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Injectable Vitamin D for Bariatric Patients Unresponsive to Oral Supplementation

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Abstract

Introduction: With an increasing incidence of obesity and weight loss surgery, there is an increased awareness of vitamin D deficiency and its metabolic sequala. The conventional treatment for vitamin D deficiency is not adequate for a subset of bariatric patients, both pre-and postoperatively. Compounded injectable vitamin D is an alternative for most people who do not respond adequately to oral Vitamin D supplements after bariatric surgery.

Method: Those patients diagnosed with vitamin D deficiency were all prescribed oral supplementations and levels rechecked in three and six months and yearly after that. Our recommendations included Vitamin D injections to those patients who had either not responded or further worsened their vitamin D levels. Repeat levels of vitamin D of both those on injection and oral supplements were rechecked. We did not include those Patients with preexisting Primary hyperparathyroidism or hypercalcemia. Their work up included medical, nutritional, and psychological evaluations, also to complete metabolic panel. At the time of the operation, all patients were older than 18 years old and younger than 67.

Results: Between February 2011 and June 2019, 147 patients were recommended vitamin D injections since oral supplements failed to improve the serum levels. There was a significant improvement in the Serum level for those patients who received Vitamin D compared to those who continued on higher dose oral supplements.

Conclusion: Compounded Vitamin D injections should be considered a treatment option for patients who do not respond to oral supplementations following weight loss surgery.

Keywords

Vitamin D; Bariatric surgery; Hypercalcemia; Oral supplements

Introduction

Worldwide, more than 1 billion people are vitamin D deficient [1]. Pregnant women, people of color (those with increased skin melanin pigmentation), obese children and adults, and children and adults who practice abstinence from direct sun exposure are exceptionally at high risk [2]. Vitamin D deficiency is prevalent in the adult population [3], reaching an epidemic level. Obesity, poor health and nutrition, and weight loss surgery are some of the risk factors associated with Vitamin D deficiency. Vitamin D absorption occurs in the proximal small intestine with bile salts' help [4]. Anatomical changes resulting from the Duodenal switch and other weight-loss surgical procedures may significantly reduce the gastrointestinal tract's vitamin D absorptive capacity. Oral vitamin D supplementation may be inadequate in the prescribed regimen for post-weight loss surgical patients.

Physiology of Vitamin D

Vitamin D is one of the four lipid-soluble vitamins. It exists in different forms. Chemically, the various forms of vitamin D are secosteroids, i.e. steroids in which one of the bonds in the steroid rings is cleaved. The two primary vitamin D forms are vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol). These are known collectively as calciferol. The active form of vitamin D with an endocrine action is synthesized in the human body sequentially in the skin, liver, and kidneys. The chemical structure of vitamin D3 results from the ultraviolet irradiation of 7-dehydrocholesterol in the skin. The human body lacks the enzyme to cleave the four rings in cholesterol. The conversion of the cholesterol ring structure is dependent on UV light exposure to the skin. Vitamin D binding protein then transports D3 to the liver, where hydroxylation to the inactive 25- hydroxyvitamin

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D form (calcidiol) occurs. In the kidneys, calcidiol is further hydroxylated by the enzyme 1-alpha-hydroxylase to active 1, 25-Dihydroxy vitamin D (calcitriol) [5]. Parathyroid hormone regulates calcium and vitamin D for skeletal bone metabolism and homeostasis. Recent epidemiologic studies have also observed relationships between low vitamin D levels and multiple disease states, including the pandemic of COVID-19 caused by its anti-inflammatory and immune-modulating properties and possible cytokine effects levels [6]. The human body stores vitamin D in the form of 25-hydroxyvitamin D.

The half-life of vitamin D in the liver is approximately one month, highlighting the need for frequent replenishment of the body's supply. Diet rich in vitamin D replenishes body source. Deficiency may result from decreased absorption, weight loss surgery, or conditions leading to malabsorption such as celiac and Crohn diseases, and drug interactions (Statin), increased catabolism caused by medications and disease conditions, and inadequate intake

Testing for vitamin D level in the blood

No definitive established guidelines exist for screening vitamin D levels in the asymptomatic population. The US Preventive Services Task Force has not made any recommendations for screening for vitamin D deficiency [7]. The testing of vitamin D levels has increased in the last decade [8]. When testing for vitamin D, serum 25-hydroxyvitamin D is the accepted biomarker. Measuring the active vitamin D 1, 25-OH-D level is not helpful because the kidney quickly and tightly regulates it. A true deficiency would be evident only by measuring 25-OH-D. The current estimated average requirements may be inadequate to correct low serum vitamin D levels [9].

Vitamin D toxicity

A literature review identifies rare case reports and vitamin D toxicity in individuals with preexisting conditions affecting calcium homeostasis 8. Vitamin D toxicity may present with fatigue, nausea, vomiting, and weakness caused by the resultant hypercalcemia and not directly related to the vitamin D excess [10]. Our patients included the subset of patients at risk factors for vitamin D deficiency, including obesity [11] and weight loss surgery [12]. In our patients, we saw no case of vitamin D toxicity.

Prevalence of vitamin D deficiency

National Health and Nutrition Examination Survey (NHANES) data collected showed insufficient vitamin D levels in 41.6% of patients [13]. The race is a significant risk factor, with African American adults having the highest prevalence rate of vitamin D deficiency (82.1%, 95% CI, 76.5%-86.5%) followed by Hispanic adults (62.9%; 95% CI, 53.2%- 71.7%). Additional risk factors for vitamin D deficiency identified included obesity, lack of college education, and daily milk consumption [14]. Low Vitamin D is critical in patients undergoing bariatric surgery as the surgery predisposes to micronutrients' malabsorption [15,16].

Treatment options

Diet and sun exposure is a primary source of vitamin D recommendations made. Physicians may also recommend supplementation to those deficient in vitamin D, but there are no current guidelines that provide the optimal dose and type of vitamin D. The Recommended dose for healthy adults is 2,000 IU daily [17]. Vitamin D2, commonly found in over-the-counter supplements, is 70% less effective than vitamin D3 to increase and maintain sufficient 25-OH D levels [18]. The most common recommendation for Vitamin D supplement is 50,000 IU for 2 to 3 months orally or three times weekly for one month, and serial follow-up of the serum levels 7. In our experience, this dosing schedule falls short of correcting or miniating the persistent Vitamin D deficiency seen in obese and post-bariatric patients. There are two treatment options for vitamin D deficiency oral and IM [19]. High-dose vitamin D injection effectively corrects deficiency with no toxicity reported [20,21]. High doses of 100 000–300 000 IU have been administered orally or intramuscularly 6-monthly or once-yearly without causing hypercalcemia or renal impairment [22]. Twenty-five to 80% of adult patients undergoing bariatric surgery may have baseline Vitamin D deficiency [23]. Even with oral supplementations postoperatively, 45% of bariatric patients continue to have insufficient vitamin D levels [24].

Statistical analysis

We chose the confidence level for all statistical analyses was set at 5% (α=0.05). P values were calculated using the ANOVA test, and when indicated, Kruskal-Wallis ANOVA was used. All statistical analyses were performed using the StatPlus:Mac Build 7.3.3.0/Core v7.3.32 (Analystsotf Inc., Walnut, CA 91789, USA).

Study

Patients who were undergoing Laparoscopic Duodenal Switch (DS) were screened for Vitamin D deficiency. The patient had consented to anonymized data collection. A retrospective analysis between 12 and 120 months was completed in October 2020. The vitamin D levels were measured preoperatively and rechecked at regular intervals postoperatively, at 3, 6, 9, 12, 24, and 36 months, and as clinically indicated. One hundred forty-seven patients were offered vitamin D injections and had ordered blood levels drawn. There were 128 females and 19 male patients with a mean age of 41.6 (Table 1). The mean BMI was 47.6 Kg/m2 (SD +/-6.8, range 35.8-68.1).

Demographics		
	Age (years)	**BMI (kg/m2)**
Mean	41.6	47.6
Standard deviation	14.1	6.8
Range as of (October-2020)	19-67	35.7-68.1

Table 1: Demographics.

The mean pre-op vitamin D level was 32 mg/dl. Follow-up post-op level of Vitamin D3 on oral supplements of 50,000I U/day was 27.1 md/dl and 22.0 mg/dl at three and six months, respectively (Table 2). The change in measured vitamin D levels represented a 15% and 19% drop for three months.

Vitamin D levels mg/dl			
	Pre-operative	Post-operative	
		3 months	6 months
Mean	32	27	22.1
Standard deviation	8.4	7.6	8
Kruskal-Wallis ANOVA P<0.001			

Table 2: Vitamin D levels mg/dl.

Vitamin D		
	Pre-op to 3 months	3 to 6 months
Change	-15%	-19%
Standard deviation	9%	17%
Kruskal-Wallis ANOVA P<0.001		

Table 3: Vitamin D.

There were no correlations noted between the age, post-operative time, the initial BMI, or the initial vitamin D level to the measured levels at 3 and 6 months. Patients were offered Vitamin D injection of 50,000/ week for six weeks (yearly regiment) or increased oral supplements of 100,000 IU/Day for one month followed by 50,000/day for one month and rechecked the levels. If the follow-up vitamin D levels did not improve, the same regimen was recommended. At 12, 24, and 36 months the injection had normalization of the vitamin D level. There were no side effects of supplementation noted in either group (Table 3).

Results

At 12 months, 47 patients continued with oral supplements, and 99 patients opted for Injections. At 24 months, 108 patients were getting injections, and at 36 months, there were 110 patients. The mean vitamin D level dropped from 32, pre-operative to 25 mg/dl (Figure 1).

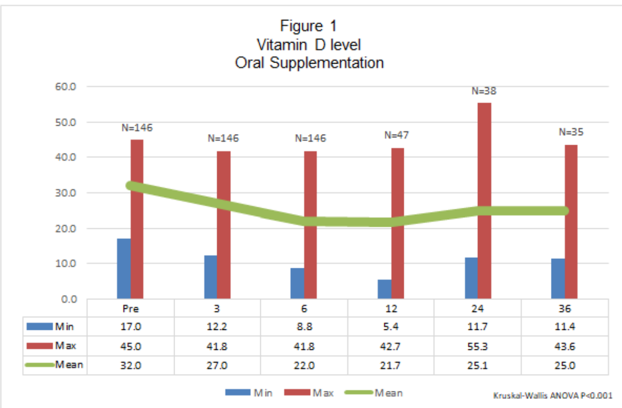

Figure 1: Vitamin D level oral supplementation.

The group that elected to have IM injection shows significant improvement of the vitamin D levels 24 and 36 months to 39.3 and 53.3 mg/dl, respectively (Figure 2). The improvement of vitamin D levels was noted in 3 months (P=0.0469) and continues to improve at 24 and 36 months (P<0.001).

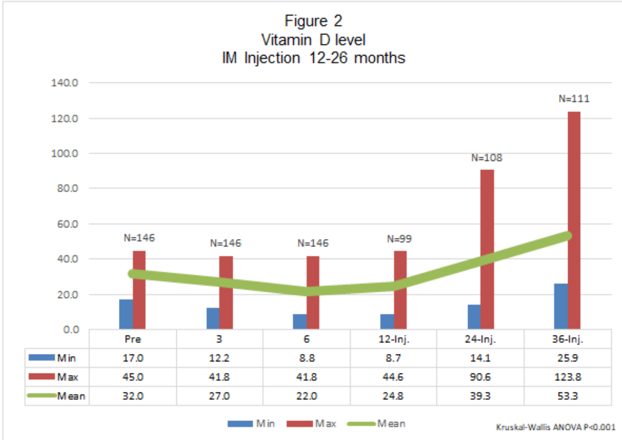

Figure 2: Vitamin D level IM Injection 12-26 Months.

The BMI of groups that took oral (mean BMI 46 kg/m2, SD 6.7) and Injectable (mean BMI 48 kg/m2, SD 6.7) form of Vitamin D were similar (p=0.14666, ANOVA). The BMI was not a factor in how the patients chose between the two modes of supplementations. The mean age was 40 for oral and injectable groups (p=0.00919, ANOVA) (Table 4). The groups' dissimilarities based on the age may have been related to the younger patients choosing to have the injections instead of taking daily medications (Figure 3).

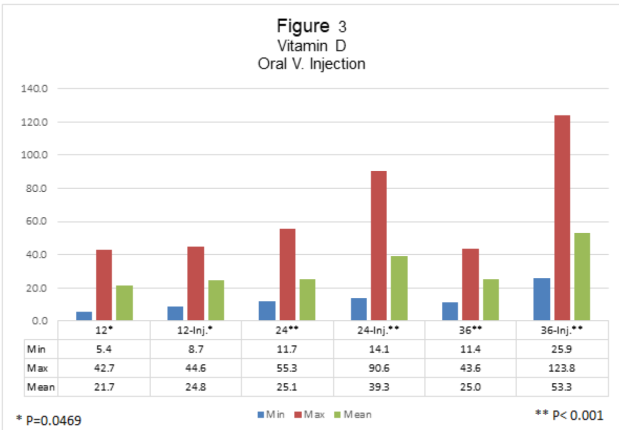

Figure 3: Vitamin D Oral vs. Injection.

Demographics of Two Groups Oral Vs. IM Vitamin D supplements					
	Mean		SD		P (ANOVA)
	Oral	IM	Oral	IM	
Age	47	40	16.5	12.8	0.00919

BMI	46	48	6.8	6.7	0.14666

Table 4: Demographics of Two Groups Oral vs. IM Vitamin D supplements.

Conclusion

Injectable vitamin D may be needed to correct the persistent vitamin D deficiency in the post-bariatric patient who do not respond to high dose oral supplementations. Frequent serum levels are needed for close monitoring and continued dose adjustment. Vitamin D toxicity is extremely rare and was not seen in this group of patients.

Setting

Private Practice, Pasadena, California, United States of America

Disclosures

No financial disclosure or funding support to report.

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