholesterol concentrations and the total lymphocyte count are also considered indicators of nutritional status^{3,18,45,46}. In the present study, these parameters showed the lowest values in group C. However, a high percentage of people in this group showed values within the normal range, as have been previously described in other studies⁴⁷. We believe that low values of these parameters, although within the normal range, should be considered unfavourable when they are accompanied by low energy intake or low values for the anthropometric parameters.

On the other hand, biochemical parameters can be altered by certain diseases^{45,48}. Anthropometric measurements, especially BMI, can be affected by dehydration or edema, and arm anthropometry is less accurate because of the physical changes with age: redistribution of fat from subcutaneous to deep adipose tissues, decreased elasticity of skin, alterations in skin thickness, and atrophy of subcutaneous adipocytes⁴⁴. An undernourished person could show an adequate energy intake, while the development of undernutrition may be due to increased metabolic demands or increased nutrient losses, because illness is frequent in the elderly⁴⁹. We believe that three groups of data should be used to diagnose undernutrition: intake, and anthropometric and analytical variables.

In conclusion, our study shows that cluster analysis is a useful statistical method for assessing the nutritional status of institutionalized elderly populations. In the studied population, we found that the overall prevalence of undernutrition or risk of undernutrition was 32.7%, whereas 32.2% of the studied subjects were malnourished or at risk of malnutrition because of an excessive energy intake, showing overweight/obesity. The undernourished or at risk of undernutrition group showed the lowest values for dietary intake and the anthropometric and analytical parameters measured. Some of the specific reference values used in the literature, on the other hand, might have failed to detect many of the undernourished or people at risk identified by cluster analysis.

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Original / Ancianos

Predicción de la masa muscular apendicular esquelética basado en mediciones antropométricas en Adultos Mayores Chilenos

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Resumen

Objetivos: Desarrollar un modelo antropométrico de predicción de masa muscular apendicular esquelética (MMAE), en adultos mayores chilenos.

Métodos: La muestra estudiada corresponde a 616 adultos ≥ 60 años ($69,9 \pm 5,2$ años), 64,6% mujeres, autovalentes, viviendo en la comunidad en Santiago, Chile, participantes del estudio ALEXANDROS. Se efectuaron mediciones antropométricas, dinamometría de mano, pruebas de movilidad y densitometría ósea (DEXA). Mediante modelos de regresión lineal paso a paso se relacionó la MMAE obtenida por DEXA con variables antropométricas, edad y sexo. La muestra se dividió en forma aleatoria en dos submuestras, obteniéndose ecuaciones de predicción para ambas, que se validaron mutuamente por doble validación cruzada. La alta correlación entre los valores de MMAE observados y pronosticados en ambas submuestras y el bajo grado de contracción permitieron desarrollar la ecuación de predicción final con la muestra total.

Resultados: El coeficiente de validez cruzada entre las ecuaciones de predicción obtenidas en las dos submuestras fue 0,941 y 0,9409 y el grado de contracción 0,004 y 0,006. La ecuación de predicción final, en la muestra total, fue: MMAE (kg) = 0,107(peso kg) + 0,251(altura rodilla cm) + 0,197(circunferencia pantorrilla cm) + 0,047(dinamometría kg) - 0,034(circunferencia cadera cm) + 3,417(sexo) - 0,020 (edad años) - 7,646 ($R^2 = 0,89$). La MMAE estimada y la medida por DEXA fueron similares ($16,8 \pm 4,0$ vs $16,9 \pm 3,7$) y concordantes según los métodos de Bland y Altman (IC 95%: -2,6 -2,7) y Lin (coeficiente correlación concordancia = 0,94).

Conclusiones: Se obtuvo una ecuación antropométrica para determinar la masa MMAE, de gran utilidad en la pesquisa de sarcopenia en adultos mayores.

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Palabras clave: Adulto mayor. Sarcopenia. Mediciones antropométricas. Ecuaciones de predicción.

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ANTHROPOMETRIC MODEL FOR THE PREDICTION OF APPENDICULAR SKELETAL MUSCLE MASS IN CHILEAN OLDER ADULTS

Abstract

Objectives: To develop a predictive model of appendicular skeletal muscle mass (ASM) based on anthropometric measurements in elderly from Santiago, Chile.

Methods: 616 community dwelling, non-disabled subjects ≥ 60 years (mean 69.9 \pm 5.2 years) living in Santiago, 64.6% female, participating in ALEXANDROS study. Anthropometric measurements, handgrip strength, mobility tests and DEXA were performed. Step by step linear regression models were used to associate ASM from DEXA with anthropometric variables, age and sex. The sample was divided at random into two to obtain prediction equations for both subsamples, which were mutually validated by double cross-validation. The high correlation between the values of observed and predicted MMAE in both sub-samples and the low degree of shrinkage allowed developing the final prediction equation with the total sample.

Results: The cross-validity coefficient between prediction models from the subsamples (0.941 and 0.9409) and the shrinkage (0.004 and 0.006) were similar in both equations. The final prediction model obtained from the total sample was: ASM (kg) = 0.107(weight in kg) + 0.251(knee height in cm) + 0.197 (Calf Circumference in cm) + 0.047 (dynamometry in kg) - 0.034 (Hip Circumference in cm) + 3.417 (Man) - 0.020 (age years) - 7.646 ($R^2 = 0.89$). The mean ASM obtained by the prediction equation and the DEXA measurement were similar (16.8 ± 4.0 vs 16.9 ± 3.7) and highly concordant according Bland and Altman (95% CI: -2.6 -2.7) and Lin (concordance correlation coefficient = 0.94) methods.

Conclusions: We obtained a low cost anthropometric equation to determine the appendicular skeletal muscle mass useful for the screening of sarcopenia in older adults.

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Keywords: Older adults. Sarcopenia. Anthropometric measurements. Prediction equations.

Abreviaturas

DEXA: dual energy x ray absorptiometry.
MMAE: masa muscular apendicular esquelética.
ASM: appendicular skeletal muscle mass.
IC 95%: intervalo de confianza del 95%.
95% CI: 95% confidence interval.
Kg: kilogramos.
Cm: centímetros.
M: meters.
Adultos mayores: AM.
Índice de Masa Corporal: IMC.
DE: desviación estándar.
EE: error estándar.
R²: coeficiente de determinación.
EEE: error estándar de estimación.

Introducción

La sarcopenia es una característica del envejecimiento biológico, que representa la progresiva pérdida de masa, calidad y fuerza muscular esquelética. Sus graves repercusiones sobre la salud de los Adultos Mayores (AM) van desde pérdida de funcionalidad, dependencia, caídas, disminución de la función inmune¹⁻⁷ y aumento de riesgo de osteoporosis⁸, hasta su asociación con fragilidad, hospitalización, institucionalización y muerte^{9,10}. Es sabido que la población AM chilena tiene una esperanza de vida cada vez mayor¹¹, pero a su vez la prevalencia de dependencia funcional es alta, ya que alrededor del 21,5% de los AM tiene algún grado de dependencia¹².

Todo ello significa además un alto y creciente costo en salud. Es así como la identificación de la sarcopenia se hace muy relevante, no sólo por sus devastadores efectos sobre la salud, sino porque se trata de una condición posible de prevenir, retardar, e incluso revertir a través de intervenciones destinadas a mejorar la nutrición y la actividad física^{1,11,13}.

Aunque la sarcopenia asociada a la edad fue descrita en los años 80's, aún no se cuenta con una definición clínica de consenso universal. Sin embargo, cualquiera sea el algoritmo utilizado para su diagnóstico, la definición de sarcopenia incluye disminución de masa muscular y función^{4,6} por lo tanto, requiere la evaluación de la masa magra y específicamente la masa magra apendicular esquelética (MMAE).

La MMAE, que es la suma de la masa magra de las piernas y los brazos, puede determinarse por DEXA, resonancia magnética o impedancia, aunque la mayor parte de los estudios clínicos de sarcopenia utilizan como "Gold Standard" la medición de la masa muscular por DEXA. En estudios poblacionales y en la atención primaria, la evaluación por estos métodos es impracticable, debido a la baja accesibilidad y el alto costo de este examen, lo que representa una dificultad para el diagnóstico de sarcopenia, realidad a la cual Chile no es ajena.

En el presente estudio se desarrolla un modelo de predicción de MMAE basado en mediciones antropométricas, en una muestra de AM (60 y más años), chilenos, de Santiago, que puede ser utilizado en usuarios de centros de atención primaria de salud y en estudios poblacionales.

Método

Diseño del estudio

Análisis secundario de datos provenientes de la medición basal del estudio Alexandros¹¹ para el desarrollo de un modelo de predicción de masa muscular en AM chilenos, basado en mediciones antropométricas y utilizando la medición DEXA como "gold standard".

El estudio Alexandros fue aprobado por el Comité de Ética del Instituto de Nutrición y Tecnología de los Alimentos (INTA) de la Universidad de Chile y cada sujeto llenó un consentimiento informado aceptando participar en el estudio¹¹.

Población objetivo

AM de 60 años y más, autovalentes, viviendo en la comunidad en Santiago de Chile.

Muestra

Para efectuar el presente estudio se dispuso de datos de 755 sujetos participantes de la cohorte Alexandros (FONDECYT 1080589) evaluados entre 2008 y 2011 que contaban con antropometría completa y DEXA.

Criterios de exclusión

Índice de Masa Corporal (IMC) <20 ó ≥40, talla ≤151 cm en hombres y 140 cm en mujeres e individuos enfermos con cáncer o enfermedad pulmonar obstructiva.

Se excluyeron 139 sujetos por presentar algún criterio de exclusión, por lo que la muestra final quedó constituida por 616 AM.

Se midieron las siguientes variables antropométricas: peso, talla, altura de rodilla, circunferencia de cintura, circunferencia de cadera, perímetro de brazo, pliegue tricipital y dinamometría. También se midió masa grasa, masa magra y masa ósea por DEXA. Todas las mediciones fueron realizadas por personal especialmente entrenado y estandarizados para el estudio.

Descripción de las variables

La talla fue medida con estadiómetro portátil SECA con el sujeto descalzo de pie, con los talones juntos, los

brazos a los lados del cuerpo, las piernas rectas, los hombros relajados y la cabeza en el plano horizontal de Frankfort con los talones, nalgas, escápula y parte posterior de la cabeza apoyados contra un muro vertical recto o una puerta. Las medidas se registraron en cm. El peso se midió usando una balanza SECA de plataforma con una precisión de 0,1 kg, con el sujeto descalzo y de pie sobre la plataforma. Se utilizaron las variables de peso y talla para calcular el índice de masa corporal (IMC = peso total en kg/altura² en metros).

La altura de rodilla fue medida con el sujeto sentado usando un calíper de rodilla, de hoja ancha; las mediciones se hicieron en la pierna izquierda, colocando la rodilla y la pierna en un ángulo de 90 grados. La parte fija del calíper se puso bajo el talón y la parte móvil se colocó de forma paralela a la fíbula sobre el maléolo e inmediatamente detrás de la fíbula, presionando las dos hojas para comprimir los tejidos blandos. Las mediciones fueron registradas en cm. con una cifra decimal.

El pliegue tricótipal se midió con un calíper Lange (Vital Signs, modelo 68902, Country Technology, Inc.) en la parte posterior del brazo, en el punto medio entre el olecranon y el acromion. Las mediciones se registraron en mm.

Las circunferencias de cintura, caderas, brazo y pantorrilla se midieron con una cinta métrica SECA 203 con una precisión de 0,1 cm. La cintura se midió con el sujeto de pie, inmediatamente por encima de la cresta ilíaca en una circunferencia paralela al piso. La circunferencia de pantorrilla se midió en el centro de la parte más voluminosa de la pantorrilla en cm. La circunferencia de caderas se midió con la misma cinta métrica, paralela al piso, en la zona de mayor circunferencia a la altura de las nalgas.

La fuerza muscular (dinamometría) se midió a través de la fuerza de agarre de la mano en kg. Esta evaluación se realizó con un dinamómetro (Hand Dynamometer T-18; Country Technology, Inc.) con una precisión de 0,1 kg, utilizando la mano dominante. La medición se hizo con el sujeto sentado, ajustando el mango hasta que los dedos del sujeto estén en un plano perpendicular al plano de la escala (reloj de lectura del aparato), pidiendo al sujeto ejercer el máximo de fuerza posible con su mano. Se realizaron dos mediciones y se registró la marca mayor.

Se determinó la masa muscular apendicular utilizando DEXA como "Gold Standard". Para el DEXA se usó un densitómetro Lunar PRODIGY (LUNAR IDEXA 13,6).

Análisis estadístico

Para obtener un modelo de predicción de MMEA, la muestra se dividió en dos submuestras de igual tamaño, en forma aleatoria ("split sampling analysis"), una muestra de predicción y una de validación, manteniendo la misma proporción por sexo. Para analizar las diferencias entre las submuestras se utilizaron pruebas t

de Student. Se obtuvieron modelos de predicción de MMAE en ambas submuestras a través del análisis de regresión lineal paso a paso, utilizando todas las variables antropométricas. Dichos modelos se validaron mutuamente por el método doble validación cruzada¹⁴. Se calculó el coeficiente de validez cruzada para cada submuestra (correlación de los valores observados de MMAE y los valores estimados en la muestra de predicción) y el estadístico de encogimiento ("shrinkage": diferencia entre el coeficiente de determinación obtenido en el modelo y la correlación al cuadrado de la predicción y los valores observados) para las dos submuestras. La alta correlación entre los valores de MMAE observados y pronosticados en ambas submuestras y el bajo grado de encogimiento ("shrinkage") permitieron calcular un modelo de regresión con toda la muestra^{14,15}. Se calculó la concordancia entre los valores estimados por el modelo de regresión y los valores obtenidos por DEXA para la MMAE por los métodos de Bland y Altman (1986)¹⁶ y por el coeficiente de concordancia de Lin (1989)¹⁷.

Todos los análisis estadísticos fueron realizados con el software estadístico STATA 12,1 (Stata Corp, College Station, TX).

Resultados

La muestra está compuesta de 616 adultos de 60 años y más (edad promedio $69,9 \pm 5,2$ años; rango 61,7-81,0), 64,6% mujeres, de similar rango etáreo en ambos sexos. Respecto a las variables antropométricas, la circunferencia de brazo ($30,5 \pm 3,2$ vs $30,3 \pm 3,3$) fue similar en ambos sexos. El IMC y la circunferencia de caderas, fueron mayores en las mujeres ($27,7 \pm 3,8$ vs $28,6 \pm 4,3$ y $98,6 \pm 7,6$ vs $100,8 \pm 8,4$; respectivamente). Con relación al resto de las variables, los hombres presentan mayores valores promedio que las mujeres (t-Student: $p < 0,01$) como se observa en la tabla I.

Las características de las submuestras obtenidas al dividir aleatoriamente la muestra total, son similares (t-Student para muestras independientes $p: 0,2427-0,9848$) (datos no mostrados).

La tabla II muestra las ecuaciones de predicción para MMAE obtenidas por el método de regresión lineal paso a paso en las submuestras y en la muestra total. Las variables seleccionadas fueron peso, altura de rodilla, circunferencia de cadera, circunferencia de pantorrilla, dinamometría, sexo y edad. Se observa que el coeficiente de validez cruzada presenta un alto valor para las dos ecuaciones (0,9410 y 0,9409; respectivamente) y el estadístico de encogimiento presenta un valor pequeño, menor que 0,01 (0,004 y 0,006; respectivamente), lo que nos permitió calcular un modelo con toda la muestra. El modelo predictivo obtenido en la muestra total, explica casi el 90% de la variabilidad total ($R^2 = 0,8889$).

El promedio de MMAE obtenida por la ecuación de predicción y las mediciones por DEXA fueron muy similares ($16,8 \pm 4,0$ vs $16,9 \pm 3,7$; $p > 0,5$).

Tabla I
Características de la muestra por sexo

Variables (promedio ± DE)	Hombres n = 218	Mujeres n = 398	Total n = 616
Edad (Años)	70,2±5,4	69,8±5,1	69,9±5,2
IC 95%	69,5-70,9	69,3-70,3	69,5-70,3
Talla (cm)	166,1±6,5	152,5±6,0**	157,3±9,0
IC 95%	165,2-166,9	151,9-153,1	156,6-158,0
Peso (Kg)	76,4±12,0	66,5±11,2**	70,0±12,4
IC 95%	74,8-78,0	65,4-67,6	69,0-71,0
BMI (Kg/m ²)	27,7±3,8	28,6±4,3*	28,2±4,1
IC 95%	27,2-28,2	28,1-29,0	27,9-28,6
Altura de rodilla (cm)	52,1±2,5	47,5±2,4**	49,1±3,3
IC 95%	51,7-52,4	47,3-47,8	48,9-49,4
Circunferencia de brazo (cm)	30,5±3,2	30,3±3,3	30,4±3,3
IC 95%	30,1-30,9	30,0-30,7	30,1-30,7
Circunferencia pantorrilla (cm)	36,5±3,5	35,0±3,3**	35,5±3,5
IC 95%	36,0-37,0	34,7-35,3	35,3-35,8
Circunferencia cintura (cm)	99,0±10,6	93,1±11,0**	95,2±11,2
IC 95%	97,5-100,4	92,1-94,2	94,3-96,1
Circunferencia caderas (cm)	98,6±7,6	100,8±8,4*	100,0±8,2
IC 95%	97,6-99,7	99,9-101,6	99,4-100,7
Dinamometría (Kg)	34,2±8,4	19,6±6,9**	24,7±10,3
IC 95%	33,1-35,3	18,9-20,3	23,9-25,6
MMAE DEXA (Kg)	21,3±2,9	14,5±2,2**	16,9±4,1
IC 95%	20,9-21,6	14,2-14,6	16,6-17,2

Prueba t de Student para muestras independientes: *p < 0,01; **p < 0,0001;
DE: desviación estándar; IC: intervalo de confianza.

La figura 1 muestra la relación entre el promedio de los valores de MMAE medidos por DEXA y los estimados por la ecuación de predicción y su diferencia (método de Bland y Altman), mostrando buena concordancia (diferencia promedio: 0,039; IC 95%: -2,6-2,7).

En la figura 2 se presenta el gráfico de validación por el método de Lin. El diagrama de dispersión de la MMAE medida por DEXA y la estimada por el modelo de predicción, así como la línea de la concordancia perfecta, permiten visualizar gráficamente la buena concordancia que presentan ambas mediciones (coeficiente de correlación concordancia de Lin = 0,94; IC 95%: 0,93-0,95).

El diagrama de cajas de la masa muscular esquelética apendicular obtenidas por DEXA y estimada por la ecuación de predicción, para ambos sexos se presenta en la figura 3. Se observa que ambas son muy similares (hombres: 21,2 ± 2,9, vs 21,1 ± 2,2; mujeres: 14,6 ± 2,2 vs 14,7 ± 2,1).

Discusión

En este estudio se obtuvo una ecuación de predicción antropométrica de masa muscular esquelética apendicular en una muestra de adultos mayores chilenos autovalentes, que participaron en el estudio Alexandros¹¹. Dicha ecuación, que tuvo un alto grado de concordancia con los resultados del DEXA, fue obtenida mediante un modelo de regresión lineal múltiple que incluye las variables antropométricas altura de rodilla, peso, circunferencia de pantorrilla, circunferencia de cadera y dinamometría, además de sexo y edad.

Diversos autores han reportado ecuaciones de predicción de MMAE específicas para las poblaciones de origen¹⁸⁻²².

Todas incluyen peso y talla, o IMC¹⁸⁻²² sin embargo algunas agregan dinamometría y circunferencia de cadera,

Tabla II
Ecuaciones de predicción obtenidas para las sub-muestras y para la muestra total

Variables	Sub-muestra 1 n = 308	Sub-muestra 2 n = 308	Muestra total n = 616
Constante ± EE	-7,625 ± 2,48	-8,710 ± 2,42	-7,646 ± 1,71
Altura de rodilla ± EE	0,260 ± 0,04	0,263 ± 0,04	0,251 ± 0,03
Peso ± EE	0,113 ± 0,01	0,102 ± 0,01	0,107 ± 0,01
Circunferencia cadera ± EE	-0,050 ± 0,02	-0,018 ± 0,02	-0,034 ± 0,01
Circunferencia pantorrilla ± EE	0,203 ± 0,03	0,190 ± 0,04	0,197 ± 0,02
Dinamometría ± EE	0,059 ± 0,01	0,035 ± 0,01	0,047 ± 0,01
Sexo (Hombre) ± EE	2,915 ± 0,30	3,864 ± 0,27	3,417 ± 0,20
Edad ± EE	-0,013 ± 0,02	-0,024 ± 0,02	-0,020 ± 0,01
R2	0,8896	0,8913	0,8889
EEE	1,3553	1,3375	1,3458
Coefficiente de validez cruzada	0,9410	0,9409	
Grado de encogimiento ("shrinkage")	0,004	0,006	

Leyenda: EE: error estándar; R²: coeficiente de determinación; EEE: error estándar de estimación.

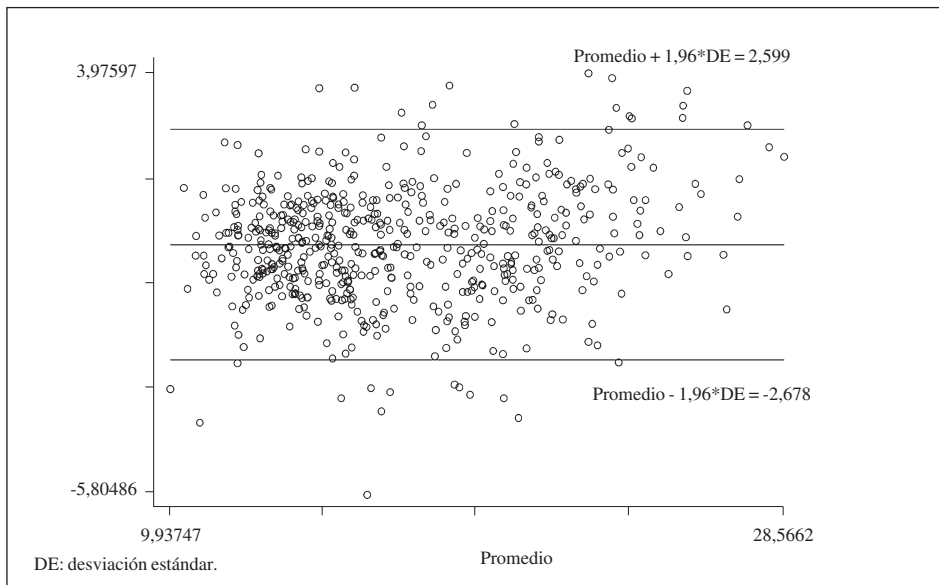


Fig. 1.—Diagrama de dispersión entre el promedio de los valores medidos por DEXA y los valores estimados por la ecuación de predicción de MMAE con su diferencia. Método de Bland y Altman (1986).

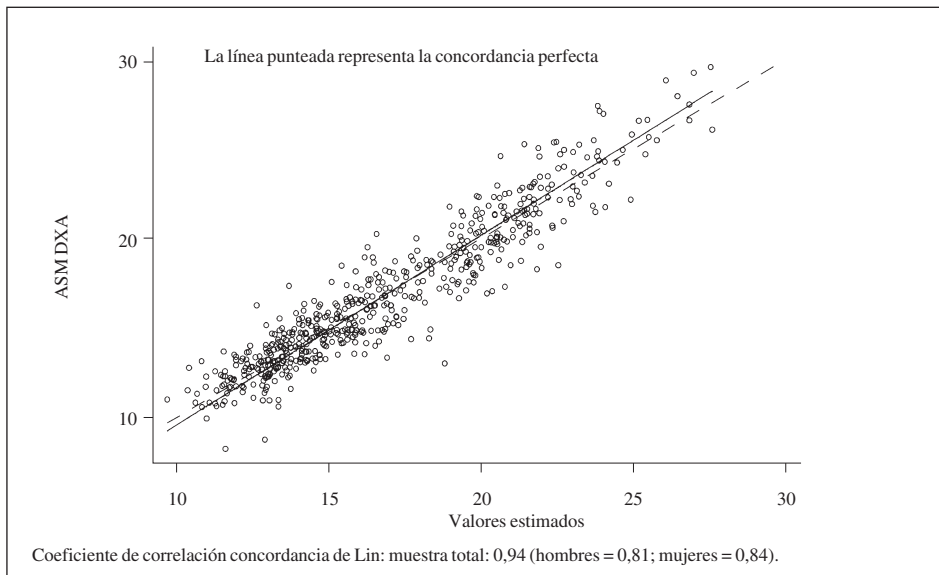


Fig. 2.—Diagrama de dispersión entre los valores medidos por DEXA y los valores estimados por la ecuación de predicción de MMAE. Coeficiente de correlación de concordancia de Lin (1989).

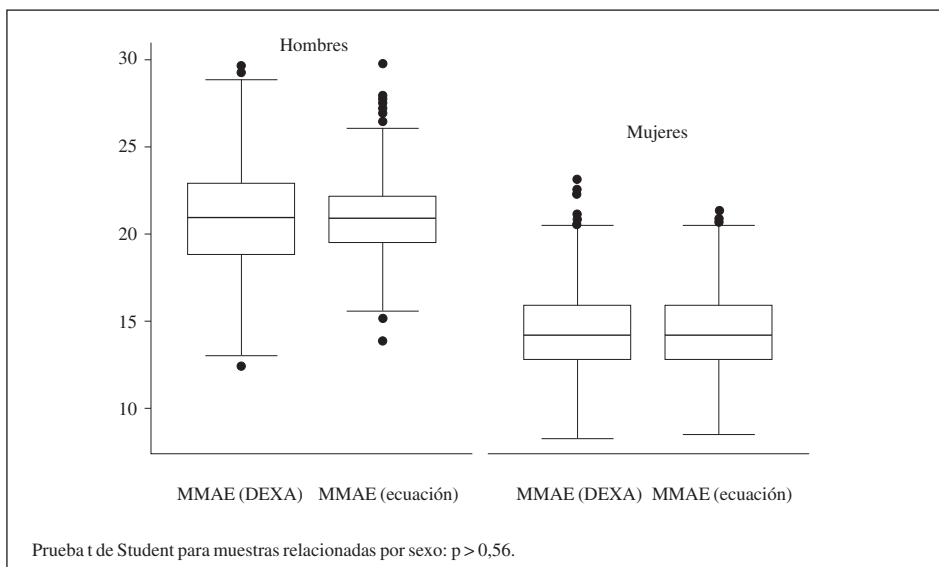


Fig. 3.—Masa muscular apendicular esquelética (MMAE) por DEXA y su estimación por la ecuación de predicción por sexo.

como es el caso de Baumgartner y cols. (1998)¹⁸, que desarrollaron y validaron un modelo en una muestra de 199 adultos mayores de Nuevo México, para las variables peso, talla, circunferencia de cadera, dinamometría y sexo. Otros autores usan circunferencia de cadera, circunferencia de pantorrilla, pliegues, etc., como Galvão y cols. (2013)²¹, que desarrollaron y validaron 10 ecuaciones de predicción sencillas y aplicables en una muestra de 234 mujeres brasileñas mayores de 60 años, sanas, en función de IMC, Masa corporal, circunferencia de cadera, circunferencia de pantorrilla, pliegues, etc. Inicialmente ellos compararon los valores de MMAE obtenidos por DXA con los valores estimados al utilizar las ecuaciones obtenidas por Baumgartner y cols. (1998) y por Tankó y cols. (2002)^{18,19}, encontrando diferencias significativas al aplicarlas, lo que demuestra que es importante determinar ecuaciones específicas para cada población. El modelo obtenido por Tankó y cols. (2002)¹⁹ fue en una muestra de 754 mujeres danesas entre 17 y 85 años de edad que contiene a las variables peso, talla y edad. En forma similar Visvanathan y cols. (2012)²⁰ desarrollaron y validaron una ecuación de predicción de MMAE en una muestra de 2275 adultos mayores de 50 años de Adelaide, que incluye peso, IMC, edad y sexo, para ser usada en la atención primaria.

Otros autores han utilizado las ecuaciones obtenidas por Baumgartner y cols. (1998) para definir sarcopenia y relacionarla con desnutrición, movilidad y actividades básicas de la vida, como Velázquez y cols.²³ en México.

Se sabe que la validación de la composición corporal por DEXA²⁴ contra un modelo de 4 compartimientos, ha detectado una leve sobreestimación de la masa libre de grasa, lo que hace necesario el uso de factores de corrección. Sin embargo, considerando que en brazos y piernas todo el tejido que no es grasa o hueso, es músculo, para definir sarcopenia se utiliza la masa muscular apendicular y a partir de ella se construye el índice de masa muscular esquelética. Aunque el modelo propuesto sobreestima ligeramente la MMAE, se obtuvo una alta concordancia entre los valores predichos por el modelo y los valores obtenidos por DEXA.

Probablemente, la mayor limitación de este estudio es que incluye la dinamometría en la ecuación de predicción, la que no se efectúa en forma rutinaria en la atención primaria. Sin embargo, considerando su asociación negativa con mortalidad, discapacidad e institucionalización²⁵, su inclusión en la ecuación podría constituir un argumento más para su incorporación al examen del AM.

Entre las fortalezas del estudio tenemos la obtención de una sola ecuación de predicción de masa muscular apendicular, simple, en función de variables antropométricas, fáciles de obtener, que explica un alto % de la variación total (89%) y cuyos valores estimados muestran una alta concordancia con los valores obtenidos por el DEXA. La inclusión de la altura de rodilla en el modelo y no de la talla, aporta mayor validez a la ecuación ya que siendo una variable altamente correlacionada con la estatura^{26,27}, no cambia con la edad.

Conclusiones

La ecuación antropométrica obtenida:

$$\begin{aligned} \text{MMAE (kg)} = & 0,107 (\text{peso en kg}) + 0,251 (\text{altura rodilla en cm}) \\ & + 0,197 (\text{circunferencia pantorrilla en cm}) + 0,047 (\text{dinamometría en kg}) \\ & - 0,034 (\text{circunferencia cadera en cm}) + 3,417 (\text{sexo Hombre}) \\ & - 0,020 (\text{edad en años}) - 7,646, \end{aligned}$$

es válida, fiable, fácil de obtener y de bajo costo para predecir la masa muscular esquelética apendicular, en adultos mayores chilenos.

Su aplicación nos permitirá calcular el índice de masa muscular apendicular esquelético para su utilización en la pesquisa de sarcopenia en adultos mayores chilenos que asisten a los centros de atención primaria de salud.

Agradecimientos

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Original / *Cáncer*

Cáncer y su asociación con patrones alimentarios en Córdoba (Argentina)

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Resumen

Introducción: La alimentación es un importante factor vinculado a la ocurrencia del cáncer. Su abordaje en términos de patrones alimentarios es de creciente interés en epidemiología nutricional, no obstante ha sido pocas veces empleado en Latinoamérica.

Objetivos: Identificar patrones alimentarios en la población adulta de Córdoba (Argentina) y estimar sus efectos sobre el riesgo de ocurrencia de cáncer colorrectal (CCR), cáncer de mama (CM), cáncer de próstata (CP) y urotelial (CU).

Métodos: Se condujeron estudios caso-control, 2006-2012, correspondientes a CCR, CM, CP y CU. Empleando un análisis factorial de componentes principales se identificaron patrones alimentarios. Se estimaron ORs mediante regresión logística multinivel.

Resultados: Se identificaron patrones característicos en la población general, y en hombres y mujeres independientemente. En población total, los patrones *Cono Sur* y *Bebidas Azucaradas* evidenciaron un efecto promotor para CCR y CU, y el *Patrón Prudente* mostró efecto protector. En mujeres, el CM se asoció de manera directa con los patrones *Cono Sur Femenino*, *Rural* y *Amiláceo*, e inversa con el *Patrón Prudente*. En hombres, los patrones *Cono Sur Masculino*, *Bebidas Azucaradas* y *Típico Medurado* mostraron un efecto promotor para CP.

Conclusión: Resulta necesario promover una ingesta habitual de vegetales, frutas y lácteos (éstos últimos de manera moderada en hombres), y disminuir el consumo de carnes rojas (fundamentalmente grasas), carnes procesadas, vegetales amiláceos, vino y bebidas azucaradas, a fin de prevenir la ocurrencia de cáncer. En hombres se sugiere moderar la ingesta de huevos, y en mujeres la de granos refinados, productos de pastelería, aceites y mayonesa.

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Palabras clave: *Patrones alimentarios. Caso control. Cáncer. Argentina.*

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CANCER AND ITS ASSOCIATION WITH DIETARY PATTERNS IN CORDOBA (ARGENTINA)

Abstract

Introduction: Feeding habits play a prominent role in carcinogenesis. The dietary patterns approach applied to the study of chronic diseases is of increasing interest in nutritional epidemiology. Nevertheless, it has been seldom used in Latin America.

Objective: To identify dietary patterns in adult population in Córdoba (Argentina) and to estimate their effects on the risk of colon-rectal (CRC), urothelial (UC), breast (BC) and prostate (PC) cancers.

Methods: Four case control studies were conducted, 2006-2012 for CRC, PC, BC and UC. To identify the dietary patterns, a Principal Components Factor Analysis was conducted. A multilevel logistic regression was adjusted for the risk analyses.

Results: Characteristic dietary patterns in the whole population, and in women and men independently, were identified. In the whole population *South Cone* and *Sweet Beverages* patterns behaved as promoters for CRC and UC while the *Prudent Pattern* had a protective effect. Female *South Cone*, *Rural* and *Starchy* patterns were associated to a higher BC risk. *Prudent Pattern* lowered BC risk. In men, *South Cone*, *Sweet Beverages* and *Typical Measured* patterns promoted PC.

Conclusion: It is necessary to promote a regular intake of vegetables, fruits and dairy products (although a moderate intake for men), and to reduce red meat (especially fat meat), processed meat, starchy vegetables, wine and sweet beverages intakes, to prevent the occurrence of cancer. In men, it is recommended a moderate intake of egg. In women, it is advised a moderate intake of refined grains, bakery products, oils and mayonnaise intake.

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Keywords: *Dietary patterns. Case control. Cancer. Argentina.*

Abreviaturas

HAAs: Aminas aromáticas heterocíclicas.

CCR: Cáncer colorrectal.

CM: Cáncer de mama.

CP: Cáncer de próstata.

CU: Cáncer urotelial.

AFCP: Análisis Factorial de Componentes Principales.

KMO: Kraisner-Meyer-Olkin.

OR: Odds Ratio.

Introducción

A nivel mundial, los tumores malignos representan la segunda causa de muerte por enfermedad, con una incidencia creciente, especialmente en países de bajos y medianos ingresos¹. Díaz y cols.², establecieron que los tipos de cáncer más frecuentes en la Provincia de Córdoba (Argentina) son los de mama, cérvix, colon y pulmón en el sexo femenino, y los de próstata, pulmón, colon y vejiga en el masculino. Los patrones espaciales no aleatorios que muestran las tasas de incidencia de estos cánceres en la provincia, sugieren que las distribuciones geográficas de esta enfermedad podrían estar asociadas, en parte, a factores epigenéticos como las características ambientales³, socioeconómicas⁴ y de estilo de vida^{5,6}. La alimentación es también considerada un factor ambiental con importante influencia en el desarrollo del cáncer. Se reconoce que el 35% de los tumores malignos están asociados con factores alimentarios, y serían prevenibles mediante una alimentación y nutrición apropiadas⁷. Sin embargo, dada la naturaleza compleja de la interacción dieta-cáncer, resta aún mucho por dilucidar en cuanto a su papel en la promoción o protección de la patología.

El efecto de la alimentación sobre la ocurrencia del cáncer, es variable. Así, dietas con alta densidad calórica, elevada proporción de carnes procesadas, alimentos refinados, grasas y alcohol, se asocian a un incremento del riesgo de desarrollar cáncer de mama, próstata y colon, mientras que una alimentación que incluya importantes cantidades de vegetales y frutas, con alto contenido de micronutrientes y fibra, se encuentra relacionada a una disminución del riesgo⁷. Además, la presencia de contaminantes naturales en el agua de bebida, como el arsénico, estaría asociada a un mayor riesgo de ocurrencia de tumores uroteliales, entre otros^{3,6}.

En Argentina, el perfil alimentario tradicional está caracterizado por un alto consumo de proteínas y grasas animales, obtenidas principalmente de las carnes rojas, y una baja ingesta de pescado, frutas y verduras^{8,9}. Además, es habitual en la región el asado de carnes a la parrilla. Se ha evidenciado que este método de cocción permite la formación de costra tostada en la superficie del alimento⁸, generándose

aminas aromáticas heterocíclicas (HAAs), potenciales promotores tumorales¹⁰. Varios estudios epidemiológicos desarrollados en Córdoba ya evidenciaron su asociación con el riesgo de ocurrencia de algunos cánceres^{8,12}. Estos hallazgos constituyen un punto de partida para profundizar el estudio de los hábitos alimentarios en esta población y su papel en la ocurrencia de cáncer.

En los últimos años, en el campo de la Epidemiología Nutricional, se ha observado un creciente interés en el enfoque de patrones alimentarios, dado que permite la caracterización de la dieta de manera integral y extrapolable a recomendaciones alimentarias. No obstante, son escasos los trabajos epidemiológicos sobre cáncer que analizan la alimentación desde esta perspectiva, siendo la mayoría provenientes de países desarrollados^{6,12-15}. Desde este enfoque, un patrón alimentario se define por la naturaleza, calidad, cantidad y proporciones de diferentes alimentos y bebidas en la dieta de un individuo, y la frecuencia con las cuales son habitualmente consumidos⁷. Analíticamente, puede ser entendido como una medida única de exposición a la dieta, que resume la información de numerosas variables de naturaleza alimentaria y que se caracteriza por aquellas que resultan dominantes en la alimentación del individuo^{7,16}. Esto conlleva la ventaja adicional de simplificar el análisis y la interpretación de un fenómeno complejo y multidimensional, la ingesta alimentaria.

Otro aspecto a considerar en estudios epidemiológicos sobre enfermedades crónicas, el cual constituye un aspecto clave en la epidemiología moderna, es que no todos los determinantes y condicionantes de la salud pueden ser conceptualizados como atributos a nivel individual, sino que resulta necesario considerar características de orden poblacional. El reconocimiento de estos niveles jerárquicos de los condicionantes del fenómeno en estudio genera desafíos metodológicos¹⁷.

Por todo lo expuesto, ante la necesidad de profundizar el estudio de la relación dieta-cáncer a nivel regional, el presente trabajo se propone identificar patrones alimentarios en la población adulta de Córdoba (Argentina) y analizar el papel que éstos ejercen en el desarrollo del cáncer colorrectal (CCR), de mama (CM) de próstata (CP) y urotelial (CU), aplicando estrategias de modelación que incorporen una dimensión explicativa adicional de orden familiar o contextual en el análisis.

Métodos

Diseño de estudios caso-control

La provincia de Córdoba (3.348.000 habitantes) se ubica en el centro de la República Argentina y está dividida en 26 departamentos. En el marco del proyecto "Exposiciones ambientales y Cáncer en Córdoba: Es-

tudio de la relación dieta-cáncer y construcción de una escala de exposición a contaminantes” (FONCyT-ANPCyT, PICT 2008-1814), llevado a cabo en la Universidad Nacional de Córdoba (Argentina), se condujeron cuatro estudios caso-control (2006-2012), uno por cada sitio tumoral de interés. Se consideraron “casos” a sujetos con diagnóstico histopatológicamente confirmado de: a) adenocarcinoma primario colorrectal (CIE-10 C18-C20), b) tumor de urotelio: carcinoma de células de transición, carcinoma epidermoide o adenocarcinoma (CIE-10 C65-68), c) adenocarcinoma de mama (CIE-10 C50), y d) adenocarcinoma de próstata (CIE-10 C61). Los “controles” fueron individuos que, siendo de igual sexo, similar edad (± 5 años) y lugar de residencia semejante a la de sus respectivos casos, no tuvieron antecedentes de la patología, ni otras asociadas, ni presentaron hábitos alimentarios particulares por enfermedad, costumbres o creencias religiosas. La identificación de casos se realizó con la colaboración de los principales efectores de salud de la región, del ámbito público y privado. Los controles fueron seleccionados aleatoriamente de las poblaciones de referencia y en función a los criterios de inclusión descritos. Por cada sujeto-caso, fueron elegidos al menos 2 controles, resultando los siguientes tamaños muestrales (casos/controles): 75/153 (colorrectal), 41/82 (urotelio), 100/294 (mama) y 135/282 (próstata).

Se obtuvo el consentimiento informado de cada participante. Este trabajo fue aprobado por el Comité Institucional de Ética de la Investigación en Salud (CIEIS) del Hospital Nacional de Clínicas (Córdoba, Argentina), e inscripto en el Registro Provincial de Investigaciones en Salud (RePIS, N° Registro 1387, 10/12/2009) del Ministerio de Salud de la Provincia de Córdoba.

Encuesta alimentaria

Cada individuo fue entrevistado en su domicilio por encuestadores entrenados centralizadamente, empleando un cuestionario estructurado que consta de dos secciones: una referida a características bio-socio-culturales, datos antropométricos y de estilos de vida, y otra al consumo alimentario habitual. Esta, incluye un cuestionario de frecuencia alimentaria cuali-cuantitativo, validado para estudios epidemiológicos sobre cáncer en Córdoba¹⁸, que permite valorar la exposición alimentaria en el pasado (5 años previos al diagnóstico y al momento de la entrevista en casos y controles, respectivamente). Complementariamente se empleó un atlas fotográfico de alimentos, también validado¹⁹, y el software Nutrio 1.2²⁰ para el análisis de composición nutricional. La base de datos sobre composición de alimentos de este software incluye datos de la tabla de composición nutricional de alimentos de CENEXA²¹ e información provenientes de otras determinaciones bioquímicas efectuadas en Argentina²².

Análisis estadísticos

Análisis Factorial de Componentes Principales para la identificación de patrones alimentarios

Con el fin de caracterizar multidimensionalmente los patrones alimentarios predominantes en la población adulta total y por sexo, de la provincia de Córdoba, fueron analizados datos sobre frecuencia de consumo alimentario, recabados sobre una muestra de sujetos adultos de ambos sexos ($n = 489$), otra de hombres ($n = 381$) y una de mujeres ($n = 294$) que actuaron como controles, durante el periodo 2006-2012, en los estudios caso-control antes mencionados. Se utilizó un Análisis Factorial de Componentes Principales (AFCP), con rotación Varimax¹⁴. Este, examina la matriz de correlaciones (rotada para facilitar su interpretabilidad) entre variables de consumo alimentario, y la reduce a un conjunto menor de dimensiones. Éstas constituyen factores (patrones), que capturan las principales características de la dieta en la población estudiada.

En el presente trabajo los grupos alimentarios definidos para la construcción de estos patrones fueron seleccionados acorde a su representatividad de la dieta regional, y/o su potencial efecto sobre el riesgo de ocurrencia de cáncer.

La matriz de correlación fue evaluada mediante el test de Esfericidad de Bartlett y el de medidas Kraiser-Meyer-Olkin (KMO) de adecuación muestral¹⁶. En los análisis propuestos el número de patrones alimentarios (factores retenidos) se definió en base a los siguientes criterios: obtención de autovalor mayor a 1, e interpretabilidad factorial¹⁶.

La denominación de cada factor (patrón) se basó en los grupos de alimentos que resultaron dominantes en el análisis, para lo cual se estableció como criterio la presencia de carga absoluta del factor rotado $\geq 0,60$.

Posteriormente, para cada individuo encuestado (casos y controles), fue estimado un coeficiente de puntuación o score para cada patrón identificado, mediante método de regresión. Este score representa el grado en que la dieta del sujeto se ajusta a dicho patrón¹⁴. Luego, tomando como referencia la distribución de scores correspondientes al total de individuos adultos (controles) estudiados, se definieron puntos de corte, adoptando los terciles de la distribución del mencionado score. Se definieron así tres categorías para cada patrón: tercil inferior, medio y superior, indicadores indirectos de un bajo, medio y alto nivel de adherencia al patrón analizado.

Estimación de riesgos: modelación multinivel

Para la estimación de riesgos de ocurrencia de cáncer (Odds Ratios, OR) ligados al nivel de adherencia a los patrones alimentarios (terciles de los scores) fueron estimados modelos generalizados multinivel²³, ajustando por variables de confusión e incorporando distintas je-

rarquías de variabilidad (individuos integrados en unidades de un nivel superior, por ejemplo, de orden familiar o geográfico). Específicamente, fueron adoptados modelos de regresión logística a dos niveles, con sujetos (nivel 1, j) anidados dentro de una dimensión familiar o poblacional (nivel 2, i). Las variables de agrupamiento fueron: antecedentes familiares de la enfermedad, para CCR, CM y CP, y la residencia urbano-rural, para CU. Las covariables propuestas para el predictor lineal fueron los patrones alimentarios identificados, controlando por variables seleccionadas de acuerdo a la red causal de cada sitio tumoral.

Todos los análisis estadísticos se llevaron a cabo con el software Stata versión 12.1²⁴.

Resultados

La tabla I resume las principales características biológicas, socio-económicas, culturales, y otras asociadas a estilo de vida de los sujetos que participaron de los estudios caso-control. Se observa que la edad media de los sujetos fue de aproximadamente 67 y 62 años, para hombres y mujeres respectivamente. Se destaca que aquellos que integraron la muestra del estudio sobre CP presentaron el mayor promedio (70,5 años) respecto del resto de los estudios. Se encontraron diferencias estadísticamente significativas en la proporción de sujetos con antecedentes familiares de la enfermedad para CCR ($p = 0,02$) y CP ($p = 0,002$), nivel de instrucción secundario completo para CP ($p = 0,006$), situación ocupación de riesgo para CM ($p = 0,04$) y hábito de fumar para CCR ($p = 0,04$) y CU ($p = 0,00004$), entre casos y controles.

La tabla II presenta el consumo promedio diario energético, de macronutrientes y de alimentos (por grupos alimentarios), en casos y controles. Como se observa, el valor energético diario y consumo medio de macronutrientes mostró diferencias significativas ($p < 0,05$) entre sujetos con CCR y sus controles. En CM, también se evidenciaron diferencias en la ingesta media energética y de lípidos. Con respecto al consumo en término de grupos de alimentos, en el estudio sobre CCR la ingesta media de cereales y vegetales amiláceos, legumbres, lácteos, carnes-huevos y azúcares-confituras resultó significativamente diferente entre casos y controles, mientras que en relación al CU se observaron diferencias en el consumo medio de lácteos y bebidas alcohólicas. Específicamente en CM, la mayoría de los grupos alimentarios obtuvieron medias estadísticamente diferentes entre grupos, contrariamente a lo observado en el estudio de CP, donde sólo el consumo de legumbres resultó significativamente menor entre los casos.

En la caracterización multidimensional de la alimentación empleando el AFCP (en la población total de adultos, y la femenina y masculina separadamente) se obtuvieron como medidas de adecuación muestral un KMO general de 0,75 para ambos sexos, 0,65 para

mujeres y 0,71 para hombres. Esto indica que se justifica el análisis realizado en virtud de la extensión de la muestra.

La tabla III muestra la matriz de cargas factoriales (rotada) para los factores (patrones) retenidos en cada uno de los grupos poblacionales estudiados. Los tres patrones emergentes de la población general fueron denominados *Patrón Cono Sur* (caracterizado por elevadas cargas factoriales para carnes rojas, vegetales amiláceos y vino), *Patrón Bebidas Azucaradas* (gaseosas y jugos), y *Patrón Prudente* (frutas y vegetales no amiláceos, y lácteos). Particularmente en la población femenina, el primer patrón alimentario identificado incluyó las carnes grasas, productos de pastelería, aceites y mayonesa como grupos alimentarios dominantes, y fue llamado *Patrón Cono Sur Femenino*, y se identificó un patrón denominado *Prudente* que incluyó frutas y vegetales no amiláceos. Por su parte, en la población masculina el *Patrón Cono Sur Masculino* se caracterizó también por la ingesta de carnes grasas, sumado a la de huevos, granos y vegetales amiláceos, mientras que el *Prudente* resultó de igual conformación que el patrón del mismo nombre en la población general. El resto de los patrones identificados fueron llamados *Patrón Rural* (carnes procesadas), y *Patrón Amiláceo* (elevada ingesta de granos refinados y baja de granos enteros) en mujeres, y en el grupo de los hombres *Patrón Bebidas azucaradas* (jugos y gaseosas) y *Patrón Típico mesurado* (carnes rojas magras e infusiones).

La tabla IV presenta los resultados de la estimación de modelos logísticos multinivel, para la obtención de las medidas de asociación (ORs) de CCR, CU, CM y CP, con los diversos patrones alimentarios identificados, y sus correspondientes medidas de agrupamiento (esto es, en función de la estructura jerárquica de los datos). Respecto al riesgo de ocurrencia de CCR, y en consideración de la presencia de antecedentes familiares de esta patología, el *Patrón Cono Sur* (OR 2,35, para el tercil superior versus el inferior) y el *Patrón Bebidas Azucaradas* (OR 2,62) evidenciaron un efecto promotor, mientras que el *Patrón Prudente* (OR 0,31), mostró un efecto protector. En cuanto a la ocurrencia de CU, también fue observado un riesgo incrementado asociado al *Patrón Cono Sur* (OR 1,75) y a una adherencia media al *Patrón Bebidas Azucaradas* (OR 2,55 para el tercil medio versus el inferior), en tanto, una adherencia elevada a este último patrón mostró una asociación inversa con la enfermedad (OR 0,72 para el tercil superior versus el inferior), observándose agregación significativa ligada a la residencia en un ámbito urbano ó rural (tabla IV). En el estudio caso-control de CM, se evidenció un efecto promotor significativo del *Patrón Cono Sur Femenino*. Scores elevados (tercil superior) para los *Patrones Rural* y *Amiláceo* fueron también positivamente asociados al riesgo de padecer cáncer de mama (OR 2,02 y OR 1,82 respectivamente), mientras que la misma categoría del *Pa-*

Tabla I
Distribución de casos y controles según variables bio-socio-culturales. Estudio caso-control de cáncer colorrectal, urotelial de mama y próstata. Córdoba. Argentina 2006-2011

	CCR		CU		CM		CP	
Edad: Media (DE)								
Sexo Masculino	67,7 (11,3)		65,1 (10,6)		-		70,5 (8,6)	
Sexo Femenino	59,8 (16,2)		67,8 (18,9)		58,80 (13,4)		-	
<i>Características biológicas, socioeconómicas y culturales †</i>	<i>Casos (n=75)</i>	<i>Controles (n=153)</i>	<i>Casos (n=41)</i>	<i>Controles (n=82)</i>	<i>Casos (n=100)</i>	<i>Controles (n=293)</i>	<i>Casos (n=135)</i>	<i>Controles (n=282)</i>
	<i>N (%)</i>	<i>N (%)</i>	<i>N (%)</i>	<i>N (%)</i>	<i>N (%)</i>	<i>N (%)</i>	<i>N (%)</i>	<i>N (%)</i>
Nivel socioeconómico								
Bajo	45 (60,0)	76 (49,7)	19 (46,34)	41 (50,0)	36 (36,0)	18 (40,3)	32 (23,7)	79 (28,0)
Medio	19 (25,3)	38 (24,8)	16 (39,02)	27 (32,9)	39 (39,0)	84 (28,7)	54 (40,0)	109 (38,6)
Alto	11 (14,7)	39 (25,5)	6 (14,63)	14 (17,1)	25 (25,0)	91 (32,1)	49 (36,3)	94 (33,3)
Nivel de instrucción								
Sin instrucción o primario incomp.	19 (25,3)	30 (19,6)	6 (14,6)	16 (18,3)	6 (6,0)	19 (6,4)	31 (22,9)	48 (17,2)
Primario completo	35 (46,7)	71 (46,4)	24 (58,5)	39 (47,6)	61 (61,0)	158 (53,9)	67 (49,6)	133 (47,2)
Secundario compl.	12 (16,0)	27 (17,6)	3 (7,3)	12 (14,4)	15 (15)	57 (19,5)	12 (8,9)*	55 (19,5)*
Terciario/ Universit.	9 (12,0)	25 (16,3)	8 (19,5)	16 (19,5)	18 (18,00)	59 (20,1)	25 (18,5)	46 (16,3)
Situación Ocupacional								
Sin riesgo	62 (82,7)	140 (91,5)	35 (85,4)	71 (86,6)	90 (90,0)*	278 (95,9)*	90d (66,7)	207 (73,7)
Con riesgo	13 (17,3)	13 (8,5)	6 (14,6)	11 (13,4)	10 (10,0)*	12 (4,1)*	45 (33,3)	74 (26,3)
Antecedentes fliares.								
No presenta	66 (88,0)*	147 (96,8)*	21 (51,22)	55 (67,1)	83 (83,00)	247 (84,0)	117 (86,7)*	269 (95,4)*
Presenta	9 (12,0)	6 (3,9)*	20 (48,78)	27 (32,9)	17 (17,00)	47 (16,0)	18 (13,3)*	13 (4,6)*
Antecedentes del estilo de vida †								
Obesidad								
No	55 (73,3)	116 (75,8)	33 (80,5)	67 (81,7)	78 (78,0)	235 (80,2)	112 (82,9)	218 (77,3)
Si	20 (26,7)	37 (24,2)	8 (19,5)	15 (18,3)	22 (22,0)	58 (19,8)	23 (17,0)	64 (22,7)
Actividad Física								
No sedentario	40 (53,3)	76 (49,7)	10 (24,4)	27 (32,9)	51 (51,00)	136 (46,4)	33 (32,6)	93 (32,9)
Sedentario	35 (46,7)	77 (50,3)	31 (75,6)	55 (67,0)	49 (49,00)	157 (53,6)	91 (67,4)	189 (67,0)
Hábito de Fumar								
No fumador	37 (49,3)*	54 (35,3)*	9 (21,9)*	50 (60,9)*	64 (64,00)	176 (60,1)	44 (32,6)	86 (30,5)
Fumador	38 (50,7)*	99 (64,9)*	32 (78,0)*	(39,0)*	36 (36,00)	117 (39,9)	91 (67,4)	196 (69,5)
Consumo alcohol								
etanol <30 g/día	58 (77,3)	119 (77,8)	32 (78,0)	69 (84,1)	93 (93,00)	282 (96,2)	92 (68,1)	180 (63,8)
etanol ≥30 g/día	17 (22,7)	34 (22,2)	9 (21,9)	13 (15,8)	7 (7,0)	11 (3,5)	43 (31,8)	102 (36,2)

CCR: cáncer colorrectal; CU: cáncer urotelial; CM: cáncer de mama; CP: cáncer de próstata.

† Comparación de proporciones (Aproximación Normal) entre casos y controles; *Significativo a un nivel $\alpha=0,05$.

trón Prudente evidenció un efecto protector (OR 0,56). Por su parte, respecto a CP, el denominado *Patrón Cono Sur Masculino* mostró un efecto promotor significativo (OR 1,91 para el tercil superior vs el tercil inferior). De la misma manera, el consumo elevado (tercil superior) de jugos y gaseosas (*Patrón Bebidas Azucaradas*) y de carnes rojas magras e infusiones (*Patrón Típico Mesurado*), mostraron una asociación positiva con la ocurrencia de la enfermedad (OR 1,66 y 1,09, respectivamente). Se destaca que aquí también se observó una agregación significativa derivada de una posible dimensión de agrupamiento familiar, los antecedentes familiares de CP.

Discusión

En el presente trabajo fueron identificados patrones alimentarios característicos en la provincia de Córdoba. Los patrones emergentes en la población general fueron denominados *Patrón Cono Sur*, *Patrón Bebidas Azucaradas*, y *Patrón Prudente*. En la población femenina los patrones identificados fueron llamados *Cono Sur Femenino*, *Rural*, *Prudente* y *Amiláceo*, y en la población masculina *Cono Sur Masculino*, *Bebidas Azucaradas*, *Típico Mesurado* y *Prudente*. La mayoría de estos patrones presentaron asociaciones significativas con la ocurrencia de CCR, CM CP y CU en la provincia de Córdoba (Argentina).

Tabla II
Ingesta diaria energética, de macronutrientes y grupos alimentarios (media, desvío estándar) en casos y controles.
Estudio caso-control de cáncer colorrectal, urotelial, de mama y próstata. Córdoba. Argentina 2006-2012

	CCR		CU		CM		CP	
	Controles Media (DE)	Casos Media (DE)	Controles Media (DE)	Casos Media (DE)	Controles Media (DE)	Casos Media (DE)	Controles Media (DE)	Casos Media (DE)
VET †								
Kilocalorías/día	3112,9* (1266,5)	3661,3* (1322,6)	3090,7 (889,0)	3171,0 (861,8)	2844,9* (1114,7)	3389,4* (1283,5)	3526,4 (1212,5)	3630,2 (1139,3)
Macronutrientes† (g/día)								
Hidratos de carbono	351,2* (158,8)	418,5* (172,2)	379,1 (126,6)	372,9 (101,2)	355,9 (146,8)	404,6 (169,3)	385,5 (125,0)	399,9 (125,0)
Proteínas	112,8* (40,3)	127,5* (2,8)	112,6 (32,1)	111,3 (32,8)	104,5 (39,5)	112,5 (36,0)	127,2 (44,6)	129,7 (45,4)
Lípidos	123,4* (61,4)	146,7* (69,6)	115,9 (45,7)	124,1 (43,5)	105,8* (57,1)	137,1* (69,1)	142,7 (70,4)	151,2 (63,9)
<i>Grupos de alimentos† (g ó cc/día)</i>								
Cereales y vegetales amiláceos	339,7* (188,1)	422,9* (196,2)	391,1 (154,6)	384,2 (109,2)	320,4* (182,8)	385,8* (196,1)	410,5 (67,7)	428,6 (203,2)
Vegetales no amiláceos y fruta	495,2 (246,9)	472,4 (416,6)	519,6 (242,7)	524,0 (257,9)	512,2* (299,9)	445,7* (241,9)	476,5 (262,2)	474,6 (283,7)
Legumbres	5,6* (8,5)	3,4* (9,2)	6,2 (9,2)	4,4 (7,6)	4,1 (10,5)	4,0 (7,5)	5,2* (12,7)	2,9* (5,1)
Lácteos	233,8* (210,6)	178,8* (162,8)	274,5* (197,5)	210,2* (215,1)	263,0 (202,4)	250,8 (217,4)	224,1 (222,3)	228,6 (202,0)
Carnes y huevo	329,7* (151,5)	392,9* (206,4)	291,1 (133,4)	296,9 (123,7)	270,8* (137,5)	319,3* (150,6)	411,8 (224,4)	423,4 (224,6)
Grasas y aceite	29,0 (23,7)	33,6 (21,2)	29,0 (20,7)	31,1 (21,7)	24,4* (21,2)	34,7* (31,9)	29,3 (26,0)	33,8 (25,7)
Azúcares y confituras	85,1* (78,5)	106,2* (90,2)	82,5 (65,9)	72,2 (70,9)	88,5* (82,2)	116,9* (99,1)	82,9 (63,0)	90,3 (63,5)
Bebidas con alcohol	173,5 (275,8)	201,1 (318,9)	112,7* (150,6)	173,0* (269,2)	40,6* (94,5)	67,6* (123,6)	245,7 (272,8)	202,3 (217,1)
Bebidas sin alcohol	297,0 (404,5)	351,1 (401,2)	241,3 (347,6)	255,0 (305,4)	242,2* (323,6)	317,0* (331,1)	247,0 (325,7)	248,7 (283,7)
Infusiones	666,6 (657,69)	655,4 (565,6)	431,0 (394,4)	529,1 (623,0)	927,0 (691,9)	1044,0 (878,0)	448,8 (356,5)	423,8 (308,2)

CCR: cáncer colorrectal; CU: cáncer urotelial; CM: cáncer de mama; CP: cáncer de próstata. DE, desvío estándar; VET, valor energético total;

† Comparación de medias entre casos y controles mediante prueba de hipótesis T de Student; *Significativo a un nivel $\alpha = 0,05$

Se ha reportado que en Argentina, las tasas de incidencia 2008 para CCR registraron valores de 25,3 en hombres y 16,7 en mujeres, por cada 100000 habitantes, y de 10,7 y 1,7 en la población masculina y femenina, respectivamente, para CU¹. Por su parte, en el mismo año, el CM presentó una tasa de 74,0 y el CP de 58,8, a nivel nacional¹. Específicamente en Córdoba se ha observado en años anteriores gran variabilidad en la magnitud de las tasas entre los 26 departamentos que componen la Provincia². Se ha sugerido que dicho patrón espacial está asociado a características culturales, económicas y ambientales (incluidos los hábitos alimentarios) y a la diferente urbanización de las poblaciones^{4,7}.

Es importante destacar que las costumbres alimentarias de los argentinos presentan ciertas particularidades que las diferencian de otros países latinoamericanos: elevado consumo de carnes rojas⁹, frecuente cocción de carnes a la parrilla⁸, habitual ingesta de vino²⁵, y el consumo típico de la infusión “mate”^{26,40,41}, entre otros. Particularmente en Córdoba, ciertas características de la dieta en la ciudad capital fueron asociadas al riesgo de cáncer en estudios anteriores^{8,11,27}. Aún en consideración de esto, en Córdoba como Argentina no se cuenta con información oficial respecto a la alimentación típica del total de la población, menos aún con estudios que describan cuál es el consumo alimen-

tario habitual en nuestra población desde el enfoque de patrones de consumo alimentario (AFCP). Solo a partir de las hojas de balance de alimentos de la FAO puede deducirse de manera indirecta que los alimentos que integran principalmente la dieta nacional son: pan, harinas y fideos, carne vacuna, azúcar, leche, quesos, aceite de girasol, papa, verduras de hoja, arroz, naranja, manzana, banana y tomate, manteca y grasa, y vino²⁸. En términos generales, la identificación de patrones alimentarios realizada en el marco de este trabajo, mostró concordancia con esto, en tanto resultaron emergentes como grupos de alimentos (o alimentos) dominantes varios de los descritos por la FAO.

Si se considera la conformación de los patrones alimentarios identificados en este estudio, encontramos que tanto en la población total, como masculina y femenina, el grupo de las carnes resultó dominante en los patrones denominados *Cono Sur*, identificados siempre en primer lugar, lo cual indica una fuerte representación de estos en la dieta de los individuos. Si bien estos patrones difieren en algunos aspectos del *Patrón Occidental (Western Pattern)* descrito en diversos estudios¹⁵, coincide con éste en presentar a las carnes rojas como grupo característico. Se observa que nuestros resultados en relación a CCR y TU fueron consistentes con los reportados en estudios previos respecto a la asociación positiva del *Patrón Occidental* con estas patologías^{11,13,15}.

Tabla III

Matriz de cargas factoriales (rotada) para los principales patrones alimentarios identificados a partir del análisis factorial de componentes principales. Córdoba. Argentina 2006-2012

<i>Población total (n = 489)^a</i>				
<i>Grupos de alimentos</i>	<i>Patrón Cono Sur</i>	<i>Patrón bebidas azucaradas</i>	<i>Patrón Prudente</i>	
Lácteos	-0,06	-0,03	0,68	
Carnes rojas	0,72	0,10	0,04	
Frutas y vegetales no amiláceos	0,05	-0,04	0,75	
Vegetales amiláceos	0,61	0,15	0,24	
Bebidas azucaradas	-0,07	0,79	-0,14	
Vino	0,68	-0,37	-0,21	
Variabilidad explicada (%)	19,47	13,13	12,43	
Variabilidad explicada acumulada (%)	19,47	32,6	46,03	

<i>Población femenina (n = 294)^b</i>				
<i>Grupos de alimentos</i>	<i>Patrón Cono Sur</i>	<i>Patrón Rural</i>	<i>Patrón Prudente</i>	<i>Patrón Amiláceo</i>
Carnes grasas	0,7319	0,15	-0,08	0,18
Carnes procesadas	0,23	0,71	-0,05	0,01
Granos refinados	0,23	-0,15	0,007	0,73
Granos enteros	-0,07	-0,08	0,03	-0,68
Productos de pastelería	0,65	0,35	-0,0006	0,14
Aceites vegetales y mayonesa	0,69	-0,08	0,23	-0,003
Vegetales no amiláceos	0,05	0,03	0,81	0,03
Frutas	0,09	-0,13	0,64	-0,12
Variabilidad explicada (%)	0,13	0,10	0,07	0,06
Variabilidad explicada acumulada (%)	0,13	0,24	0,31	0,37

<i>Población masculina (n = 381)^c</i>				
<i>Grupos de alimentos</i>	<i>Patrón Cono Sur</i>	<i>Patrón bebidas azucaradas</i>	<i>Patrón Típico medido</i>	<i>Patrón Prudente</i>
Lácteos	-0,0014	-0,0114	-0,1221	0,7915
Huevos	0,6304	-0,1821	-0,0458	0,0215
Carnes rojas magras	-0,1128	-0,2575	0,6282	0,1412
Carnes rojas grasas	0,7367	-0,1206	0,0810	-0,0046
Frutas y vegetales no amiláceos	0,1072	0,1083	0,2804	0,6779
Granos y vegetales amiláceos	0,6005	0,2355	0,1219	0,0897
Infusiones	0,1132	0,1311	0,7223	-0,0734
Bebidas azucaradas	0,0422	0,8006	0,0415	-0,0591
Variabilidad explicada (%)	20,10	13,04	10,48	8,46
Variabilidad explicada acumulada (%)	20,10	33,14	43,62	52,08

NOTA: Cargas $\geq 0,60$ (**en negrita**) definen los grupos dominantes para cada factor. La Tabla solo presenta los grupos alimentarios que resultaron dominantes en algún factor. No obstante, las dimensiones o variables intermedias definidas para la construcción de patrones alimentarios, tras las pruebas estadísticas de adecuación muestral, fueron:

^aCereales y productos derivados, Vegetales amiláceos, Vegetales no amiláceos y frutas, Lácteos, Carnes procesadas, Carnes rojas, Carnes blancas, Huevos, Azúcares y confituras, Bebidas azucaradas, Vino, Grasas y aceites.

^bLeche y yogur, quesos duros, quesos blandos, carnes magras, carnes grasas, carnes procesadas, huevos, vegetales amiláceos, vegetales no amiláceos, frutas, cereales integrales, cereales refinados, legumbres, productos de panadería, dulces (helados, chocolates, mantecol, dulce de leche), azúcares y dulces (azúcar, mermelada, miel, dulce de leche), manteca y crema de leche, aceites vegetales y mayonesa, bebidas alcohólicas y bebidas no alcohólicas.

^cLácteos, carnes rojas magras, carnes rojas grasas, huevos, frutas y vegetales no amiláceos, cereales y vegetales amiláceos, azúcares y confituras, grasas, aceites vegetales, infusiones, vino, bebidas sin alcohol.

También en cuanto a CM y CP este patrón ha mostrado, en la mayoría de los casos y coincidentemente con nuestros resultados, un riesgo incrementado^{16,29-32}, aunque existe también evidencia contradictoria al respecto^{33,34}.

Los patrones alimentarios denominados Prudente en el presente estudio, presentaron similares característi-

cas a otros publicados bajo esta y otras denominaciones tales como *Patrón Saludable* ó *Vegetales y frutas*^{13,35,36}. Coincidentemente con nuestros hallazgos, los resultados de la mayoría de estos estudios evidenciaron un efecto favorable de este patrón en la reducción del riesgo de CCR¹⁵ y CM³⁷⁻³⁹, aunque existe evidencia que in-

Tabla IV

Estimación de medidas de asociación (ORs ajustados por variables de confusión seleccionadas) mediante Modelos Logísticos Multinivel para cáncer colorrectal, urotelial, de mama y de próstata. Córdoba. Argentina 2006-2012

<i>Estudio caso-control según sitio tumoral</i>	<i>Patrón alimentario Referencia: Tercil I</i>	<i>OR (IC 95%)</i>	<i>p valor</i>
Cáncer colorrectal ¹	Patrón Cono Sur, II	1,92 (1,51-2,46)	<0,001
	Patrón Cono Sur, III	2,35 (2,25-2,46)	<0,001
	Patrón Bebidas Azucaradas, II	1,54 (0,86-2,75)	0,144
	Patrón Bebidas Azucaradas, III	2,62 (2,32-2,95)	<0,001
	Patrón Prudente, II	0,84 (0,51-1,41)	0,516
	Patrón Prudente, III	0,31 (0,22-0,43)	<0,001
Cáncer urotelial ²	Patrón Cono Sur, II	2,63 (1,99-3,47)	<0,001
	Patrón Cono Sur, III	1,75 (1,10-2,78)	0,017
	Patrón Bebidas Azucaradas, II	2,55 (1,28-5,07)	0,008
	Patrón Bebidas Azucaradas, III	0,72 (0,60-0,85)	<0,001
	Patrón Prudente, II	0,66 (0,25-1,70)	0,386
	Patrón Prudente, III	0,31 (0,08-1,23)	0,097
Cáncer de mama ¹	Patrón Cono Sur Femenino, II	1,63 (1,59-1,69)	<0,001
	Patrón Cono Sur Femenino, III	3,13 (2,58-3,78)	<0,001
	Patrón Rural, II	1,44 (0,64-3,26)	0,370
	Patrón Rural, III	2,02 (1,21-3,37)	<0,001
	Patrón Prudente, II	1,10 (0,88-1,37)	0,370
	Patrón Prudente, III	0,56 (0,41-0,77)	<0,001
Cáncer de próstata ¹	Patrón Amiláceo, II	1,36 (1,04-1,76)	0,020
	Patrón Amiláceo, III	1,82 (1,18-2,79)	<0,001
	Patrón Cono Sur Masculino, II	1,39 (0,981-1,99)	0,064
	Patrón Cono Sur Masculino, III	1,91 (1,734-2,11)	<0,001
	Patrón Bebidas Azucaradas, II	1,17 (0,728-1,89)	0,509
	Patrón Bebidas Azucaradas, III	1,66 (1,094-2,55)	0,017
	Patrón Típico Mesurado, II	1,30 (0,970-1,74)	0,079
	Patrón Típico Mesurado, III	1,09 (1,052-1,14)	<0,001
	Patrón Prudente, II	0,94 (0,620-1,44)	0,798
	Patrón Prudente, III	1,26 (0,705-2,27)	0,431

OR, odds ratio; IC, intervalo de confianza; II y III, tercil medio y superior de los escores del patrón alimentario. Variable de agrupamiento: ¹Antecedentes familiares de la patología, ²Residencia urbano-rural.

dica asociación nula o positiva respecto a este último sitio tumoral³⁰. Sin embargo, mientras la bibliografía refiere un efecto anti-tumorigénico de las frutas y vegetales^{5,7,40}, este patrón no evidenció efecto en la ocurrencia de CP ni CU en nuestro estudio.

Otro patrón alimentario emergente en la población de Córdoba que se asoció a un riesgo incrementado de CCR y CP en este estudio fue el *Patrón Bebidas Azucaradas*. Este patrón, compuesto básicamente por el consumo de jugos y gaseosas no ha sido identificado en otras áreas de Sudamérica, ni como tal en ningún otro

estudio, por lo que constituiría un patrón particular de esta región^{5,6}. Elevadas ingestas de bebidas azucaradas se asociaron con un incrementado riesgo de presentar CCR y CP en otros estudios epidemiológicos^{40,41}, aunque algunos no corroboran tal asociación para CCR⁴². El incremento del riesgo de CCR y CP estaría vinculado con el elevado índice glucémico de estas bebidas, es decir su capacidad para aumentar notablemente la glucemia luego de su ingesta. La hiperglucemia provocada estimula secreciones elevadas de insulina que actúa per se como un factor de crecimen-

to, y a su vez, induce un incremento del factor de crecimiento similar a la insulina tipo I (IGF-1), hormona que promueve la mitosis y la proliferación celular, a la vez que inhibe la apoptosis en células normales y cancerosas⁴³. Otras vías metabólicas que involucran a la insulina, han sido también vinculadas a un riesgo incrementado, específicamente, de CP⁴⁴.

Cabe destacar que los patrones alimentarios identificados en la población masculina de Córdoba presentaron mayor similitud con los de la población total, que los identificados en la población femenina. Esto si bien puede en parte explicarse por la diferente proporción de hombres y mujeres (mayoría de controles de sexo masculino) que integraron la muestra en la población total, también puede deberse a diferencias entre los hábitos alimentarios entre hombres y mujeres⁴⁵. Las principales diferencias entre los patrones *Cono Sur Femenino* con el patrón *Cono Sur* identificado en la población total pueden justificarse por las diferencias de género en lo referente al hábito de beber. Es conocido que, tradicionalmente, las mujeres argentinas consumen menos bebidas alcohólicas que los hombres, lo cual podría explicar la ausencia de altas cargas en ese grupo alimentario en los patrones emergentes para dicha población. De acuerdo a la Encuesta Nacional de Factores de Riesgo llevada a cabo en el año 2009 en Argentina, el consumo regular de alcohol de riesgo y consumo de alcohol episódico excesivo en la provincia de Córdoba fue superior en hombres que en mujeres⁴⁶.

Por otra parte, la identificación en la población femenina de un patrón *Rural* con carnes procesadas como grupo dominante, coincide con los resultados de un estudio llevado a cabo en otro país sudamericano (Uruguay), en el cual fue reportado que, al estratificar los patrones por género, la población femenina presentó cargas más elevadas para carnes procesadas que la población masculina¹².

Es necesario hacer mención a algunas limitaciones de este trabajo concernientes al diseño del estudio y las metodologías empleadas. Es posible que el tamaño de las muestras sea insuficiente para detectar el verdadero efecto de los patrones alimentarios. Sin embargo, la particular metodología estadística propuesta admite tamaños muestrales reducidos. Además, en el análisis factorial de componentes principales se obtuvieron medidas de KMO satisfactorias, indicando un adecuado tamaño muestral para el análisis realizado.

En los estudios de casos y controles se reconoce la posibilidad de sesgos de selección (debido a una selección no aleatoria de sujetos), de información (por la realización de mediciones imperfectas) y de confusión (generados por asignaciones no aleatorias de la exposición). Sin embargo, en el presente estudio fueron implementadas numerosas estrategias desde su diseño hasta su análisis a fin de minimizar la posibilidad de su ocurrencia. Estas tácticas incluyeron el desarrollo de un detallado manual de procedimientos, así como un riguroso entrenamiento de los entrevistadores, la estandarización de los procedimientos de recolección de datos y el minu-

cioso monitoreo de esta etapa del estudio para evitar una clasificación errónea de la exposición. Además, la mayoría de los entrevistadores fueron enmascarados respecto de las principales hipótesis del estudio, a fin de remover una importante fuente de sesgos, particularmente cuando éstos tienen conocimiento sobre la condición de caso o control dentro del estudio. Sin embargo errores en la medición de la exposición a la dieta podrían aún existir. No obstante, la distribución equitativa de éstos entre casos y controles –a excepción del sesgo del recuerdo– hace suponer que su influencia sea despreciable.

A fines de evitar potencialmente importantes sesgos de selección y por factores confundentes no medidos, en este estudio se procuró una distribución similar de características relevantes en el grupo casos y controles. Es decir, se recurrió a la selección de los controles según sexo, edad y lugar de residencia de los casos, para formar grupos tan similares como sea posible, excepto por la presencia de cáncer, y fueron entrevistados en el mismo período de tiempo. Adicionalmente, se incluyeron en los modelos diversas covariables para considerar alguna confusión residual y obtener estimaciones más precisas del efecto de los patrones alimentarios en la ocurrencia de cáncer.

En virtud de lo hasta aquí expuesto, podemos decir que en términos generales nuestros hallazgos contaron con suficiente plausibilidad biológica y consistencia respecto a otros estudios en la temática. Este trabajo además da muestra de un desarrollo metodológico novedoso en el campo de la epidemiología nutricional, lo cual puede orientar futuras investigaciones.

Conclusiones

Las enfermedades crónicas no transmisibles, y entre ellas el cáncer, sin dudas representan actualmente una importante carga de enfermedad en Córdoba (Argentina) como en el mundo. Esto amerita el esfuerzo concertado de los diferentes actores sociales, incluida la comunidad científica y académica, para paliar su impacto en las poblaciones. En ese sentido, consideramos que el presente trabajo aporta valiosa evidencia acerca del papel de los patrones alimentarios en la compleja etiología de diversos cánceres, en tanto la alimentación constituye un estilo de vida potencialmente modificable. Es así que, en consideración de las estrategias de prevención del cáncer ya conocidas y divulgadas, los resultados de esta investigación corroboran la necesidad de enfatizar recomendaciones alimentarias tendientes a fomentar la ingesta habitual de vegetales, frutas y lácteos (éstos últimos de manera moderada en hombres), así como disminuir el consumo de carnes rojas (fundamentalmente las de alto contenido graso), carnes procesadas, vegetales amiláceos, granos refinados, vino y bebidas azucaradas. Particularmente en hombres se sugiere moderar la ingesta de huevos, y en mujeres la de productos de pastelería, aceites y mayonesa.

Finalmente, se destaca la contribución que este estudio realiza a la caracterización de hábitos alimentarios poblacionales en una región en la que existen escasos antecedentes al respecto, más aún ligados a una problemática de salud que reviste particular importancia el escenario de la sociedad moderna y que se reconoce fuertemente ligada a determinantes ambientales, como lo es el cáncer.

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Original / *Cáncer*

The Inflammatory-Nutritional Index; assessing nutritional status and prognosis in gastrointestinal and lung cancer patients

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Abstract

Objective: To evaluate the prognostic capacity of the Inflammatory-Nutritional Index (INI) in gastrointestinal and lung cancer patients.

Methods: Longitudinal study, including patients from a chemotherapy service in Brazil, between July 2008 and May 2010. INI (Albumin/CRP) and nutritional status (by Subjective Global Assessment - SGA) were evaluated. Risk INI was defined as lower than 0.35. The mean follow-up of survival was 1.6 year. Statistical analyses were performed using Stata 11.1™.

Results: 74 patients participated in the study, mean age 63.4, most of them male (58%) and presenting gastrointestinal cancer (71%). Malnutrition was identified in 87% of the patients (22% severely malnourished). The mean INI was 2.67 and 54% of the patients had INI levels considered as risk. During the follow-up there were 49 deaths (66%). The median survival time for INI risk patients was significantly shorter than for normal INI ones ($p = 0,002$). It took 0.78 year for the INI risk subsample to decline 50%, while it took 2.78 year for the normal INI subsample. INI risk and severe malnutrition were independent predictors for poor survival.

Conclusion: The INI showed prognostic capacity in this sample and may be a useful tool, based on routinely available blood tests, to assess cancer patients.

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Keywords: *Biomarkers. Cachexia. Longitudinal study. Serum markers.*

ÍNDICE INFLAMATORIO-NUTRICIONAL; EVALUACIÓN DEL ESTADO NUTRICIONAL Y PRONÓSTICO EN PACIENTES CON CÁNCER DE TRACTO GASTROINTESTINAL Y DE PULMÓN

Resumen

Objetivo: Evaluar la capacidad pronostica del Índice Inflamatorio-Nutricional (INI) en pacientes con cáncer del tracto gastrointestinal y pulmón.

Métodos: Estudio longitudinal, con pacientes de un servicio de quimioterapia en Brasil, entre Julio de 2008 y Mayo de 2010. INI (Albúmina/CRP) y el estadio nutricional (Valoración Global Subjetiva-SGA) fueran evaluados. INI de riesgo fue definido como menor que 0.35. El tiempo medio de acompañamiento fue 1.6 año. Análisis estadísticas fueran realizadas con el programa Stata 11.1™.

Resultados: Fueron evaluados 74 pacientes, con edad media de 63.4 años, la mayoría hombres (58%) e con cáncer gastrointestinal (71%). Desnutrición fue identificada en 87% de los pacientes (22% con desnutrición grave). El INI medio fue 2.67 y 54% de los individuos presentaban INI de riesgo. Durante el acompañamiento hubieran 49 óbitos (66%). El tiempo mediano de supervivencia de los pacientes con INI de riesgo fue significativamente más corto que de los pacientes con INI normal ($p = 0.002$). El grupo con INI de riesgo llevó 0.78 año para decaer 50%, en cuanto el grupo con INI normal llevó 2.78 año ($p = 0.001$). INI de riesgo y desnutrición grave fueron factores independientes de peor supervivencia. Conclusión: El INI demostró capacidad pronostica en esta muestra y puede ser una herramienta útil, basada en tests rutinarios y disponibles, para evaluar pacientes con cáncer.

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Palabras clave: *Biomarcadores. Caquexia. Estudio longitudinal. Marcadores séricos.*

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Abbreviations

BMI: Body Mass Index.
CI: Confidence Interval.
CRP: C-Reactive Protein.
GPS: Glasgow Prognostic Score.
HR: Hazard Ratio.
INI: Inflammatory-Nutritional Index.
IQR: Inter Quartile Range.
NSCLC: Non Small Cells Lung Cancer.
PINI: Prognostic Inflammatory Nutritional Index.
SGA: Subjective Global Assessment.

Introduction

Mortality in cancer is closely linked to the patient's nutritional status, with one third of deaths being caused by malnutrition, and not by the disease itself¹. Cancer cachexia is defined as a multifactorial and complex handling syndrome, which leads to weight loss based mostly on muscle mass and, consequently, to progressive functional impairment. Such condition can be divided in three stages: pre-cachexia, in which there is a weight loss of less than 5% accompanied by anorexia and metabolic changes; cachexia, with weight/muscle loss aggravation and the onset of systemic inflammation; and refractory cachexia, the final stage of the syndrome characterized by intense catabolism, non responsiveness to anticancer treatment, poor functionality and a life expectancy of less than three months².

As cachexia progresses to irreversible stages and contributes to the death of cancer patients, it is necessary to identify this condition as early as possible. Weight loss must be assessed and observed, specially the decrease in muscle mass. Furthermore, systemic inflammation, which plays an important role in cachexia genesis and progression, should be evaluated³, considering that it implies worsening in prognosis⁴.

For that purpose, the tools that can help the identification of the nutritional and inflammatory status of the cancer patients are useful in anticancer therapy. A previous study⁵ has demonstrated an association between the Inflammatory-Nutritional Index (INI = serum Albumin / serum C Reactive Protein [CRP]) and the nutritional status according to the Subjective Global Assessment (SGA)^{6,7}, which is used to early detect malnutrition/nutritional risk.

As INI considers an increase in CRP levels and a decrease in albumin levels in the evaluation of the systemic inflammation, it probably has some prognostic value for cancer patients, since it has already been associated with the *Glasgow Prognostic Score* (GPS)⁵. Moreover, other studies have found an association between inflammatory markers (such as Albumin and CRP) and scores based on them, and survival prognosis in cancer^{4,8-15}.

Therefore, the aim of this study was to perform a survival analysis and to evaluate the prognostic

capacity of the INI as an independent predictor of mortality in a cohort of gastrointestinal and lung cancer patients with a 3.5 year follow-up, and whose baseline data were collected before the first chemotherapy cycle.

Methods

This survival longitudinal study consisted of cancer patients attended at the Chemotherapy Service of the Teaching Hospital of the Federal University of Pelotas-RS/Brazil. The baseline data collection occurred from July 2008 to May 2010, and the follow-up was conducted until June 2012.

Patients aged 18 years and older, diagnosed with gastrointestinal (including annex glands) or lung cancer, and receiving chemotherapy for the first time, were considered eligible. After signing a consent form, the patients had an appointment with a nutritionist. Socio-economic, disease and treatment (tumor site/stage and chemotherapy type –those gathered from the patient medical records) data were collected using standardized questionnaires. Patients had their nutritional status evaluated by the SGA^{6,7} and anthropometric measurements (weight and height) collected for a further calculation of the Body Mass Index (BMI = Weight [kg] / Height[m]²).

After the appointment, patients were conducted to the laboratory for the measurement of serum albumin and CRP and subsequent calculation of the INI⁵. For this study, INI values lower than 0.35 were determined as risk INI, considering the cut point of normality for serum albumin (3.5 g/dL) and CRP (10 mg/dL).

After 3.5 years from the baseline, phone calls were made to check the patients' conditions. When the phone contact was not possible, the government database of death records was consulted to verify whether death has occurred and when.

Data were double entered and the consistency was checked using EpiInfo™ 6.04d software. Statistical analyses were performed by Stata™ 11.1 package. For survival analyses, it was used the Kaplan-Meier curves. Associations to death were tested with Student's t, χ^2 or Fischer's exact tests, according to the variable nature. Those variables which test presented $p < 0.20$ in univariate analysis were included in multivariate analysis by Cox Proportional Hazard regression model.

This study was approved by the Research Ethics Committee of the School of Medicine of the Federal University of Pelotas, responsible for the Hospital where it was conducted (of. 066/2006).

Results

Seventy-four patients, mean aged 63.4 ± 11.9 years old, most of them male (58.1%) participated in the

Table I <i>Description of the characteristics of cancer patients evaluated at the Chemotherapy Service of the Teaching Hospital of the Federal University of Pelotas - RS - Brazil</i>		
Characteristic	n	Frequency (%)
Gender		
Male	43	58.1
Female	31	41.9
Tumor site		
Esophagus/Stomach	16	21.6
Colon/Rectum	33	44.6
Pancreas/Gall bladder	4	5.4
Lung	21	28.4
Tumor stage		
II	19	25.7
III	24	32.4
IV	21	28.4
Unknown	10	13.5
Chemotherapy type		
Curative	1	1.3
Neoadjuvant	23	31.1
Adjuvant	10	13.5
Palliative	40	54.1
Nutritional status (SGA*)		
Well nourished (A)	10	13.5
Suspected/moderated malnutrition (B)	48	64.9
Severe malnutrition (C)	16	21.6
BMI**		
Under nutrition	6	8.1
Normal	43	58.1
Excessive weight (≥ 25.0 kg/m ²)	25	33.8
Risk INI***		
Yes	40	54.1
No	34	45.9
Total	74	100.0

*Subjective Global Assessment.

**Body Mass Index.

***Inflammatory-Nutritional Index.

study. The most prevalent tumor site was colon/rectum (44.6%) followed by lung cancer (28.4%). Around 30% of the patients had stage IV disease and 54.1% received indication of palliative chemotherapy. The detailed sample's description is shown in table I.

With regard to the nutritional status, according to SGA, almost 87% of the sample had some degree of malnutrition. The mean BMI of the patients was 23.3 kg/m², ranging from 15.5 to 36.6 kg/m²; only six patients (8.1%) were classified as malnourished according to this indicator, and most of them (58.1%) were eutrophic.

Serum CRP levels presented mean of 39.29 \pm 48.61 mg/dL (median 13.25 IQR: 3.28; 59.3 mg/dL), while serum albumin levels had mean of 3.73 \pm 0.39 g/dL (ranging from 2.66 to 4.41 g/dL). The mean INI was 2.67 \pm 8.08 (median of 0.27 IQR: 0.06; 1.30), with most of the sample (54.1%) presenting Risk INI (< 0.35). Table II compares the subjects characteristics according to the INI categories (risk or not).

Table II <i>Comparison of characteristics of the patients with risk INI (< 0.35) and normal INI</i>			
Characteristic	Normal INI n (%)	Risk INI n (%)	P value*
Gender			
Male	18 (41.9)	25 (58.1)	0.406
Female	16 (51.6)	15 (48.4)	
Age (years old)**			
Mean \pm SD	60.9 \pm 11.6	65.5 \pm 11.8	0.094
Tumor site***			
Esophagus/Stomach	10 (62.5)	6 (37.5)	1.000
Colon/Rectum	16 (48.5)	17 (51.5)	0.357
Pancreas/Gall bladder	3 (75.0)	1 (25.0)	0.639
Lung	5 (23.8)	16 (76.2)	0.176
Tumor stage***			
II	11 (57.9)	8 (42.1)	0.112
III	14 (58.3)	10 (41.7)	
IV	6 (28.6)	15 (71.4)	
Unknown	3 (45.9)	7 (54.1)	
Chemotherapy type***			
Curative	14 (60.9)	9 (39.1)	1.000
Neoadjuvant	7 (70.0)	3 (30.0)	0.616
Adjuvant	0 (0.0)	1 (100.0)	0.227
Palliative	13 (32.5)	27 (67.5)	0.028
Nutritional status (SGA)***			
Well nourished (A)	7 (70.0)	3 (30.0)	0.178
Suspected/moderated malnutrition (B)	22 (45.8)	26 (54.2)	
Severe malnutrition (C)	5 (31.3)	11 (68.7)	
BMI***			
Under nutrition	3 (50.0)	3 (50.0)	1.000
Normal	20 (46.5)	23 (53.5)	
Excessive weight (≥ 25.0 kg/m ²)	11 (45.9)	14 (54.1)	
Death			
No	17 (68.0)	8 (32.0)	0.007
Yes	17 (34.7)	32 (65.3)	
Total	34 (45.9%)	40 (54.1%)	

* χ^2 test.

**Student's T test.

***Fischer's Exact test.

The mean survival follow-up was 1.6 \pm 1.2 years, with a minimum of 0.01 years (early deaths around the baseline period) and maximum of 3.6 years. During this period, there were 49 deaths (66.2%) and, according to the bivariate analysis, its occurrence was associated to increased age ($p = 0.005$), tumor location ($p = 0.001$, lower mortality rate in colon/rectum cancer patients and higher mortality rate in pancreatic cancer), palliative chemotherapy ($p = 0.001$), worsening of the nutritional status according to SGA ($p < 0.001$) and Risk INI ($p = 0.007$), as shown in table III.

The subsample with Risk INI had a 50% survival decrease in 0.78 year, while the subsample of patients with Normal INI had a 50% survival decrease in 2.78 years ($p = 0.001$ – fig. 1), with a hazard ratio of 2.56 (CI95%: 1.41 ; 4.64) for mortality in the Risk INI group. The median survival time for the Normal INI patients was 2.33 years (IQR: 1.13; 2.86 years), while

Table III
Comparison of characteristics of the patients according to mortality

Characteristic	Survivor n (%)	Deceased n (%)	P value*
Gender			0.447
Male	13 (30.2)	30 (69.8)	
Female	12 (38.7)	19 (61.3)	
Age (years old)**			0.005
Mean ± SD	58.1 ± 11.4	66.1 ± 11.3	
Tumor site***			0.001
Esophagus/Stomach	2 (12.5)	14 (87.5)	1.000
Colon/Rectum	19 (57.6)	14 (42.4)	0.003
Pancreas/Gall bladder	0 (0.0)	4 (100.0)	0.046
Lung	4 (19.1)	17 (80.9)	0.592
Tumor stage***			0.138
II	10 (52.6)	9 (47.4)	
III	8 (33.3)	16 (66.7)	
IV	6 (28.6)	15 (71.4)	
Unknown	1 (10.0)	9 (90.0)	
Chemotherapy type***			0.001
Curative	10 (43.5)	13 (56.5)	1.000
Neoadjuvant	8 (80.0)	2 (20.0)	0.053
Adjuvant	0 (0.0)	1 (100.0)	0.388
Palliative	7 (17.5)	33 (82.5)	0.025
Nutritional status (SGA)***			<0.001
Well nourished (A)	8 (80.0)	2 (20.0)	1.000
Suspected/moderated malnutrition (B)	16 (33.3)	32 (66.7)	0.009
Severe malnutrition (C)	1 (6.3)	15 (93.7)	<0.001
BMI***			0.189
Under nutrition	1 (16.7)	5 (83.3)	
Normal	12 (27.9)	31 (72.1)	
Excessive weight (≥ 25.0 kg/m ²)	12 (48.0)	13 (52.0)	
Risk INI			0.007
No	17 (50.0)	17 (50.0)	
Yes	8 (20.0)	32 (80.0)	
Total	34 (33.8%)	49 (66.2%)	

* χ^2 test.

** Student's T test.

*** Fischer's Exact test.

Risk INI patients presented significantly poor survival time (median of 0.79 years, IQR: 0.21; 1.88. P value = 0.002 – Mann-Whitney Test).

After the Cox Proportional Hazard analysis (table IV), severe malnutrition according to SGA ($p = 0.009$) and Risk INI (0.003) remained as independent predictive factors for mortality. In this sample, site tumor in colon/rectum was considered a protective factor for survival.

Discussion

Several studies have proposed the assessment of prognostic factors for survival in patients with cancer and most of them were focused on inflammatory markers, isolate or combined, to form index or scores.

In their study on esophagus-gastric cancer patients, followed by a mean period of 3.5 years, Noble et al (2013) found pre-treatment serum albumin (< 3.5 g/dL) as an independent prognostic factor for the reduction of disease-free survival ($p = 0.042$)⁸. Of the 29 studies in gastrointestinal cancer (most of them about colorectal cancer), 26 found albumin as an independent predictive factor of survival in a systematic review of the literature concerning the prognostic value of pre-treatment serum albumin, which included studies published between January 1995 and June 2010. The same result was found in 9 of 10 articles on lung cancer, most of them in non-small cell lung tumors¹¹. In a study with 51 advanced colorectal cancer patients, Read et al found a mean survival of 4 months in those with low serum albumin (< 3.5 g/dL) when compared to those patients with normal serum albumin ($p = 0.017$)¹³. The serum albumin was also described as an independent survival predictor (HR: 0.556 IC95%: 0.313-0.986) in a study by Utech et al in which 136 men diagnosed with various types of cancer (48.5% of them with gastrointestinal or lung cancer). In addition, an increase in inflammatory markers, such as Interleukin 6 (IL6) and Tumor Necrosis Factor alpha (TNF- α), were also associated with higher mortality⁹.

With regard to the inflammatory markers based index, the use of the GPS stands out in the literature. Read et al found GPS as a mortality predictor (HR: 2.27 CI95%: 1.09-4.73) while studying advanced colorectal cancer¹³. In a study with 165 cancer patients, Elahi et al reported that there was a linear reduction of the survival time with a high GPS score, both in patients with colorectal tumors (mean survival of 12.1 months for GPS = 0, 6.1 months for GPS = 1 and 1.7 month for GPS = 2 - $p < 0.001$) and in gastric cancer patients (mean survival of 6.1 months for GPS = 0, 3.1 months for GPS=1 and 1.6 month for GPS = 2 - $p = 0.002$)¹⁴. In a study with 56 non-small cell lung cancer (NSCLC) patients (98% staged III/IV), presenting 77% of deaths in a mean follow-up of 54 months, the GPS was a survival prognostic factor (HR: 2.10 CI95%: 1.30-3.40)¹⁰. Forrest et al evaluated 161 inoperable NSCLC patients and found that the combined scores of low albumin and high CRP had a prognostic value (HR: 1.70 CI95%: 1.23-2.35- $p = 0.001$) when compared to scores based on stage and Performance Status (HR: 1.48 CI95%: 1.12 – 1.95 – $p = 0.005$)¹⁵. In contrast, Walsh et al used the Prognostic Inflammatory Nutritional Index (PINI= [alpha 1-acid glycoprotein \times CRP] divided by [albumin \times pre-albumin]) and did not find any prognostic value in 50 advanced cancer patients (26% of them with lung cancer); besides, it is an index based on non-routine and more expensive laboratorial tests compared to serum albumin and CRP, and is widely used in the assessment of critically ill patients¹⁶. The present study showed that Risk INI is an independent survival predictor and a simple scoring system based on routine and easily available laboratorial tests. A previous study has demonstrated its association to GPS⁵.

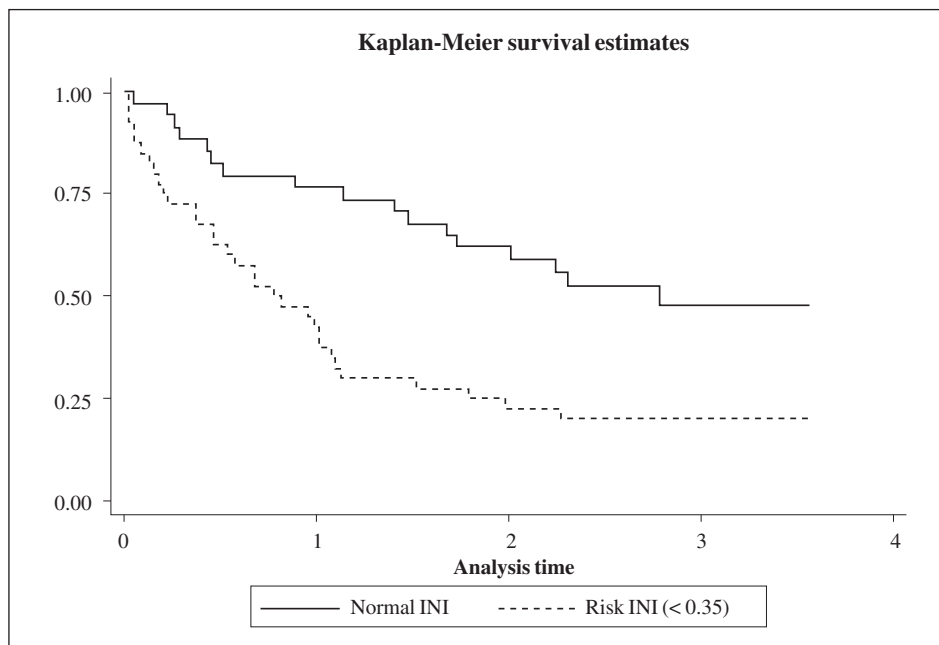


Fig. 1.—Kaplan-Meier survival curves according to Inflammatory-Nutritional Index categories (Normal or Risk) of the gastrointestinal and lung cancer patients ($p = 0.001$).

Variable	Hazard ratio	95% CI	p value
Age (as a continuous variable)	0.998	0.966-1.031	0.902
Tumor stage			
II	1.000		
III	1.076	0.405-2.861	0.883
IV	0.874	0.313-2.440	0.798
Unknown	1.487	0.486-4.545	0.487
BMI			
Under nutrition	1.000		
Normal	1.331	0.403-4.400	0.639
Excessive weight ($\geq 25.0 \text{ kg/m}^2$)	1.526	0.425-5.482	0.517
Chemotherapy type			
Curative	1.000		
Neoadjuvant	0.218	0.025-1.877	0.166
Adjuvant	0.129	0.010-1.695	0.119
Palliative	0.330	0.040-2.698	0.301
Tumor site			
Esophagus/Stomach	1.000		
Colon/Rectum	0.293	0.132-0.649	0.002
Pancreas/Gall bladder	2.321	0.745-7.234	0.147
Lung	0.671	0.305-1.477	0.322
Nutritional status (SGA)			
Well nourished (A)	1.000		
Suspected/moderated malnutrition (B)	3.338	0.779-14.303	0.104
Severe malnutrition (C)	7.453	1.646-33.748	0.009
Risk INI			
No	1.000		
Yes	2.845	1.432-5.656	0.003

Bold values indicate statistically significant.

This study revealed that a worsening in nutritional status, evaluated by SGA, was associated with higher mortality and that severe malnutrition could be

considered an independent predictor of mortality, with an increased rate of up to seven times when compared to well nourished patients. Read et al, also using SGA to classify the nutritional status of their advanced colorectal cancer patients, found less malnutrition (SGA “B” + “C” = 56%) than the present study, possibly because the tumor site (colorectal) affects less the ingestion, digestion and absorption of nutrients. Moreover, the presence of any degree of malnutrition was associated with a higher mortality rate ($p = 0.02$), with mean survival around 8 months lower than that of well nourished patients¹³. Utech et al evaluated a six-month weight loss history prior to the recruitment of the study participants (one of the SGA components) and found it to be an independent survival predictor ($p = 0.002$)⁹. A study conducted in the United Kingdom, using albumin $< 30 \text{ g/L}$ or BMI $< 18.5 \text{ kg/m}^2$ or a recent weight loss history as criteria to define malnutrition, classified 28% of its sample (642 patients) as malnourished, being such condition an independent mortality predictor (HR: 1.43 CI95%: 1.11 – 1.85)¹⁷. Using BMI, which in this study was not associated with survival, Meek et al found patients with BMI lower than 20 Kg/m^2 having twice the risk of death (HR 2.33 CI95%: 1.07 – 5.08) when compared to those with higher BMI values¹⁰.

In his 2009 review, McMillan D.C. emphasized that the use of prognostic scores based on systemic inflammation allows the identification of patients with cachexia or those in risk of developing such condition, who are more likely to have a poorer response to treatment and shorter survival¹². In the present study, the INI was considered an independent survival predictor, being previously associated with well known tools, such as GPS and SGA⁵.

Conclusion

The INI was an independent survival predictor for this sample of cancer patients and it was associated to nutritional status. Thus, INI emerges as a possible tool for routine use in the assessment of cancer patients in and outside hospitals, with easy and quick calculation based on affordable and routinely available laboratory tests.

More studies in different cancer types may further demonstrate whether INI will be widely used in oncology.

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Original / *Deporte y ejercicio*

Efecto de dos dietas hipocalóricas y su combinación con ejercicio físico sobre la tasa metabólica basal y la composición corporal

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Resumen

El Síndrome Metabólico (SMet) se diagnostica por el cumplimiento de al menos tres criterios: hipertriglicéridemia, HDL-C disminuido, hipertensión arterial, glucemia alterada en ayunas y obesidad. Dicha obesidad constituiría el punto inicial para el desarrollo del SMet. Según la evidencia científica, las dietas hipocalóricas, incluyendo la mediterránea y la reducida en grasa con alto contenido en carbohidratos, reducen la masa grasa (MG) de estos pacientes y su efecto se potencia al combinarse con ejercicio físico (EF), pero se desconoce aún su influencia sobre la tasa metabólica basal (TMB).

Objetivo: Conocer el efecto de dos dietas hipocalóricas: mediterránea y baja en grasas, combinadas o no con EF, sobre la TMB y la composición corporal (CC) de adultos con SMet.

Métodos: 36 voluntarios, > 50 años, ambos sexos, con diagnóstico de SMet. Se asignaron aleatoriamente a uno de los cuatro grupos de intervención: Dieta hipocalórica mediterránea (MED), Dieta hipocalórica baja en grasa (CHO) ó ambas asociadas a EF (MEDE y CHOE respectivamente). Se evaluó CC (antropometría) y TMB (calorimetría indirecta) antes y después de la intervención.

Resultados: La adición de EF a los dos tratamientos hipocalóricos produjo mayor pérdida de peso y MG que las dietas por sí solas, siendo esta pérdida en CHOE > MEDE ($p < 0,05$). Dichos grupos descendieron la TMB siendo MEDE > CHOE ($p < 0,05$). La Dieta Mediterránea, combinada o no con EF, disminuyó la MM siendo MEDE > MED ($p < 0,05$).

Conclusiones: CHOE fue el tratamiento que mayor pérdida de peso y MG produjo, induciendo menor reducción de TMB y manteniendo un mejor perfil de CC que MEDE.

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Palabras clave: *Síndrome metabólico. Dieta hipocalórica baja en grasas. Dieta hipocalórica mediterránea. Ejercicio físico. Tasa metabólica basal.*

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EFFECT OF TWO HYPOCALORIC DIETS AND THEIR COMBINATION WITH PHYSICAL EXERCISE ON BASAL METABOLIC RATE AND BODY COMPOSITION

Abstract

Background: Metabolic syndrome (MetS) is diagnosed by the detection of at least three criteria (hypertriglyceridemia, low HDL-C, hypertension, obesity and altered fasting glucose). Visceral fat excess would be the starting point for its development. Scientific evidence supports hypocaloric diets -mediterranean or low fat diet and rich in complex carbohydrates diet included- as the best treatment to reduce fat mass (FM), maximizing its impact by combining them with physical exercise (PE). However, the effects of these treatments on basal metabolic rate (BMR) of patients with MetS, are unknown.

Objective: To study the effect of the hypocaloric diet -mediterranean or low fat diet- with or without PE on the BMR and body composition (BC) of adults with MetS.

Methods: 36 volunteers, MetS, both sexes, > 50 years, meeting the inclusion criteria. They were randomly assigned to a group of intervention (3 months) of hypocaloric diet: mediterranean diet (MED), low fat and rich in complex carbohydrates diet (CHO) and both combined with PE (MEDE and CHOE respectively). Anthropometric data was taken (weight, muscle mass (MM) and FM) and BMR was determined by indirect calorimetry, before and after intervention.

Results: The addition of PE to both hypocaloric treatments produced greater FM loss and weight loss than dieting alone, being this loss in CHOE > MEDE ($p < 0.05$). These groups decreased the BMR after treatment being MEDE > CHOE ($p < 0.05$). Mediterranean diet with or without PE lost MM ($p < 0.05$) being MEDE > MED

Conclusions: CHOE induces less reduction of BMR while supporting a better profile of BC than MEDE.

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Keywords: *Metabolic syndrome. Low fat hypocaloric diet. Mediterranean hypocaloric diet. Physical exercise. Basal metabolic rate.*

Abreviaturas

CC = Composición Corporal.
CHO = Dieta Hipocalórica Baja en Grasas con alto contenido en Hidratos de Carbono.
CHOE = Dieta CHO combinada con Ejercicio Físico Aeróbico.
EF = Ejercicio Físico.
FC = Frecuencia cardíaca.
FCmáx = FC máxima.
Gr = grasas.
HCO = Hidratos de Carbono.
HDL-c = Colesterol HDL.
HT = Hormonas Tiroideas.
HTA = Hipertensión Arterial.
HURS = Hospital Universitario Reina Sofía.
Kg = Kilogramos.
LDL-c = Colesterol LDL.
Lpm = Latidos por minuto.
MB = Metabolismo Basal.
MED = Dieta Hipocalórica Mediterránea.
MEDE = Dieta MED combinada con Ejercicio Físico Aeróbico.
MET = Tasa Equivalente Metabólica.
MG = masa grasa.
MM = masa muscular.
PC = Peso Corporal.
Pr = Proteínas.
SMet = Síndrome Metabólico.
T = Talla.
TG = Triglicéridos plasmáticos.
TMB = Tasa Metabólica Basal.
VO₂ = Consumo de O₂.
VCO₂ = Producción de CO₂.

Introducción

La creciente prevalencia de Síndrome Metabólico (SMet) en países desarrollados lo coloca dentro de las principales problemáticas de salud pública. Dicho síndrome constituye una entidad de dudoso significado nosológico y se diagnostica por la presencia de al menos tres de los siguientes criterios: triglicéridos plasmáticos (TG) en ayunas ≥ 150 mg/dl, HDL-c plasmático < 40 mg/dl en hombres y < 50 mg/dl en mujeres, hipertensión arterial (HTA) (tensión arterial sistólica y/o diastólica ≥ 130 y ≥ 85 mmHg respectivamente o tratamiento para la HTA), glucemia alterada en ayunas (GAA) (glucemia en ayunas ≥ 100 mg/dl) y obesidad abdominal (perímetro de cintura > 88 cm en mujeres y > 102 cm en hombres)^{1,2}. En Estados Unidos se da la mayor prevalencia de SMet a nivel mundial (41% en hombres y 37% en mujeres entre los 40-59 años y 52% en hombres y 54% en mujeres mayores de 60 años)³. En España, diferentes estudios epidemiológicos aportan cifras similares a otros países desarrollados, con un 40% de SMet en poblaciones mayores de 60 años^{4,5}.

Algunos autores consideran que el desarrollo de SMet podría deberse a la acumulación excesiva de grasa abdominal, lo que se atribuye, al menos en una gran mayoría de los pacientes, al desequilibrio entre la ingesta y el gasto calórico diario⁶⁻⁸. Dicho gasto energético es utilizado tanto para mantener el metabolismo basal (MB) (entre el 45-70% del gasto diario) como para realizar actividad física –cotidiana y ejercicio físico– (20-45% del gasto diario) y responder a la respuesta metabólica inducida por alimentos (10% del gasto diario)⁹.

La energía utilizada para el MB suele medirse en un período de tiempo determinado (comúnmente 24 horas) y se denomina tasa metabólica basal (TMB). La TMB queda determinada principalmente por factores no modificables, como la edad y el género, pero también puede variar en función al nivel de entrenamiento físico del sujeto así como de su composición corporal, dependiendo tanto del peso total como de las proporciones de masa grasa (MG) y masa muscular (MM)⁹. De acuerdo con ello, un tratamiento óptimo para el descenso de la MG y la consecuente mejoría de los factores de riesgo del SMet, sería aquél que induzca el mejor efecto sobre ambos elementos de la balanza energética. Es decir, aquél que permita disminuir el ingreso de energía y aumentar su gasto, provocando una pérdida de peso proveniente de MG sin deteriorar significativamente la MM ni la TMB.

Actualmente, la evidencia científica apoya que una dieta hipocalórica, bien sea el modelo de Dieta mediterránea o el de una Dieta pobre en grasas con un alto contenido en carbohidratos (HCO), es el tratamiento de elección para reducir la grasa visceral y el SMet¹⁰⁻¹². Además, diferentes estudios muestran que la combinación de dichas dietas con un programa de ejercicio físico (EF) produce una mayor reducción del peso corporal y de la grasa visceral, mejorando aún más el perfil cardio-metabólico de estos pacientes¹³⁻¹⁶. Sin embargo, no se ha valorado aún el efecto sobre la TMB de ninguna de las dietas mencionadas, ya sea con o sin EF, en pacientes con SMet.

Objetivos

Principal: Conocer el efecto de dos intervenciones dietéticas hipocalóricas: Dieta mediterránea y Dieta baja en grasas con alto contenido en HCO, en dos modalidades: sin la adición de actividad física programada o combinadas con un programa semanal de ejercicio físico aeróbico, sobre la TMB de adultos con SMet.

Secundario: Analizar las variaciones de PC, MG y MM a fin de establecer una relación entre dichos cambios con la modificación de la TMB en los diferentes grupos de tratamiento.

Métodos

Población: se seleccionó a través de la consulta externa del Servicio de Medicina Interna del Hospital

Universitario Reina Sofía (HURS) en el contexto de un estudio de intervención dietética y ejercicio físico titulado “Efectos a largo plazo de dos dietas mediterráneas hipocalóricas con diferente aporte proteico y su combinación con un programa estructurado de ejercicio físico, sobre los factores de riesgo en pacientes con síndrome metabólico”

Criterios de inclusión: personas adultas (50-70 años de edad) de ambos sexos, con al menos 3 criterios de SMet según ATP III: TG en ayunas ≥ 150 mg/dl, HDL-c plasmático < 40 mg/dl en hombres y < 50 mg/dl en mujeres, HTA (tensión arterial sistólica y/o diastólica ≥ 130 y ≥ 85 mmHg respectivamente o tratamiento para la HTA), GAA (glucemia en ayunas ≥ 100 mg/dl) y obesidad abdominal (perímetro de cintura > 88 cm en mujeres y > 102 cm en hombres)^{1,2}.

Criterios de exclusión: ser fumador, consumir alcohol en una cantidad > 20 g y > 30 g al día en mujeres y hombres respectivamente; antecedentes de infarto agudo de miocardio (IAM); dieta o restricción calórica sistemática en los 3 meses previos al estudio; ejercicio físico o actividad física vigorosa superior a 2 horas semanales.

Diseño

El presente estudio fue un ensayo clínico experimental aleatorizado cuya primera etapa consistió en una entrevista médica a los posibles candidatos voluntarios, llevada a cabo por un médico de familia para determinar los criterios de inclusión y exclusión. Luego, 36 pacientes con SMet fueron incluidos en la muestra y distribuidos aleatoriamente en uno de los cuatro grupos de intervención: Dieta hipocalórica mediterránea (MED), Dieta hipocalórica baja en grasas con un alto contenido en HCO (CHO) y la combinación de ambos tratamientos dietéticos con un programa semanal de ejercicio físico aeróbico (MEDE y CHOE respectivamente). Se determinó TMB, MG y MM en forma previa a intervención y al finalizar la misma. Todos los procedimientos fueron aprobados por el Comité de ética del HURS.

Tasa Metabólica Basal

Se determinó mediante calorimetría indirecta de circuito abierto con un equipo Jaeger (Oxycon Pro 2007, Alemania). Los participantes fueron instruidos para concurrir al centro por la mañana, con 12 horas de ayuno nocturnas, sin haber bebido cafeína el día previo, ni consumido medicamentos, ni haber realizado EF intenso. Además, debieron concurrir realizando el mínimo de actividad posible (se indicó asistir en coche como acompañante o en su defecto en autobús). Antes de iniciar la prueba, los sujetos permanecieron recostados en reposo durante un mínimo de 10 minutos, a fin de normalizar la frecuencia cardíaca (FC) y alcanzar el máxi-

mo nivel de reposo posible^{17,18}. Una vez realizada la calibración del equipo (volúmenes, tiempo de retraso y determinación de concentraciones específicas de CO₂ y O₂) se colocó sobre el paciente una máscara tipo Canopy (Oxycon Jaeger tm) y se inició la medición. Durante la prueba el sujeto permaneció decúbito supino sobre la camilla durante un período medio de 30 min mientras se procedía a medir el consumo de O₂ (VO₂) y producción de CO₂ (VCO₂) utilizando un sistema de cámara de mezcla y una campana con cámara de mezcla de gases espirados. Para el análisis de los datos obtenidos y basándose en estudios previos se adoptó el criterio de eliminación de los 10 primeros min de la prueba, como plazo necesario de adaptación a la misma^{19,20}. El tiempo mínimo de evaluación consistió en 5 min. Por lo tanto, la TMB de aquellos sujetos que no pudieron cumplimentar 15 min totales de evaluación se obtuvo descontando un plazo inicial de adaptación que permitiera evaluar al menos los 5 min finales. Los valores de MB obtenidos fueron extrapolados a 24 h y expresados en kcal/día para obtener la TMB.

Composición Corporal

El análisis de la composición corporal se realizó mediante estudio antropométrico siguiendo el protocolo estandarizado de la Sociedad Internacional para el Avance de la Cineantropometría (International Society for the Advancement of Kinanthropometry, ISAK)²¹. Los pacientes debieron concurrir en un estado de ayunas de 12 h, evitar la práctica de ejercicio, no tomar medicamentos diuréticos en las 24 h previas y orinar al menos 30 min antes del examen.

Se valoró el PC y la talla (T) mediante balanza de precisión con tallímetro (MB 201T Plus). Los perímetros musculares (brazo relajado, antebrazo, cintura mínima, muslo medial y pantorrilla) fueron obtenidos mediante el uso de una cinta antropométrica metálica flexible no extensible (Rosscraft). Y los pliegues grasos (bíceps, tríceps, subescapular, cresta ilíaca, supraespinale, abdominal, muslo anterior, pantorrilla medial) fueron medidos por triplicado, usando luego el valor de la mediana, con un calibrador de pliegues cutáneos (Harpender). La MM fue estimada según la Ecuación de Martin y cols., 1990²² y la MG mediante la fórmula de Durnin & Womersley, 1974²³.

Ingesta dietética inicial y prescripción de las dietas

Determinación de la ingesta: todos los sujetos completaron un registro dietético de 3 días no consecutivos (dos días laborables y un día de fin de semana). Se utilizó el método de pesada, entregándose una balanza digital (Mettler Toledo® precisión $\pm 0,5$ g) a los sujetos que les permitió registrar prospectiva y detalladamente cada uno de los alimentos y líquidos consumidos (hora, día, cantidad, marca). La ingesta habitual de energía y

nutrientes fue analizada usando el software Dietsource (Novartis 2000, España).

Prescripción dietética: en base a los datos obtenidos de la valoración de la ingesta se prescribió la dieta personalizada a cada paciente ya sea mediterránea o baja en grasas.

La proporción de macronutrientes en la dieta mediterránea hipocalórica fue: 50% de hidratos de carbono (HCO), 30% de grasas (Gr) conformado por un 20% de ácidos grasos monoinsaturados, provenientes de aceite de oliva virgen, 5% de ácidos grasos saturados y 5% de ácidos grasos poliinsaturados y 20-22% de proteínas (Pr). Para la dieta baja en grasas los porcentajes fueron: < 20% de Gr (con la misma proporción de ácidos grasos que la dieta mediterránea), 55-58% de HCO y 20-22% de Pr. En ambos tratamientos se redujo el 40% de energía respecto a la ingesta habitual para promover la pérdida de peso de forma progresiva: 20% el primer mes, 10% el segundo y tercer mes. Se utilizaron réplicas y fotografías de alimentos para explicar el tratamiento dietético y se instruyó al paciente sobre la selección de alimentos y técnicas culinarias adecuadas.

Programa de ejercicio físico

Protocolo de prueba: se realizó una prueba submáxima de ejercicio en el Laboratorio de Ejercicio físico y Metabolismo del HURS a todos los pacientes asignados a un tratamiento con ejercicio físico (MEDE y CHOE) con el fin de conocer su capacidad cardiopulmonar máxima y determinar las cargas de ejercicio individuales que se utilizaron luego durante la fase de intervención. Para ello, los sujetos se ejercitaron en un cicloergómetro (Ergonomics 800; Ergoline, Barcelona España) hasta alcanzar el 85% de su FC máxima (FCmáx) determinada según la ecuación específica de Tanaka²⁴. El protocolo de prueba comenzó con 2 min de reposo. Luego, se inició el ejercicio con una carga de esfuerzo inicial de 25 W durante los tres primeros min de actividad. La segunda carga se determinó según la FC alcanzada por el sujeto en esta fase de la siguiente manera: si en el tercer minuto de carga inicial su FC era < 80 lpm, la carga inicial de incremento consistió en 125 W; entre 80 a 89 lpm se aplicó una carga de 100 W; entre 90 a 100 lpm la carga aplicada fue de 75 W y >100 lpm, la carga fue de 50 W. A partir de la segunda carga se incrementó 25 W de intensidad cada tres min de ejercicio hasta finalizar la prueba. Además, se monitorizó la FC con un pulsímetro y la cadencia de pedaleo se mantuvo constante en 50 rpm durante todo el ejercicio.

Programa semanal de ejercicio aeróbico: para ambos grupos de ejercicio, el programa semanal consistió en dos sesiones supervisadas realizadas en el HURS y una sesión no supervisada fuera de la institución. En ambos casos la intensidad del ejercicio fue del 75% de la FC máx y se prescribió a partir de los valores de FC

alcanzados durante el protocolo de prueba. Las sesiones supervisadas constaron de 30 min de ejercicio aeróbico intermitente (esfuerzos de alta intensidad y corta duración, seguidos por periodos de ejercicio de baja intensidad). Se realizó pedaleo sobre cicloergómetro en series discontinuas con períodos de alta intensidad (75% de la FCmáx) y periodos de recuperación (45% de la FCmáx). Se utilizó también un ergómetro de brazo, donde la FC fue 5% inferior a la fijada para el cicloergómetro. La sesión no supervisada consistió en ejercicio aeróbico continuo durante 30-60 minutos (caminata), cuya intensidad (velocidad de caminata) se incrementó mensualmente (65, 70 y 75% FC máx en cada mes de tratamiento).

Análisis Estadístico

Los datos se presentan como media y error estándar (ES). La normalidad de la muestra fue calculada utilizando el test Shapiro-Wilk. Para el análisis del efecto de las diferentes intervenciones, MED, MEDE, CHO y CHOE, (variables independientes) sobre la TMB, PC, MM y MG (variables dependientes) se utilizó un análisis de varianza (ANOVA) con medidas repetidas de dos factores intrasujeto: grupo y tiempo: [4 (grupo) × 4 (tiempo)]. La corrección de Tukey fue utilizada para ajustar los valores de la P en relación al número de contrastes llevados a cabo. La significancia estadística fue establecida en $p < 0,05$. Se utilizó el software SPSS 15.0 de Windows.

Resultados

36 pacientes con diagnóstico de SMet completaron el tratamiento asignado, distribuidos en 4 grupos de intervención: CHO (n = 8), CHOE (n = 10), MED (n = 8) y MEDE (n = 10). La edad media (años) fue $58,2 \pm 1,0$, $58,8 \pm 0,6$, $57,2 \pm 1,0$ y $58,8 \pm 1,1$, el IMC medio fue $38,0 \pm 1,8$, $37,9 \pm 1,6$, $39,0 \pm 1,6$ y $37,8 \pm 0,7$, la media de MM (kg) fue de $3,8 \pm 3,4$, $35,3 \pm 3,5$, $36,8 \pm 3,0$, $36,4 \pm 2,3$ y la MG (kg) media fue de $34,6 \pm 4,3$, $34,6 \pm 1,0$, $35 \pm 3,0$ y $35,2 \pm 1,7$ para CHO, CHOE, MED y MEDE respectivamente. También se registró el uso de estatinas e antihipertensivos, así como la media de colesterol LDL (LDL-c), HDL-c, colesterol total, TG, glucemia, realización de actividad física total en (METs/w), ejercicio de resistencia y caminata y actividades sedentarias. Ninguna de las variables mencionadas presentó diferencias estadísticamente significativas entre grupos.

Tasa Metabólica Basal (TMB)

Se valoró y comparó entre grupos la media obtenida de TMB (Kcal) antes y después de la intervención para cada uno de los grupos. Además, se comparó entre

tratamientos el porcentaje de variación de la TMB entre los momentos pre y post intervención. Todos los datos se presentan como media +/- ES en las figuras 1 y 2, donde puede verse que tanto MEDE como CHOE sufrieron un descenso estadísticamente significativo de la TMB luego de la intervención ($p < 0,05$) y respecto a ambos grupos sin EF ($p < 0,05$). Dicha disminución de TMB fue mayor en MEDE que en CHOE ($p < 0,05$).

Peso corporal

Se valoró y comparó entre grupos el descenso de PC (kg) como porcentaje de variación entre los momentos pre y post intervención.

La figura 3 presenta los datos como media +/- ES evidenciando un descenso de PC estadísticamente significativo en todos los grupos luego de la intervención

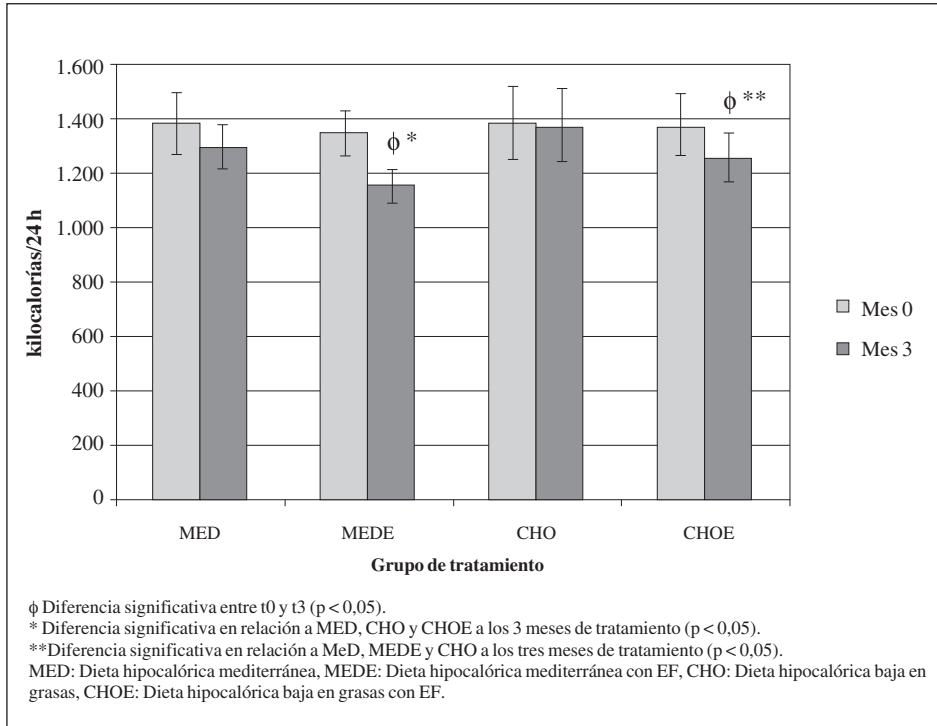


Fig. 1.—Tasa metabólica basal promedio según tratamiento al inicio y final de los 3 meses de intervención (media \pm ES).

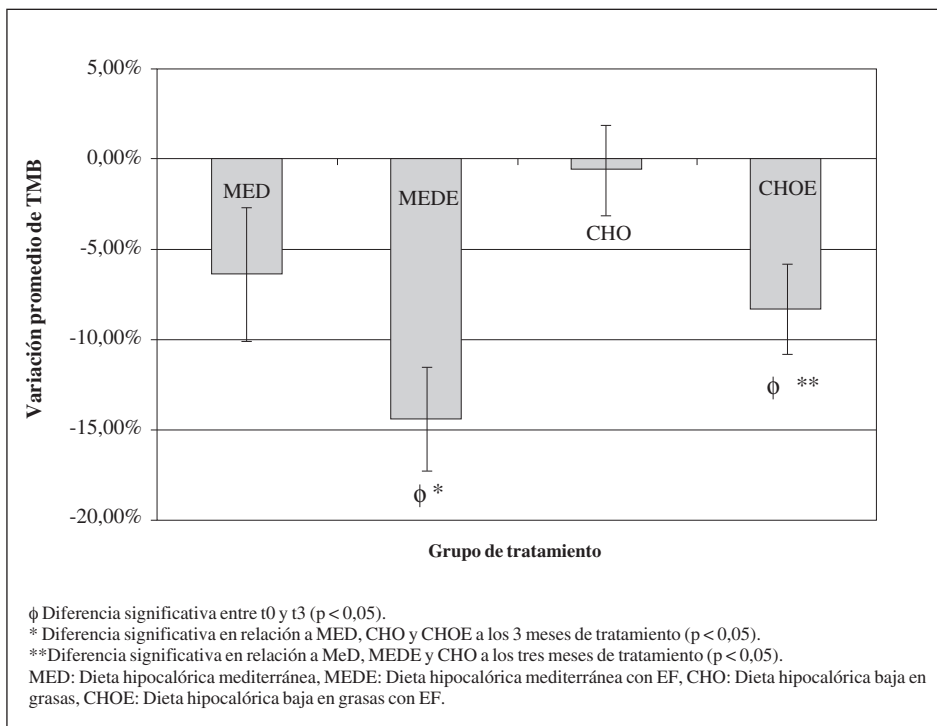


Fig. 2.—Porcentaje de variación de la TMB según tipo de tratamiento entre los momentos pre y post intervención (media \pm ES).

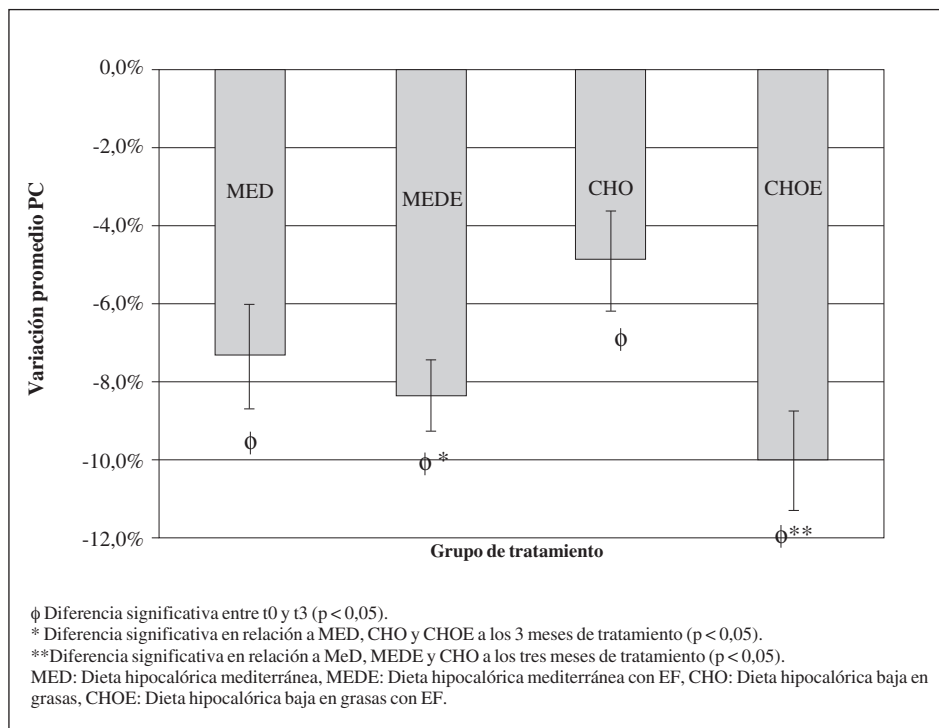


Fig. 3.—Porcentaje de variación del peso corporal según tipo de tratamiento entre los momentos pre y post intervención (media \pm ES).

($p < 0,05$). Al comparar los distintos tratamientos, se obtiene que la pérdida de PC fue mayor en ambos grupos con EF respecto a los dos tratamientos con intervención dietética solamente ($p < 0,05$). Entre los grupos con EF, CHOE perdió más peso que MEDE ($p < 0,05$).

Kilogramos de masa grasa (MG)

Se valoró y comparó entre grupos el descenso de MG (kg) como porcentaje de variación entre los momentos pre y post intervención. Los datos se presentan como media \pm ES en la figura 4 y muestran un des-

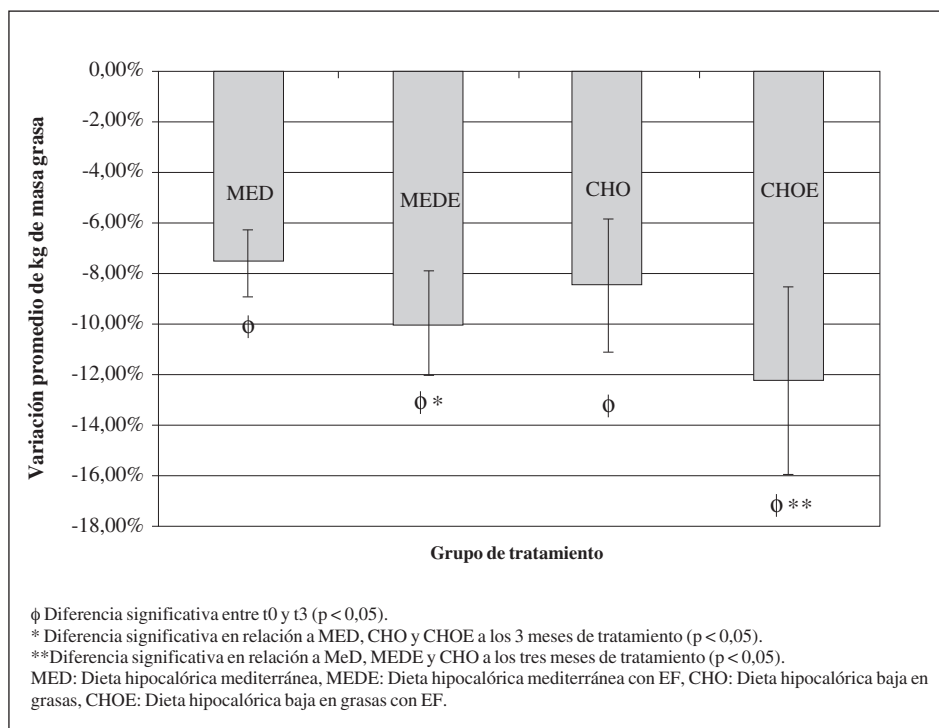


Fig. 4.—Porcentaje de variación de la MG según tipo de tratamiento entre los momentos pre y post intervención (media \pm ES).

censo de la MG estadísticamente significativo en todos los grupos luego de la intervención ($p < 0,05$). La comparación entre tratamientos arroja una mayor pérdida de MG en ambos grupos con EF respecto a los dos tratamientos con intervención dietética solamente ($p < 0,05$). Entre los grupos con EF, CHOE provocó mayor pérdida de MG que MEDE ($p < 0,05$).

Kilogramos de masa muscular (MM)

Se valoró y comparó entre grupos la modificación de la MM (kg) como porcentaje de variación entre los momentos pre y post intervención. La figura 5 presenta los datos como media \pm ES. Ambos tratamientos con dieta hipocalórica mediterránea, MED y MEDE, sufrieron una pérdida significativa de MM al finalizar la intervención ($p < 0,05$), siendo MEDE $>$ MED ($p < 0,05$). Dicha pérdida de MM en MEDE y MED fue mayor que en ambos grupos con dieta hipocalórica baja en Gr con alto contenido en HCO, CHOE y CHO ($p < 0,05$).

Discusión

Este estudio permitió observar que una Dieta baja en grasa y con alto contenido en hidratos de carbono combinada con un programa semanal de ejercicio físico aeróbico (CHOE), induce la mayor reducción de PC y MG respecto al resto de grupos (CHO, MED y MEDE). Al mismo tiempo provoca menor reducción de la TMB respecto a una Dieta hipocalórica mediterránea combi-

nada con EF (MEDE) y preserva la MM más efectivamente que esta última.

Se conoce que la dieta hipocalórica eficiente es aquella que disminuye el aporte calórico, lo que favorece la movilización de grasa almacenada en el tejido adiposo, con el consiguiente descenso progresivo del PC a causa de la pérdida de MG. Sin embargo, una dieta hipocalórica puede conllevar una pérdida fisiológica no deseada de MM, metabólicamente activa, conduciendo a una reducción de la TMB. Dicha pérdida podría limitar el éxito del tratamiento en el largo plazo, causando un efecto compensatorio del gasto energético capaz de obstaculizar la progresión de la pérdida de PC^{25,26}. Por lo tanto, el tratamiento más efectivo no sólo será aquél que provoque la mayor pérdida de PC y MG sino también el que permita mantener, o incluso aumentar, la MM y la TMB. Ambos tratamientos dietéticos hipocalóricos (Dieta mediterránea y Baja en grasa con alto contenido de hidratos de carbono complejos) son más efectivos para lograr una pérdida de peso y grasa corporal cuando se combinan con un programa regular de EF. Dicho resultado coincide con estudios previos que combinaron otros modelos hipocalóricos con EF aeróbico¹³⁻¹⁶. Por otra parte, la TMB no varió significativamente en los tratamientos dietéticos sin EF (CHO y MED), coincidiendo con el estudio realizado por Sénéchal y cols., 2010, quienes no observaron diferencias en la TMB tras un tratamiento dietético hipocalórico en mujeres post-menopáusicas obesas²⁷. MED, a diferencia de CHO, produjo una reducción significativa de MM, pero que no se corresponde con un descenso de la TMB. Dos posibles hechos podrían explicar este hallazgo: primero, es cono-

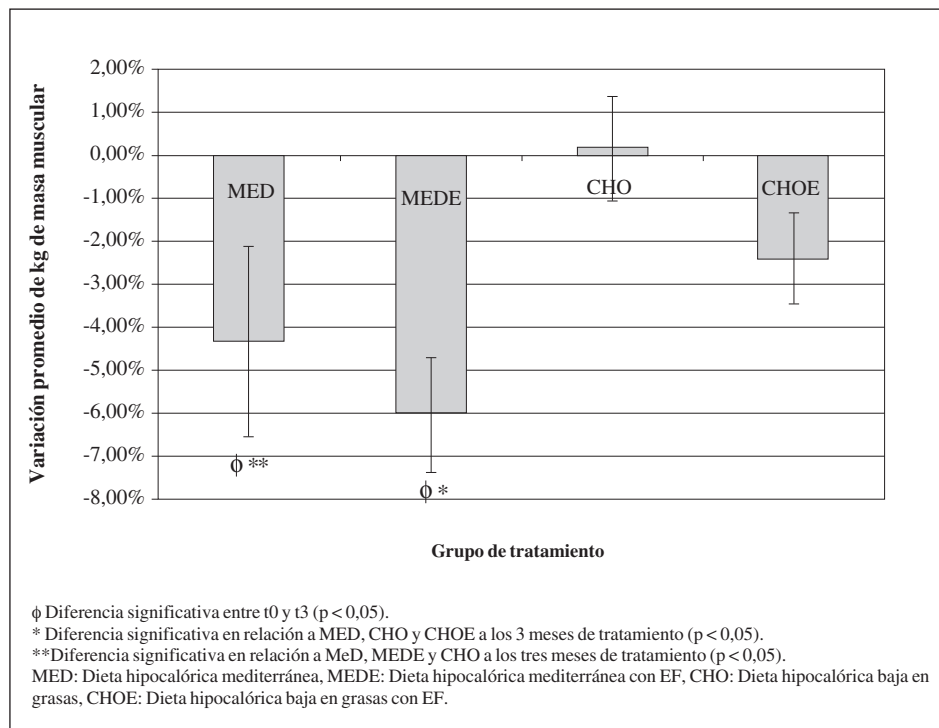


Fig. 5.—Porcentaje de variación de MM según tipo de tratamiento entre los momentos pre y post intervención (media \pm ES).

cido que la MM no constituye el único factor regulador del MB, interviniendo otros como la reducción en la secreción de hormonas tiroideas (HT) que actúan sinérgicamente provocando la reducción de la TMB. Sin embargo, esta reducción en la concentración de HT ocurre sólo ante una pérdida aguda de PC^{28,29}. Éste no fue el caso de MED, el cual redujo un 7% del PC en 3 meses de tratamiento. Quizás sea razonable explicarlo por el tamaño muestral, ya que MED mostró una tendencia negativa de la TMB, aunque no significativa, que podría alcanzar significancia estadística con un mayor número de sujetos, correspondiéndose con la pérdida de MM de este grupo.

Respecto a la intervención con EF, MEDE indujo la mayor pérdida de MM junto con una pronunciada reducción de la TMB en relación con CHOE. Como se ha explicado anteriormente, la TMB disminuye cuando se pierde tejido metabólicamente activo ya que al disminuir su tamaño y actividad, se requiere menos energía para sostener sus demandas²⁸. Sin embargo, MEDE y CHOE fueron igualmente hipocalóricas y normoproteicas, por lo cual, se sugiere que las diferencias inducidas en la masa MM y en la TMB podrían estar relacionadas con la menor ingesta de ingesta de HCO en el grupo MEDE (50% vs 55-58% en el grupo CHOE). Dicho nutriente es un factor clave para la estimulación de la secreción de insulina, principal hormona anabólica requerida para la recuperación del glucógeno muscular (utilizado durante las sesiones de ejercicio y también en la re-síntesis de proteínas musculares) que aumenta su catabolismo cuando el sujeto realiza actividad física. Además, los HCO constituyen la única fuente de glucógeno muscular y, por ende, funcionan como principal abastecimiento energético para la contracción, mantención y regeneración de la MM. Por lo tanto, la menor proporción de dicho nutriente en MEDE podría haber afectado los mecanismos mencionados, favoreciendo los procesos de catabolismo muscular y la consecuente pérdida de MM. Simultáneamente, el EF incrementa la demanda de HCO potenciando así el desequilibrio entre la disponibilidad y utilización muscular de este nutriente con la consecuente utilización de la proteína endógena, desgastando el tejido muscular. Conjuntamente, aunque no fue objetivo del presente estudio analizar la ingesta dietética pre y post ejercicio, un bajo consumo de HCO en las comidas posteriores a la sesión de ejercicio, limitaría la recuperación del glucógeno muscular y provocaría aún mayor pérdida progresiva de MM³⁰. Estas evidencias en su conjunto, podrían ser las causas de que MEDE haya provocado la mayor variación negativa de TMB y MM respecto al resto de los grupos. Distinto es el caso de CHOE el cual resultaría a primera vista el tratamiento más efectivo, produciendo el mayor descenso de PC y MG sin pérdida significativa de MM. Sin embargo, CHOE también indujo una reducción de la TMB. Dicha variación podría deberse a la pérdida aguda de PC y MG que provocó este tratamiento, significativamente mayor que en el resto de los grupos. Como se explicó anteriormente, la

pérdida aguda de PC puede afectar parámetros hormonales capaces de alterar el MB independientemente de la masa magra, como la acción de las HT^{28,29}.

Este estudio analiza por primera vez la influencia de una dieta hipocalórica combinada con EF sobre la TMB en pacientes con SMet. Aparentemente, la Dieta baja en grasas y con alto contenido en HCO complejos combinada con un programa semanal de EF podría ser la opción que mejor conserva la TMB y la MM. Aún así, debería examinarse la posibilidad de incrementar la proporción de HCO de la dieta mediterránea para mantener los efectos beneficiosos de ésta sobre el resto de factores de riesgo del SMet^{31,32} controlando la pérdida de MM y consecuentemente la disminución de la TMB.

Finalmente, la principal limitación del estudio queda determinada por el reducido tamaño muestral que no permite aún extrapolar los resultados a la población general con SMet, por lo que este estudio lo consideramos base suficiente de una hipótesis que habrá que validarla con estudios a más largo plazo y con mayor tamaño muestral.

Conclusiones

En conclusión, una Dieta hipocalórica baja en grasas y con alto contenido en hidratos de carbono complejos combinada con un programa regular de ejercicio físico aeróbico semanal induce menor reducción de la tasa metabólica basal al tiempo que favorece un mejor perfil de composición corporal que la Dieta hipocalórica mediterránea combinada con el mismo protocolo de ejercicio físico.

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Original / *Deporte y ejercicio*

Gender- and hydration-associated differences in the physiological response to spinning

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Abstract

Introduction: There is scarce and inconsistent information about gender-related differences in the hydration of sports persons, as well as about the effects of hydration on performance, especially during indoor sports.

Objective: To determine the physiological differences between genders during indoor physical exercise, with and without hydration.

Methods: 21 spinning sportspeople (12 men and 9 women) participated in three controlled, randomly assigned and non-sequential hydration protocols, including no fluid intake and hydration with plain water or a sports drink (volume adjusted to each individual every 15 min), during 90 min of spinning exercise. The response variables included body mass, body temperature, heart rate and blood pressure.

Results: During exercise without hydration, men and women lost ~2% of body mass, and showed higher body temperature (~0.2°C), blood pressure (~4 mmHg) and heart rate (~7 beats/min) compared to exercises with hydration. Body temperature and blood pressure were higher for men than for women during exercise without hydration, differences not observed during exercise with hydration. Between 42-99% of variance in body temperature, blood pressure and heart rate could be explained by the physical characteristics of subjects and the work done.

Conclusions: During exercise with hydration (either with water or sport drink), the physiological response was similar for both genders. Exercise without hydration produced physical stress, which could be prevented with either of the fluids (plain water was sufficient). Gender

RESPUESTAS FISIOLÓGICAS ASOCIADAS AL GÉNERO E HIDRATACIÓN DURANTE EL SPINNING

Resumen

Introducción: La información sobre las diferencias relacionadas con el sexo en cuanto a la hidratación de las personas deportistas, así como sobre los efectos de la hidratación sobre el rendimiento, especialmente en deportes de interior, es escasa e inconsistente.

Objetivo: Determinar las diferencias fisiológicas entre sexos durante el ejercicio físico en el interior con y sin hidratación.

Métodos: Veintiuna personas deportistas (12 hombres y 9 mujeres) participaron en tres protocolos de hidratación, no secuenciales, controlados y distribuidos al azar, que incluían falta de hidratación, hidratación con agua corriente e hidratación con una bebida para deportistas (ajustando el volumen a cada individuo cada 15 minutos), durante 90 minutos de ejercicio spinning. Las variables de respuesta incluían masa corporal, temperatura corporal, frecuencia cardíaca y presión sanguínea.

Resultados: Durante el ejercicio sin hidratación los hombres y mujeres perdieron cerca de un 2 % de la masa corporal y mostraron una temperatura corporal (~0,2°C), presión sanguínea (~4 mm Hg) y frecuencia cardíaca (~7 latidos/min) superiores en comparación con los ejercicios sin hidratación. La temperatura corporal y la presión sanguínea fueron superiores en hombres que en mujeres durante el ejercicio sin hidratación, diferencias que no se observaron durante el ejercicio con hidratación. Entre el 42 y el 99 % de la varianza de la temperatura corporal, la presión sanguínea y la frecuencia cardíaca pudo explicarse por las características físicas de los individuos y el trabajo realizado.

Conclusiones: Durante el ejercicio con hidratación (ya fuese con agua o una bebida para deportistas), la respuesta fisiológica fue similar en ambos sexos. El ejercicio sin hidratación produjo estrés físico que pudo ser evitado con cualquiera de los dos tipos de líquidos (el agua corriente fue suficiente). Las diferencias en la respuesta fisiológica al spinning (temperatura corporal, presión

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differences in the physiological response to spinning (body temperature, mean blood pressure and heart rate) can be explained in part by the distinct physical characteristics of each individual.

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Introduction

Dehydration is a common problem among athletes. The most important causes are poor nutritional education of both athletes and their trainers, environment factors, inappropriate diets before and after exercise^{1,2}, ignorance about the effects of dehydration on health and performance^{3,4}, a lack of thirst stimulus during exercise⁵ and deficits in planning and organization by sports authorities⁶.

It is known that athletes must be euhydrated (280-290 mOsm/kg) to have good physical performance during exercise. However, there are several environmental conditions that provoke a considerable loss of water (1-5% of body mass) and electrolytes (10-80 mEq/L Na⁺, 3-15 mEq/L K⁺, and 5-60 mEq/L Cl⁻)^{7,8}, including intense sun light, high temperatures and high relative humidity, as well as a lack of ventilation and proper clothing. At a certain threshold, the higher body temperature and physical stress of dehydrated athletes lowers physical performance compared to their euhydrated counterparts^{5,7,9}.

While some authors propose that the rate of sweating is lower in female than male athletes^{10,11}, others pose that women take more time than men to start sweating¹². Since there is scant information on the relation between physical performance and hydration of sports persons, and because these differences could affect the homeostasis and performance of females, it is necessary to gain insights into this subject.

Most of the studies on male and female athletes have evaluated the effects of dehydration on exercise performance outdoors, especially under extreme environmental conditions (temperature > 30°C; relative humidity > 60%)^{7,8}, however, there are few reports on sports persons practicing indoor sports. Since the latter activities are generally carried out with poor ventilation, and in some cases require clothing impermeable to air flow, the problem of dehydration tends to be worse indoors than outdoors in spite of *ad libitum* drinking. For example, a loss of water representing more than 2% of body mass has been reported during judo¹³, nearly 3.4% during indoor soccer¹⁴, between 1-2 kg of body mass/h during badminton¹⁰ and tennis¹⁵.

Dehydration is a problem with the aforementioned indoor sports even though they involve displacement of the involved person, leading to a certain degree of

sanguínea media y la frecuencia cardíaca) pudieron explicarse en parte por características físicas individuales diferenciales.

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ventilation and therefore heat loss by convection and evaporation. Hence, dehydration becomes an even more serious problem with spinning, an activity in which sports person are stationary, i.e., Mora-Rodríguez et al. (2007)¹⁶ reported a mean body mass loss of 2.3% after 60 min of spinning. When adding ventilation (air flow: 2.55 m/s), dehydration was lower by 0.5% and body temperature by 0.5°C. According to Coyle (2004)⁵, physical performance is not affected during spinning provided that sports person are well hydrated and the body mass loss is below 2%. Although these guidelines have been established for spinning, to the best of our knowledge there is only one report that explore the different hydration status of male sports person of this sport¹⁷. This factor is important because it may affect performance. Thus, here we study the gender-related physiological response during 90 min of spinning exercise with and without hydration in healthy young adult volunteers.

Methods

Subjects

Twenty one amateur spinning sports persons (12 men and 9 women) volunteered to participate in a case series study (each subject is its proper control) (table I). All sports persons were accustomed to practicing spinning 3 to 5 days per week, in sessions lasting at least 1 hour. They were asked not to smoke, drink caffeinated beverages or consume alcohol during the entire study, not to exercise 48 h prior to a session, and to arrive to the physiology lab between 9:00 am and 2:00 pm. All participants were found to be in good health, corroborated by a medical check-up (University medical service) and an electrocardiogram before the tests. The study was carried out with the approval of the institution's Ethics Committee, and each volunteer signed an informed consent letter in accordance with the Declaration of Helsinki of the World Medical Association Ethics Code.

Anthropometry

Height (stadiometer Seca Model 206, Mexico) and body fat (Quantum X RJL, USA) were determined

immediately before the first exercise session. Body mass (*Bame* Aut model O.C.N. 5282; *Torrey*, Mexico) was measured before and after each session, weighing the sports person with an empty bladder (at the end of the exercise the individuals did not want to urinate) and no clothing, and when completely dry.

Exercise and hydration protocols

Environmental indoor conditions during the exercise sessions were kept constant, with a temperature of 23°C, relative humidity of 23%, barometric pressure of 659 mmHg, and no ventilation (it is important to notice that in Ciudad Juarez, few gyms have ventilation). Participants wore sports clothes commonly used in cycling and were free to have their habitual breakfast 3 to 5 hours before the exercise sessions. On the first day they were given 15 min to adapt to the stationary bicycle of the lab (Monark 828E, Vansbro Sweden), during which time they learned about the modified Borg scale (from 0 to 10)¹⁸. Afterwards, they were programmed for three exercise sessions, each with a distinct hydration protocol: exercise without fluid intake and exercise accompanied by hydration (either with plain water or a sports drink). In every session the participant exercised continuously for 90 min and maintained the psychosomatic perception of effort between six and seven (heavy to very heavy exercise) on the modified Borg scale. With this in mind, they were allowed to freely increase or reduce both ergometer resistance and pedaling revolutions and a member of the team monitored her/his perception of the Borg scale.

During the first session (48 hours after the 15 min adaptation period), the protocol for all participants was exercise without fluid intake. The order of the other two protocols was randomized. Based on the loss of body mass during the first protocol, we determined the amount of fluid, either plain water or the sports drink (Gatorade®: 324 mmol/L of carbohydrates, 19.9 mmol/L of Na⁺ and 3.2 mmol/L of K⁺), that each participant needed to prevent dehydration. In accordance with the literature, this quantity of fluid was divided into six equal parts and supplied every 15 min during the respective exercise protocol^{5,19}, and was kept in refrigeration at 4°C. The time elapsed between the three exercise sessions was two weeks for men and three months for women. This protocol was established for women so that each exercise session would be in the middle of their follicular phase of menstruation, since hormonal changes within the menstrual cycle affect body temperature, corporal water retention and physical performance²⁰.

Physiological parameters measurement

Physical stress was evaluated by body temperature (Digital infrared Ear 424 USA), heart rate (Polar

RS100, Finland), blood pressure (Aneroid Baumanometer and EM Rescue stethoscope, USA), and mean blood pressure [(diastolic blood pressure + (systolic blood pressure – diastolic blood pressure)/3)]²¹. Psychosomatic perception of effort (fatigue) was evaluated by the modified Borg scale. The distance traveled was calculated in km, and the resistance applied to the bicycle ergometer was measured in N. Only one person was in charge of recording blood pressure, one for body temperature, one for heart rate and one for psychosomatic perception of effort (Borg scale) every 15 min during exercise (without stopping the exercise) and at rest.

Statistical Analyses

Differences in physical characteristics between genders were analyzed by the Student's *t* test of independent samples. Differences between hydration protocols, time and sex were analyzed by the General Linear Model (GLM). Repeated measurements and comparisons between factors were evaluated by the Sidak test. The homogeneity of variances on Student's *t* test and GLM analysis was checked by Levene's test. The independency of associated parameters on changes in heart rate, body temperature and blood pressure was analyzed by multiple linear regression analysis through the stepwise method. The Statistical analyses were carried out with the 18.0 PASW program. Data are presented as the mean ± standard deviation (SD) in tables and ± standard error of the mean (SEM) in figure. The significance was set at $p < 0.05$.

Results

Body mass was constant for both men and women during the hydration protocols

Men showed higher values in relation to age, height and body mass than women; contrarily, men had a lesser percentage of body fat. At rest, men had higher blood pressure (systolic, diastolic and mean) and a lower heart rate ($p < 0.01$; table I). During the exercise session without fluid intake, the loss of body mass was slightly higher for men ($2.2\% \pm 0.9$) than women ($2.0\% \pm 1.2$), but the difference was not statistically significant (table II). Accordingly, men needed more fluid than women to prevent dehydration. During the exercise sessions with a sports drink, the consumption for women versus men was as follows: 72 ± 40 vs 103 ± 38 g of carbohydrates, 564 ± 312 vs 807 ± 298 mg of Na⁺, and 154 ± 85 vs 220 ± 81 mg of K⁺. While both genders lost body mass during the exercise sessions without fluid intake, this parameter was stable (± 0.2 kg) for both men and women during the two hydration protocols (table II).

Table I
Physical characteristics of participants

	Women (n = 9)	Men (n = 12)
Age (years)	24.1 ± 4.5	30.0 ± 6.2 ^a
Body mass (kg)	62.2 ± 2.4	77.4 ± 16.7 ^a
Height (m)	1.65 ± 0.05	1.75 ± 0.05 ^a
Body fat (%)	33.9 ± 4.2	18.0 ± 6.2 ^a
BMI (kg/m ²)	22.9 ± 1.7	25.2 ± 5.1
Heart rate (beats/min)	69 ± 9	58 ± 7 ^a
Systolic blood pressure (mmHg)	107 ± 9	124 ± 12 ^a
Diastolic blood pressure (mmHg)	67 ± 5	74 ± 7 ^a
Mean blood pressure (mmHg)	80 ± 5	91 ± 8 ^a

Values are the mean ± SD. BMI: Body mass index. ^a p < 0.01. Differences evaluated by the Student's *t* test.

Hydration prevented physical stress, but did not change physical performance

Men traveled a longer distance and applied greater resistance to the ergometer than women (distance, ~50.0 vs ~43.4 km; resistance, ~19 vs ~14 N). There was no statistical difference in these values between any three exercise sessions (with and without fluid consumption) for either men or women (table II). However, the increase in body temperature (p < 0.01), mean blood pressure (p < 0.01) and heart rate (p < 0.01) was higher for both men and women during the exercise session without fluid intake than during the sessions with hydration. This corroborates that there is an increase in physical stress when sports person are deprived of hydration; furthermore, there was no statistical difference in these values between the two exercise sessions with hydration (table II), suggesting that this protocol prevented physical stress regardless of the composition of the fluid.

Men had higher body temperature and mean blood pressure than women during exercise, but similar heart rate

During exercise (after 30-40 min and on) men had higher body temperature (p < 0.01) and mean blood pressure (p < 0.001) than women (fig. 1); however, women had a slightly higher heart rate than men, even at rest, but this difference was not significant (p = 0.12; table II). Analysis of the associations between parameters showed that: (a) 42% of the variance in body temperature could be explained by differences in age, heart rate, Δ body mass and resistance applied to the ergometer (p < 0.001); (b) 74% of the variance in mean blood pressure could be explained by gender and differences in heart rate (p < 0.001); (c) 99% of the variance in heart rate could be explained by differences in body temperature (p < 0.001; table III).

Dehydration increases physiological parameters independently of gender

Exercise with no fluid intake yielded higher numbers in all parameters evaluated, independently of gender (fig. 1), which were maintained throughout the 90 min spinning period. It is worth to mention that, even though statistical significance was obtained for body temperature in men (p < 0.05), no difference was set in the blood pressure and heart rate among sexes but they were higher when no hydration consumption was the protocol. Furthermore, hydration yielded similar results despite it was plain water or sports fluid (fig. 1).

Discussion

The results of the present study show that the dehydration provoked by 90 min of spinning, performed in comfortable environmental indoor conditions (23°C and 23% relative humidity) but without ventilation, did not

Table II
Physiological and performance changes for women and men caused by hydration protocols

	Women (n = 9)			Men (n = 12)		
	EFW	EPW	ESD	EFW	EPW	ESD
Loss of body mass (kg)	-1.21 ± 0.72	-0.05 ± 0.35 ^a	0.16 ± 0.25 ^a	-1.69 ± 0.68	-0.17 ± 0.50 ^a	-0.03 ± 0.61 ^a
Loss of body mass (%)	-2.0 ± 1.2	-0.08 ± 0.6 ^a	0.3 ± 0.4 ^a	-2.2 ± 0.9	-0.2 ± 0.7 ^a	0.0 ± 0.8 ^a
Distance travelled (km)	45.0 ± 3.6	44.1 ± 3.0	43.3 ± 3.1	49.3 ± 5.6 ^b	50.1 ± 5.6 ^b	51.4 ± 6.5 ^b
Resistance applied to the ergometer * (N)	13.4 ± 2.1	14.3 ± 2.0	14.1 ± 2.2	19.6 ± 4.1 ^b	19.8 ± 2.8 ^b	18.2 ± 3.3 ^b
Body temperature* (°C)	36.9 ± 0.3	36.7 ± 0.5 ^a	36.7 ± 0.3 ^a	37.3 ± 0.5 ^b	36.9 ± 0.3 ^{ab}	37.0 ± 0.4 ^{a,b}
Mean blood pressure* (mmHg)	94 ± 5	91 ± 4 ^a	88 ± 6 ^a	114 ± 8 ^b	112 ± 10 ^{ab}	111 ± 7 ^{ab}
Heart rate* (bpm)	154 ± 16	145 ± 19 ^a	145 ± 17 ^a	147 ± 12	141 ± 14 ^a	142 ± 16 ^a

Values are expressed as the mean ± SD. EFW = exercise without fluid intake; EPW = exercise accompanied by hydration with plain water; ESD = exercise accompanied by hydration with a sports drink. ^aDifferent with respect to the protocol of exercise without fluid replacement. ^bDifferent with respect to women. p < 0.01. Statistical analysis of independent variables by GLM, and of repeated measures by the Sidak test for multiple comparisons. * Mean value for the 90 minutes of exercise.

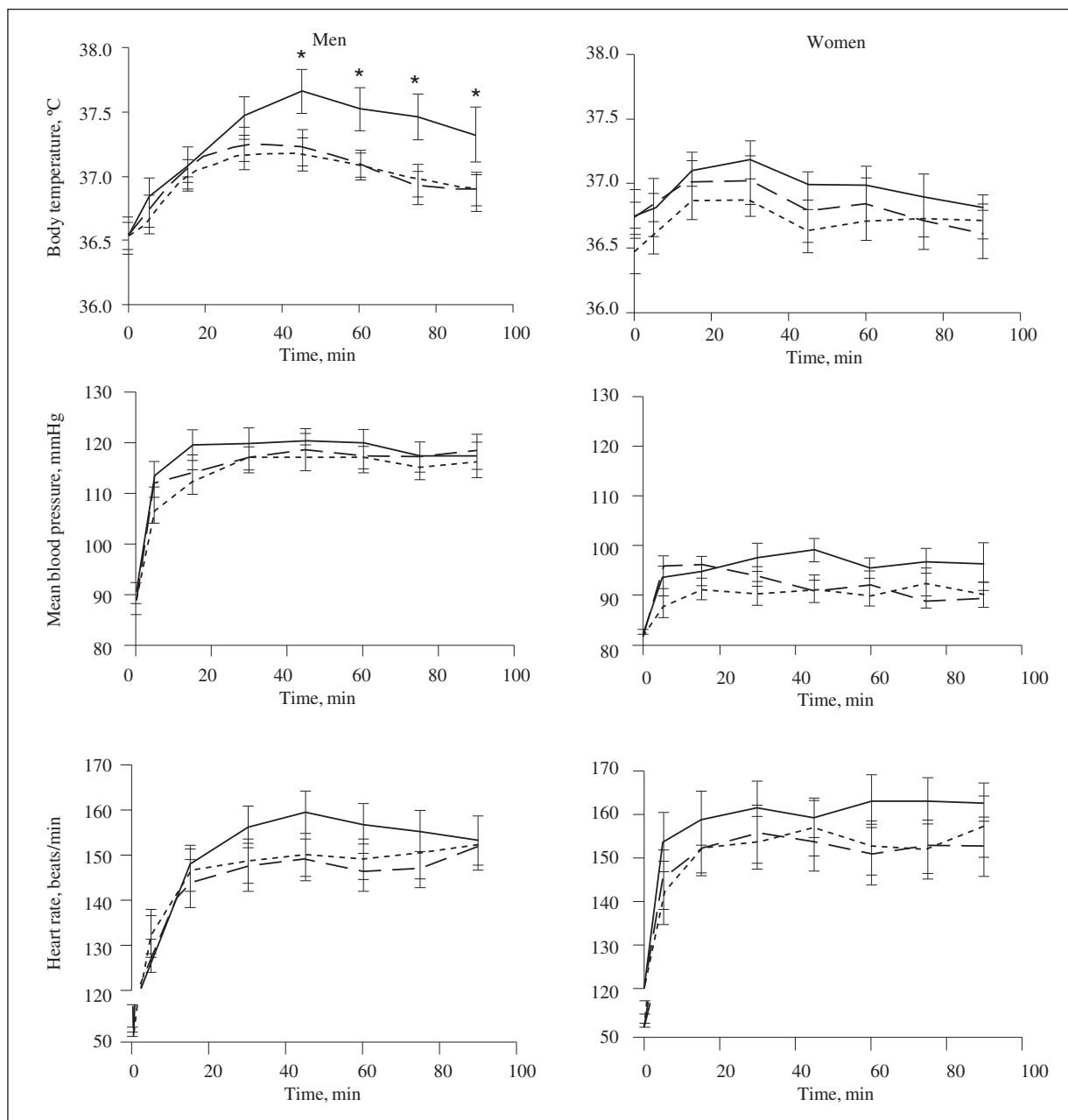


Fig. 1.—Kinetics (Time course) of body temperature, mean blood pressure and heart rate during 90 minutes of spinning. The results are shown as the mean \pm SEM. (—) Continuous lines for dehydration, (---) dashed lines for hydration with plain water, (••••) Stitch lines for hydration with sports drink.

Table III
Multiple linear regression models for body temperature, blood pressure and heart rate

Regression Equations	R ²	p level
Body temperature = 34.3 + 0.25 age (years) + 0.01 heart rate (bpm) - 0.12 Δ body mass (kg) + 2.4 resistance applied to the ergometer (N)	0.42	< 0.001
Mean blood pressure = 62.1 + 22.7 sex (0 = women, 1 = men) + 0.20 heart rate (bpm)	0.74	< 0.001
Heart rate = 3.9 body temperature (°C)	0.99	< 0.001

diminish physical performance but increased physical stress, since all the parameters measured were higher in this condition (similar results for men have been reported previously)¹⁷. The physical stress apparently experienced by the sports person during the exercise session without fluid intake was absent for both men and women, when exercise was accompanied by hydration (either with plain water or a sports drink). The physiological response was similar in both genders, explained in part by the physical characteristics of the subjects.

In relation to the water balance in men and women after spinning, reported data are inconsistent. Some uncontrolled studies carried out with *ad libitum* hydration indicate that the absolute and relative rates of sweating are higher for men versus women (1.12 vs 0.57 L/h, and 2.16 vs 1.49%, respectively) during a 90 min spinning session with artificial ventilation.¹¹ On the other hand, in a controlled experiment, also with *ad libitum* hydration but without ventilation, no gender differences in sweating in relation to time (60 vs 90 min of spinning) were found, although women consumed less fluid than men²².

Since it has been shown that *ad libitum* hydration is not sufficient to prevent dehydration during and after exercise^{10,11,14,15,22}, we decided to replace the exact amount of fluid (euhydration) lost by each individual during 90 min of spinning. Comparing both euhydration and dehydration, we found that there are no gender differences in water balance after spinning, in agreement with other's findings²². In the present study, the loss of body mass was slightly but not significantly higher in men than women, which is also in agreement with Johannsen et al²².

One possible explanation for the differences between genders found by Hazelhurst & Claassen (2006)¹¹, could be that women have greater body surface area/kg of body mass than men²³. This would allow for a greater loss of heat by convection and evaporation in women than men during experiments with artificial ventilation. However, heat production without ventilation increases sweating and loss of body mass in a similar way for both genders. Hence, a lack of ventilation and displacement of the athlete²² and the current contribution, diminishes the possibility of heat loss by convection and evaporation, and in consequence practically eliminates the differences between men and women in regard to a loss of body mass.

Besides heat production, another factor that influences perspiration during exercise is the number of sweat glands. On this question there is controversy, as some authors reported that women have a higher density of sweat glands per cm² than men²⁴, while others report the opposite²³. However, some authors have shown that when variability in sweating is corrected by physical capacity as well as by morphological and anthropometrical characteristics, there are no differences due to gender²⁵.

Contrary to our findings, there is one report that women had a higher body temperature than men regard-

less of exercise intensity and climate conditions²⁶. However, that study did not consider the variability of temperature during the menstrual cycle. It has been reported that the body temperature of women can vary as much as 0.6°C, even at rest, depending on the phase of the menstrual cycle²⁷. In the present study this variation was avoided by planning all the spinning sessions for women at the same phase of the menstrual cycle.

According to Gagnon & Kenny (2012)²⁸, differences between genders in body temperature are related to distinct physical characteristics; also Havenith & van Middendorp (1990)²⁵ reported that 54 to 70% of the variance in body temperature could be explained by physical characteristics. The results of the present study disagree with these reports, since we found that the modifications in age, heart rate, Δ body mass and resistance applied to the ergometer accounted for only 42% of the variance in body temperature.

This contradiction can be explained by the distinct methods of calculating body temperature. According to the Havenith & van Middendorp regression equation [Rectal temperature = 36.7 + 0.26 (Body fat) + 82.3 (body surface area) + 0.18 (VO₂ max), among other parameters], body temperature rises with an increase in body fat, body surface area, and maximum volume of O₂ consumption (VO₂ max). However, the equation seems to be flawed, as the results it gives are not as expected. For example, a higher percentage of fat tissue implies the presence of less lean mass and therefore a lower metabolic rate, which in turn should produce less (not greater) heat. Moreover, a greater body surface area provokes higher heat dissipation, which should lead to a lower (not higher) body temperature. Finally, a higher VO₂ max indicates a better adaptation to exercise stress, which should result in a lower (not higher) body temperature. Hence, we propose the following regression equation (table III) since it sounds more adequate:

$$\text{Body temperature} = 34.3 + 0.25 \text{ age (years)} + 0.01 \text{ heart rate (bpm)} - 0.12 \Delta \text{ body mass (kg)} + 2.4 \text{ resistance applied to the ergometer (N)}$$

In relation to mean blood pressure, our results are similar to studies that involve maximum intensity exercise, in which this parameter is higher for men than women, even at rest²⁹. In addition, the present results show that 74% of the variance in mean blood pressure could be explained by gender and differences in heart rate.

On the other hand, it has been shown that heart rate is higher for women than men when exercise is above the anaerobic threshold²⁹. In the present study, heart rate was higher for women than men, both at rest and during exercise. Moreover, 99% of the variance in heart rate during exercise was explained only by body temperature.

In the present study, dehydration did not affect physical performance, but increased physical stress since all physiological parameters augmented. This can best be explained by the fact that the participants were

asked to exercise at the same subjective work intensity (6-7 on the modified Borg scale) and had a dehydration rate below 3%, which is the critical point above which sweating is reduced, body temperature increased, and there is a greater subjective perception of effort, thus affecting performance¹².

Dehydration and body temperature have an additive effect under extreme weather conditions (temperature $\geq 35^{\circ}\text{C}$ and relative humidity $\geq 50\%$), increasing peripheral vascular resistance and heart rate, while decreasing systolic volume, cardiac output and mean blood pressure.³⁰ Together these changes lead to an enormous decrease in physical performance³¹. However, in the controlled indoor conditions of the present study (23°C and 23% relative humidity) it is understandable that physical performance was not affected; in this regard, our results agree with those by Abián-Vicén et al. (2012)¹⁰, in relation to exercise under non-extreme conditions. The fact that the distance traveled and the resistance applied to the ergometer was higher for men than women, is probably due to the well-recognized differences in body mass and physical strength between genders.

Conclusions

Both men and women had higher values for body temperature, mean blood pressure and heart rate during the exercise without fluid replacement, confirming that dehydration provokes physical stress. Consumption of plain water is sufficient for preventing physical stress in both genders, provided that an adequate volume is consumed to replace the loss of body fluid caused by sweating. The differences found in body temperature, mean blood pressure and heart rate between women and men are due, in part to the distinct physical characteristics and work load of the subjects. Since *ad libitum* water consumption as a response to thirst has proven inadequate, the present results suggest that it would be helpful for sports person to evaluate their own dehydration rate before participating in a competition. They would then be able to program the correct intake of fluid, based on continuous drinking, to avoid dehydration, diminish physical stress, and therefore maintain a good performance level.

Limitations of the study

Is it worth to mention that participants of the study are considered Mexican mestizo and it is recommended to test this kind of experiments with other populations in order to compare results.

Competing interests

The authors declare that they have no competing interests.

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Original / *Valoración nutricional*

Evaluación del riesgo nutricional de los adolescentes escolarizados en Cantabria

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Resumen

Objetivo: Evaluar el riesgo nutricional, por edad y sexo, que presentan los adolescentes escolarizados en la Comunidad Autónoma de Cantabria.

Sujetos: Se realizó un estudio transversal, analizando una muestra de 1101 adolescentes, de los que 51,6% eran varones y 48,4% fueron mujeres de edades comprendidas entre los 10 y los 17 años, escolarizados en centros de enseñanza pública, mediante el cuestionario Krece Plus.

Resultados: Se observa un elevado porcentaje de adolescentes que presentan un riesgo nutricional elevado (35%). Los varones presentan un riesgo nutricional alto en un porcentaje ligeramente superior a las mujeres (37,8% vs 32,1%). Además, el riesgo nutricional alto sufre un notable incremento a medida que la edad de los jóvenes aumenta. Se aprecian diferencias estadísticamente significativas tanto en los grupos de edad de los varones ($p = 0,024$), de las mujeres ($p < 0,001$) como en el grupo global ($p = 0,001$). En los tres casos, la distribución del riesgo nutricional en los grupos de menor edad es muy similar (entre 35,2 y 35,8% en los ♂, entre 27,9 y 29,7% en las ♀, y entre 31,7 y 32,7% en el grupo total). Mientras que en el grupo de mayor edad estos valores prácticamente se duplican (57,1% en los ♂, 69,0% en las ♀, y 62,2% en el grupo total).

Conclusión: Los resultados obtenidos muestran una realidad preocupante debido, principalmente, al elevado porcentaje de adolescentes que presentan un riesgo nutricional elevado. Siendo los varones y los adolescentes de mayor edad los sectores en los que este riesgo nutricional elevado es superior.

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Palabras clave: *Adolescencia. Riesgo nutricional. Nutrición. Alimentación.*

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ASSESSMENT OF NUTRITIONAL RISK AMONG IN-SCHOOL ADOLESCENTS FROM CANTABRIA

Abstract

Objective: To analyse nutritional risk, by age and sex, among primary and secondary education adolescents from Cantabria.

Methodology: a cross-sectional study was carried out, analysing a sample of 1101 adolescents: 568 (51.6%) were men and 533 (48.4%) were women, aged 12 to 17, attending 16 different primary and secondary education centres in Cantabria, by means of a Krece Plus questionnaire.

Results: A high percentage of adolescents with a high nutritional risk (35%) can be observed. Men show a high nutritional risk slightly higher than women (37.8% ♂ vs 32.1% ♀). Moreover, the high nutritional risk experiences a notable increase as young people get older. Significant statistical differences can be seen both in male and female groups, and as a global group. In all three cases, the nutritional risk distribution in the youngest group is very similar (35.2-35.8% in ♂, 27.9-29.7% in ♀, 31.7-32.7% in the global group); whereas in elder adolescents, those values are practically doubled (57.1% in ♂, 69.0% in ♀, y 62.2% in the global group).

Conclusions: Results are alarming mainly given the high percentage of adolescents with a high nutritional risk. Men and older adolescents are the groups in which high nutritional risk is more evident.

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Keywords: *Adolescence. Nutritional risk. Feeding. Nutrition.*

Introducción

La Organización Mundial de la Salud (OMS) define la malnutrición como “el desequilibrio entre el suministro de nutrientes y de energía a nivel celular y la demanda o necesidad que el cuerpo tiene de los mismos para asegurar el crecimiento, el mantenimiento y las diversas funciones concretas”¹.

La edad infantil y juvenil se caracteriza por ser el periodo en que se expresan los fenómenos de crecimiento y maduración como un proceso fisiológico integral, que obtiene como resultado una etapa adulta condicionada en toda su dimensión por este intervalo precedente². El potencial de crecimiento genéticamente determinado depende, entre otros factores, de la disponibilidad y del consumo adecuado de nutrientes³.

El crecimiento y el desarrollo son dos procesos biológicos resultantes de la interacción entre los factores genéticos y los ambientales. Entre estos últimos, la nutrición es un factor determinante de aquellos. Es por esto, que la evaluación de la situación nutricional se considera como uno de los indicadores más importante del estado de salud de las personas en general y de los niños o adolescentes en particular⁴.

A pesar de que no existe una definición de adolescencia aceptada internacionalmente, tanto las Naciones Unidas como la Organización Mundial para la Salud (OMS) establecen que los adolescentes son personas con edades comprendidas entre los 10 y los 19 años; considerándose en la misma dos fases, la adolescencia temprana 10 a 14 años y la adolescencia tardía 15 a 19 años⁵. La adolescencia es un buen momento para adquirir hábitos saludables de alimentación y ejercicio, que pueden contribuir al bienestar físico y psicológico durante ese periodo, y para reducir la probabilidad de que en la edad adulta aparezcan enfermedades crónicas relacionadas con la nutrición. Promover modos de vida sanos también es fundamental para atajar la rápida progresión de la epidemia de obesidad⁶. No obstante, los profundos cambios biológicos, psicológicos y sociales que se producen a lo largo de esta etapa permiten considerar a los adolescentes como un grupo de riesgo nutricional⁷⁻¹⁰.

La evaluación del estado nutricional de un individuo o colectividad consiste en la determinación del nivel de salud y bienestar desde el punto de vista de su nutrición y depende del grado en que las necesidades fisiológicas, bioquímicas y metabólicas de nutrientes estén cubiertas por la ingestión de alimentos en la dieta¹¹. En la evaluación del estado nutricional de un individuo o de una colectividad pueden emplearse determinados y variados métodos de medida, tales como el estudio bioquímico y hematológico, el estudio antropométrico, la historia dietética, la historia clínica y el examen físico y la valoración psicosocial. Dependiendo del interés de la investigación se empleará uno u otro, y si lo que se busca es un estudio exhaustivo del individuo o de la población, habría que llevar a cabo todo el conjunto de métodos mencionados¹²⁻¹⁴. De acuerdo con la OMS, el

principal fin de la valoración nutricional es mejorar la salud de los humanos.

Es evidente que en los centros de enseñanza casi nunca se dispone de los recursos ni del tiempo necesario para llevar a cabo una evaluación exhaustiva del estado nutricional; por esta razón, y en consonancia con lo expresado en el *Estudio enKid*, el empleo de instrumentos cortos para la evaluación del riesgo nutricional y los desequilibrios alimentarios, es de sumo interés por su fácil realización¹⁵.

El objetivo del presente estudio es evaluar el riesgo nutricional de los adolescentes de ambos sexos, con edades comprendidas entre 10 y 17 años, escolarizados en la Comunidad Autónoma de Cantabria, empleando para ello el “Cuestionario *Krece Plus*”, de fácil administración, que fue elaborado y validado dentro del “Estudio enKid”¹⁵.

Metodología

Se realizó un estudio epidemiológico observacional de carácter transversal, cuya población objetivo fueron los adolescentes, de ambos sexos, escolarizados y con edades comprendidas entre 10 y 17 años.

La muestra fue recogida entre el alumnado que cursaba alguna de las modalidades académicas de las Enseñanzas Primaria, Secundaria y Bachillerato, matriculado en 16 centros de enseñanza de carácter público de la Comunidad autónoma de Cantabria: 4 institutos de Enseñanza Secundaria y 12 colegios de enseñanza infantil y primaria de, a lo largo del curso 2010-11. El número total de encuestados ascendió a 1.101 adolescentes.

El cuestionario fue presentado al alumnado o bien por los autores principales del artículo, o bien por los profesores colaboradores que se citan al final del mismo. El alumnado contestó a las preguntas durante una hora del tiempo escolar reservado a tal efecto.

La participación del alumnado fue voluntaria y de carácter anónimo, a fin de respetar la confidencialidad. En todo momento se siguieron las normas de buena práctica clínica y la Declaración de Helsinki.

La encuesta consistió en un formulario en el que se recogían aspectos tales como: datos del individuo (sexo, fecha de nacimiento, fecha de la encuesta), variables de imagen corporal, test de alimentación sana del estudio EnKid, aspectos de actividad física y sedentarismo, consumo de polivitamínicos y minerales, tabaquismo, vigilancia por el pediatra, prácticas alimentarias. Además, a los participantes se le realizaron una serie de medidas antropométricas y tuvieron que llevar a cabo determinadas pruebas físicas.

Para el desarrollo del presente artículo el instrumento empleado para la obtención de los datos fue el “Cuestionario *Krece Plus*”. Este cuestionario fue elaborado y validado dentro del estudio denominado “Estudio enKid”¹⁵. Las 16 variables que componen el mismo son las que se detallan en la tabla I.

Tabla I
Ítems del cuestionario Krece Plus

Pregunta	Puntuación
No desayuna	-1
Desayuna un lácteo (leche, yogur, etc.)	+1
Desayuno un cereal o derivado	+1
Desayuna bollería industrial	-1
Toma una fruta o zumo todos los días	+1
Toma una segunda fruta todos los días	+1
Toma un segundo lácteo a lo largo del día	+1
Toma verduras frescas o cocinadas una vez al día	+1
Toma verduras más de una vez al día	+1
Toma pescado con regularidad (≥ 2-3/semana)	+1
Acude una vez o más a la semana a un fast food	-1
Toma bebidas alcohólicas (≥ 1/semana)	-1
Le gusta consumir legumbres (≥ 1/semana)	+1
Toma golosinas varias veces al día	-1
Toma pasta o arroz casi a diario (≥ 5/semana)	+1
Utilizan aceite de oliva en casa	+1

La valoración del riesgo nutricional se halló en función de la siguiente puntuación:

- Menor o igual a 5: nivel nutricional muy bajo. Conviene corregir urgentemente los hábitos alimentarios. Consulta con el pediatra o dietista.
- De 6 a 8: nivel nutricional medio. Es necesario introducir algunas mejoras en la alimentación. Acude al pediatra en seis meses.
- Mayor o igual a 9: nivel nutricional alto. Sigue así.

El análisis estadístico, que se realizó con el programa informático SPSS v21, consistió en una estadística descriptiva bivalente. Para la comparación de las variables cualitativas se utilizó la prueba de χ^2 de Pearson. Las asociaciones se realizaron en función del grupo de edad y del sexo.

Resultados

Datos sociodemográficos

Como se puede apreciar en la tabla II, la edad de la mayoría de los adolescentes estaba comprendida entre

Tabla II
Distribución según la edad

Edad	Hombre	Mujer	Total
10	22,0%	22,1%	22,1%
11	27,6%	25,5%	26,6%
12	13,6%	14,3%	13,9%
13	10,2%	9,6%	9,9%
14	9,7%	11,1%	10,4%
15	6,0%	8,3%	7,1%
16	7,0%	6,6%	6,8%
17	3,9%	2,6%	3,3%
Total	100,0%	100,0%	100,0%

los 10 y los 11 años. Con relación al sexo de los mismos, de los 1101 adolescentes que respondieron a esta pregunta, 568 (51,6%) eran varones y 533 (48,4%) fueron mujeres.

En la tabla III, se describe la distribución de la población analizada en función del curso académico, siendo los niveles correspondientes a la Educación Primaria donde se concentra el mayor número de alumnado participante.

Con relación a la distribución geográfica de la muestra, para realizar la misma se consideraron tres áreas preferentes: Santander y poblaciones colindantes, resto de la zona costera e interior. De acuerdo a esta distribución se obtuvieron los siguientes resultados (tabla IV).

Valoración del riesgo nutricional

La valoración del riesgo nutricional se halló en función de la puntuación mencionada en la metodología. De acuerdo a la misma, los 1031 adolescentes de ambos sexos (532 ♂ y 499 ♀) que completaron íntegramente (los 16 “ítems”) el cuestionario se distribuyeron de la siguiente forma: 15% de riesgo nutricional bajo; 50% de riesgo medio y 35% de riesgo nutricional alto (fig. 1).

Con relación al estudio del riesgo nutricional en función del sexo de los adolescentes, no se observan diferencias estadísticamente significativas ($p = 0,118$) entre los varones y las mujeres, pero los primeros presentan un riesgo nutricional alto en un porcentaje ligeramente superior al de las segundas (37,8 % ♂ vs 32,1 % ♀). Por otro lado, el porcentaje de mujeres que presentan un riesgo bajo es ligeramente superior al de los varones (16,0 % ♀ vs 13,2 % ♂) (fig. 2).

Tabla III
Distribución del alumnado en función del curso académico

Curso	Hombre	Mujer	Total
5º Primaria	29,0%	28,0%	28,5%
6º Primaria	30,1%	28,7%	29,4%
1º ESO	8,1%	7,7%	7,9%
2º ESO	11,3%	11,1%	11,2%
3º ESO	8,8%	11,1%	9,9%
4º ESO	7,2%	9,4%	8,3%
1º Bachillerato	5,5%	4,1%	4,8%
Total	100,0%	100,0%	100,0%

Tabla IV
Distribución geográfica de la muestra

Habitat	Varones	Mujeres
Santander	115 (20,2%)	396 (20,8%)
Resto zona costera	432 (76,1%)	111 (74,3%)
Interior	21 (3,7%)	26 (4,9%)

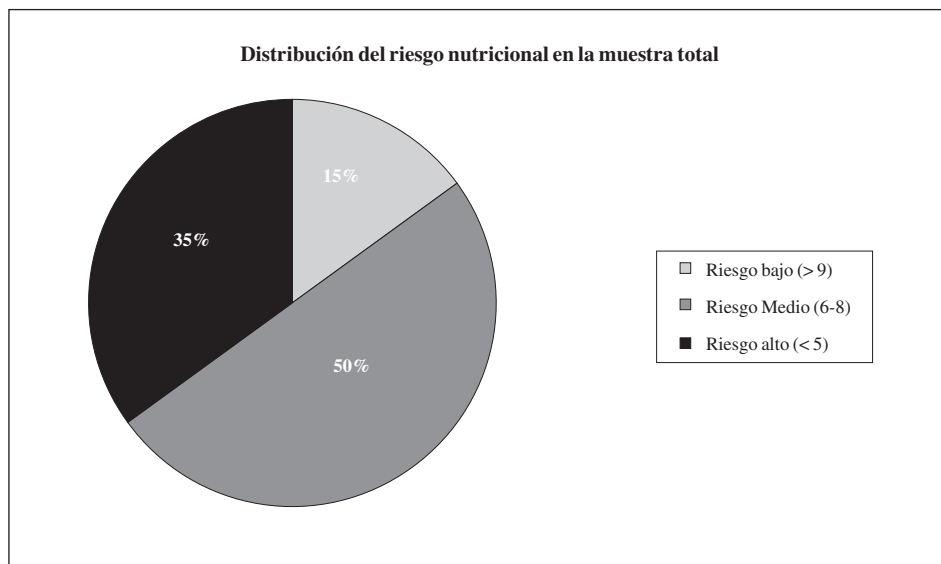


Fig. 1.—Riesgo nutricional global.

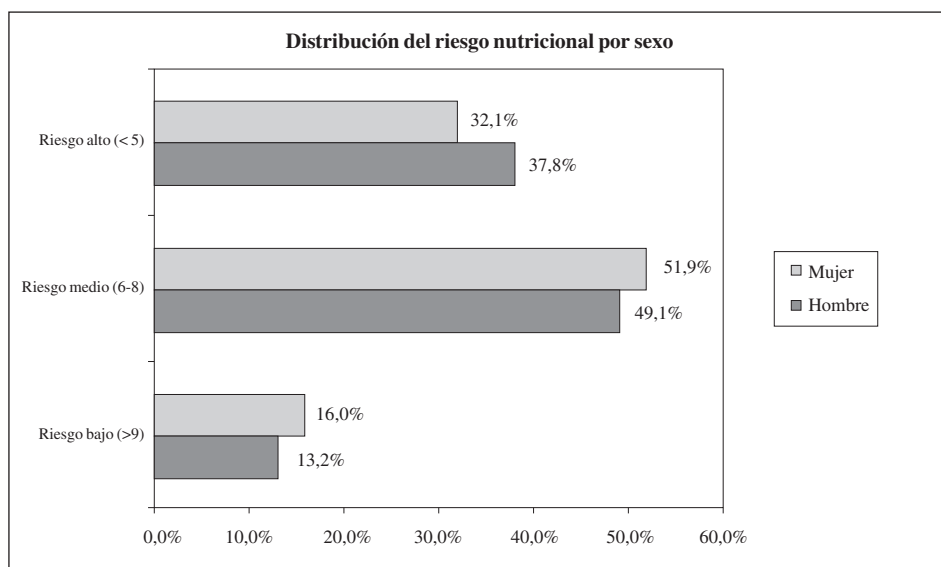


Fig. 2.—Riesgo nutricional en función del sexo.

También se analizó la evolución del riesgo nutricional según la edad de los adolescentes. En la figura 3, se observa claramente las diferentes tendencias de los riesgos, destacando como el riesgo nutricional alto sufre un notable incremento a medida que la edad de los jóvenes aumenta.

En el análisis del riesgo nutricional en función de la edad y el sexo de los adolescentes, se aprecian diferencias estadísticamente significativas tanto en los grupos de edad de los varones ($p = 0,024$), de las mujeres ($p < 0,001$) como en el grupo global ($p = 0,001$). En los tres casos, la distribución del riesgo nutricional en los grupos de menor edad (10-11 y 12-15 años) es muy similar presentando un riesgo elevado entre un 35,2 y 35,8% en los ♂, entre un 27,9 y 29,7% en las ♀, y entre el 31,7 y 32,7 % en el grupo total; mientras que en el grupo de mayor edad estos valores prácticamente se duplican

pasando a ser del 57,1 % en los ♂, del 69,0 % en las ♀, y del 62,2 % en el grupo total (tabla V).

Finalmente, es importante destacar que el 31,7% de los adolescentes de 10 y 11 años presentan un riesgo nutricional elevado.

Discusión

Los resultados obtenidos muestran una realidad preocupante debido, principalmente, al elevado porcentaje (35%) de adolescentes que presentan un riesgo nutricional elevado, máxime cuando en un estudio anterior realizado sobre los adolescentes de la ciudad de Santander, el porcentaje de aquellos que presentaban un riesgo elevado era del 17%¹⁶. No obstante, los datos obtenidos son más favorables que los hallados por Gar-

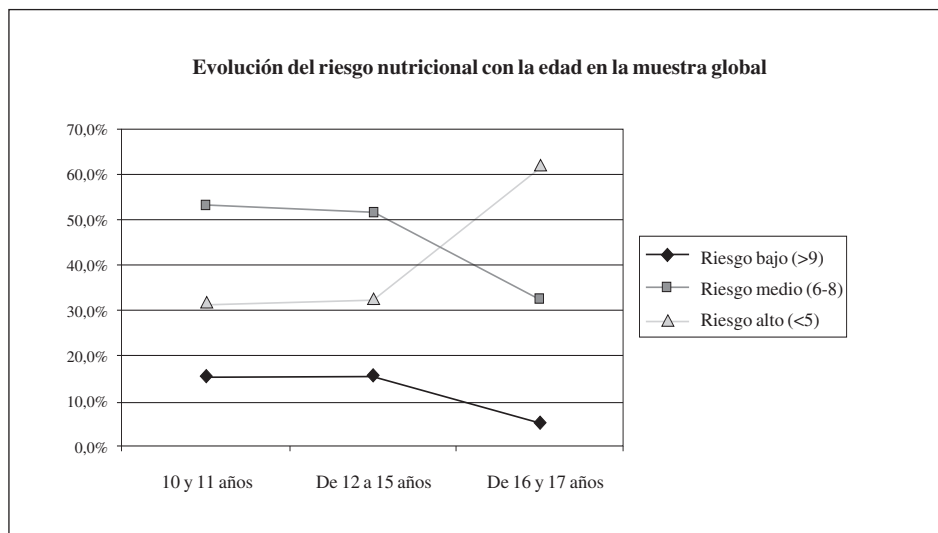


Fig. 3.—Riesgo nutricional en función de la edad.

Tabla V
Distribución porcentual del riesgo nutricional en función de la edad y del sexo

		10 y 11 años	De 12 a 15 años	De 16 y 17 años	Total
Varón	Riesgo Bajo (>9)	13,3%	15,1%	5,4%	13,2%
	Riesgo Medio (6-8)	51,5%	49,1%	37,5%	49,1%
	Riesgo alto (<5)	35,2%	35,8%	57,1%	37,8%
Mujer	Riesgo Bajo (>9)	17,4%	16,7%	4,8%	16,0%
	Riesgo Medio (6-8)	54,9%	53,6%	26,2%	51,9%
	Riesgo alto (<5)	27,7%	29,7%	69,0%	32,1%
Total	Riesgo Bajo (>9)	15,2%	15,9%	5,1%	14,5%
	Riesgo Medio (6-8)	53,1%	51,4%	32,7%	50,4%
	Riesgo alto (<5)	31,7%	32,7%	62,2%	35,0%

cía MA y col. en la población de 6 a 12 años de la ciudad de Sevilla, en la que refirieron los siguientes resultados: 11% de riesgo nutricional bajo; 41,7% de riesgo medio y 47,4% de riesgo nutricional alto¹⁷.

En el análisis del riesgo nutricional en función del sexo, el riesgo nutricional alto es más frecuente entre los varones que entre las mujeres. Resultado que es coincidente con el observado entre los adolescentes de la Comunidad Valenciana, en los que la prevalencia de riesgo nutricional alto en los escolares era más elevado en los varones (42,97 %) que en las mujeres (40,61%)¹⁸. Sin embargo, aquel es totalmente contrario al observado en un estudio anterior llevado a cabo entre los adolescentes de la ciudad de Santander¹⁶.

De igual forma, la constatación de que el riesgo nutricional alto es mucho más elevado entre los adolescentes de mayor edad es coincidente con el resultado obtenido en una población de 829 escolares de 11 a 16 años de la Comunidad Valenciana¹⁸.

Un dato preocupante es el elevado porcentaje (31,7%) de escolares de 10 y 11 años de edad que presentan un riesgo nutricional elevado. Máxime cuando

en el estudio Enkid, de ámbito nacional, este porcentaje fue del 18 %¹⁵.

Conclusiones

Los resultados obtenidos muestran una realidad muy preocupante al constatarse un importante porcentaje de adolescentes que presentan un riesgo nutricional elevado. Este riesgo es incluso más alto que el observado en estudios de ámbito nacional en el rango de edades de 10 a 15 años. Por otro lado, se ha puesto de manifiesto como dicho riesgo nutricional es destacadamente más elevado en los adolescentes de mayor edad.

A la vista de los resultados obtenidos se hace necesario seguir trabajando en la Educación para la salud en general y en la Educación alimentaria y nutricional en particular. La Organización Mundial de la Salud (OMS), en su Carta de Ottawa para la Promoción de la Salud, establece que la promoción de la salud es el proceso que permite a las personas incrementar el control sobre su salud para mejorarla¹⁹⁻²². Desde este punto de

vista es necesario que todos los centros educativos sean promotores de salud. La Educación para la Salud desarrollada en las escuelas e institutos de enseñanza secundaria es un instrumento esencial de las intervenciones en salud. Ha de lograrse una mejora en la “alfabetización” sanitaria, entendida ésta en una concepción holística, en la que no sólo se contemple la adquisición de mayores conocimientos por parte de los escolares, sino fomentar el desarrollo de habilidades personales que conduzcan a la salud individual y de la comunidad.

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Original / *Valoración nutricional*

Association between magnesium-deficient status and anthropometric and clinical-nutritional parameters in postmenopausal women

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Abstract

Background: During menopause occurs weight gain and bone loss occurs due to the hormone decline during this period and other factors such as nutrition. Magnesium deficiency suggests a risk factor for obesity and osteoporosis.

Objective: To evaluate the clinical and nutritional magnesium status in a population of postmenopausal women, assessing intake and serum levels of magnesium in the study population and correlation with anthropometric parameters such as body mass index (BMI) and body fat, and biochemical parameters associated.

Subjects and Method: The study involved 78 healthy women aged 44-76, with postmenopausal status, from the province of Grenade, Spain. The sample was divided into two age groups: group 1, aged < 58, and group 2 aged ≥ 58. Anthropometric parameters were recorded and nutritional intake was assessed by 72-hour recall, getting the RDAs through Nutriber[®] program. To assess the biochemical parameters was performed a blood sample was taken. Magnesium was analyzed by flame atomic absorption spectrophotometry (FAAS) in erythrocyte and plasma wet-mineralized samples.

Results: Our results show that 37.85% of the total subjects have an overweight status. Magnesium intake found in our population is insufficient in 36% of women, while plasma magnesium deficiency corresponds to 23% of the population and 72% of women have deficient levels of magnesium in erythrocyte. Positive correlations were found between magnesium intake and dietary intake of calcium, of phosphorus, and with prealbumin plasma levels, as well as with a lower waist / hip ratio. Magnesium levels in erythrocyte were correlated with lower triglycerides and urea values.

Conclusion: It is important to control and monitor the nutritional status of magnesium in postmenopausal

ASOCIACIÓN DE LA DEFICIENCIA DE MAGNESIO CON PARÁMETROS ANTROPOMÉTRICOS Y CLÍNICO-NUTRICIONALES EN MUJERES POSMENOPÁUSICAS

Resumen

Introducción: Durante la menopausia se produce un aumento de peso y de pérdida de masa ósea debido a la disminución hormonal producida durante este periodo y a otros factores como la nutrición. La deficiencia de magnesio podría ser un factor de riesgo para la obesidad y la osteoporosis.

Objetivo: Evaluar el estado clínico-nutricional en una población de mujeres postmenopáusicas, evaluando la ingesta y los niveles séricos de magnesio, y su correlación con parámetros antropométricos, como el índice de masa corporal (IMC) y la grasa corporal, así como con parámetros bioquímicos asociados.

Sujetos y Metodología: En el estudio participaron 78 mujeres sanas en situación de postmenopausia de la provincia a de Granada, con edades comprendidas entre los 44-76 años. La muestra se dividió en dos grupos de edad: grupo 1, mujeres postmenopáusicas con edad menor de 58 años y grupo 2, de edad mayor o igual a 58 años. Se registraron parámetros antropométricos y se valoró la ingesta nutricional mediante recordatorio de 72 horas, obteniendo las RDAs a través del programa Nutriber[®]. Para valorar los parámetros bioquímicos se realizó una extracción de sangre y el magnesio se analizó mediante espectrofotometría de absorción atómica de llama (FAAS) en muestras de eritrocitos y plasma previamente mineralizadas por vía húmeda.

Resultados: Nuestros resultados muestran que el 37.8% de las mujeres presentan sobrepeso. La ingesta de magnesio encontrada en nuestra población es insuficiente en el 36% de las mujeres, mientras que la deficiencia de magnesio plasmático y eritrocitario corresponde al 23% y el 72% de las mujeres, respectivamente. Se observaron correlaciones significativas positivas entre el aporte de magnesio en la dieta y el aporte de calcio, de fósforo, y los niveles plasmáticos de prealbúmina, además de con una menor relación cintura/cadera. Los niveles de magnesio en eritrocito se correlacionaron con los niveles de triglicéridos y con menores valores de urea.

Conclusión: Es importante un control y seguimiento de la situación nutricional en magnesio d la mujer postme-

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women to prevent nutritional alterations and possible clinical and chronic degenerative diseases associated with magnesium deficiency and with menopause.

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Keywords: *Postmenopause. Osteoporosis. Magnesium. Obesity.*

nopáusica para prevenir alteraciones clínico-nutricionales y posibles enfermedades crónico-degenerativas relacionadas con la deficiencia del magnesio y la menopausia.

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Palabras clave: *Menopausia. Osteoporosis. Magnesio. Obesidad.*

Introduction

Menopause is a natural status of the woman and is determined by the cessation ovarian hormone secretion, leading to the disappearance of menstrual cycles and the emergence of a set of physiological changes causing among others, bone loss, increased abdominal adiposity, insulin resistance, hypertension and dyslipidemia, factors that increase the risk of chronic degenerative diseases such as cardiovascular disease, diabetes and osteoporosis^{1,2}. It appears at an age that, in Spain, is around age of 51, with a spectrum ranging from 48 to 54³.

In this situation women menopause presents a greater risk of obesity, by increasing fat percentage and fat distribution with higher accumulation in the abdominal area, while lean body mass decreases and bone tissue^{4,5}.

One of the main causes of this weight gain is related to decreased hormone produced during this period and others depend on several factors such as age, lack of physical activity and increased caloric intake, resulting in a decrease in energy expenditure. Moreover, at this stage, occurs accelerated bone loss can cause osteoporosis⁶ and significant increase in fracture risk, being an important factor in the pathogenesis both estrogen and nutrition lack. Nutritional factors have multiple effects by acting on the peak bone mass, bone loss related to age and strength muscular⁴. Therefore, we cannot forget the importance of maintaining healthy eating habits for achieving the goal of bone health.

Magnesium is involved as an essential cofactor in numerous enzymatic reactions involved in energy metabolism and the synthesis of proteins and nucleic acid, and about half of a body contained in the bone is therefore not surprising that an increasing number of clinical disorders such as diabetes, osteoporosis and vascular diseases, are associated with deficiency Himself^{7,8}. Postmenopausal women are often associated with a low dietary intake of magnesium and decreased serum levels thereof in numerous studies showing that magnesium deficiency suggests a risk factor for obesity and osteoporosis⁸⁻¹⁰.

Therefore, a healthy and balanced is essential at this stage and help ensure optimal health. Menopause can be a consolidation phase eating habits practiced correctly that help prevent and mitigate some problems as described above, achieving healthy aging.

In addition to conducting a proper and healthy diet is necessary to maintain or incorporate into daily life a number of lifestyles also considered healthy example would be the daily practice of physical exercise and avoiding harmful habits that affect bone health as snuff, and alcohol consumption^{11,12}.

The aim of this study is to evaluate the clinical and nutritional status in a population of postmenopausal women, assessing magnesium status in the study population, by ingestion and analysis of biological samples, and finally, to study possible associations with anthropometric parameters such as BMI and body fat, and clinical parameters-related nutritional magnesium metabolism.

Subjects and methods

Study Design

A cross-sectional study, which measures both the prevalence of exposure and effect in a population sample in a single moment in time. The study has approval from the Ethics Committee of the University of Granada.

Study Subjects

The sample consisted of 78 female volunteers in the province of Granada, Spain, in postmenopausal status aged between 44 and 76. The sample was divided into two age groups: group 1, postmenopausal women aged fewer than 58 and group 2 aged greater than or equal to 58. All received detailed information about the purpose of the study, accompanied by informed consent form to be signed prior to recording his acceptance to be part of it. Inclusion criteria were based on the agreement to participate in the study, by postmenopausal women of any age, which do not have any pathology that could affect their nutritional status and were not undergoing hormone replacement therapy.

Methods

Subjects underwent an interview nutritional and fasting blood extraction for subsequent biochemical

tests. Interview Nutritional Data collection to assess food and nutrient intake of each of the participating women was conducted by personal interview at the time of the appointment. A questionnaire consisting of a section for personal information and one for socio-demographic, age, weight and height (with which was calculated the body mass index-BMI-), and finally, a 72h-recall (where includes two days and one holiday). The anthropometric evaluation was performed at the Institute of Nutrition and Food Technology, University of Granada, by measures of size, made with measuring rod SECA® Model 274, waist circumference determined anthropometric tape SECA® Model 201, and body composition performed with impedance meter TANITA® BC-420-P column. To assess the extent of nutrient intake was used *Nutriber*® software program (Mataix and Garcia-Díz, 2006), containing the recommendations for healthy population.

Removing blood

Blood sampling for determination of relevant biochemical parameters were performed on women participating voluntarily, after the completion of the survey the day of the appointment.

Biochemistry was performed after 12 hours of fasting first thing in the morning, by specialists, by puncturing the cubital vena cava determining the parameters for postmenopausal women. Biochemical assessment was performed in hospital laboratories, based on the analysis parameters in blood samples by *vacutainer* tubes (Venoject®): glucose, creatinine, urea, uric acid, triglycerides, total cholesterol, total proteins, transferrin, prealbumin and albumin. For determining mineral, analytical techniques were as

follows: Calcium and magnesium were analyzed by atomic absorption spectrophotometry (AAS) in erythrocytes and plasma samples wet mineralized. The phosphorus was determined with the colorimetric method of Fiske-Subbarow.

Statistical Analysis

All data are entered, processed and analyzed using SPSS 17.0 for Windows (SPSS Inc. Chicago, IL, USA), represented by their mean values and standard deviation (SD).

In the study of data or numeric variables we used the independent samples test for comparisons between groups and test for related sample to assess the statistical significance of the change in the numerical variables during the study. For this, we used the statistical analysis of variance (ANOVA), having used the test of Student t test for parametric methods, both in the case of independent samples, and related samples. Linear regression analysis was used for bivariate correlations search using the Pearson correlation coefficient. The estimation of the degree of association between each of the analyzed plasma parameters and clinical outcomes was performed using logistic regression analysis. Those were accepted as significant difference with a probability of being due to chance of less than 5% ($p < 0.05$).

Results

Table I represents the age, BMI and nutrient intake in all postmenopausal women participating in the study and separated by age groups (Group 1: aged < 58 and group 2: aged ≥ 58).

Table I						
Evolution of general and nutritional characteristics of the total sample and in different age groups						
	Total population		Group 1		Group 2	
						Reference values
Age (years)	58.1 ± 8.3		51.6 ± 4.05		65.7 ± 4.8**	
BMI (kg/m ²)	27.0 ± 4.6		26.9 ± 4.8		27.1 ± 4.3	18.5-24.9
Abdominal perimeter (cm)	89.0 ± 12.7		88.0 ± 9.4		90.2 ± 13.1	a
Hip (cm)	105.8 ± 10.4		105.7 ± 9.5		105.8 ± 11.6	
Waist / hip ratio	0.83 ± 0.08		0.82 ± 0.08		0.85 ± 0.07	b
Fat Mass (%)	37.5 ± 5.9		37.4 ± 5.5		37.8 ± 6.4	
		% RDA		% RDA		% RDA
Energy (Kcal/day)	1378.5 ± 337.4	69.0	1357.2 ± 393.1	65.4	1404.1 ± 258.6	73.3
Carbohydrates (g/day)	149.7 ± 42.5	54.2	146.3 ± 47.2	50.8	153.6 ± 36.5	58.2
Protein (g/día)	61.5 ± 15.3	148.7	61.1 ± 16.9	146.3	62.1 ± 13.5	151.4
Lipids (g/día)	59.0 ± 20.6	82.4	58.2 ± 23.1	76.8	60.0 ± 17.7	88.9
Calcium (mg/day)	829.5 ± 257.2	103.7	802.3 ± 286.1	100.3	861.0 ± 218.6	107.6
Phosphorus (mg/day)	1038.8 ± 304.9	129.4	1037.3 ± 283.9	129.6	1040.5 ± 331.7	129.2
Magnesium (mg/day)	237.9 ± 79.8	78	219.8 ± 67.7	70.8	259.0 ± 88.3*	86.3

a>88 elevated risk of obesity; b>0.85 obesity. Significant differences between group 1 and group 2: ** $p < 0.01$ * $p < 0.05$.

We note, by the comparison test of means in anthropometric parameters, no significant differences between the age groups, except between age ($p < 0.01$), being higher in the older group.

In our results, the mean BMI indicates that the total population is overweight type I, 37.85% of the total subjects are overweight, which is not surprising when you consider that from that age significantly decreases basal metabolism in women, and often not accompanied by a reduction in the intake caloric.

RDAs according to both the total population and in the different age groups, these values were below in total energy intake, carbohydrates, fats and magnesium above protein, calcium and phosphorus (table I).

When comparing age groups, regarding nutritional intake, no significant differences, both groups showed similar values, except for magnesium intake is higher in the older group ($p < 0.05$).

Moreover, we found that the total study sample, has a 36% of subjects with inadequate intake of magnesium ($< 2/3$ RDA).

Biochemical characteristics of the total sample and in the two age groups are shown in table II. Overall, our study population presented clinical parameters within normal, except cholesterol levels that are above the reference values, and whose difference is negligible in both groups. These are healthy women without apparent disease, since one of the inclusion criteria was that women had not established pathologies

When comparing age groups, significant differences ($p < 0.05$) in the levels of creatinine, urea, uric acid, prealbumin, albumin and glucose ($p < 0.01$), being higher in older women, with the exception of q albumin is higher in younger women.

Observed that magnesium values in both plasma and red blood cells are suitable, are within the reference values and there are almost no differences in body

magnesium status between age groups. The 23% of people are deficient in magnesium levels in plasma and 71.8% deficiency in magnesium levels in erythrocytes.

According to Pearson correlations, there were significant positive correlations between age and glucose levels ($p < 0.001$, $r = 0.421$), urea ($p = 0.009$, $r = 0.299$), uric acid ($p = 0.001$, $r = 0.378$), and total bilirubin ($p = 0.009$, $r = 0.298$).

Also between BMI with the lowest energy ($p = 0.040$, $r = -0.234$) and glucose levels ($p = 0.019$, $r = 0.266$) and uric acid ($p = 0.015$, $r = 0.277$).

As for magnesium related parameters, positive correlations were observed between the contribution of dietary magnesium and calcium intake ($p < 0.001$, $r = 0.498$), phosphorus ($p < 0.001$, $r = 0.580$) and plasma levels of prealbumin ($p = 0.035$, $r = -0.266$), along with a smaller waist / hip ratio ($p = 0.042$, $r = -0.235$).

Regarding magnesium levels in erythrocytes were obtained correlations between erythrocyte magnesium levels with triglycerides ($p = 0.011$, $r = 0.287$) and lower values of urea ($p = 0.017$, $r = -0.272$).

Discussion

The prevalence of overweight was found similar to that reported by other studies¹³⁻¹⁵, being similar in both age groups, however this situation has no relation to the average caloric intake of the diet study, which appears insufficient. This may be due, in addition to hormonal changes associated with menopause, which leads to increased weight, the age-related factors, since although the energy requirements decrease with age (about 5% per decade after age 40), women at this stage remains the same eating habits, to which we must add the low energy expenditure characteristic of this age^{9,20}.

Table II
Biochemical characteristics of the total sample and in different age group

Analyzed parameters	Total population Media \pm DS	Group 1 aged < 58 Media \pm DS	Group 2 aged \geq 58 Media \pm DS	Reference values
Glycemia (mg/dL)	92.1 \pm 15.9	87.4 \pm 12.3	97.4 \pm 17.8**	70-110 mg/dL
Creatinine (mg/dL)	0.69 \pm 0.13	0.67 \pm 0.08	0.70 \pm 0.16*	0.5-0.9 mg/dL
Urea (mg/dL)	34.5 \pm 9.08	32.2 \pm 8.02	37.2 \pm 9.6*	10-50 mg/dL
Uric acid (mg/dL)	4.4 \pm 1.07	4.1 \pm 0.8	4.7 \pm 1.2*	2.4-5.7 mg/dL
Triglycerides (mg/dL)	108.2 \pm 67.9	108.2 \pm 82.0	108.1 \pm 48.3	50-200 mg/dL
Cholesterol (mg/dL)	220.4 \pm 34.3	219.1 \pm 33.6	222.0 \pm 35.5	110-200 mg/dL
Transferrin (mg/dL)	280.2 \pm 45.8	278.9 \pm 43.1	281.8 \pm 50.0	200-360 mg/dL
Prealbumin	25.2 \pm 5.1	25.6 \pm 4.5	24.6 \pm 5.8*	20-40 mg/dL
Albumin (mg/dL)	4.4 \pm 0.2	4.5 \pm 0.2	4.4 \pm 0.1*	3.5-5.2 mg/dL
Total protein (g/dL)	7.1 \pm 0.5	7.1 \pm 0.5	7.0 \pm 0.5	6.6-8.7 mg/dL
Calcium (mg/dL)	9.2 \pm 0.4	9.1 \pm 0.4	9.2 \pm 0.5	8.6-10.2 mg/dL
Phosphorus (mg/dL)	3.5 \pm 0.5	3.4 \pm 0.5	3.6 \pm 0.4	2.7-4.5 mg/dL
Mg plasma (mg/dL)	1.8 \pm 0.2	1.8 \pm 0.2	1.8 \pm 0.2	1.7-2.6 mg/dL
Mg erythrocyte (mg/dL)	3.9 \pm 0.7	4.0 \pm 0.6	3.9 \pm 0.8	4.2-6.7 mg/dL

Significant differences between group 1 vs group 2: ** $p < 0.01$, * $p < 0.05$.

Regarding nutritional intake no significant differences, both groups showed similar values (fig. 1), except for magnesium intake is higher in the older group. Macronutrient intake in our population is similar to the results observed in other studies^{9,16}.

Consumption of total carbon hydrates is low, which would explain the results obtained energy intake, since women had intakes carbon hydrates significantly lower than recommended.

Fat intake is decreased but close to the recommendations, so it follows that these women are socially aware of the risk of diseases of overconsumption of them, probably due to having greater access to nutritional information and their level of education, although it would be wise to consider the quality of the fat, because as will be seen below, cholesterol levels are increased.

It is well documented that excessive intake of protein increases urinary excretion of calcio^{17,18} may have significant impact on the health of postmenopausal women presenting progressive bone loss, however, reciente¹⁹ study has shown that this excess protein in the diet does not affect bone status.

As for the intake of the major minerals involved in bone metabolism, our results show adaptation to nutritional needs in calcium and high in phosphorus, an important fact that must be taken into account, since

excessive drinking to be present in high percentage foods may decrease intestinal absorption of calcium and magnesium²⁰, affecting bone density.

Regarding magnesium intake, postmenopausal women have lower than recommended media in a high percentage, as can be seen in several studies^{21,16}, noting that women have higher age range increased intake of magnesium, possibly due to increased intake of foods rich in magnesium or greater energy intake.

In our study, insufficient intake of magnesium through diet corresponds to 36% of the sample (fig. 2), this group is quite large when you consider that the study was conducted in a developed area where supply and food availability is high.

Several authors have shown that magnesium deficiency in menopausal women was associated with an increased IMC^{22,9}. In our study, insufficient intake of magnesium is associated with increased waist/hip ratio, which could lead to a situation similar to those cited.

In our study, practically all biochemical values are within the normal range in both age groups, highlighting the plasma levels of prealbumin, located on the edge, correlated with intake of magnesium deficiency in our study. The plasma magnesium is one more readily available for use in its multiple functions, so these results may inform you to depletions prealbumin,

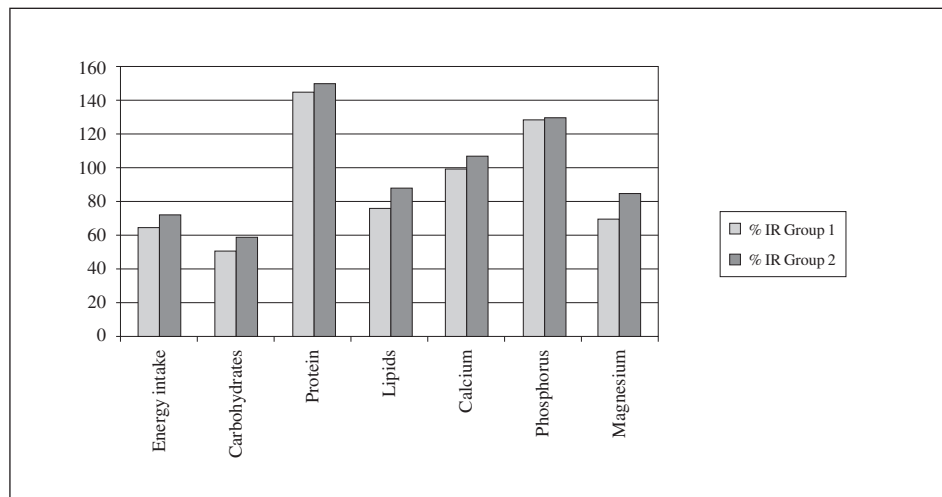


Fig. 1.—Percentage of intake of macronutrients and minerals in relation to the RDA in both age groups.

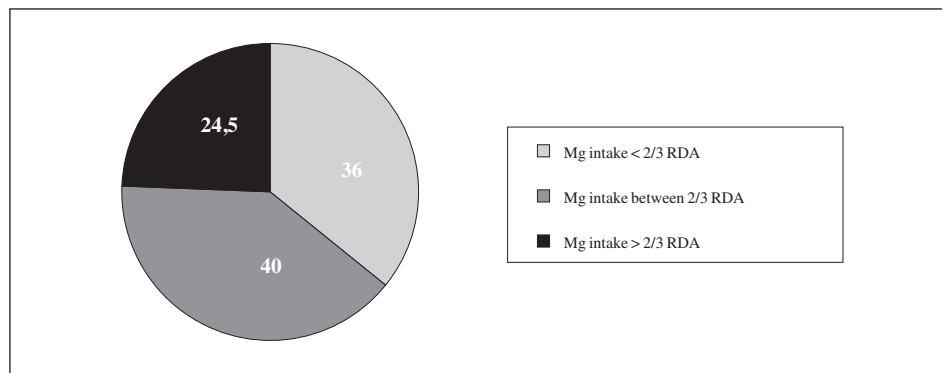


Fig. 2.—Percentage of intakes of magnesium in the total sample.

are released higher amounts of magnesium, for example to act in situations of increased oxidative stress which may occur in the postmenopausal stage.

Our results show that a high percentage of the sample (fig. 3) provides adequate levels of magnesium in plasma and approximately a third of the population has some blood magnesium levels below the reference value, similar results to those obtained by Laires et al (2004)¹⁶, so we can say that postmenopausal women in our study have a magnesium deficiency in erythrocyte considerably, probably due to insufficient intake of magnesium and deregulation of the factors controlling Mg homeostasis during menopause.

This decrease in erythrocyte magnesium levels possibly due to increased physiological demands at this stage of the woman, which leads to depletion in this compartment.

Considering the direct correlation between the Mg-erythrocyte and triglyceride levels, there appears to be direct cardiovascular risk in our women, but would have to take into account other lipid profiles such as cholesterol, high in our women, although this relationship may also be due to the involvement of both the insulin pathway. Other studies, such as that conducted by Farhangi et al (2011)²³, determined in a group of postmenopausal women no correlation between erythrocyte Mg and triglyceride levels.

Numerous studies have demonstrated that postmenopausal osteoporosis is often associated with a low dietary intake of magnesium and reducing Mg levels in the serum and bone^{24,25}. In our study we have not been able to assess whether magnesium deficiency may contribute to osteoporosis, but if we observe that body magnesium levels measured in plasma and erythrocyte are deficient in many cases and may be a risk factor for the occurrence of osteoporosis with higher incidence during this stage postmenopausal.

Conclusions

We conclude that at this menopausal stage is very important proper nutritional intake, both to maintain optimal levels of nutrients, such as to maintain a proper

body weight, so as to counteract the increased risk of several pathologies associated with this status. The data show that both age groups of women have low nutritional intake.

As for magnesium intake found in our population is insufficient in 36% of women, with a higher intake in women of upper age range, while plasma magnesium deficiency corresponds to 23% of the population, being in both groups of similar age and 72% of women have lower levels of magnesium in erythrocyte.

Our results confirm the need for control and monitoring of mineral status, particularly magnesium, given its functional spectrum and greater needs, in postmenopausal women. The high prevalence of deficiencies found in this element as essential to good health osteo –muscular, nervous, antioxidant, immune, etc., leads us to emphasize the importance of an intervention with nutrition education and healthy habits in this group as vulnerable because the inevitable suffering drastic changes at this age.

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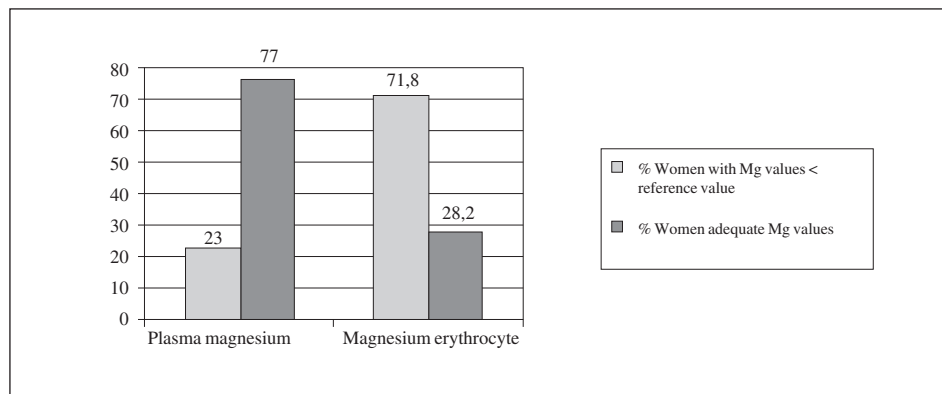


Fig. 3.—Percentage of population with magnesium values in plasma and erythrocytes appropriate and inappropriate.

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Original / *Valoración nutricional*

Evaluación del estado nutricional de estudiantes adolescentes de Extremadura basado en medidas antropométricas

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Resumen

Antecedentes y objetivos: Una correcta alimentación es uno de los pilares para un adecuado desarrollo corporal y un estado nutricional óptimo. Los métodos antropométricos son los más utilizados para el análisis de la composición corporal y constituyen una parte fundamental en la valoración del estado nutricional de individuos y poblaciones. Este estudio tiene como objetivo valorar el estado nutricional de adolescentes extremeños, determinar las variaciones en la composición corporal de acuerdo a los percentiles obtenidos, y proponer esos valores como referencia del estado nutricional de la población adolescente en Extremadura.

Material y Métodos: Se realizó un estudio transversal analítico en la Comunidad Extremeña, incluyendo un total de 816 estudiantes de Educación Secundaria Obligatoria y Bachillerato, de ambos sexos y de todas las edades que comprende la adolescencia. Los centros educativos seleccionados pertenecían a poblaciones de diferentes tamaños (de menos de 5.000 a más de 60.000 habitantes). A partir de las medidas tomadas, se determinaron distintos índices antropométricos y se hallaron los percentiles 3, 10, 25, 50, 75, 90, 95 y 97 del peso, la talla y la complexión.

Resultados y conclusiones: Se encontraron diferencias significativas en varios parámetros en función del sexo. Los chicos presentaban una mayor altura, peso y área muscular del brazo; por el contrario, el pliegue tricéptico y el área grasa del brazo fue mayor en las chicas. Al comparar con estudios nacionales, la altura media de nuestra población era inferior en unos 3 cm en ambos sexos. El peso fue similar, pero presentaban una mayor proporción de grasa en el brazo. Las chicas extremeñas parecen tener un crecimiento más rápido, alcanzando la altura definitiva a una edad más temprana que la media nacional; sin embargo, la talla final es menor a la media. Los chicos presentaban un crecimiento más continuado en todas las edades, con medias en altura similares a las nacionales.

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Palabras clave: *Antropometría. Composición corporal. Adolescentes. Percentiles. Estado nutricional.*

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NUTRITIONAL EVALUATION OF ADOLESCENT STUDENTS FROM EXTREMADURA BASED ON ANTHROPOMETRIC MEASUREMENTS

Abstract

Introduction and objectives: Nutrition is one of the pillars for proper body development and optimal nutritional status. Anthropometric methods are most commonly used for body composition analysis and are an essential part in the assessment of the nutritional status of individuals and population groups. This study aims to assess the nutritional status of adolescents from Extremadura (Spain); to determine variations in body composition according to the percentiles obtained; and to propose these values as a reference to the nutritional status of the adolescent population in Extremadura.

Material and methods: A cross sectional study in the community of Extremadura was performed, including a total of 816 students of Secondary School Education of both sexes; and of all ages in the adolescence stage. The selected secondary schools belonged to populations of different sizes (less than 5,000 to more than 60,000 inhabitants). From the measurements taken, different anthropometric indices were determined and the percentiles 3, 10, 25, 50, 75, 90, 95 and 97 for weight, height and complexion were found.

Results and conclusions: There were significant gender differences for height, weight, triceps skinfold, arm muscle area and arm fat area. Boys showed greater figures for height, weight and arm muscle area; however, the triceps skinfold and arm fat area was higher in girls. When compared to other national studies, the average height of our population was lower by about 3 cm in both sexes; the average weight was similar, but our adolescents had a higher proportion of fat in the arm. Extremadura girls seem to have a faster growth, reaching final height at an earlier age than the national average, although this height is below average. The boys had a continuous growth in all ages, maintaining national averages.

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Keywords: *Anthropometry. Body composition. Adolescents. Percentiles. Nutritional status.*

Introducción

En los últimos años la sociedad española está sufriendo una evolución notable en los hábitos alimentarios de los ciudadanos como consecuencia del impacto de los nuevos estilos de vida que han condicionado la organización familiar. La adquisición de unos patrones dietéticos adecuados puede ser vital en la edad escolar para conseguir un crecimiento y estado de salud óptimos¹. Esto ha hecho que, desde el punto de vista institucional tanto a nivel nacional como regional, se hayan llevado a cabo diferentes iniciativas, para potenciar un adecuado estado de salud en las personas, como el llevado a cabo por la Agencia Española de Seguridad Alimentaria y Nutrición (AESAN) en 2010 o, en Extremadura, con el desarrollo de la Ley 10/2001 de 28 de junio de Salud de Extremadura. El estudio de los aspectos relacionados con la valoración del estado nutricional de un individuo o colectividad nos permite obtener datos de gran utilidad para la estimación del nivel de salud y bienestar de la población². Mediante la evaluación del estado nutricional se pueden detectar de forma temprana y sistemática los grupos de pacientes con riesgo de malnutrición, tanto por exceso como por defecto; establecer los valores basales para controlar la eficacia de diferentes regímenes dietéticos; y desarrollar programas de salud y nutrición adecuados³. Para su evaluación se pueden emplear diferentes parámetros, como los antropométricos, dietéticos y de actividad física. Para una valoración nutricional, los métodos más empleados son los antropométricos, por su simplicidad de uso y bajo coste^{4,6}. Estos pueden clasificarse en dos grupos; aquellos que nos permiten realizar una valoración de la masa global del cuerpo, como el peso y la talla; y aquellos que evalúan el compartimento muscular y graso, entre los que se incluyen el perímetro braquial y los pliegues cutáneos⁷.

Uno de los grupos de mayor interés para realizar estudios nutricionales es la población adolescente. La adolescencia es un período crucial en el proceso de desarrollo que se caracteriza por un crecimiento y maduración tanto desde el punto de vista somático como psicológico. La nutrición en esta etapa desempeña un gran papel para este proceso. Todos los cambios morfológicos y funcionales (incremento de la velocidad de crecimiento longitudinal, incremento de depósito de tejido graso, maduración sexual, etc.) necesitan una mayor demanda energética y de nutrientes para producirse de forma adecuada. Asimismo, durante la adolescencia se dan cambios psicológicos que llevan a una modificación en la conducta emocional y social, que puede influir en las variaciones de las preferencias y aversiones alimenticias de los adolescentes y, por tanto, en sus hábitos alimentarios⁸. Aunque todos esos cambios que se producen en el adolescentes dificultan su descripción, en los países occidentales los estudios de alimentación y antropometría nutricional tienen una especial relevancia desde diversas perspectivas, incluida la de la epidemiología nutricional^{4,9-12}.

Aunque se han realizado estudios de la composición corporal, si exceptuamos el estudio de Córdoba y cols.¹³, realizado con escolares de la ESO de la ciudad de Badajoz (Extremadura), el resto de estudios no aportan datos de la población extremeña, sino que corresponden a otras regiones, o incluso a países diferentes. Se echa en falta, por ello, un estudio en el que se analice el estado nutricional de escolares de la Comunidad Autónoma de Extremadura. Con el presente trabajo se pretende describir y evaluar el estado nutricional de un amplio grupo de adolescentes extremeños distribuidos por poblaciones de distintos tamaños mediante el análisis de las características antropométricas. Los resultados obtenidos nos permitirían aportar datos referenciales para su utilización en estudios nutricionales en esta Comunidad Autónoma.

Material y métodos

Muestra Poblacional

Se obtuvo una muestra poblacional de 816 adolescentes durante el curso escolar 2009/2010, 450 chicas y 366 chicos, con edades comprendidas entre los 13 y 18 años de edad. De ellos, 529 estudiantes cursaban 2º de ESO (Educación Secundaria Obligatoria) y 287 cursaban 1º de Bachillerato. Los estudiantes procedían de un total de 23 Centros de Educación Secundaria, 17 centros públicos y 6 privados/concertados de poblaciones de toda Extremadura. Asimismo se tuvo en cuenta el tamaño de la población de procedencia, escogiéndose desde poblaciones rurales, de menos de 5.000 habitantes, a poblaciones urbanas (con más de 60.000 habitantes). Con ello se pretendió asegurar la heterogeneidad y representatividad de la muestra, así como la validez del estudio para toda la población adolescente extremeña.

Recogida de datos y material

A cada sujeto de la muestra se le determinaron las medidas antropométricas: talla, peso, perímetro braquial, perímetro del antebrazo, pliegue cutáneo tricipital (PT) y circunferencia de la muñeca. A partir de esas medidas, y mediante la aplicación de las correspondientes fórmulas¹⁴ se obtuvieron el área braquial, área muscular braquial, área grasa braquial y complexión. Todas las medidas se tomaron por triplicado utilizando material antropométrico homologado y siguiendo la metodología recomendada por el IBP (Programa Internacional de Biología)¹⁵.

- *Talla*: se realizó la medida de cada individuo con un tallímetro SECA (Ltd., Birmingham, England) con escala métrica desmontable de dos secciones y una longitud de 2.300 mm (precisión de 1 mm).

- *Peso*: se tomaron las medidas de cada uno de los estudiantes con una balanza TEFAL (Bodysignal) con un peso máximo de 160 kg y una precisión de 100 g.
- *Circunferencia de la muñeca y Perímetro del brazo y antebrazo*: se midieron con una cinta métrica flexible, no elástica, con un espacio sin graduar antes del cero, precisión de 1mm y con una anchura de 1 cm y longitud de 200 cm.
- *Pliegue cutáneo tricipital (PT)*: se midió el pliegue de la cara posterior del brazo no dominante, a nivel mesobraquial, con un lipocalibre o adipómetro digital.

Determinación de índices indirectos

Para los índices indirectos se calcularon el Área del brazo (Circunferencia del brazo² (mm)/12,56); el Área Muscular del brazo (Circunferencia del brazo (mm) – 3,14*Pliegue tricipital (mm))²/12,56); Área Grasa Brazo (Área del brazo-Área Muscular del brazo) y Complejión (Talla (cm)/circunferencia muñeca (cm)).

Tratamiento de los datos y análisis estadístico

Los datos fueron procesados con el paquete estadístico SPSS v. 19.0, realizándose un análisis descriptivo e inferencial. Se consideraron significativas aquellas diferencias cuya probabilidad fue inferior al 5% (p < 0,05), utilizando un análisis de varianza (ANOVA), siguiendo los procedimientos de una vía y realizando un test de comparación de medias por el método Tukey. Se obtuvieron las medias aritméticas y desviaciones es-

tándares de cada uno de los datos investigados, además de distintos percentiles entre 3-97 para la talla, peso y complejión por género y edad.

Resultados y discusión

Análisis del estado nutricional de adolescentes extremeños

En la tabla I se muestran el tamaño de la muestra, los resultados medios y la desviación estándar de las distintas medidas antropométricas de la población de adolescentes estudiada. Al analizar las edades medias de la población de niñas y niños no se encontraron diferencias significativas de edad; por tanto, las diferencias encontradas en las medidas antropométricas fueron debidas al sexo. En cuanto a la talla media y el peso, puede observarse que son significativamente mayores en niños que en niñas. Resultados similares se obtuvieron en el estudio piloto AVENA realizado por González-Gross y cols.¹⁶ para adolescentes españoles. La media de altura de nuestra población, tanto en niños como en niñas, es 3 cm inferior que la del estudio nacional realizado por Carrascosa y cols.¹⁷ sobre españoles en edad de crecimiento; por el contrario, el peso medio de nuestros estudiantes fue similar al de dicho estudio, no observándose diferencias en función del sexo. En lo que respecta a la circunferencia del brazo, como se muestra en la tabla I, no encontramos diferencias significativas entre chicas y chicos. Mientras que sí encontramos diferencias significativas entre chicos y chicas en lo que respecta al pliegue tricipital y el área grasa del brazo mayor en la población femenina. Con respecto al área

Tabla I
Descripción de la población adolescente del estudio por sexo

	Chicas (n = 450) (x ± DS)	Chicos (n = 366) (x ± DS)	p
Edad	15,22 ± 1,61	15,17 ± 1,52	0,610
Talla (m)	1,59 ± 0,06	1,66 ± 0,09	0,000
Peso (kg)	56,70 ± 11,44	61,68 ± 13,90	0,000
Circunferencia del brazo (cm)	25,64 ± 3,31	25,90 ± 3,45	0,270
Área Brazo (cm ²)	53,20 ± 14,14	54,35 ± 14,97	0,259
Área Muscular brazo (cm ²)	25,94 ± 7,45	31,07 ± 10,06	0,000
Área Grasa brazo (cm ²)	27,25 ± 9,60	23,27 ± 9,59	0,000
Circunferencia del antebrazo (cm)	22,42 ± 2,06	23,79 ± 2,28	0,000
Pliegue cutáneo tricipital (mm)	24,68 ± 6,62	20,33 ± 7,22	0,000
Complejión (cm)	10,63 ± 0,71	10,31 ± 0,57	0,000
Circunferencia de la muñeca (cm)	15,06 ± 1,20	16,17 ± 1,04	0,000

Los datos se presentan como la Media (x) ± DS (Desviación estándar). p<0,01 denota diferencias altamente significativas entre géneros.

muscular del brazo, también se encontraron diferencias significativas en función del sexo, siendo la media de los chicos superior, presentando por tanto un mayor porcentaje de músculo que las chicas estudiadas.

En la tabla II se muestran los valores medios, desviación estándar, tamaño de la muestra de las distintas medidas antropométricas de la población en función de la edad y sexo. Respecto a la talla, en las adolescentes extremeñas se observan diferencias significativas para el rango de edad estudiado, correspondiendo los menores valores a los 13 años. Comparando con el estudio a nivel nacional de Carrascosa y cols.¹⁷, a los 13 años, las adolescentes extremeñas tenían una talla mayor, pero para el resto de las edades la talla fue entre 1,5-3,5 cm inferior en todos los casos. Estos resultados parecen indicar que nuestras adolescentes alcanzarían su altura definitiva a una edad más temprana que la media nacional; a pesar de ello, la talla final sería menor a la media nacional.

Se encontraron diferencias significativas en el peso de las niñas para los rangos de edad estudiados, encontrándose el peso más bajo a los 13 años. Si se comparan los valores con los de Carrascosa y cols.¹⁷, obtenidos a nivel nacional, las chicas extremeñas tuvieron medias superiores entre 0,5 y 3 kg desde los 13 a los 18 años; las mayores diferencias entre ambas poblaciones se encontraron entre los 13 y los 15 años. Estos resultados, unidos a los de la altura, parecen indicar que las chicas extremeñas alcanzan el pico de crecimiento rápido de-

bido a la adolescencia antes y muestran un peso y talla más alto y constante en las edades estudiadas, más similar al mayor peso de la edad adulta, viéndose que a partir de los 15 años la media se estabiliza en torno a 59,5 kg. Esto explicaría que las adolescentes extremeñas tuvieran menos diferencias con respecto al estudio nacional a la edad de 16, 17 y 18 años, cuando alcanzan su desarrollo. No hubo diferencias en el pliegue tricótipal en las chicas de los 13 a los 18 años. El índice antropométrico área muscular del brazo mostró diferencias significativas en el rango estudiado, siendo las chicas de 15 años las que tuvieron el valor mayor. En cuanto al área del brazo y área grasa del brazo, tampoco hubo diferencias significativas entre las distintas edades pero fue el grupo de 15 años el de valores más altos. Los mayores valores de los parámetros anteriores se reflejan en el parámetro circunferencia del brazo; aunque no se encontraron diferencias significativas en el rango estudiado, las chicas de 15 años fueron las que tuvieron un valor más alto.

Los chicos extremeños presentaban diferencias significativas en la altura a las diferentes edades estudiadas, siendo los de menor estatura los de 13 años y los más altos los de 18. Al comparar las medias de la talla por edad con las nacionales¹⁷, los adolescentes extremeños muestran una media de 2-3 cm superior a los 13, 16 y 18 años, similar a los 14 años, e inferior a la media nacional a los 15 y 17 años. Con respecto al peso, también hubo diferencias significativas en el rango de edad

Tabla II
Descripción de la población adolescente del estudio por estratos de edades

	13 años (n = 269) (x ± DS)	14 años (n = 181) (x ± DS)	15 años (n = 67) (x ± DS)	16 años (n = 160) (x ± DS)	17 años (n = 99) (x ± DS)	18 años (n = 40) (x ± DS)	p
CHICAS							
Edad	13,62 ± 0,24	14,32 ± 0,27	15,45 ± 0,31	16,66 ± 0,24	17,31 ± 0,25	18,19 ± 0,21	0,000
Talla (m)	1,57 ± 0,06 a	1,59 ± 0,06 ab	1,59 ± 0,05 ab	1,61 ± 0,06 b	1,61 ± 0,07 b	1,61 ± 0,06 ab	0,000
Peso (kg)	54,64 ± 11,37 a	55,93 ± 10,84 ab	59,52 ± 14,57 b	58,94 ± 11,71 ab	59,45 ± 9,42 ab	59,50 ± 12,21 b	0,010
Circunferencia del brazo (cm)	25,17 ± 3,24 a	25,37 ± 3,15 a	26,82 ± 4,76 a	25,88 ± 3,13 a	26,07 ± 2,73 a	26,45 ± 3,99 a	0,074
Área Brazo (cm ²)	51,27 ± 13,57 a	52,02 ± 12,92 a	59,01 ± 22,02 a	54,09 ± 13,44 a	54,69 ± 11,60 a	56,93 ± 17,71 a	0,058
Área Muscular brazo (cm ²)	25,11 ± 7,00 ab	24,93 ± 6,11 a	29,23 ± 11,71 b	26,39 ± 7,04 ab	26,49 ± 5,80 ab	28,59 ± 11,91 ab	0,029
Área Grasa brazo (cm ²)	26,15 ± 9,54 a	27,09 ± 9,04 a	29,79 ± 13,20 a	27,70 ± 8,95 a	28,20 ± 8,74 a	28,34 ± 11,99 a	0,426
Circunferencia del antebrazo (cm)	22,11 ± 1,95 a	22,47 ± 2,02 a	23,07 ± 2,87 a	22,46 ± 1,92 a	22,74 ± 1,83 a	22,81 ± 2,46 a	0,122
Pliegue cutáneo tricótipal (mm)	24,10 ± 6,75 a	24,86 ± 6,40 a	25,35 ± 7,97 a	24,91 ± 6,05 a	25,24 ± 6,33 a	24,83 ± 8,13 a	0,842
Complejión (cm)	10,50 ± 0,80 ab	10,60 ± 0,58 ab	10,22 ± 1,04 a	10,85 ± 0,62 b	10,75 ± 0,49 b	10,80 ± 0,60 b	0,000
CHICOS							
Edad	13,65 ± 0,24	14,37 ± 0,31	15,38 ± 0,28	16,54 ± 0,26	17,39 ± 0,32	18,38 ± 0,28	0,000
Talla (m)	1,60 ± 0,09 a	1,64 ± 0,08 ab	1,68 ± 0,07 ab	1,73 ± 0,06 ab	1,72 ± 0,06 ab	1,78 ± 0,06 b	0,000
Peso (kg)	55,62 ± 11,70 a	59,22 ± 13,22 ab	61,92 ± 14,20 abc	69,67 ± 13,85 cd	66,20 ± 11,51 bc	74,33 ± 11,87 d	0,000
Circunferencia del brazo (cm)	24,90 ± 3,26 a	25,41 ± 3,17 ab	25,74 ± 4,04 ab	27,50 ± 3,39 bc	26,47 ± 2,89 abc	28,34 ± 3,20 c	0,000
Área Brazo (cm ²)	50,22 ± 13,28 a	52,21 ± 13,43 ab	54,00 ± 18,66 ab	61,10 ± 15,44 bc	56,44 ± 12,84 abc	64,73 ± 15,05 b	0,000
Área Muscular brazo (cm ²)	27,30 ± 7,28 a	28,91 ± 7,44 ab	33,54 ± 12,01 b	34,60 ± 10,64 b	33,65 ± 12,01 b	42,92 ± 10,42 c	0,000
Área Grasa brazo (cm ²)	22,91 ± 9,02 ab	23,30 ± 9,50 ab	20,46 ± 9,50 a	26,50 ± 11,36 b	22,78 ± 8,36 ab	21,80 ± 7,78 ab	0,047
Circunferencia del antebrazo (cm)	22,84 ± 2,26 a	23,49 ± 2,18 ab	23,73 ± 2,26 abc	25,01 ± 1,93 cd	24,50 ± 1,83 bcd	25,57 ± 1,80 d	0,000
Pliegue cutáneo tricótipal (mm)	20,88 ± 6,72 ab	20,77 ± 7,05 ab	17,39 ± 6,41 a	21,94 ± 8,56 b	19,80 ± 7,27 ab	16,81 ± 5,01 a	0,010
Complejión (cm)	10,15 ± 0,57 a	10,18 ± 0,53 a	10,35 ± 0,61 ab	10,47 ± 0,50 abc	10,63 ± 0,53 bc	10,71 ± 0,47 c	0,000

Los datos se presentan como la Media ± Desviación estándar (x ± DS). p denota diferencias significativas entre estratos de edades. El número de alumnos estudiados de 13 años es 269 (156 y 103), 181 de 14 años (91 y 90), 67 de 15 años (26 y 41), 160 de 16 años (98 y 62), 99 de 17 años (55 y 44), y 40 de 18 años (24 y 16).

estudiado, a diferencia de lo que se observaba en las chicas, en estos no se encontró una relación con la edad, ya que a los 13 años hay una diferencia de 5,3 kg y de 4 kg a los 16 y 18 años con respecto a los estudios nacionales¹⁷; en todas las edades la media de peso es superior en los adolescentes extremeños excepto la de 15 años que presenta un valor similar. La circunferencia del brazo mostró diferencias significativas, observándose los valores más altos a los 16 y 18 años. Los valores encontrados en los chicos de 14, 15, 16 y 17 años no mostraron diferencias significativas entre ellos. En el área muscular del brazo se encontraron diferencias significativas entre las edades estudiadas, siendo el menor valor en los chicos de 13 y el mayor en los de 18. Los primeros no mostraron diferencias significativas con respecto al grupo de 14 años, y este último tampoco mostró diferencias con los de 15, 16 y 17.

El pliegue tricaptal y el área grasa del brazo, indicadores de la grasa del brazo, también mostraron diferencias significativas. Para el área grasa del brazo y pliegue tricaptal hay que destacar las diferencias significativas encontradas a la edad de 16 años, mostrando valores superiores al resto de edades. Encontramos los valores más bajos a los 15 y 18 años y, por el contrario, a los 13 y 16 años presentaban la mayor proporción de grasa en brazo, aunque las diferencias significativas sólo fueron apreciables para el grupo de 16 años. Suele haber una relación inversamente proporcional entre la cantidad de grasa y la de músculo; en nuestro estudio, esta relación se ve más clara a la edad de 18 años, donde observamos los valores de mayor área muscular del brazo y los de menor pliegue tricaptal.

En la tabla II se muestra asimismo la complejión media de los alumnos participantes en el estudio; este índice de complejión corporal o constitución corporal (*r*) permite clasificar cada persona como de complejión pequeña (> 10,4 en hombre y > 11 en mujer), mediana (entre 9,6-10,4 en hombre; y de 10,1-11 en mujer) o grande (< 9,6 en hombre y < 10,1 en mujer)¹⁸. Si comparamos nuestros valores con los de referencia del valor *r*, se puede considerar que, de media, ambos sexos presentan una complejión mediana. Según los datos obtenidos, la mayoría de los alumnos (un 45,52%) presentaron una complejión mediana, seguido de un 43,63% que tenían complejión pequeña; y sólo un 10,84% presentaron una complejión grande. En el caso de las chicas, el 51,42% eran de complejión mediana, seguido de un 28,0% de complejión pequeña y de un 20,57% de complejión grande. Estos resultados contrastan con los obtenidos por Jiménez y cols.¹² con alumnos de 14 a 20 años de México D.F., en el que la mayoría de los alumnos (el 78,25%) eran de complejión pequeña, mientras que el 20,58% tenían una complejión mediana y el 1,16% grande. Por otra parte, al analizar la complejión de nuestros adolescentes por edades (tabla II), se observaron diferencias dependiendo del sexo. Las chicas presentaban una complejión mediana a todas las edades estudiadas; mientras que la de los chicos fue mediana hasta los 15 años y pequeña a

partir de esa edad. Estos resultados complementan lo indicado anteriormente para la talla, demostrando que el tamaño corporal de nuestros alumnos es menor al esperado, especialmente a partir de los 15 años; sin embargo, en las chicas esto no queda tan patente, al no haber diferencias en la complejión. En lo que respecta a la circunferencia de la muñeca, no observamos diferencias en función de la edad, encontrándose valores similares en alumnas de 13 a 18 años (datos no mostrados); esto contrasta con los resultados de Sánchez¹⁹ con un grupo de alumnas de 12 a 16 años, que muestran una estabilización de la circunferencia de la muñeca a partir de los 14 años. Por el contrario, en el caso de los chicos, hubo diferencias entre los de 13 años, con los menores valores para ese parámetro (15,83 cm), y los de 16 y 18 años (16,53 y 16,64 cm respectivamente), lo que muestra una cierta evolución en el tamaño corporal, tal y como se ha indicado para la complejión. Sin embargo, este no parece ser el parámetro más adecuado para determinar la evolución del tamaño corporal de los adolescentes.

Comparación en base a los percentiles de la población de adolescentes extremeños con otras poblaciones

Comparando los pesos y las alturas medias (tabla I) de los adolescentes extremeños con los percentiles elaborados por Carrascosa y cols.¹⁷ con datos de la población española, ambos sexos se encontraban dentro del mismo percentil para esos dos parámetros. El valor medio de peso se situó en el percentil 50 y la altura entre el percentil 25 y 50; según los datos tabulados por estos autores, la talla de nuestra población estaría por debajo de la media nacional. Nuestros valores se situarían en esos mismos percentiles al comparar con las tablas de Frisancho²⁰, que obtuvieron una altura media de 1,70 m en niños y de 1,63 m en niñas de esa edad. En relación al peso, la media obtenida por estos autores coincide tanto en chicos como en chicas con la de la población extremeña. Comparando con el estudio de López de Lara y cols.²¹ con chicos de Madrid, los percentiles de peso tanto en chicos como chicas coinciden con los valores anteriores; por el contrario, la altura de los chicos estaría en el percentil 20 y cercana al 50 en las chicas. En lo que respecta a la circunferencia del brazo, nuestros adolescentes de ambos sexos se encuadrarían en el percentil 75, siguiendo a Hernández y Sastre²²; mientras que si se siguen las tablas de Alastrué y cols.²³, las chicas se situarían entre los percentiles 50-75 y los chicos en torno a 25-50. Empleando las tablas de diferentes autores, el valor medio del pliegue tricaptal de nuestra población es bastante superior al percentil 50; entre el 75-90 en ambos sexos²⁴, o por encima del percentil 90²²; esto indicaría una mayor proporción de grasa en esta localización del brazo en la población extremeña estudiada. Por lo que se refiere al área muscular del brazo, al comparar con los resultados de Alastrué y cols.²⁵ y te-

niendo en cuenta la edad, nuestros valores se encuentran por debajo de la media de la población española, situándose entre el percentil 10-25 y el 5-10 en chicas y chicos, respectivamente.

Observando los valores medios de las chicas por edades (tabla II), la talla en todo el rango de edad estudiado se encuadró en los mismos percentiles de los estudios de la población española elaborados por Carrascosa y cols.¹⁷ y López de Lara y cols.²¹, situándose los valores medios a esas edades entre el percentil 25-50 con respecto a ambos estudios. El peso se comportó igual para todas las edades al compararlo con el estudio de población española de Carrascosa y cols.¹⁷, situándose entre el percentil 50-75. Al comparar con la población de López de Lara y cols.²¹, el peso de las adolescentes extremeñas se encuentra en el percentil 50-75 para las de 13, 14 y 16 años, y en el 75-80 para las de 15, 17 y 18 años. En el caso de la circunferencia del brazo, nuestros adolescentes se encuentran siempre entre los percentiles 75-90, si se sigue a Hernández y Sastre²². Si comparamos con el estudio a nivel nacional de Alastrué y cols.²⁵ para el rango de 16-18 años, nuestros valores se encuadran en percentiles más bajos, entre el 50 y 75. Los valores de pliegue tripital de la población extremeña se encontrarían siempre por encima del percentil 90 obtenido por Alastrué y cols.²⁵ y por Hernández²⁶, siendo especialmente significativo a los 15, 17 y 18 años donde los valores se encuadran entre el 90 y 97²⁵. El índice antropométrico área muscular del brazo mostró, en el caso de las niñas, diferencias significativas en el rango estudiado. Comparando los datos de la población extremeña con los de Alastrué y cols.²³, se observó que para la mayoría de las edades estudiadas, las medias se encuadraban entre el percentil 20-25, no superando en ningún caso el percentil 50. Estos datos, junto a los del pliegue tripital, parecen indicar que las

adolescentes extremeñas presentan una mayor proporción de grasa y una menor masa muscular en brazos que las adolescentes nacionales. Esto puede estar relacionado con el tipo de alimentación, o con una menor actividad física realizada por las chicas.

Al analizar la talla de los chicos por edades (tabla II) y compararla con los percentiles, se observó que los chicos de todas las edades estaban entre el percentil 50 y 75; solamente los chicos de 17 años estarían situados en el percentil 25. En cuanto al peso, al compararlo con los datos percentilados de otros estudios de la población española (Carrascosa y cols.¹⁷; López de Lara y cols.²¹), el peso en todas las edades se encuentra entre el percentil 50 y el 75, con excepción de los de 17 años, que se encuentra entre 25 y 50. Comparando los valores medios de la circunferencia del brazo con los percentiles descritos por Hernández y Sastre²², estos se encuadran entre el percentil 75-90 para todas las edades estudiadas, exceptuando los chicos de 17 años que están situados en el percentil 50-75. Por su parte, los valores medios del área muscular del brazo corresponden, según las tablas de Alastrué y cols.²³, para la mayoría de las edades, a los percentiles 10-25, excepto a los 13 años que se sitúa entre 25-50. Esto muestra que la musculatura de los brazos de los chicos extremeños estaría por debajo de los valores de estos autores. Con respecto al pliegue tripital, comparando los valores medios por edad con los percentiles descritos por Hernández²⁶, a los 13, 14 y 16 años mostraron valores comprendidos en el percentil 90-97, a los 15 años se situarían en el percentil 90, y los de 17 y 18 años tuvieron una menor cantidad de grasa, situándose entre los percentiles 75-90.

En la tabla III se muestran los valores medios, desviación estándar y percentiles de la talla de la población de adolescentes estudiada por edad y sexo. Para su realización se han analizado los índices antropométricos de la talla, el peso y la complexión, hallando los percentiles 3,

Tabla III
Valores medios, desviación estándar y percentiles de la talla (cm) por sexo y edad

	Media	Desviación estándar	Percentil								
			3	5	10	25	50	75	90	95	97
Chicas											
13 años	1,57	0,06	1,45	1,47	1,50	1,54	1,58	1,62	1,66	1,67	1,68
14 años	1,59	0,06	1,49	1,50	1,52	1,55	1,59	1,63	1,67	1,68	1,70
15 años	1,59	0,05	1,51	1,52	1,53	1,56	1,60	1,63	1,64	1,65	1,66
16 años	1,61	0,06	1,50	1,50	1,53	1,58	1,62	1,65	1,67	1,70	1,72
17 años	1,61	0,07	1,49	1,51	1,52	1,57	1,61	1,66	1,68	1,70	1,72
18 años	1,61	0,06	1,51	1,54	1,54	1,56	1,60	1,65	1,68	1,69	1,70
Chicos											
13 años	1,60	0,09	1,43	1,44	1,49	1,55	1,61	1,67	1,71	1,73	1,75
14 años	1,64	0,08	1,48	1,51	1,54	1,59	1,65	1,71	1,74	1,76	1,77
15 años	1,68	0,07	1,57	1,58	1,59	1,63	1,67	1,73	1,78	1,78	1,82
16 años	1,73	0,06	1,63	1,64	1,65	1,69	1,72	1,77	1,82	1,84	1,85
17 años	1,72	0,06	1,59	1,61	1,66	1,68	1,73	1,76	1,78	1,80	1,82
18 años	1,78	0,06	1,66	1,70	1,73	1,74	1,80	1,82	1,85	1,86	1,86

5, 10, 25, 50, 75, 90, 95 y 97. En el caso de las chicas, se observa que la mayoría de los valores de los percentiles son menores que los de referencia, tanto en los percentiles estudiados como para todas las edades estudiadas. Hay una mayor diferencia entre nuestra población y la de Madrid²², siendo los valores más parecidos a los del estudio nacional (Carrascosa y cols.¹⁷). Las mayores diferencias se observan con los valores del percentil 97, donde las tallas a los 15 y 18 años son 9 cm inferior para este percentil con respecto a los estudios de Carrascosa y cols.¹⁷ y López de Lara y cols.²¹. En general, las diferencias son de 2-5 cm para los percentiles 3, 25, 50 y 75, siendo los percentiles 90 y 97 los que mostraron mayores diferencias para todas las edades estudiadas. Comparando con los datos del estudio con adolescentes de Navarra²⁷, las chicas extremeñas miden 2 cm menos en todos los percentiles y en la media a la edad de 14 años. Por su parte, los adolescentes norteamericanos presentaban tallas superiores respecto a los de nuestro estudio²⁸.

Analizando los percentiles para cada una de esas edades, y comparándolos con los datos obtenidos a nivel nacional y en la Comunidad de Madrid^{17,21}, se observa que los percentiles de nuestra población son de 2 a 4 cm más elevados para la edad de 13 años²². Los adolescentes extremeños con valores más bajos fueron los de 15 y 17 años, hallándose las mayores diferencias (de hasta 5-6 cm), en los percentiles más altos (75, 90 y 97), siendo por lo general las diferencias con la población madrileña mayores que con los que comparamos con el estudio a nivel nacional¹⁷. Por el contrario, al comparar los valores obtenidos para las edades de 16 y 18 años con el estudio de adolescentes madrileños, los extremeños resultaron ser más altos en todos los percentiles estudiados menos en el 97. La mayoría de los percentiles resultaron ser más altos en el estudio nacional¹⁷, exceptuando los percentiles 50 y 75 de los chicos de 18 años y el percentil 3 de los de

16. Cuando comparamos nuestro estudio con los adolescentes de 14 años de Navarra²⁷, para los percentiles 10, 25 y 50 apenas hubo una diferencia de 1 cm, mientras que en los percentiles extremos (3 y 97), los navarros eran 3-4 cm más altos que los extremeños de 14 años. Sin embargo López de Lara y cols.²¹, comparando los datos de su estudio, realizado en Madrid, con el realizado a nivel nacional, afirmaban que el patrón antropométrico en España era similar, al no encontrar diferencias con los patrones de Andalucía, Aragón, Cataluña, País Vasco y Madrid.

En la tabla IV se muestran los valores medios, desviación estándar y percentiles del peso de la población de adolescentes por edad y sexo. Comparados con los obtenidos por Kuczmarski y cols.²⁸ para adolescentes estadounidenses, observamos que los valores del peso son menores que en nuestro estudio. En el caso de las adolescentes, comparando las medias con las obtenidas en el estudio nacional para esos mismos rangos de edad¹⁷. Analizando los valores representados por los percentiles, las adolescentes extremeñas tienden a tener un mayor peso para cada uno de los percentiles. También observamos que las mayores diferencias se encuentran a partir del percentil 75; esto indica que hay más chicas con peso alto en la población extremeña que en las otras poblaciones, siendo los percentiles 90 y 97 en los que se encontraron las mayores diferencias, incluso superiores a los 16 kg para el mismo percentil de la población madrileña. Por lo general también las diferencias son mayores con esta población que con el estudio nacional, por lo que se podría decir que las adolescentes de la Comunidad de Madrid tienen una mayor diferencia de peso con las extremeñas que con respecto al estudio nacional. En el estudio realizado en adolescentes de Navarra por Durá y cols.²⁷, las chicas extremeñas de 14 años mostraron hasta el percentil 50 mayores pesos que las mostradas por esta

Tabla IV
Valores medios, desviación estándar y percentiles del peso (kg) por sexo y edad

	Media	Desviación estándar	Percentil								
			3	5	10	25	50	75	90	95	97
Chicas											
13 años	54,64	11,37	37,17	38,55	40,60	46,88	52,40	60,58	68,95	77,600	81,97
14 años	55,93	10,84	39,02	41,50	44,50	48,50	53,50	62,35	67,90	77,70	79,97
15 años	59,52	14,57	40,88	42,08	43,95	49,28	58,15	65,95	77,40	84,98	89,43
16 años	58,94	11,71	45,05	46,29	47,77	51,35	56,25	63,15	74,99	79,26	87,23
17 años	59,45	9,42	47,49	47,74	48,78	52,80	57,10	64,70	74,70	76,59	78,28
18 años	59,50	12,21	44,93	46,25	46,86	52,25	56,65	62,75	77,42	85,56	87,38
Chicos											
13 años	55,62	11,70	35,69	37,54	41,46	46,50	54,40	63,50	68,92	75,70	79,08
14 años	59,22	13,22	41,31	44,18	45,30	50,45	55,55	67,03	72,37	81,27	85,95
15 años	61,92	14,20	41,18	43,10	48,00	52,70	59,70	66,60	76,30	85,60	95,68
16 años	69,67	23,43	51,16	51,59	56,63	59,83	64,90	78,33	89,03	95,77	98,05
17 años	66,20	11,21	50,08	51,15	53,44	57,98	63,35	72,80	80,97	83,08	87,25
18 años	74,33	11,87	58,61	59,15	59,95	64,08	75,40	83,43	87,05	90,85	92,95

población. Sin embargo, en los percentiles más altos de 90 y 97 las chicas de Navarra superan los pesos de las adolescentes extremeñas hasta en 5 kg. La media de la población para esta edad fue superior en la población extremeña con 55,93 de media frente a los 54,14 de las chicas de Navarra.

En los chicos las diferencias están repartidas de igual modo en todo el rango de edad, a diferencia de lo observado en las chicas, en las que las mayores diferencias se encuentran a edades más tempranas. El comportamiento de los percentiles para este rango de edad es similar al descrito en el de las chicas, encontrándose las mayores diferencias en el percentil 97, con valores de hasta 15 kg por encima de los obtenidos en otras poblaciones. Comparándolo con los adolescentes navarros del estudio de Durá y cols.²⁷, el comportamiento fue más homogéneo, ya que tanto la media de ambas poblaciones, 59,22 (Extremadura) y 59,15 (Navarra), como los percentiles del 3 al 25 fueron iguales. Los valores de los percentiles 50 y 90 fueron de 2-3 kg menores en la población extremeña, mientras que el 97 nuevamente mostró el mismo comportamiento en las dos poblaciones. En general, los adolescentes extremeños presentan una altura inferior a las referencias nacionales, aunque mayor en peso.

Por último, en la tabla V se muestran los valores medios, desviación estándar y percentiles de la complejión de la población de adolescentes estudiada, separados por edad y sexo. Al analizarlos observamos que el percentil 50 varió entre 10,44 y 10,91 para las chicas; y entre 10,22 y 10,79 para los chicos, dependiendo en ambos casos de la edad. En las chicas de todas las edades analizadas el percentil 50 correspondió a una complejión mediana; por el contrario, en los chicos ese percentil correspondió a una complejión mediana entre los 13 y los 15 años; y a una complejión pequeña entre los 16 y 18 años.

Conclusiones

Se han encontrado diferencias significativas en función del sexo en los parámetros antropométricos talla, peso, pliegue tricúspital, área muscular del brazo y área grasa del brazo. La talla, el peso y el área muscular del brazo fueron mayores en los chicos, aunque presentaron valores medios menores para el pliegue tricúspital y el área grasa del brazo. Al comparar con estudios nacionales, la media de altura de nuestra población era inferior en unos 3 cm, mientras que el peso fue similar a los estudios nacionales. Analizando el pliegue tricúspital, la circunferencia del brazo y el área muscular del brazo, se observó que la población extremeña estudiada tenía una mayor proporción de grasa en el brazo, y menor de músculo en ambos sexos. Algunos de esos valores generales contrastan en el estudio en función de la edad. Las chicas extremeñas son más altas que las referencias nacionales e internacionales únicamente a los 13 años y tienen un peso superior en todo el rango de edades estudiadas, aunque las mayores diferencias se observan a los 13 años. Nuestras adolescentes parecen tener un crecimiento más rápido, alcanzando su altura definitiva a la edad de 15 años, más temprana que la media nacional; sin embargo, la talla final fue menor a la media nacional, mientras que las diferencias en el peso fueron menores a partir de esa edad. Todo ello, unido a que la complejión fue constante en todo el periodo parece estar relacionado con un desarrollo puberal más temprano que en otras poblaciones. Por su parte, los chicos extremeños tuvieron una talla igual o algo superior y un peso mayor a los valores de referencia, con un crecimiento más continuado a todas las edades y similar a la media nacional. En lo que respecta a la circunferencia de la muñeca, a diferencia de en las chicas, sí se observaron diferencias en función de la edad en los chicos. En am-

Tabla V
Valores medios, desviación estándar y percentiles seleccionados de la complejión r (cm) por sexo y edad

	Media	Desviación estándar	Percentil								
			3	5	10	25	50	75	90	95	97
Chicas											
13 años	10,50	0,79	9,33	9,52	9,78	10,07	10,54	10,97	11,39	11,48	11,54
14 años	10,59	0,58	9,45	9,52	9,81	10,24	10,66	10,98	11,22	11,61	11,66
15 años	10,22	1,04	7,97	8,25	8,89	9,86	10,44	10,83	11,37	11,43	11,50
16 años	10,85	0,62	9,60	9,85	10,04	10,46	10,91	11,24	11,62	11,93	11,98
17 años	10,75	0,49	9,78	9,94	10,08	10,45	10,78	10,96	11,49	11,62	11,67
18 años	10,80	0,60	9,70	9,80	10,04	10,43	10,77	11,36	11,53	11,67	11,70
Chicos											
13 años	10,15	0,57	9,33	9,52	9,44	9,79	10,22	10,46	10,85	10,99	11,06
14 años	10,18	0,53	9,45	9,54	9,52	9,90	10,23	10,54	10,76	10,94	11,03
15 años	10,31	0,61	7,97	8,25	9,64	9,92	10,37	10,71	11,00	11,25	11,30
16 años	10,47	0,50	9,60	9,85	9,84	10,15	10,47	10,87	11,14	11,21	11,31
17 años	10,63	0,53	9,78	9,94	10,00	10,24	10,52	11,15	11,38	11,48	11,51
18 años	10,72	0,47	9,70	9,80	10,11	10,38	10,79	11,12	11,27	11,31	11,33

bos sexos, la conformación del brazo da una idea de una población con una proporción de grasa superior a las poblaciones referenciadas, y una conformación muscular menor. Aunque estos datos no permiten determinar el porcentaje de grasa total del organismo, al relacionarlos con el peso parecen indicar un grado de adiposidad mayor en los adolescentes extremeños con respecto a los del resto de España, lo que supondría un mayor riesgo de sobrepeso y obesidad.

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Original / *Valoración nutricional*

Assessment of risk factors and test performance on malnutrition prevalence at admission using four different screening tools

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Abstract

Background & aims: Malnutrition is very common in patients when admitted to the hospital. The aim of the present study was: a) to determine the prevalence of malnutrition at admission in a tertiary care hospital and identify risk factors for malnutrition, and b) to test the sensitivity and specificity of different screening tests for malnutrition compared to subjective global assessment (SGA).

Methods: We conducted a prospective study at 24h of admission in order to assess malnutrition in 537 adult subjects (56.4% males, mean age of 61.3±17.7 years) using 4 different screening tools: mininutritional assessment short form (MNA-SF), nutritional risk screening 2002 (NRS2002), malnutrition universal screening tool (MUST), and SGA. Anthropometrics and co-morbidities were registered.

Results: The overall rate of undernutrition was 47.3%. Specific rates were 54.2% in patients > 65y vs. 40.7% < 65y (p = 0.002) and 63.4% in medical vs. 34.0% surgical department (p < 0.001). Identified risk factors of malnutrition at admission were: the presence of heart disease (OR 1.74 CI 95% 1.16-2.60 p = 0.007) for MNA-SF (AUC 0.62); liver disease (OR 4.45 CI 95% 1.9410.22 p < 0.001), > 65y (OR 2.10 CI 95% 1.19-3.93 p = 0.011), medicine department (OR 3.58 CI 95% 1.93-6.62 p < 0.001) for SGA (AUC 0.96); lung disease (OR 3.34 CI 95% 1.45-7.73 p = 0.005), medicine department (OR 2.55 CI 95% 1.09-5.98 p = 0.032) for NRS 2002 (AUC 0.97). Recent unintentional weight loss was a common factor.

Conclusions: Undernourishment at hospital admission is frequent. Comorbidities may contribute to the presence of undernutrition at admission. Nonetheless, SGA, NRS2002, MNA-SF or MUST can be used in our setting.

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VALORACIÓN DE LOS FACTORES DE RIESGO Y VALIDEZ DE CUATRO TESTS DE CRIBAJE SOBRE LA PREVALENCIA DE DESNUTRICIÓN AL INGRESO HOSPITALARIO

Resumen

Antecedentes y objetivos: La desnutrición es muy frecuente en los pacientes que ingresan en el hospital. El objetivo de nuestro estudio es a) determinar la prevalencia de desnutrición al ingreso en un hospital de tercer nivel e identificar los factores de riesgo para desnutrición. b) Estudiar la sensibilidad y especificidad de diferentes test de cribado de desnutrición comparados con las valoración global subjetiva (VGS).

Material y métodos: Realizamos un estudio prospectivo a las 24 h del ingreso hospitalario a individuos (56.4% hombres con una edad media de 61,3 ± 17 años) utilizando 4 test de cribado diferentes: mininutritional assessment short form (MNA-SF), nutritional risk screening 2002 (NRS2002), malnutrition universal screening tool (MUST) y VGS. Además, se recogieron medidas antropométricas y comorbilidades.

Resultados: La prevalencia global de desnutrición fue de 47.3%. Las tasas específicas fueron 54,2% para > 65 años, 40,7% en < 65 años (p = 0,002), 63,4% en las áreas médicas, 34,0% áreas quirúrgicas (p < 0,001). Los factores que influían en la presencia de desnutrición al ingreso fueron: cardiopatía (OR 1,74 IC 95% 1,16-2,60 p = 0,007) en el MNA-SF (AUC 0,62); hepatopatía (OR 4,45 IC 95% 1,9410,22 p < 0,001), > 65años (OR 2,10 IC 95% 1,19-3,93 p = 0,011), áreas médicas (OR 3,58 IC 95% 1,93-6,62 p < 0,001) en la VGS (AUC 0,96); neumopatía (OR 3,34 IC 95% 1,45-7,73 p = 0,005), áreas médicas (OR 2,55 IC 95% 1,09-5,98 p = 0,032) en el NRS 2002 (AUC 0,97). La pérdida de peso involuntaria fue común a todos los test.

Conclusiones: La desnutrición es frecuente al ingreso hospitalario. La presencia de comorbilidades puede influir en la presencia de desnutrición al ingreso, sin embargo, podemos utilizar cualquiera de los tests propuestos para su detección en nuestro hospital.

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Palabras clave: *Desnutrición. Prevalencia. Enfermedad crónica. Morbilidad.*

Abbreviations

MNA: Mini nutritional Assessment.

MNA-SF: Mini nutritional Assessment short form.

MUST: Malnutrition Universal Screening Tool.

NRS 2002: Nutritional risk Screening 2002.

SGA Suggestive Global Assessment.

BAPEN: British Association of parenteral and enteral nutrition.

ESPEN: European society for clinical nutrition and metabolism.

Yo: Years old.

BMI: Body mass index.

ROC: Receive operative curves.

AUC: Area under the curve.

CI: Confidence interval.

SPSS: Statistical Package for the Social Sciences.

Introduction

About 10-85% patients are undernourished when admitted to the hospital. Some data exist in relation to the prevalence of malnutrition in Spanish hospitals.¹⁻⁴ However, as well as surveys conducted in other countries,⁵⁻⁶ a wide range of malnutrition prevalence has been reported, as a result of type of population or institution studied, expertise in screening or assessing nutritional status and tool used, but also on the different diagnostic criteria used to define nutritional status.⁷

Malnutrition is associated with many adverse outcomes including depression of the immune system, impaired wound healing, muscle wasting, longer lengths of hospital stay, higher treatment costs and increased mortality.⁸⁻¹⁰ Referral rates for dietetic assessment and treatment of malnourished patients have proven to be suboptimal, thereby increasing the likelihood of developing such aforementioned complications. Nutrition risk screening using a validated tool is a simple technique to rapidly identify patients at risk of malnutrition, and provides a basis for prompt dietetic or specialized nutritional support referrals.^{11,12}

Screening tools need to be low cost and time consuming, reliable, simple and adapted to the clinical setting where it will be used. Therefore, within last decades, several screening tools have been developed to detect malnutrition in worldwide hospitals, home care institutions and community patients. The most used tools in clinical practice are the Mininutritional Assessment (MNA) Test, the Malnutrition Universal Screening Tool (MUST), the Nutritional Screening Risk (NRS2002) and the Suggestive Global Assessment (SGA) tests. Each one of these screening tools have been developed to fit in a certain scenario and validated for this.

The MNA was developed to screen and assess frail elderly individuals living in community or hospitalized as a result of a decrease in caloric intake even before changes in weight or albumin occur.¹³ The MUST was validated for home-dwelling population,¹⁴ although it is

now being also used for patients at hospital admission, and institutionalized individuals. The NRS-2002 was developed for inpatients and, the SGA screening tool, initially designed to screen surgical patients, it is now recognized as an accurate nutritional screening tool used as a gold standard test in many conditions.¹⁵

The primary objective of the present study was to estimate the prevalence of malnutrition at hospital admission in a randomized sample of patients from our hospital. We also aim to compare the predictive capability of different screening tools to evaluate malnutrition and identify the factors most likely to influence the nutritional state of our screened patients.

Individuals and methods

Patients

We conducted prospective study evaluating individuals at 24h of hospital admission in medical and surgical departments during the period March-June 2010. All adult individuals entering to Son Llatzer Hospital during this period were considered potential participants. Refusing to participate or to sign the informed consent has been considered exclusion criteria for the study. Patients admitted for major ambulatory surgery, eye surgery, or those admitted to the rheumatology, gynecology, obstetrics, psychiatry departments or the intensive care unit were also excluded for the study.

The Son Llatzer Hospital Research Committee approved the study protocol and written informed consent was obtained in all subjects.

Anthropometric measurements and screening malnutrition tools used

Ad hospital admission, trained dietitians conducted the anthropometric measurements and assessed the risk of malnutrition using 4 different tools: MNA-SF, SGA, NRS2002, and MUST. Comorbidities were obtained by medical history and confirmed by medical records. Body height was measured to the nearest 0.5 cm with a stadiometer in patients who could stand, and recumbent height or alternatively, demispan calculated formula was used to estimate height in patients who were unable to stand up. Body weight was measured to the nearest 0.1 kg with a scale or hoist with attached weighing device for patients who were bed-ridden while subjects wore hospital gowns. The body mass index (BMI) was calculated as weight (kg) divided by height (m²) (kg/m²). If unable to measure height or weight, we used recently documented or self-reported measurements if they were realistic or reliable.

Percentage of weight loss was derived by the following equation: [(usual weight-current weight)/current weight]* 100.

SGA questionnaire. The SGA test was performed as previously described,¹¹ classifying individuals as A = well nourished, B = suspected malnourished or moderately malnourished, and C = severely malnourished. This test was used as the gold standard for statistical analysis.¹⁰

Mininutritional Assessment short form questionnaire. The MNA test⁸ was originally developed to detect the risk of malnutrition. However, we used the short-form that has also been validated^{12,13} as a screening tool and shown as high sensitivity (97%) and specificity compared to the MNA full test.¹⁴ With this questionnaire, patients were scored and classified as: 0-7, undernourished; 7-11, at risk of undernourishment; and 12-14, well nourished.

Nutritional Risk Screening 2002. The NRS-2002 was performed as described by ESPEN guidelines.¹⁵ Thus, patients are classified as: without risk, 0; at low risk, 1-2; at medium risk, 3-5, and at high risk, > 5 of malnutrition.

Malnutrition Universal Screening Test. The MUST test was conducted accordingly to BAPEN guidelines.¹⁶ The overall risk of undernutrition using this tool was classified as: 0, low risk; 1, medium risk; and > 2, high risk of malnutrition.

Risk factors for malnutrition assessment

The following factors have been considered *a priori* risk factors for malnutrition: age (> 65 years), sex, weight loss > 5% in previous 6 months, food intake below 75% of energy requirements one week prior to admission, type of diet (solid, liquid or puree), hospitalization or surgery 6 months prior to admission, and the intake of nutritional supplements before the hospital admission. The presence of the following disease comorbidities were also considered to potentially increase the risk of malnutrition: hypertension, diabetes mellitus, dyslipidemia and other reported chronic conditions such as: a) chronic heart disease (coronary heart disease, hypertensive myocardiodiopathy, moderate or severe valvulopathy), b) chronic pulmonary disease (obstructive or asthma), c) chronic liver disease of any etiology, and d) chronic kidney disease (eGFR < 60 ml/min/1.73m²).

Statistical analysis

The sample size was calculated based on the 20-50% prevalence of hospital malnutrition in local studies carried out in different hospitals and regions in Spain with similar characteristics to ours. Based on estimated prevalence assuming of 20%, an accuracy of 3% and a significance level of 5%, an estimated 15% dropout, the final sample calculated was 599 patients to be included. 67 patients were not included in data analysis due to exclusion criteria (refusing to participate or not being able to answer questionnaires).

We classified patients into 2 groups based on malnutrition risk: undernourished (including those at risk of undernutrition, SGA = B + C, MNA-SF < 11 MUST < 1, NRS-2002 < 3) and well-nourished (when no risk of undernourishment was present). They were also reclassified as medicine and surgical patients according the hospital ward admitted. The qualitative variables were described in percentages and quantitative by means, standard deviation, and range values. The χ^2 test was used to compare two categorical variables, and the t-test to compare two continuous variables. Univariate and multivariate logistic regression analysis were used to assess the associations between malnutrition and potential risk variables. ROC curves were used to assess reliability of each test. Sensitivity, specificity and predictive values were calculated to evaluate the different nutritional scores. SGA was considered the gold standard test for statistical analysis. The *k* statistic was calculated to measure agreement between tools (STAT 509), and the Shrout classification was used to interpret the *k* values as follows: 0-0.1, virtually none; 0.11-0.40, slight; 0.41-0.60, fair; 0.61-0.80, moderate; and 0.81-1, substantial. Data were analyzed using the SPSS statistical package version 18.0 for Windows (SPSS Inc., Chicago, IL, USA). The level of significance was set at 0.05.

Results

A total of 537 adult subjects (56.4% males, n = 303) with a mean age of 61.3 ± 17.7 years were assessed in medical (45%, n = 243) and surgical (55%, n = 294) wards. General physical characteristics of the population by gender are shown in table I.

No differences in general physical characteristics (sex, weight, height, BMI and body weight loss) between individuals of surgical and medical wards were shown except for age. Individuals admitted to medical wards were older (medical vs. surgical patients 68.1 ± 16.3 vs. 55.6 ± 16.8 years; P < 0.001). The most frequent comorbidities observed in our population were hypertension (38.7%), chronic heart diseases (29.7%), chronic lung diseases (29.5%), dyslipidemia (28.1%), and diabetes (20.9%). Table II shows the prevalence of comorbidities for medical and surgery patients. Type 2 diabetes mellitus, chronic heart and lung disease, and hospital admission in the last 6 month were significant more frequently observed in individuals admitted to the medical wards compared to those admitted to the surgical wards.

Table III shows the prevalence of malnutrition determined using different screening tools. The prevalence of malnutrition determined by the presence of at least one of malnutrition screening tool was 47.3%; 54.2% in patients older than 65 years vs. 40.7% in patients < 65 years old (P = 0.002). The prevalence of malnutrition determined by the presence of at least one of malnutrition screening tools was significantly different

Table I
General physical characteristics of participants

	Men (n = 303)		Women (n = 234)	
	Mean	SD	Mean	SD
Age (years)	61.5	17.65	60.98	17.56
Current weight (kg)	69.37	16.17	77.39	14.63
Usual weight (kg)	69.63	16.01	78.33	14.11
Height (cm)	157.65	7.75	169.75	8.04
Body mass index (kg/m ²)	27.9	6.12	26.82	4.55
Weight loss (%)	0.139	6.97	1.14	6.74

Weight loss was measured as: [(Usual weight-current weight)/current weight* 100].

Table II
Comorbidities present in the total population studied

	Medical wards (n = 243)			Surgery wards (n = 294)	
	Number	%		Number	%
Diabetes mellitus	73	30.0	39	13.3	<0.000
Hypertension	102	42.0	106	36.1	0.161
Dyslipemia	74	30.5	77	26.2	0.274
Heart disease	115	47.3	44	15.0	<0.000
Lung disease	127	52.3	31	10.6	<0.000
Liver disease	22	9.1	26	8.8	0.932
Kidney disease	24	9.9	27	9.2	0.785
Surgical procedures < 6 months	28	11.5	44	15.0	0.244
Hospital admission < 6 months	92	37.9	78	26.5	0.005

Weight loss was measured as: [(Usual weight-current weight)/current weight* 100].

between medical and surgical patients, being higher in surgical patients (63.4% vs. 34.0%, $P < 0.001$). The prevalence of malnutrition in those individuals older than 65 years was 31.8, 29.9, 28.4 and 23.9% by MNA-SF, SGA, NRS2002 and MUST, respectively. Accuracy values for different tests classified by age and type of wards are shown in table IV.

Specificity for NRS2002, MUST and MNA-SF were relatively high in overall the sample (> 90%), age category (> 90%) and type of wards groups (> 80%), although sensitivity was lower (between 59.7 and 84.9%). All the tests showed fair agreement with the subjective global assessment (considered the gold standard tool) except for MUST in case of < 65 year old ($k = 0.464$). Negative predictive values were also high in all the screening tests for different settings (between 91.5%- and 98.5%) except for medical wards (82.7% to 85.1%) and elderly individuals (82.3% to 89.6%).

Positive predictive values were lower for NRS-2002 and MUST than MNA-SF in all settings. Comparison of AUC showed no differences among tests compared to SGA. In the multivariate analysis, factors associated to the presence of malnutrition at admission were the presence of heart disease (OR 1.74; 95% CI 1.16-2.60, $P = 0.007$) for the MNA-SF test (AUC = 0.62); liver disease (OR 4.45; 95% CI 1.94-10.22 $P < 0.001$), age > 65 years (OR 2.10; 95% CI 1.19-3.93 $P = 0.011$), medical wards (OR 3.58; 95% CI 1.93-6.62 $P < 0.001$) for SGA (AUC=0.97); lung disease (OR 3.34; 95% CI 1.45-7.73 $P = 0.005$), medical ward (OR 2.55 95% CI 1.09-5.98 $P = 0.032$) for NRS-2002 (AUC = 0.97). Recent unintentional weight loss was a common factor among SGA, NRS 2002 and MUST. Neither the rest of comorbidities nor the type of diet or previous nutritional support influenced the presence of malnutrition at admission.

Table III
Prevalence of malnutrition using different screening tools

	MNA-SF	SGA	NRS 2002	MUST	Any tool ^a
<i>Overall population</i>					
Malnourished	17.7 (97)*	19.5 (107)	21.3 (115)	18.8 (102)	47.3 (254)
Wellnourished	82.3 (442)	80.4 (430)	78.7 (422)	81.2 (435)	52.7 (283)
<i>Medical wards</i>					
Malnourished	35.4 (86)	32.9 (80)	33.7 (82)	26.3 (64)	63.5 (154)*
Wellnourished	64.6 (157)	32.9 (163)	66.3 (161)	73.7 (179)	36.6 (89)
<i>Surgical wards</i>					
Malnourished	25.3 (74)	8.6 (25)	10.9 (32)	12.6 (37)	34.0 (100)
Wellnourished	74.7 (219)	91.4 (267)	89.1 (261)	87.4 (256)	66.0 (194)

MNA: Mini-nutritional assessment test; SGA: Subjective assessment questionnaire; NRS: Nutritional risk screening; MUST: Malnutrition universal screening test.

^aPresence of malnutrition by using any tools.

*Expressed as percentage and (number).

χ² test (*P < 0.05 Medical vs. Surgical wards).

Table IV
Accuracy values for screening test compared to the Subjective Global Assessment test

	NRS 2002	MUST	MNA-SF
<i>Overall</i>			
Sensitivity	68.9% (59.4%-77.1%)	64.1% (54.5%-72.7%)	69.9% (60.5%-77.9%)
Specificity	90.1% (86.9%-92.6%)	91.9% (89.0%-94.1%)	94.7% (92.2%-96.4%)
NPV	92.4% (89.5%-94.6%)	91.5% (88.5%-93.8%)	93.0% (90.2%-95.0%)
PPV	62.3% (53.1%-70.6%)	65.3% (55.7%-73.9%)	75.8% (66.3%-83.3%)
k value	0.567	0.564	0.666
<i>< 65 years (n = 265)</i>			
Sensitivity	56.7% (39.2%-72.6%)	60.0% (42.3%-75.4%)	70.0% (52.1%-83.3%)
Specificity	97.9% (95.3%-99.1%)	91.8% (87.6%-94.6%)	95.1% (91.6%-97.2%)
NPV	94.8% (91.3%-96.9%)	94.4% (91.3%-97.1%)	96.3% (93.0%-98.0%)
PPV	77.3% (56.6%-89.9%)	47.4% (32.5%-62.7%)	63.6% (46.6%-77.8%)
k value	0.618	0.464	0.623
<i>> 65 years (n = 272)</i>			
Sensitivity	72.6% (61.4%-81.5%)	65.8% (54.3%-75.6%)	69.9% (58.6%-79.2%)
Specificity	90.1% (85%-93.5)	92.1% (87.4%-95.2%)	94.2% (90.0%-96.8%)
NPV	89.6% (84.5%-93.2%)	87.6% (82.3%-91.4%)	82.3% (71.0%-89.8%)
PPV	73.6% (62.4%-82.4%)	76.2% (64.4%-85.0%)	89.1% (84.1%-92.7%)
k value	0.629	0.605	0.672
<i>Medicine wards (n = 243)</i>			
Sensitivity	68.8% (57.8%-78.1%)	59.7% (48.6%-70%)	64.9% (53.8%-74.7%)
Specificity	82.5% (76.0%-87.6%)	89.7% (83.5%-93.0%)	92.2% (87.1%-95.4%)
NPV	85.1% (78.8%-89.8%)	82.7% (76.5%-87.5%)	85.0% (79.1%-89.5%)
PPV	64.6% (53.8%-74.1%)	71.9% (59.9%-81.4%)	79.4% (67.8%-87.5%)
k value	0.505	0.512	0.6
<i>Surgery wards (n = 294)</i>			
Sensitivity	69.2% (50%-83.5%)	76.9% (57.9%-89.0%)	84.6% (83.3%-98.0%)
Specificity	94.8% (91.4%-96.9%)	93.7% (90.1%-96.0%)	96.3% (93.3%-98.0%)
NPV	96.9% (94.1%-98.4%)	97.7% (95.0%-98.9%)	98.5% (96.1%-99.4%)
PPV	56.3% (39.3%-71.8%)	54.1% (38.4%-69.0%)	68.8% (51.4%-82.0%)
k value	0.508	0.593	0.733

NRS: Nutritional risk screening; MUST: Malnutrition universal screening test; MNA: Mini-nutritional assessment test; NPV: Negative predictive value; PPV: Positive predictive value.

*Expressed as percentage and 95% interval confidence.

Discussion

The present study is the first conducted in Spain assessing test performance and risk factors for malnutrition using four different screening tools. Our data confirm that NRS2002, MNA-SF, and SGA have high reliability as screening tools for patients admitted at a hospital and invalidate the MUST for that setting after adjusting for risk factors. Despite that, the MUST test sensitivity, sensitivity, precision and validity has shown to be similar to previously described.^{22,23} This is probably because, weight loss and BMI < 20 kg/m² (the 2 items of MUST test) are not frequent in our population as shown in our data.

Overall malnutrition rates are similar whatever different screening tools used in our study. Those rates are also similar to previously published in Spanish^{1,4,21,24} and other developed countries using NRS2002^{7,25,26} for similar level of healthcare. Likewise, a higher prevalence of malnutrition in medical ward was observed in our study compared to the surgery wards.^{27,28} Recent unintentional total weight loss and chronic lung, heart and liver diseases have been delimited as the most frequent risk factors influencing the prevalence of malnutrition at admission in our study. These risk factors for malnutrition also have been identified in some studies conducted in other hospitalized populations.²⁹⁻³²

Differences in the prevalence malnutrition identified by the SGA, MNA-SF and MUST screening tests could be explained by severity of underlying disease, population setting (homecare, free-living) and age of the population studied.³ Therefore, those with end-stage disease, homecare and elderly being the most like to be undernourished when admitted at hospital.³³ The advanced stage of a chronic medical condition is characterized by an inflammatory status that enhances energy expenditure and decreases functional capacity which leads to an utter loss of weight and cachexia.³⁴ Also, elderly patients, particularly those in a homecare setting, are commonly admitted in medicine wards.³⁵

Our study has some limitations. It was conducted in a second level hospital from Spain; therefore, our results could not be extrapolated to other type hospitals from other countries. In addition, because our hospital is not the hospital of reference in our province, in our study we do not have assessed other high risk of malnutrition patients like transplants or surgery of the upper gastrointestinal track. Nevertheless, it is remarkable that we have screened 100% of the patients admitted in our hospital and thus, the sample it is representative of our population and permit to analyze the possible determinants of malnutrition in our hospital. Finally, our results are also consistent with Predyces, the only multicentric study performed in Spain.²⁴

In conclusion, undernourishment at hospital admission is frequent. The results of our study suggest that for screening hospital malnutrition at admission, it can be used any of the listed screening test. Nonetheless,

it's worth to mention that it is recommended to choose the easiest and less time consuming test. Therefore, we would recommend NRS2002 as the screening tool in our hospital accordingly to ESPEN guidelines.

Statement of authorship

All authors have made substantial contributions to all of the following: the conception and design of the study, acquisition of data, or analysis and interpretation of data; b) drafting the article or revising it critically for important intellectual content, and c) final approval of the version to be submitted.

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Original / Otros

Safe intake of an oral supplement containing carbohydrates and whey protein shortly before sedation to gastroscopy; a double-blind, randomized trial

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Abstract

Objective: To investigate the gastric emptying of an oral supplement containing carbohydrate plus whey protein drunk before sedation for gastroscopy.

Methods: This is a randomized double-blind trial including adult patients (ages 18-65) with a chief complaint of epigastric burning and who were candidates to elective gastroscopy. After overnight fast subjects were randomized to drink 200 mL of an oral nutritional supplement containing maltodextrin in addition to whey protein 150 to 210 min before the gastroscopy (intervention group, n = 12) or to undergo the endoscopic procedure with no supplement (control group, n = 12). The residual gastric volume (RGV) suctioned and measured during the exam was the main endpoint of the study.

Results: There were no complications during all exams. The median (range) fasting time was greater ($P < 0.001$) in control group (770 min, ranging from 660-917 min) than in the study group (175min ranging from 150 to 210 min). The median (range) RGV was similar in between the two groups (control group: 25 (10-70) mL versus intervention group: 10 (0-100) mL; $p = 0.32$).

Conclusion: Gastric emptying 150-210 min after the ingestion of an oral supplement containing carbohydrate plus whey protein is similar to an overnight fasting condition. Although limited by the number of cases, the sedation for endoscopic procedures is safe with this fasting protocol.

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Keywords: *Residual gastric volume. Preoperative fasting. Whey protein. Randomized trial.*

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INGESTA SEGURA DE UN SUPLEMENTO ORAL QUE CONTIENE HIDRATOS DE CARBONO Y PROTEÍNAS DE SUERO DE LECHE POCO ANTES DE SEDACIÓN PARA ENDOSCOPIA; UN ENSAYO DOBLE CIEGO Y ALEATORIZADO

Resumen

Objetivo: Investigar el vaciado gástrico de un suplemento oral que contiene hidratos de carbono, más proteínas de suero de leche tomado antes de la sedación para endoscopia.

Método: Se trata de un estudio doble ciego aleatorizado, que incluyó pacientes adultos (18-65 años de edad) por presentar epigastralgia y que eran candidatos a gastroscopia electiva. Después de una noche de ayuno los pacientes fueron asignados aleatoriamente para tomar 200 ml de un suplemento nutricional oral que contiene maltodextrina y proteína de suero de leche, de 150 a 210 minutos antes de la sedación, para gastroscopia (grupo de intervención, n = 12) o continuar en ayuno para el procedimiento endoscópico (grupo control, n = 12). El volumen gástrico residual (RGV) aspirado y medido durante el examen fue la variable de evaluación principal del estudio.

Resultados: No hubo complicaciones durante los exámenes. El tiempo medio de ayuno (rango) fue mayor ($P < 0,001$) en el grupo control (770 min, 660 - 917 min) que en el grupo de estudio (175 min, 150-210 min). El RGV (mediana y rango) fue similar entre los dos grupos (grupo control: 25 (10-70) ml y grupo de intervención: 10 (0-100) ml, $p = 0,32$).

Conclusión: El vaciado gástrico 150-210 minutos después de la ingestión de un suplemento oral que contiene hidratos de carbono y proteína de suero de leche es similar al ayuno tradicional durante toda la noche. Aunque limitado por el número de casos, la sedación para procedimiento endoscópico es segura con este protocolo de ayuno.

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Palabras clave: *Ayuno preoperatorio. Proteína de suero de leche. Volumen gástrico residual. Estudio controlado aleatorizado.*

Introduction

The main reason for the traditional prescription of 6-8 hours (h) of preoperative fasting for either gastroscopy or elective operations is to reduce the volume and acidity of stomach contents, thus decreasing the risk of regurgitation and aspiration recognized as Mendelson's syndrome¹. In the 1980s, it was already known that gastric emptying of water and other noncaloric fluids followed an extremely fast exponential curve in volunteers^{2,3}. Various randomized controlled studies⁴⁻⁶ and a meta-analyse⁷ have consistently documented that oral intake of water and other clear fluids up to 2 h before induction of anesthesia does not increase gastric volume or acidity. The use of carbohydrate (CHO)-rich beverage in the immediate preoperative period is not only safe, but may also reduce the catabolic stress response, nausea, vomiting, and thus enhance postoperative recovery^{8,9}.

Several studies have also shown the nutritional qualities of soluble whey proteins. Whey protein contains a high level of essential amino acids especially branched-chain amino acids¹⁰. The branched-chain amino acids (leucine, isoleucine, and valine) are rapidly used by skeletal muscle during stress and highly stimulate protein synthesis. In addition, they are precursors of endogenous synthesis of glutamine, the main energy source for enterocytes^{11,12}. Whey protein has also been described as an excellent source of cysteine, a precursor of glutathione synthesis, which acts as an endogenous antioxidant. Moreover, whey protein has a high degree of digestibility and rapid absorption in the small bowel¹⁰⁻¹².

However, only a few studies have investigated the gastric emptying of formulas containing carbohydrate combined with a nitrogen source such as protein or amino acids^{13,14}. This is most important because these formulas could be prescribed 2-3 h before either gastroscopy or surgical procedures needing light sedation or general anesthesia^{15,16}. We thought that gastroscopy would be an excellent tool to verify the contents of the gastric camera and assess the safety in the use of such drinks before general anesthesia for elective operations. Moreover the visualization of the entire gastric camera and the duodenum is essential for providing excellence in diagnostic and therapeutic endoscopy and data are most necessary on this matter. Thus, the aim of the study was to investigate the residual gastric volume (RGV) found during a gastroscopy 150-210 minutes after the ingestion of a carbohydrate plus whey protein enriched-drink.

Materials and methods

This was a randomized, double-blind, clinical study carried out at Gastroclinica, Cuiaba, Brazil. The study was approved by the Julio Muller Hospital Research Ethics Committee registered under number

194294/CEP-HUJM/13 and is in accordance with the ethics principals set out in the Helsinki Declaration (2000), and meets Brazilian national legal specifications. The study was registered in ClinicalTrials.gov under the number NCT01828645.

Adult patients scheduled to upper digestive endoscopy due to chief complaint of epigastric burning were eligible for inclusion in this trial. Exclusion criteria were: decline to participate, American Society of Anesthesiologists (ASA) score above II, diabetes mellitus, pregnancy, history of renal or hepatic failure, gastro-esophageal reflux, acute cholecystitis, use of corticosteroids up to 6 months previously, use of any prokinetic drug up to 6 weeks previously, and any noncompliance or violation on the assigned protocol of preoperative fasting. Patients who ingested the drink either less than 150 minutes (min) or more than 210 min before of the exam were also excluded.

Randomization

A staff not involved with the study was in charge of the randomization process. A computer program generated random numbers to assign patients to the two groups. Patients were randomized to receive either an overnight fast (minimum of 8 hours; control group) or fast for solids for the same period and drink 200 milliliters (mL) of an oral nutritional supplement (Composition per 200 mL: 0g lipids; 8 g whey protein; 67g carbohydrate being 88% maltodextrin and 12% sacharose; osmolality: 680 mOsm/L; and total energy: 300 kcal; Fresubin Jucy, Fresenius Kabi, Brazil) 150-210 minutes before the exam (intervention group).

Preoperative protocol

All patients received both oral and written information about the protocol at the outpatient clinic. Gastroscopies were scheduled to begin at 8:30 AM. The evening before operation patients were allowed to ingest solid food until 11:00 PM. The patients belonging to the intervention group received written instructions to ingest the above beverage at 6:00 AM (200 mL), and be at the endoscopy unit at 7:00 AM.

Endoscopic procedure

All endoscopic procedures were performed by one board-certified endoscopist (JSM) who was blind to the study design. Sedation was performed by a certified anesthesiologist who was also blind to the investigation with a bolus intravenous injection of 2 mL of lidocaine hydrochloride (Astra Zeneca, Sao Paulo, Brazil) in association of 100 to 150 mg of propofol before endoscopy. Digital oximetry was carried out throughout the procedure. Patients were positioned in left lateral recumbent throughout the endoscopy. A

flexible electronic videoendoscope (EG2770K; Pentax Corporation, Tokyo, Japan), 9 mm in outer diameter, was used for conventional and sedated endoscopy, according to a standard protocol recommended by the manufacturer. Special attention was done for the RGV. All gastric fluid was thoroughly suctioned through an endoscope side port, measured to the nearest mL and recorded.

Outcome variables

The main endpoint of the study was the RGV. Secondary endpoint was the judgment of the endoscopist on how confident he was to visualize all the gastric and duodenal mucosa. The satisfaction of the patient with the exam was also registered. Satisfaction with the protocol fast was evaluated by patients 2-4 weeks after the gastroscopy using a four-point scale (1, very good; 2, good; 3, moderate; 4, not satisfactory) after the question: "please rate your level of satisfaction with the fasting protocol?".

Statistical analysis

The sampling calculation was based on a previous study which reported that 80% of patients had less than 25 mL of RGV after either an overnight fast or 2-3 h after the ingestion of a carbohydrate alone or in addition to peptides enriched-drink¹⁶. A quantity of 12 cases in each study arm was judged to be sufficient to ensure 80% power (beta error) and 5% significance (alpha error) expecting a difference of a maximum of 25% in the RGV between the groups. Correlation between the fasting time and the RGV was done with the Pearson test. Comparison of RGV between the two groups was done by the Mann-Whitney test. A 5% level was adopted for significance. Data was presented as median (interquartile range) and range. All the calculations were made on a computer using the Statistical Package for the Social Sciences (SPSS) for Windows 11.0.

Results

There were no complications during the endoscopic procedures. The two groups had homogeneous demographics and clinical characteristics (table I). Overall patient satisfaction was excellent, with no difference between groups. The gastroscopist reported that in all cases, the aspiration of gastric contents was very easy and did not increase the time of the procedure. In all cases the gastroscopist was confident on his diagnosis, meaning that he had seen the entire gastric cavity, and the first portions of the duodenum. All patients had an endoscopic diagnosis of gastritis. Figure 1 shows the flowchart of the study. Forty six patients were eligible and 11 declined to participate. From the 35 randomized

Table I
Demographics and clinical characteristics of the patients in the two groups. Data are the mean (range) or the number of cases (%)

Variable	Control group	Intervention group	p
Sex (n,%)			1.00
Female	10	9	
Male	2	3	
Age (years)	40 (23-53)	35 (21-49)	0.88
Weight (kg)	72 (53-96)	70 (52-97)	0.83
Body mass index (kg/m ²)	27 (19-35)	24 (21-38)	0.89
ASA* score			
I	11	10	
II	1	2	

*, American Society of Anesthesiologists.

subjects 11 were subsequently excluded due to either current use of prokinetic agents (4 in control group) or noncompliance with the protocol (7 in intervention group). In all noncompliance cases the individuals ingested the drink out of the range of the protocol (less than 150 minutes or more than 210 minutes from the exam). No more patients were excluded and the analysis was done in 12 patients in each group. The median (range) fast period was greater ($p < 0.001$) in control group (770 min, ranging from 660-917 min) than in the study group (175 min ranging from 150 to 210 min).

The findings of RGV in the two groups can be seen in figure 2. There was no correlation between the fasting time and the RGV ($R = 0.10$; $p = 0.66$). Only two cases in each group had a RGV of 60 mL or above (2 cases with 60 mL in each group, one case with 70mL in control group, and one case with 100 mL in the intervention group). A median (interquartile range) of 25 (27) ranging from 10 to 70 mL was found in the control group and 10 (55) ranging from 0 to 100 mL in the intervention group ($p = 0.32$).

Discussion

Modern guidelines of various societies of anesthesiologists, and perioperative care now recommend 6-8h fast for solids and allow clear fluids or beverages containing carbohydrate up to 2h before surgery¹⁷⁻¹⁹. The findings of this randomized trail showed that the abbreviation of fasting up to 2 hours with 200 mL of an oral nutritional supplement containing whey protein along with carbohydrate was safe and was not associated with complications during the sedation for upper digestive endoscopy. Furthermore the RGV was similar in either fasted patients or in the group treated with abbreviation of the procedure fasting to 150-210 minutes. Moreover there was no significant correlation between time of fasting and RGV. These data suggest that this type of nutritional supplement can safely be

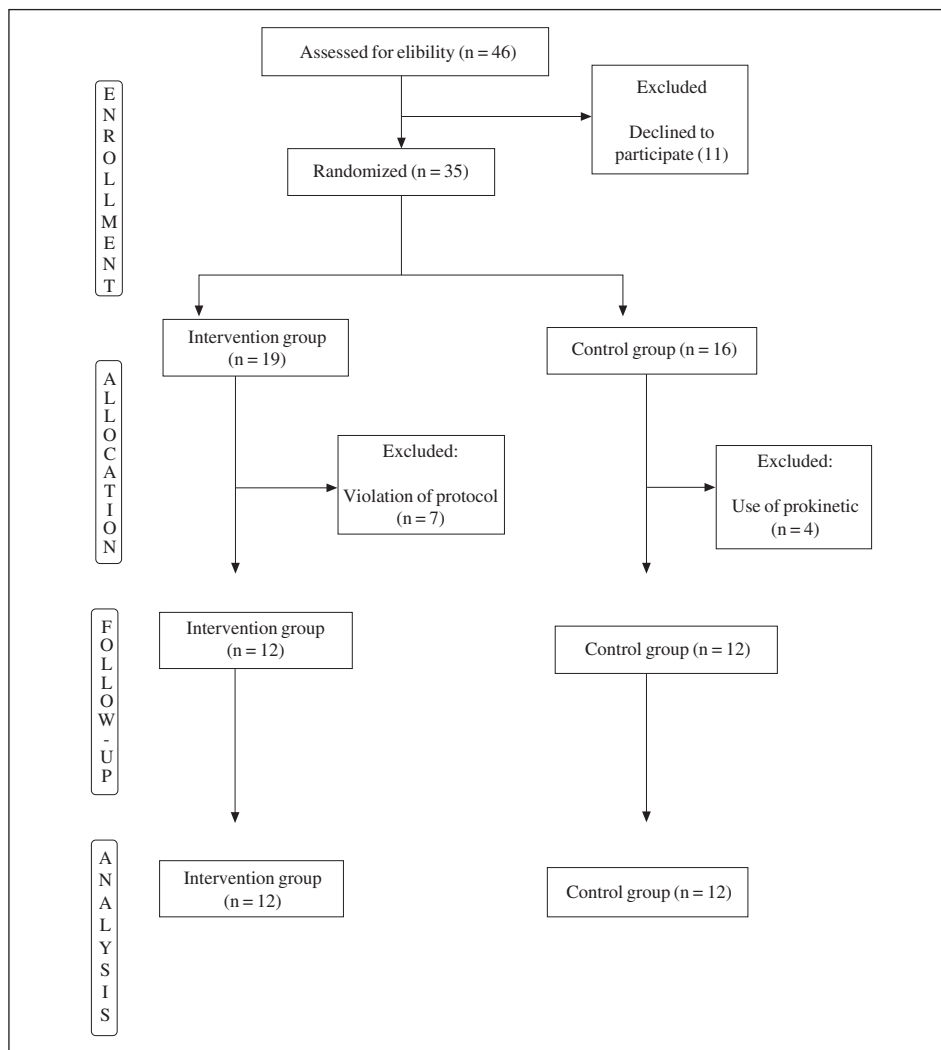


Fig. 1.—Flowchart of the study.

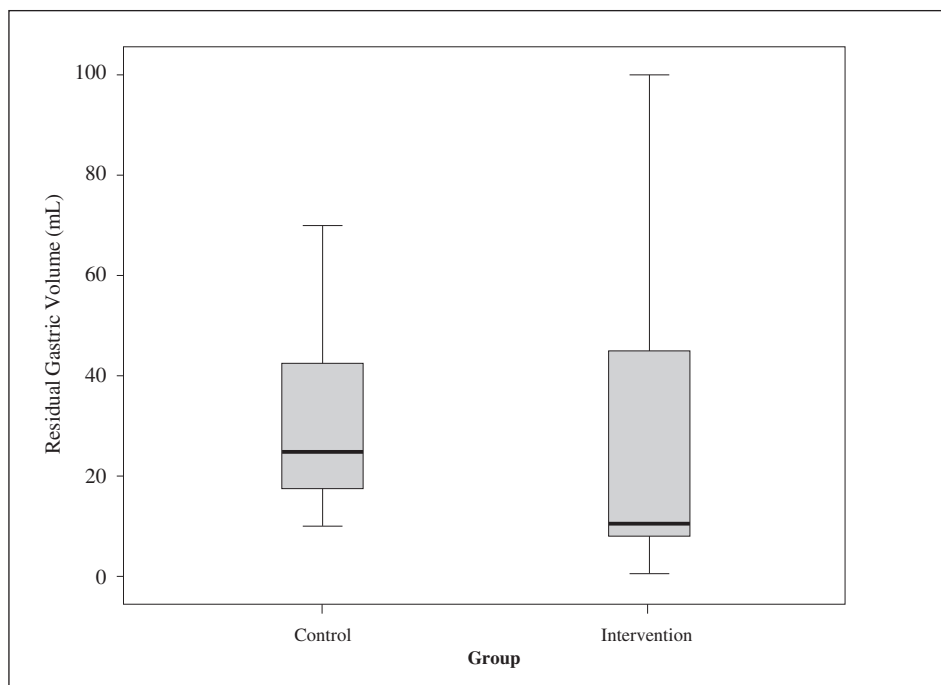


Fig. 2.—Boxplot of the residual gastric volume found during upper digestive endoscopy in the two groups. Data are the median, interquartile range, and interval ($P = 0.32$).

used to abbreviate fasting before anesthesia thus encouraging further studies.

After an overnight fast, the gastric camera is almost never completely empty and the RGV in healthy volunteers can range from 0 to 120 ml with a mean ranging from 19-37 mL²⁰ because the stomach continuously secretes up to 50 ml/h of acidic fluid even in fasting patients²¹. Our findings are in accordance to the above figures. Gastric emptying can be assessed by various methods. Since the introduction of radionuclide gastric emptying tests, considerable improvement has been achieved in both methodology and operational equipment, and scintigraphy has become the 'gold standard' for measurements of gastric emptying in research and in the clinical setting²². Recently magnetic resonance image has been proved to be an excellent method²³. All the above techniques are non-invasive which is very important to the comfort of the patients. Other studies however have reported the use of nasogastric intubation to collect gastric contents^{16,23}. Although this method is useful at the surgical unit on the other hand it is comprehensible imprecise. We have assessed the gastric emptying by gastroscopy. Gastroscopy is not only reliable but effective because the gastroscopist can visualize the whole gastric camera and then suctioning all contents²⁴. This method was recently used as gold standard to assay the efficacy of a mathematical model for ultrasound assessment of the RGV²⁵.

Another importance of these findings is that it keeps opened the gate for testing other proteins or amino acids in addition to carbohydrate-enriched drinks aiming to abbreviate the period of preoperative fasting. The use of whey protein in addition to carbohydrate beverage may theoretically benefit patients undergoing elective operation. Not only insulin resistance can be decreased but acute phase postoperative response can be diminished¹⁵. Insulin resistance is a mark of metabolic response to both prolonged fasting and trauma, and the intake of oral nutritional supplements containing either only carbohydrate or carbohydrate in addition to protein or aminoacids may promote additional benefits^{9,13,15,16,23}.

One methodological limitation of this trial is the small number of cases. However it was based on sample calculation with sufficient power analysis. In addition, the RGV was assessed by a direct and reliable technique and the study design was a randomized, double-blind controlled trial which increase the reliability for the results. Overall, the findings of this randomized trial indicate that this type of oral nutritional supplement is safe to be drunk up to 150 minutes before anesthesia. However, further studies are necessary to confirm these findings. The present findings allow us to conclude that the gastric empty 150-210 minutes after the ingestion of 200 mL of a carbohydrate plus whey protein enriched-drink is similar to an overnight fast. These data reinforces the idea of safety of such types of drinks 2-3 h before sedation or anesthesia.

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Conflict of interest: Jose Eduardo de Aguilar-Nascimento has received in the last 2 years travel reimbursement and honoraria from Fresenius-Kabi, Abbott, and Nestle for participation in Congresses.

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Original / Otros

Composición mineral de los distintos tipos de gofio canario; factores que afectan a la presencia de Na, K, Mg, Ca, Mn, Fe, Cu y Zn

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Resumen

En este trabajo se ha estudiado la composición mineral de Na, K, Mg, Ca, Mn, Fe, Cu y Zn en 181 muestras de diversos tipos de gofio elaborados con diferentes cereales. Las muestras se analizaron mediante espectrometría de emisión óptica con plasma acoplado inductivamente (ICP-OES). Considerando un consumo medio diario de 30 g de gofio en adultos y de 15 g de gofio en niños, se estimaron las ingestas diarias de cada metal y sus contribuciones porcentuales a las IDR establecidas para la población española. El elemento que presentó la mayor concentración de todos los estudiados fue el K en muestras de gofio de cereales, con una concentración media de 2189 ± 766 mg/kg. El de menor concentración fue el Cu en muestras de gofio de maíz, con $2,05 \pm 0,36$ mg/kg. Con respecto a la ingesta, cabe destacar que el gofio contribuye de manera significativa a la ingesta de cobre (53,77% - 71,45% de la IDR), en función del grupo de población que se trate y del tipo de gofio.

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DOI:10.3305/nh.2014.29.3.7099

Palabras clave: Gofio. Minerales. Espectrometría de emisión óptica con plasma acoplado inductivamente. Ingesta.

Abreviaciones

ICCA: Instituto Canario de Calidad Agroalimentaria
HNO₃: Ácido nítrico.

ICP: Espectrometría de plasma acoplado inductivamente.

IDR: Ingestas Dietéticas de Referencia.

FESNAD: Federación Española de Sociedades de Nutrición, Alimentación y Dietética.

ENCA: Encuesta de nutrición de Canarias.

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MINERAL COMPOSITION OF DIFFERENT TYPES OF CANARIAN GOFIO; FACTORS AFFECTING THE PRESENCE OF NA, K, MG, CA, MN, FE, CN AND ZN

Abstract

The contents of Na, K, Mg, Ca, Mn, Fe, Cu and Zn were analyzed and evaluated in 181 samples of various types of gofio produced from different roasted cereal grains. Samples were analyzed by ICP-OES. Based on a daily gofio intake of 30 g/day for adults and 15 g/day for children, the daily intake of each metal, and its percentage contribution to the RDAs established for the Spanish population, were estimated. The metal with the highest concentration was K (2189 ± 766 mg/kg). The lowest concentration was observed for Cu in corn gofio samples (2.05 ± 0.36 mg/kg). With respect to daily intake, it is noteworthy that gofio contributes significantly to the recommended allowance of copper (53.77% - 71.45% of the RDI), depending on the population group considered and on the type of gofio.

(Nutr Hosp. 2014;29:687-694)

DOI:10.3305/nh.2014.29.3.7099

Keywords: Gofio. Minerals. Inductively coupled plasma optical emission spectrometry. Intake.

Introducción

El gofio es un producto alimenticio tradicional de las Islas Canarias que ha sido la base de la alimentación de las clases populares durante cientos de años, hecho constatado por innumerables referencias históricas^{1,2}.

Este alimento, de aspecto harinoso, se elabora principalmente con granos enteros de trigo y/o maíz, aunque también se utilizan otros cereales o legumbres para su elaboración como la cebada, el centeno, la avena, el garbanzo, los altramuces o las habas. Presenta un alto valor nutricional ya que mantiene todos los nutrientes propios del cereal, destacando altos contenidos en minerales³ que, generalmente, se concentran en la capa de la aleurona del cereal⁴.

Según un estudio de mercado realizado por el ICCA (Instituto Canario de Calidad Agroalimentaria) en 2009, hay que destacar la elevada presencia del gofio en los hogares canarios, hasta en un 83% de los mismos

está presente este producto. Además, se observa que a más edad del consumidor y al ser Canarias como su lugar de nacimiento, mayor probabilidad de que se consuma gofio en ese hogar. Por otro lado, el gofio está más presente en los hogares canarios que el café soluble, los cereales de desayuno o el cacao en polvo.

Actualmente, se consumen diversos tipos de gofio elaborados con distintas mezclas de cereales y/o legumbres. Sin embargo, los gofios con mayor consumo son los de trigo, maíz o mezcla de ambos cereales. El consumo típico suele ser con la leche en el desayuno, espolvoreado sobre potajes, cazuelas y caldos de pescado, o como acompañamiento a modo de pan con distintas comidas.

Algunos minerales son necesarios para el desarrollo de la vida, como el Na, K, Ca y Mg, denominados macroelementos, ya que se requieren cantidades diarias en gramos. Y otros minerales imprescindibles son los denominados microelementos esenciales como el Fe, el Zn, el Mn y el Cu, que cumplen una función fisiológica en el organismo y son necesarios en menores cantidades, entre miligramos o microgramos.

Los niveles de macroelementos y microelementos esenciales presentes en este alimento se deben exclusivamente a las cantidades presentes en los cereales de partida, excepto para el sodio, que puede depender de la adición o no de sal marina en el proceso de elaboración; y para los elementos traza, que pueden obtenerse contenidos mayores si se utiliza maquinaria metálica susceptible de ceder metales al alimento⁵.

Las concentraciones de los elementos metálicos en el gofio pueden variar fundamentalmente por las características de las zonas de producción, es decir, del suelo existente como sustrato de los granos utilizados en la elaboración de este producto, así como por los procesos (tueste y molturación) a los que se someten los cereales. Los granos, generalmente, son importados, puesto que los cereales de producción local son cada vez más escasos; y suelen ser de origen argentino, francés o norteamericano.

Material y métodos

Muestras

El muestreo se realizó entre los meses de enero y junio de 2010 mediante la visita a las 51 industrias productoras de gofio de toda Canarias (28 en la isla de Tenerife, 14 en Gran Canaria, 5 en La Palma, 3 en La Gomera y 1 en Lanzarote) y se recogieron 181 muestras entre gofio envasado o a granel en envases plásticos de cierre adecuado. Las muestras se dividieron en 66 muestras de gofio de maíz, 50 de gofio de trigo, 15 de gofio de maíz canario, 23 de gofio de trigo maíz y 27 de gofio de cereales, con el fin de determinar posibles diferencias significativas en función de los niveles de elementos metálicos y otros parámetros como los cereales empleados, la isla de fabricación, la adición o no de

sal y si se realiza tamización después de la elaboración del gofio.

Tratamiento de las muestras

En cápsulas de porcelana se pesaron 10 g de muestra utilizando material de plástico desechable para evitar una posible contaminación de metales. Debido a que se trata de un alimento con muy baja humedad, la muestra no se sometió a una desecación previa por lo que se incineró directamente en horno mufla a $450^{\circ}\text{C} \pm 25^{\circ}\text{C}$, alcanzándose esta temperatura gradualmente aumentando no más de 50°C en intervalos de 30 min durante 24 h. Posteriormente, las cenizas resultantes se sometieron a una digestión ácida con HNO_3 al 10% para ayudar a oxidar la materia orgánica que pudiera quedar, eliminando los restos de ácido por evaporación sobre un baño de arena. A continuación, se introdujo de nuevo en el horno mufla siguiendo el procedimiento anterior otras 24 h, hasta obtener cenizas blancas. Una vez obtenidas las cenizas se disolvieron en HNO_3 al 5% hasta un volumen de 50 ml.

Procedimiento analítico

Los macroelementos (Na, K, Ca y Mg) y microelementos esenciales (Cu, Fe, Zn y Mn) se determinaron por espectrometría de emisión óptica con plasma acoplado inductivamente (ICP-OES), usando el modelo Thermo Jarrel Ash AtomScan 25^o. En el caso de los macroelementos, debido a la alta concentración de estos metales, se realizó una dilución 1/50, tomando 1 ml de la muestra ya preparada y diluyéndola en 50 ml de HNO_3 al 5%. Se realizaron dos lecturas de cada muestra y las concentraciones se calcularon mediante extrapolación sobre rectas de calibrado construidas a partir de soluciones patrón de concentraciones conocidas. Los límites de detección fueron 0,01 mg/l para el Na, Ca, Mg, Cu y Mn; 0,1mg/l para el K y 0,002 mg/l para el Fe y Zn.

Análisis estadístico

Se usó el programa de análisis de datos SPSS Inc., versión 18.0. En primer lugar, se realizó un estudio descriptivo de la totalidad del conjunto de datos y posteriormente, teniendo en cuenta que los gofios han sido elaborados con diferentes ingredientes, se realizó el estudio estadístico descriptivo para cada uno de los grupos establecidos en función del cereal empleado. Con el fin de determinar las diferencias significativas en el contenido mineral de los distintos gofios y para poder considerar otras variables se estudió la normalidad mediante las pruebas de *Kolmogorov-Smirnov* y *Shapiro-Wilk*⁷ con el objetivo de poder comparar los distintos grupos de muestras, en función de seguir o no

una distribución normal, y sobre homogeneidad de las varianzas con la aplicación del estadístico de *Levene*⁸. Una vez realizadas estas pruebas, se observó que existía gran cantidad de grupos de gofio que no cumplían las condiciones de aplicación de las pruebas paramétricas por lo que se recurrió a la prueba de *Kruskal-Wallis* para verificar las diferencias significativas y la prueba de *U de Mann-Whitney* para verificar las diferencias significativas entre los grupos⁹. También se utilizó el modelo de distribución de probabilidad de *t de Student* para comparar aquellos grupos de gofios en los que la distribución de los datos seguía un comportamiento normal, aplicándose cuando el tamaño de la muestra es grande, a partir de 30 casos¹⁰.

Resultados y discusión

Niveles de macroelementos: Na, K, Ca y Mg

En la tabla I, se presentan las concentraciones de sodio, potasio, calcio y magnesio para los gofios de maíz, trigo, maíz canario, trigo-maíz y cereales. El K es el macroelemento más abundante seguido del Na, Mg y Ca. La mayor concentración de K se detecta en el gofio de cereales, con una media de 2.189 ± 766 mg/kg con un intervalo de concentraciones que oscila entre 1.300 y 2.300 mg/kg. Asimismo, existen diferencias significativas entre los distintos tipos de gofio estudiados. En el caso del Na, el cereal utilizado para la elaboración del gofio no parece influir en la concentración de este macroelemento, destacando la amplia variabilidad de los datos. El mayor valor de Na se encuentra en el gofio de trigo-maíz (1257 ± 725 mg/kg) y el menor en el gofio elaborado solamente con maíz (529 ± 707 mg/kg). Por otro lado, se han relacionado los niveles de Na con la isla de producción del gofio sin diferenciar los ingredientes utilizados y se observa que, mientras las muestras producidas en Gran Canaria son las que menos Na presentan, los gofios tinerfeños son los que mayor contenido de este metal poseen.

Con respecto al calcio, este mineral se encuentra bien representado en el gofio pues su concentración suele ser alta en los cereales de partida. El trigo es el que presenta mayores niveles de este Ca ($259 \pm 66,5$ mg/kg) seguido por el gofio de cereales, trigo-maíz, maíz canario y maíz. Los resultados estadísticos muestran diferencias significativas entre ellos exceptuando

el “gofio de maíz” con el de “maíz de origen canario” y entre los gofios de cereales y de trigo.

El gofio elaborado con maíz canario es el que presenta mayor concentración de Mg ($581 \pm 47,9$ mg/kg) a diferencia del gofio de trigo, llegando a ser el menor nivel encontrado de este mineral ($495 \pm 63,6$ mg/kg). Por otro lado, se puede afirmar que los grupos de los distintos gofios presentan diferencias en sus niveles de Mg excepto para los gofios de trigo y trigo-maíz y entre los gofios de trigo-maíz con los de cereales.

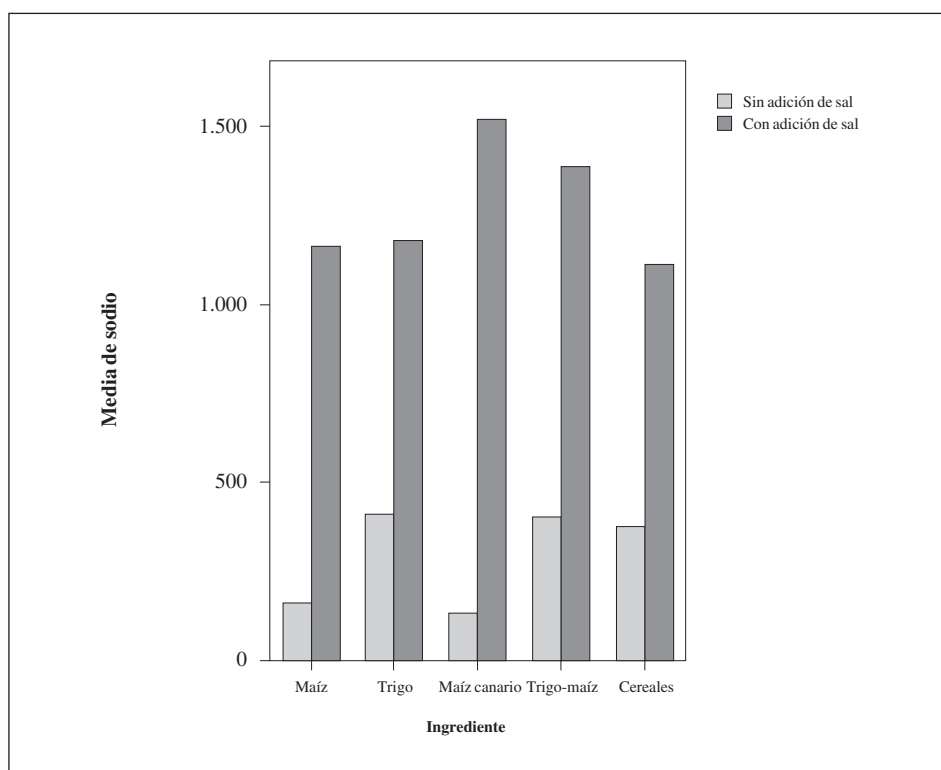
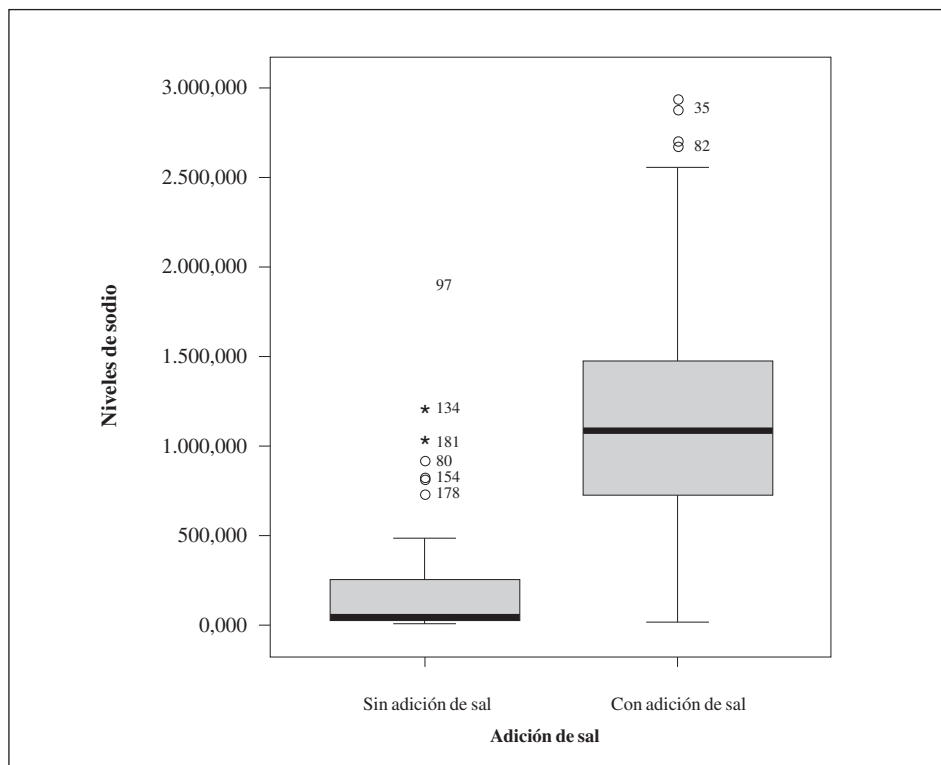
Niveles de macroelementos en función de la adición o no de sal

Para el estudio del Na se tuvo en cuenta el hecho de la adición o no de sal marina añadida en el proceso de elaboración del gofio, ya que generalmente, depende del maestro molinero y de la demanda del consumidor. En la figura 1 se representan los niveles de este elemento en la totalidad de los gofios estudiados y en función de la adición o no de sal. Para ello, se estudiaron 119 muestras de gofio con sal y 62 muestras de gofio sin sal, y es evidente que la diferencia a simple vista es significativa. La isla de producción también es importante, pues de ello depende la adición de sal marina. Es destacable observar que las islas de Tenerife y La Palma, es donde existe mayor tradición de adicionar sal al gofio. Por el contrario, en la isla de Gran Canaria, únicamente le adiciona sal al gofio en algunas empresas y de forma exclusiva al gofio de trigo⁵. En la isla de Tenerife la mayoría de las muestras de gofio comercializadas como “sin sal” poseen valores altos de este elemento mineral. Esto puede deberse a que se producen contaminaciones de sodio en el interior de los molinos o a que se almacena este gofio “sin sal” en depósitos con restos de sal (por ejemplo, depósitos usados previamente para gofio con sal). Por lo tanto, las concentraciones de sodio en el gofio dependerán la adición de NaCl (fig. 2). Las industrias de gofio instaladas en las islas de Gran Canaria y Lanzarote son las que producen las muestras con menores concentraciones de sodio. Además, las industrias que más sal le añaden al gofio, son todas pertenecientes a la isla de Tenerife.

En la tabla II se exponen los efectos de la adición de sal en las concentraciones de potasio, calcio y magnesio teniendo en cuenta la totalidad de los gofios estudiados. Los niveles de potasio parecen ser mayores en aquellos gofios a los que se les ha adicionado sal, excepto para el

Tabla I
Concentraciones de Na, K, Ca, Mg, Cu, Fe, Zn y Mn en función del tipo de gofio (mg/kg)

	Na	K	Ca	Mg	Cu	Fe	Zn	Mn
Maíz	529 ± 707	1804 ± 520	90,3 ± 44,3	541 ± 49,4	2,05 ± 0,36	27,2 ± 7,54	23,3 ± 2,09	7,05 ± 2,85
Trigo	1021 ± 614	2053 ± 452	259 ± 66,5	495 ± 63,6	3,27 ± 0,44	36,8 ± 5,76	24,1 ± 2,74	32,6 ± 3,09
Maíz canario	775 ± 812	1909 ± 92	106 ± 40,5	581 ± 47,9	2,23 ± 0,32	29,0 ± 4,96	26,2 ± 1,78	8,26 ± 2,77
Trigo-maíz	1257 ± 725	1897 ± 315	203 ± 47,8	500 ± 29,7	2,74 ± 0,39	31,7 ± 4,15	23,9 ± 1,95	22,6 ± 5,97
Cereales	1032 ± 617	2189 ± 766	238 ± 54,6	519 ± 35,9	3,21 ± 0,62	35,9 ± 7,12	24,7 ± ,76	23,5 ± 4,44



gofio de trigo-maíz en el que las concentraciones se muestran de forma inversa. No obstante, a la vista de los resultados no podemos concluir que la adición de sal afecte a los niveles de potasio en los gofios pudiendo atribuir las variaciones observadas al azar. Para el cal-

cio, la adición de sal en los gofios supone un incremento de los niveles para todos los tipos de gofios y los resultados para el magnesio nos permiten deducir que no se puede concluir que la adición de sal afecte a los niveles de este metal en los gofios estudiados.

Tabla II
Concentraciones de K, Ca y Mg teniendo en cuenta la adición o no de sal marina (mg/kg)

Adición de sal		Potasio	Calcio	Magnesio
Sin adición de sal	N	62	62	62
	Media \pm σ	2093,5 \pm 699,5	117,1 \pm 82,8	543,3 \pm 59,06
Con adición de sal	N	116	116	116
	Media \pm σ	1955,9 \pm 646,9	222,2 \pm 103,5	521,6 \pm 63,9

Niveles de macroelementos en función de la tamización o no del gofio

En la tabla III se muestran las concentraciones de Na, K, Ca y Mg en los gofios estudiados teniendo en cuenta si tras su elaboración se ha llevado a cabo una tamización o no. Se puede apreciar que debido al pequeño número de muestras para los distintos grupos de gofios no se puede establecer "a priori" que existan diferencias y mucho menos valorar las mismas si éstas existieran, excepto para el gofio de maíz para el cual se analizaron 50 muestras de gofios sin tamización posterior y 15 gofios a los que si se les realizó tal operación.

Se observa que los niveles de Na, K y Ca en el gofio de maíz son mayores en el gofio sin tamizar, sin embargo para el magnesio ocurre lo contrario. Este hecho se podría deber a que al eliminarse las partículas más gruesas, que serían fundamentalmente las cascarrillas del cereal, se pierden los minerales que con mayor concentración se encuentran en ella, lo que daría lugar a que la concentración mineral en el gofio tamizado sea más baja.

Niveles de microelementos esenciales: Cu, Fe, Zn y Mn

En la tabla I, también se exponen los resultados obtenidos de los microelementos en los gofios de maíz, trigo, maíz canario, mezcla de trigo-maíz y de cereales.

Cabe destacar que los gofios que poseen menor cantidad de Cu son los de maíz.

Por otro lado, se puede afirmar que las concentraciones de Fe de los diferentes gofios son distintas, si bien no se hallaron diferencias entre los gofios de maíz y aquellos de origen canario, ni entre los de maíz de origen canario con los de trigo-maíz, ni tampoco entre el de trigo con el de cereales.

Para el Zn, los resultados obtenidos se pueden observar en la tabla V. En ella queda de manifiesto que para

cualquier tipo de gofio, el Zn, se encuentra en cantidades similares. Esto puede deberse a que durante el proceso de producción del gofio no se generan muchas variaciones en la concentración inicial de zinc como ocurre en el caso de los cereales que son refinados. Teniendo en cuenta los ingredientes utilizados en la elaboración del gofio, se comparan las poblaciones de gofio elaborado de cereales y de maíz de origen canario, observándose que existen diferencias significativas entre las medias de Zn de ambos grupos de gofios. Además, se evidencia que hay diferencias entre los distintos grupos de gofios excepto para los gofios de maíz con trigo; maíz con trigo-maíz y trigo con trigo-maíz en los que las medias de niveles de Zn parecen ser las mismas. Por ello, podemos concluir que no hay diferencias entre los gofios elaborados con maíz y los elaborados de trigo, salvo para el caso de que el maíz sea producido en Canarias, en cuyo caso la concentración aumenta aproximadamente en 2 mg/kg.

En el caso del Mn, los gofios presentan distintas concentraciones en función del ingrediente utilizado para su elaboración. Destacan las altas concentraciones que presentan los gofios de trigo si las comparamos con las de maíz, siendo las medias 32,6 y 7,05 mg/kg, respectivamente.

Estimación de la ingesta de los macro y microelementos

Para estimar la ingesta debida al consumo de gofio por la población, se ha considerado el consumo medio diario de 30 g de gofio ya que esta cantidad es la que se aproxima a las 2 cucharadas soperas, que es la que habitualmente se consume acompañando ciertos alimentos. No obstante, para el grupo de población de niños se ha considerado el consumo de 15 g de gofio, la mitad que el considerado para adultos. Se han tenido en cuenta la Ingestas Dietéticas de Referencia (IDR) de la po-

Tabla III
Concentraciones de K, Ca y Mg teniendo en cuenta la tamización o no del gofio (mg/kg)

Ingrediente	Tamización	N	Na	K	Ca	Mg
Maíz	Si	50	572,88 \pm 710,4	1843,6 \pm 557,7	93,605 \pm 45,57	538,60 \pm 51,28
	No	15	385,21 \pm 700,6	1670,6 \pm 350,2	78,503 \pm 36,99	550,07 \pm 43,16
	Total	65	529,57 \pm 707,2	1803,7 \pm 519,9	90,173 \pm 43,96	541,24 \pm 49,44

Tabla IV

IDRs y contribución porcentual de la misma para el consumo de gofio de maíz, trigo, maíz canario, trigo-maíz y cereales

	IDRs (mg/día)			IDE (mg/día)		Contribución a la ingesta (%)		
	Niños	Hombres	Mujeres	Niños	Hombres y mujeres	Niños	Hombres	Mujeres
MAÍZ								
Na	1200	1500	1500	7,940	15,87	0,661	1,058	1,058
K	1550	3100	3100	27,06	54,12	1,746	1,746	1,746
Mg	145	350	300	1,355	2,709	0,934	0,774	0,903
Ca	750	900	1000	8,115	16,23	1,082	1,803	1,623
Mn	1,5	2,3	1,8	0,031	0,062	2,050	2,674	3,417
Fe	8,5	9,0	18	0,408	0,816	4,800	9,067	4,533
Cu	0,65	1,1	1,1	0,350	0,699	53,77	63,55	63,55
Zn	6,5	9,5	7,0	0,106	0,212	1,627	2,226	3,021
TRIGO								
Na	1200	1500	1500	15,32	30,63	1,276	2,042	2,042
K	1550	3100	3100	30,80	61,59	1,987	1,987	1,987
Mg	145	350	300	3,885	7,770	2,679	2,220	2,590
Ca	750	900	1000	7,425	14,85	0,990	1,650	1,485
Mn	1,5	2,3	1,8	0,049	0,098	3,270	4,265	5,450
Fe	8,5	9,0	18	0,552	1,104	6,494	12,27	6,133
Cu	0,65	1,1	1,1	0,362	0,723	55,62	65,73	65,73
Zn	6,5	9,5	7,0	0,489	0,978	7,523	10,30	13,97
MAÍZ CANARIO								
Na	1200	1500	1500	11,63	23,25	0,969	1,550	1,550
K	1550	3100	3100	28,64	57,27	1,847	1,847	1,847
Mg	145	350	300	1,590	3,180	1,097	0,909	1,060
Ca	750	900	1000	8,715	17,43	1,162	1,937	1,743
Mn	1,5	2,3	1,8	0,033	0,067	2,230	2,909	3,717
Fe	8,5	9,0	18	0,435	0,870	5,118	9,667	4,833
Cu	0,65	1,1	1,1	0,393	0,786	60,46	71,45	71,45
Zn	6,5	9,5	7,0	0,124	0,248	1,906	2,608	3,540
TRIGO-MAÍZ								
Na	1200	1500	1500	18,86	37,71	1,571	2,514	2,514
K	1550	3100	3100	28,46	56,91	1,836	1,836	1,836
Mg	145	350	300	3,045	6,090	2,100	1,740	2,030
Ca	750	900	1000	7,500	15,00	1,000	1,667	1,500
Mn	1,5	2,3	1,8	0,041	0,082	2,740	3,574	4,567
Fe	8,5	9,0	18	0,476	0,951	5,594	10,57	5,283
Cu	0,65	1,1	1,1	0,359	0,717	55,15	65,18	65,18
Zn	6,5	9,5	7,0	0,339	0,678	5,215	7,137	9,686
CEREALES								
Na	1200	1500	1500	15,48	30,96	1,290	2,064	2,064
K	1550	3100	3100	32,84	65,67	2,118	2,118	2,118
Mg	145	350	300	3,570	7,140	2,462	2,040	2,380
Ca	750	900	1000	7,785	15,57	1,038	1,730	1,557
Mn	1,5	2,3	1,8	0,048	0,096	3,210	4,187	5,350
Fe	8,5	9,0	18	0,539	1,077	6,335	11,97	5,983
Cu	0,65	1,1	1,1	0,371	0,741	57,00	67,36	67,36
Zn	6,5	9,5	7,0	0,353	0,705	5,423	7,421	10,07

blación española según la FESNAD¹¹ (2010) para poder conocer la contribución porcentual a la ingesta. Los grupos de población se han dividido en niños, hombres adultos y mujeres adultas.

En la tabla IV, se observan las IDRs para los macro y microelementos y se señalan los porcentajes de la ingesta a los que contribuye el consumo de gofio para los distintos tipos de gofio.

En Canarias se ha observado que la ingesta de magnesio y calcio, por la población anciana está por debajo de las ingestas diarias recomendadas, así tenemos que de magnesio se consume aproximadamente 275 mg/día y de calcio 930 mg/día¹², lo cual acentúa aún más la importancia que tiene el consumo de productos ricos en esos minerales como podría ser el gofio. Con respecto al Ca, las concentraciones en el gofio no son nada despreciables aunque el porcentaje de la ingesta diaria alcanzada por el consumo de 30 g de gofio es menor que para otros minerales. Por ello, a pesar de que el gofio es un alimento rico en Ca, los valores altos de la IDR hacen que el consumo de gofio no sea una fuente dietética importante de este metal.

Se observa que el gofio contribuye de manera significativa a la ingesta de Cu, pues para todos los grupos de población contribuye entre un 53,77 y un 71,45% de la IDR para hombres y mujeres, respectivamente. El gofio elaborado con maíz canario resulta ser el que más contribuye a la IDR de Cu.

En cuanto al Fe, se encuentra bien representado en el gofio, pero su estado de oxidación hace que se encuentre en la forma menos biodisponible como ocurre igual cuando este metal proviene de fuentes vegetales. No obstante, en dietas equilibradas, con frutas u otros alimentos que posean sustancias reductoras, la absorción intestinal de Fe se puede ver favorecida¹³.

Las ingestas de Fe varían significativamente en función del grupo de población que se esté estudiando. Las mujeres y los niños tienen unos requerimientos mayores por lo que en estas poblaciones es donde únicamente contribuye de menor manera, siendo los porcentajes alcanzados del 4 al 6% aproximadamente (tablas VI-X). Para los hombres, todos los tipos de gofio llegan a aportar más del 9% de la IDR. El consumo de gofio es una fuente de hierro interesante, formando parte de ese 75% de hierro que se aconseja ingerir a través de alimentos de origen vegetal¹⁴.

El contenido de Zn en el gofio permite abarcar parte de su recomendación, cubriendo un porcentaje de un 2,2 a 10 % para la población adulta. Se puede afirmar que, teniendo en cuenta que la ingesta de zinc es difícil de conseguir con la dieta habitual, la contribución del gofio a la ingesta de este metal cobra aún mayor importancia ya que son pocas las veces que quedan cubiertas las ingestas recomendadas con la dieta habitual¹³.

Para el Mn, el consumo de 30 g/día de gofio de maíz aporta, hasta un 2,6 % de la IDR para hombres adultos. Sin embargo, para el gofio de trigo la ingesta contribuye hasta un 5,4 % de la IDR en el caso de las mujeres.

Comparación de los resultados con otros autores

Si comparamos los valores de los macroelementos (Na, K, Ca y Mg) obtenidos en este estudio con los realizados por otros autores, destacamos que las concentraciones de Ca encontradas en los gofios estudiados no discrepan con las halladas por *Cerpa* y cols. (2001)² de 30 y 310 mg/kg para los gofios de maíz y trigo respectivamente, existiendo la mayor diferencia en el gofio de maíz en el cual, según los resultados de este estudio, se obtuvo una media de 90,3 mg/kg.

Para el Mg, las concentraciones encontradas fueron inferiores a las que establece *Suarez-Fraga* y cols. (1990)¹⁵ de 970 y 920 mg/kg para el gofio de trigo y maíz, respectivamente. También fueron más bajas que las descritas por *Cerpa* y cols. (2001)², de 1.100 y 960 mg/kg para el de maíz y trigo, respectivamente.

La tabla V muestra la comparación de las concentraciones de Cu, Fe, Zn y Mn con las obtenidas por otros autores. El gofio de trigo se compara con el cereal entero y su harina y el gofio de maíz solamente con harina de maíz por la escasez de estudios similares.

Los niveles de Cu observados se encuentran dentro de los rangos obtenidos por *Conti* y cols. (2000)¹⁶ en los trigos analizados. Sin embargo, obtuvimos concentraciones superiores a los aportados por *Nardi* y cols. (2009)¹⁷.

Si ahora comparamos nuestros resultados con las harinas de trigo analizadas por otros autores, debido a la falta de estudios encontrados sobre el gofio, se observan valores significativamente inferiores a los encontrados en este estudio. Este hecho era de esperar ya que el gofio se elabora con el grano entero de trigo o maíz y la harina se obtiene eliminando las partes externas del grano, las cuales contienen la mayor parte del contenido mineral.

Para el caso del Fe, se obtuvieron valores similares a los recogidos por *Kot* y *Zareba*, (2005)¹⁸, concentraciones superiores a las obtenidas por *Koplík* y cols. (2004)¹⁹ y por *Tang* y cols. (2009)²⁰, y por último, niveles medios de hierro inferiores a los encontrados por *Singh* y *Garg*, (2006)²¹.

Podemos observar como las concentraciones de Zn obtenidas en este estudio para los dos tipos de gofio analizados son significativamente superiores a los resultados encontrados por otros autores^{17,19,20,22}, ligeramente superiores a las concentraciones obtenidas por *Singh* y *Garg*, (2006)²¹ e inferiores a las de *Conti* y cols. (2000)¹⁶.

En el caso del Mn, la concentración media para el gofio de maíz es mayor que los valores obtenidos para las harinas de maíz analizadas por *Santos* y cols. (2004)²³ y *Koplík* y cols. (2006)¹⁹. Sin embargo, el valor medio en el gofio de trigo es ligeramente superior a las concentraciones recogidas por *Kot* y *Zareba*, 2005¹⁸ y *Singh* y *Garg*, 2006²¹ y bastante superior a los valores encontrados por el resto de autores^{17,20,22}.

Conclusiones

Los niveles de sodio en los gofios canarios dependen fundamentalmente de la adición de sal durante el pro-

ceso de elaboración, que a su vez depende de la isla de producción. Es fundamental para aquellos consumidores que tienen limitada la ingesta de sal, la lectura de la indicación de la presencia de sal en los ingredientes que se señala en los envases

Se debe recomendar el consumo de gofio en la dieta de la población anciana canaria ya que contribuye a cubrir los déficits nutricionales de los siguientes microelementos esenciales: cobre, hierro, zinc y manganeso.

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Caso clínico

Abordaje de una posible reacción de hipersensibilidad a nutrición parenteral; a propósito de un caso

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Resumen

La nutrición parenteral (NP) constituye un elemento esencial en el tratamiento de muchos pacientes hospitalizados. Sin embargo, su administración no está exenta de complicaciones quedando sujeta a la aparición de reacciones adversas de diversa índole como las de hipersensibilidad, por lo que es considerada por el ISMP (Institute for Safe Medication Practice) como medicación de riesgo. Se presenta el caso de una paciente oncológica con desnutrición severa, que tras recibir NPT durante varios días, desarrolla una reacción de hipersensibilidad que, ante la posibilidad de estar asociada a la administración de la mezcla intravenosa, nos plantea la dificultad de la nutrición preoperatoria y nos llevó a analizar las causas probables de esta reacción.

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Palabras clave: Nutrición parenteral. Alergia. Hipersensibilidad.

HYPERSENSIBILITY REACTION TO PARENTERAL NUTRITION APPROACH; A CASE REPORT

Abstract

Parenteral nutrition (PN) is essential in the treatment of many hospitalized patients. However, administration of PN is not without potential complications and patients are exposed to related possible adverse reactions such as hypersensitivity. For that reason and because of the complexity of this treatment, PNs are considered by the ISMP (Institute for Safe Medication Practice) a high risk medication. Following is introduced the case of an oncologic patient with severe malnutrition, who after receiving PN for several days, developed a hypersensitivity reaction that could have been associated with intravenous mixture administration. Our aim is to analyze the difficulties related with pre-surgery nutrition and to clarify the main possible causes of the reaction.

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Keywords: Parenteral nutrition. Allergy. Hypersensitivity.

Introducción

La nutrición parenteral (NP) constituye un elemento esencial en el tratamiento de muchos pacientes hospitalizados, siendo muchas veces la única vía de alimentación posible para tratar pacientes desnutridos o con riesgo de estarlo. Sin embargo, su empleo no está exento de complicaciones.

Tal es así, que es considerada por el ISMP (Institute for Safe Medication Practice) como medicación de

riesgo y está, por tanto, sujeta a la aparición de reacciones adversas de diversa índole¹. Una de las menos comunes pero que pueden comprometer el aporte nutricional de los pacientes son las reacciones de hipersensibilidad. Se ha observado que de todas las reacciones alérgicas, entre un 6-10 %, son debidas a fármacos². Estas reacciones de hipersensibilidad se categorizan en 4 tipos, destacando la tipo I que es provocada por re-exposición a un tipo específico de antígeno.

El cáncer de cervix es la segunda causa de cáncer en mujeres a nivel mundial³. La histerectomía radical se ha convertido en el standard de manejo de esta patología en los estadios iniciales, pero la aplicación de radiación mediante braquiterapia o irradiación externa cada vez es más utilizada. Ambos tipos de radiación han sufrido un desarrollo en clínica muy rápido cuyas consecuencias terapéuticas aún no están claras. Se ha observado que ambas técnicas pueden producir toxicidad

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aguda y complicaciones a largo plazo sobre todo a nivel gastrointestinal pudiendo ocasionar obstrucción, perforación, abscesos, síndrome de malabsorción, alteración del tránsito o aparición de fístulas con necesidad de reintervenciones quirúrgicas⁴.

Existen datos suficientes en la literatura que apoyan el uso de la nutrición preoperatoria, en especial en aquellos individuos con desnutrición o riesgo de desarrollarla que incluso, han llevado a sentar un grado de recomendación A al respecto⁵.

En el presente trabajo se expone el caso de una paciente oncológica con desnutrición severa, que tras recibir NPT durante varios días, desarrolla una reacción de hipersensibilidad que, ante la posibilidad de estar asociada a la administración de la mezcla intravenosa, nos planteo la dificultad de la nutrición preoperatoria y nos llevó a analizar las causas probables de esta reacción.

Caso clínico

Mujer de 43 años diagnosticada de cáncer de cervix en 2007 tratada con braquiterapia y radioterapia. Tras presentar un cuadro de sigmoiditis actínica y obstrucción intestinal a finales de 2009 es intervenida de resección intestinal a lo Hartman con resultado de colostomía de descarga. En ese momento la paciente pesaba 41,5 kg, 165 cm (IMC = 15). Durante el periodo posterior su peso fluctuó entre 38 y 42 kg a pesar del seguimiento nutricional sufriendo hasta cinco ingresos uno de ellos por absceso intrabdominal y fístula ureteroenteral por lo que se practica una nefrostomía izquierda.

En noviembre de 2011 es intervenida de resección ileocecal con anastomosis laterolateral por fístula intestinal. En el postoperatorio presenta un cuadro comicial secundario a imipenem que provocó el ingreso en UCI. Preciso soporte nutricional por vía parenteral durante 20 días.

En enero 2012 sufre nuevo ingreso por insuficiencia renal crónica grado III multifactorial instaurándose tratamiento nutricional con dieta de protección renal. La situación clínica requiere de nuevo NP durante 10 días por vómitos incoercibles e imposibilidad de ingesta oral.

En septiembre de 2012 reingresa a causa de una fístula suprapúbica, iniciando de nuevo NP con el objetivo de renutrir a la paciente para afrontar una nueva intervención quirúrgica, en ese momento presentaba IMC = 13 (37 kg, 169 cm). Al décimo tercer día, tras ganancia ponderal de 4 kg, la paciente desarrolla un cuadro alérgico que inicia con eritema y prurito. Se procede a la suspensión del Antibiótico (9 días con meropenem) y se administra tratamiento con corticoides y antihistamínico. La evolución continúa tórpida en las horas siguientes apareciendo edemas y dificultad para respirar. En ese momento se decide suspender NP observándose una mejoría en la sintomatología. Dado la necesidad imprescindible de nutrición preoperatoria, se elabora un protocolo de reintroducción de NP:

1. Inicio de NPT con aporte exclusivo de aminoácidos, glucosa y electrolitos, utilizándose una fuente de aminoácidos distinta a la de la preparación anterior. Iniciar siempre en horario de mañana con monitorización estrecha de la paciente.
2. Tras 48 h, si no ha habido manifestaciones de reaparición de la alergia, añadir cantidades crecientes de lípidos a la parenteral durante las próximas 72 h.
3. En caso de buena tolerancia, valorar la necesidad de añadir vitaminas y oligoelementos a la mezcla.

Se reinicia NP con buena tolerancia y sin complicaciones, aportando hacia el 4º día NP completa con macro y micronutrientes según necesidades de la paciente.

Tras objetivarse recuperación nutricional se decide intervención quirúrgica con mala evolución postoperatoria y necesidad de ingreso en Unidad de Cuidados Intensivos por desarrollo de shock séptico de origen abdominal y fracaso multiorgánico que finaliza en el fallecimiento de la paciente.

Discusión

Se expone el caso de una paciente que tras recibir braquiterapia presenta toxicidad y diversas complicaciones a largo plazo similares a las descritas en la bibliografía³. En este caso la toxicidad se centra en daño a nivel intestinal desarrollando fistulizaciones y abscesos que obligaron a realizarle diversas intervenciones quirúrgicas, entre ellas una resección intestinal que dificulta una adecuada nutrición.

En primer lugar fue necesario establecer alguna relación de causalidad entre la alergia y la NP. Dado que la paciente había recibido NP en ingresos previos, cabía la duda de la relación entre ambos.

Teniendo en cuenta que las reacciones inmunológicas requieren un período previo de sensibilización al fármaco y por ello nunca se pueden producir en la 1º dosis administrada, precisando un período más o menos prolongado de contacto con dicho fármaco, se deduce que la reacción alérgica puede ocurrir como mínimo en la 2º administración, o bien al cabo de muchos tratamientos.

El estudio de la alergia a cualquier fármaco precisa pruebas de reacción cutánea, pero ante la imposibilidad de realizarlas en nuestro centro, utilizamos el Algoritmo de Naranjo⁶ obteniendo un valor de 3 puntos (escala del 1 al 13) por lo que clasificamos la relación de causalidad entre la NPT y la reacción de hipersensibilidad como probable.

Revisando la historia clínica constatamos que la paciente había presentado convulsiones en un ingreso previo a causa de tratamiento con imipenem, por lo que se planteó la posibilidad de una reacción cruzada a meropenem. Sin embargo, la bibliografía expone que para considerar una reacción alérgica fármaco-dependiente, ésta debe diferir de la acción farmacológica o no estar

contemplada como reacción adversa esperable⁷. En este caso las convulsiones relacionadas con imipenem eran un evento adverso ampliamente descrito por lo que esta posibilidad se descartó. Además, según la evolución médica la reacción de hipersensibilidad continuó exacerbándose una vez fue suspendido el antibiótico y, por el contrario, mejoró tras la retirada de la NP.

Uno de los principales problemas con el que nos encontramos fue la identificación del alérgeno ya que la NP es una mezcla intravenosa compleja con multitud de componentes.

Si bien se han descrito en la bibliografía casos de hipersensibilidad tras infusión de emulsiones lipídicas⁷, es necesario destacar que los datos publicados datan de los años 80 en los que se utilizaban emulsiones lipídicas de 1º generación (a base de aceite de soja purificado). La mezcla i.v. administrada a nuestra paciente contenía una emulsión grasa de tercera generación aunque con una parte de aceite de soja en su composición por lo que no podíamos descartarlo como posible alérgeno a pesar del precedente de exposición previa sin reacción alguna.

Las soluciones de aminoácidos y sobre todo las proteínas de la soja⁸ también han sido asociadas a casos de hipersensibilidad; en el caso que nos ocupa no utilizamos proteínas de la soja en la mezcla i.v. por lo que consideramos menos probable su responsabilidad en la reacción.

La hipersensibilidad a los micronutrientes, vitaminas y oligoelementos, y excipientes de la NP son las más frecuentemente descritos⁹, por ello, pesar de ser los mismos compuestos que se administraron en la primera exposición no los descartamos como probables alérgenos.

Ante la necesidad de continuar con el tratamiento nutricional preoperatorio, fundamental para renutrir a la paciente y disminuir el riesgo de complicaciones, se decidió la prueba de provocación para lo que se elaboró un protocolo basado en un caso similar¹³, en el que se propuso la introducción paulatina de macro y micro nutrientes a fin de poder detectar si algún componente era el causante de la reacción.

Finalmente se reinstauró la nutrición artificial sin manifestación clínica de hipersensibilidad. A pesar de los resultados del test de causalidad no logramos constatar que la reacción sea debida a la NPT.

Si bien, la NP se considera un fármaco de riesgo, son pocos los casos de alergia descritos en la bibliografía durante los últimos años, esto puede deberse al avance en la tecnología de la formulación de los compuestos, sin embargo ante la aparición de una reacción de hipersensibilidad en un paciente polimedicaado que además recibe NP, debe sospecharse su relación de causalidad y realizarse un estudio minucioso para confirmarla, sin que esto perjudique el estado de nutrición del paciente.

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