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CONGRESO NACIONAL
DE LA SOCIEDAD ESPAÑOLA
DE FARMACIA HOSPITALARIA

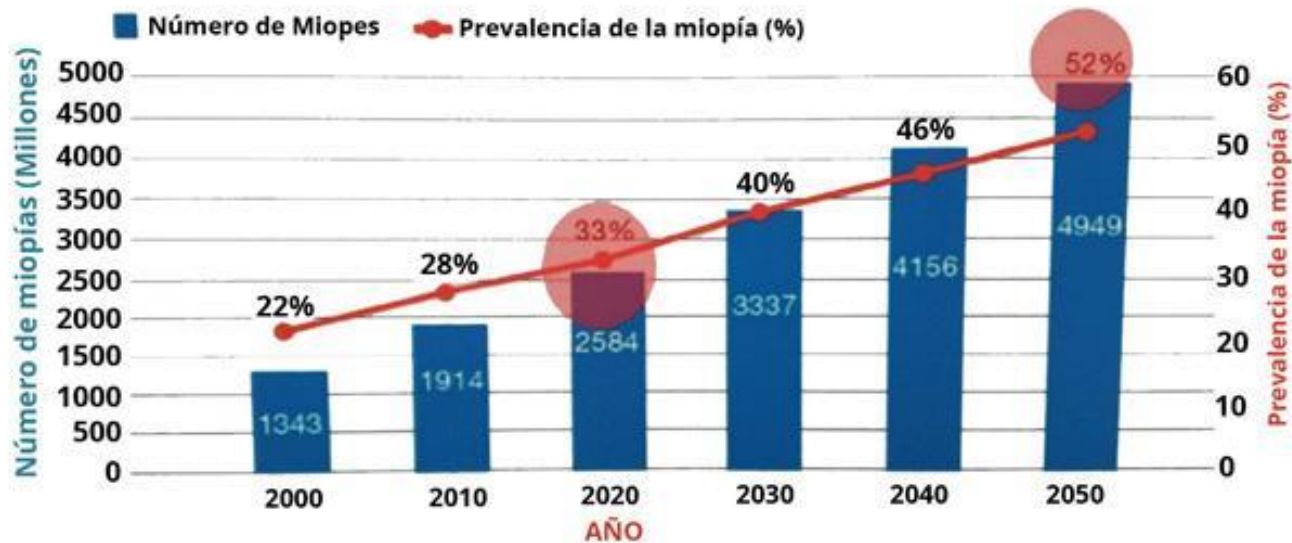
SEVILLA 17/19 OCT 2019

MEDIDAS FARMACOLÓGICAS EN EL CONTROL DE LA MIOPIA EN LA INFANCIA

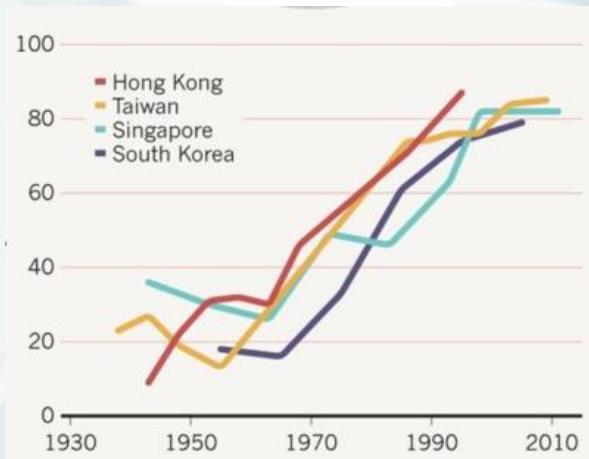


MIOPÍA: EPIDEMIA DEL SIGLO XXI

PREVALENCIA GLOBAL DE LA MIOPIA



MIOPÍA: EPIDEMIA DEL SIGLO XXI



MIOPÍA: EPIDEMIA DEL SIGLO XXI

	Glaucoma	Catarata	Desprendimiento de retina	Maculopatía Miópica
-1.00 a -3.00	2,3	2,1	3.1	2.2
-3.00 a -5.00	3,3	3,1	9.0	9,7
-5.00 a -7.00	3,3	3,5	21,5	40,6
<-7.00	-	-	44,2	126,8

Probabilidades de aumentar el riesgo de tener una patología ocular en relación con el incremento del grado de miopía (número de dioptrías) - Flitcroft, 2012 Reproduced from Gifford, 2016

ARMAS FARMACOLÓGICAS

- **Agentes antimuscarínicos**
 - Atropina
 - Pirenzepina
 - Otros (tropicamida / escopolamina)
- **Hipotensores**
- **Metilxantina 7-MX**
- Análogos colinérgicos nicotínicos
- Inhibidores de acetilcolinesterasa
- Agonistas dopamina
- GABA
- Neuropéptidos
- Óxido nítrico
- Ácido retinoico
- Otros factores de crecimiento



Ganesan P. Pharmaceutical intervention for myopia control. Expert Rev Ophthalmol 2010 Dec;5:759-787.

ATROPINA

“Si instilamos un colirio de atropina a diario durante un periodo prolongado de tiempo a niños con miopía, frenaremos su progresión”

ATOM₁

Atropina 1% - placebo

Ophthalmology 2006;113:2285–2291

Atropine for the Treatment of Childhood Myopia

Wei-Han Chua, FRCSEd(Ophth), FAMS,^{1,2} Vivian Balakrishnan, FRCS(Ed), FRCOphth,¹
Yiong-Huak Chan, PhD,³ Louis Tong, FRCS(Ed),¹ Yvonne Ling, FRCS(Ed), FRCOphth,¹
Boon-Long Quah, FRCS(Ed), MMed(Ophth),¹ Donald Tan, FRCS(Ed), FRCOphth^{1,2,3}

- Randomizado
- Doble ciego
- Grupo control placebo

ATOM₂

Atropina 0.5% - 0.1% - 0.01%

Atropine for the Treatment of Childhood Myopia: Safety and Efficacy of 0.5%, 0.1%, and 0.01% Doses (Atropine for the Treatment of Myopia 2)

Audrey Chia, FRANZCO,^{1,2} Wei-Han Chua, FRCSEd(Ophth), FAMS,^{1,2} Yin-Bun Cheung, PhD,^{1,4}
Wan-Ling Wong, MChostas,² Anushka Lingham, SRN,⁴ Allan Fong, FRCSEd(Ophth),^{1,2}
Donald Tan, FRCS, FRCOphth^{1,2,3}

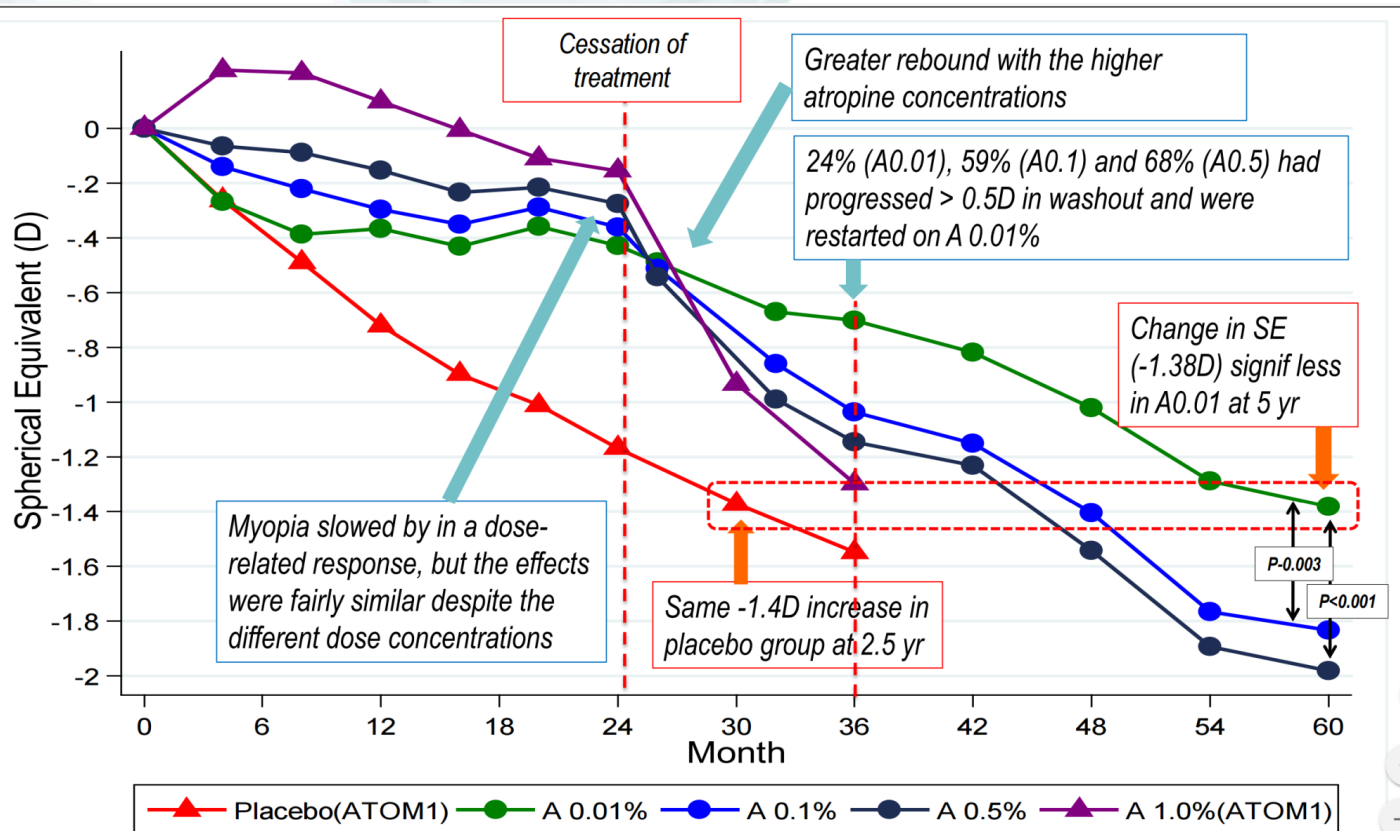
Ophthalmology 2012;119:347–354 ©

- 400 niños
- 6-12 años
- -1.00 ↔ -6.00D

Dioptrías	2 años	1 año lavado	5 años
Atropina 0.5%	-0.30 ± 0.60	-0.87	-1.98
Atropina 0.1%	-0.38 ± 0.60	-0.68	-1.83
Atropina 0.01%	-0.49 ± 0.63	-0.28	-1.38
Placebo	-1.20 ± 0.69	-0.38	x

Longitud Axial	2 años	1 año lavado	5 años
Atropina 0.5%	0.27	0.35	0.87
Atropina 0.1%	0.28	0.33	0.85
Atropina 0.01%	0.41	0.19	0.75

- ¿efectos secundarios a largo plazo? → fármaco usado desde 1900
- A dosis 0.01%:
 - no efecto clínico sobre AV cerca / pupila / acomodación
 - Mínima probabilidad de conjuntivitis alérgicas /dermatitis¹
 - ¿Sequedad ocular?



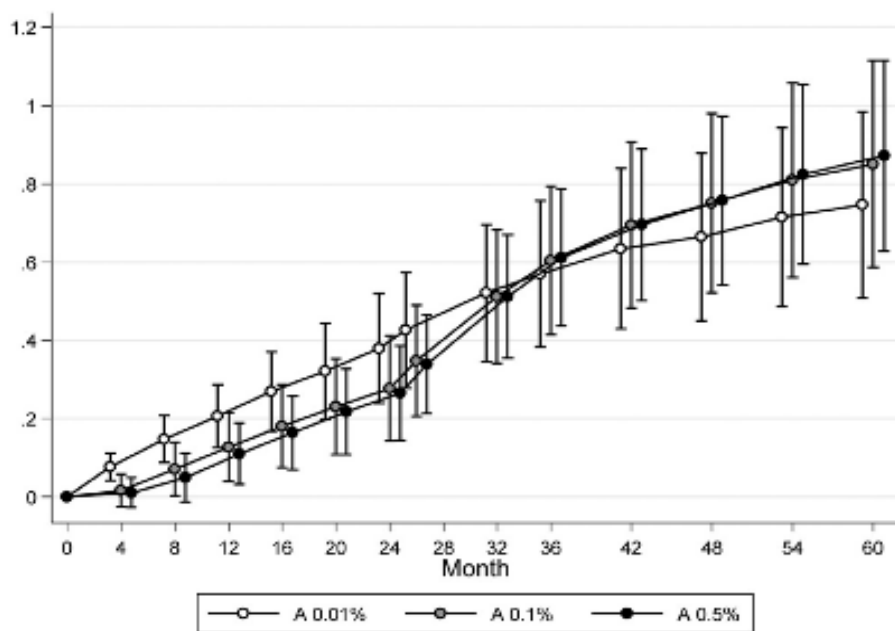
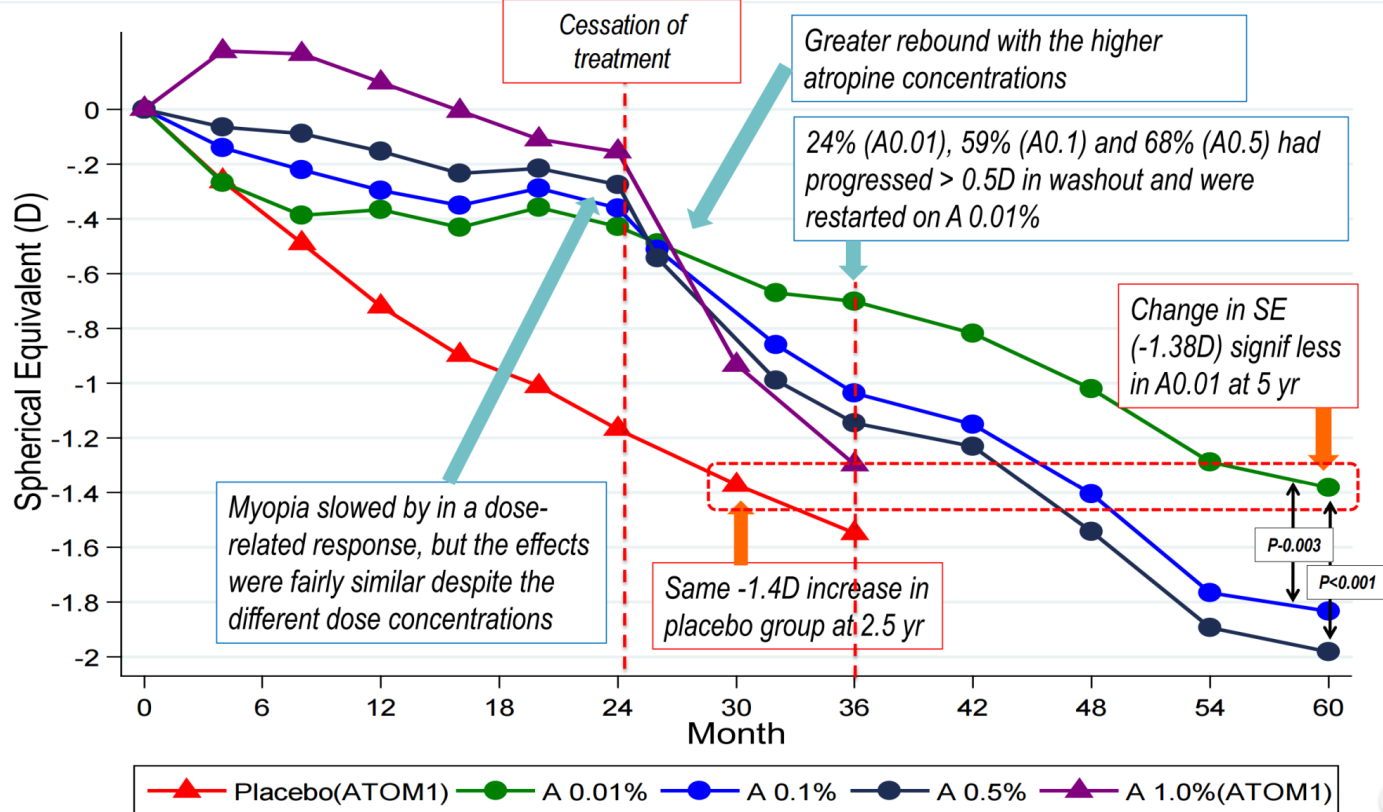
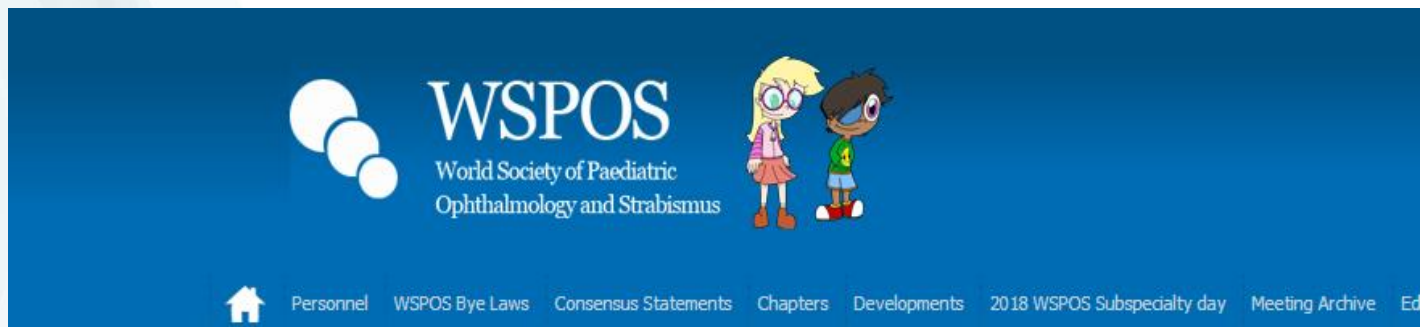


Figure 5. Mean change in axial length (AL) over time within different treatment groups (atropine 0.01%, 0.1%, and 0.5%). Error bars represent 1 standard deviation.



ATROPINA



Conclusions: Atropine 0.01% dose appears to offer an appropriate risk-benefit ratio, with no clinically significant visual side effects balanced against a reasonable and clinically significant 50% reduction in myopia progression. Orthokeratology contact lenses also appear to slow axial length elongation but infective keratitis is a risk. Peripheral defocussing lenses in the form of spectacles or contact lenses may both have a role in slowing the rate of myopic progression in a subset of children and further help our understanding of the physiologic control of ocular growth. Increasing daylight exposure and reducing intense periods of near work may be helpful.



Efficacy Comparison of 16 Interventions for Myopia Control in Children

A Network Meta-analysis

Jinhai Huang, MD,^{1,2,*} Daizong Wen, MD,^{1,3,*} Qinmei Wang, MD,^{1,2,*} Colm McAlinden, MB BCh, PhD,^{1,4,5,*}
Ian Flitcroft, FRCOphth, DPhil,^{6,*} Haisi Chen, MD,^{1,2} Seang Mei Saw, PhD,⁷ Hao Chen, MD,¹
Fangjun Bao, MD,^{1,2} Yune Zhao, MD,^{1,2} Liang Hu, MD,^{1,2} Xuexi Li, MD,³ Rongrong Gao, MD,^{1,2}
Weicong Lu, MD,^{1,2} Yaoqiang Du, MD,¹ Zhengxuan Jinag, PhD,⁸ Ayong Yu, PhD,^{1,2} Hengli Lian, MS,⁹
Qiunuo Jiang, MD,^{1,2} Ye Yu, MD,^{1,2} Jia Qu, MD, PhD^{1,2}

Conclusions: This network analysis indicates that a range of interventions can significantly reduce myopia progression when compared with single vision spectacle lenses or placebo. In terms of refraction, atropine, pirenzepine, and progressive addition spectacle lenses were effective. In terms of axial length, atropine, orthokeratology, peripheral defocus modifying contact lenses, pirenzepine, and progressive addition spectacle lenses were effective. The most effective interventions were pharmacologic, that is, muscarinic antagonists such as atropine and pirenzepine. Certain specially designed contact lenses, including orthokeratology and peripheral defocus modifying contact lenses, had moderate effects, whereas specially designed spectacle lenses showed minimal effect. *Ophthalmology* 2016; 123:697-708 © 2016 by the American Academy of Ophthalmology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).



Ophthalmic Technology Assessment



Atropine for the Prevention of Myopia Progression in Children

A Report by the American Academy of Ophthalmology

Stacy L. Pineles, MD,¹ Raymond T. Kraker, MSPH,² Deborah K. VanderVeen, MD,³ Amy K. Hutchinson, MD,⁴ Jennifer A. Galvin, MD,⁵ Lorri B. Wilson, MD,⁶ Scott R. Lambert, MD⁷

Conclusions: Level I evidence supports the use of atropine to prevent myopic progression. Although there are reports of myopic rebound after treatment is discontinued, this seems to be minimized by using low doses (especially atropine 0.01%). *Ophthalmology* 2017;124:1857-1866 © 2017 by the American Academy of Ophthalmology

ATROPINA

Optom Vis Sci. 2014 Mar;91(3):342-50. doi: 10.1097/OPX.0000000000000178.

Atropine slows myopia progression more in Asian than white children by meta-analysis.

Li SM¹, Wu SS, Kang MT, Liu Y, Jia SM, Li SY, Zhan SY, Liu LR, Li H, Chen W, Yang Z, Sun YY, Wang N, Millodot M.

⊕ Author information

Abstract

PURPOSE: To conduct a meta-analysis on the effects of atropine in slowing myopia progression and to compare Asian and white children and randomized controlled trials (RCTs) and observational studies.

METHODS: Randomized controlled trials and observational studies that assessed the effects of all concentrations of atropine in slowing myopia progression in children were searched from MEDLINE, EMBASE, and the Cochrane Library up to April 2013. Jadad scoring was used to evaluate the quality of RCTs, and the Newcastle-Ottawa Scale was used for observational studies.

RESULTS: Four RCTs and seven cohort studies (a kind of observational study) with 1815 children aged 5 to 15 years were included. The children had a baseline refraction of -0.50 to -9.75 diopters (D) and were followed up for 22.0 months (range, 12.0 to 36.5 months). The weighted mean differences in myopia progression in RCTs and cohort studies of Asian children were 0.55 D per year ($p < 0.01$) and 0.54 D per year ($p < 0.001$), respectively, and 0.35 D per year ($p = 0.01$) in cohort studies of white children. Compared with placebo, the risk of fast myopia progression (>1.0 D per year) using atropine was significantly decreased in both RCTs (odds ratio [OR], 0.14; $p < 0.01$) and cohort studies (OR, 0.08; $p < 0.01$), and the benefit of slow myopia progression (<0.50 D per year) using atropine was significantly increased in both RCTs (OR, 6.73; $p < 0.01$) and cohort studies (OR, 22.10; $p < 0.01$).

CONCLUSIONS: Atropine could significantly slow myopia progression in children, with greater effects in Asian than in white children. Randomized controlled trials and cohort studies provided comparable effects.

ATROPINA

Arch Soc Esp Oftalmol. 2018 Apr;93(4):182-185. doi: 10.1016/j.oftal.2017.12.015. Epub 2018 Feb 15.

Superdiluted atropine at 0.01% reduces progression in children and adolescents. A 5 year study of safety and effectiveness. (n=18)

[Article in English, Spanish]

Diaz-Llopis M¹, Pinazo-Durán MD².

⊕ Author information

Abstract

OBJECTIVE: To confirm the clinical security and effectiveness of the daily application of 0.01% superdiluted atropine eyedrops in the progression of myopia in children.

MATERIAL AND METHODS: A total of 200 children 9-12 years of age were randomised into a treated group and a control without treatment. Refraction under cycloplegia was performed.

RESULTS: Myopia progression of the treated group was -0.14±0.35 versus -0.65±0.54 in the control group without treatment. Only 2% of patients were forced to stop treatment due to side effects. (al año, no LA)

CONCLUSION: Atropine superdiluted atropine 0.01% eyedrops is effective and well tolerated, and reduced myopia progression by 25%.

MULTICÉNTRICO ESPAÑOL

- Galicia
- Castilla León
- Castilla La Mancha
- Navarra
- País Vasco



NOT AUTHORIZED

- Madrid
- Cataluña
- Andalucía

ATROPINA



- Hay **nivel de evidencia I** de que la atropina reduce la progresión de la miopía en la infancia como máximo 1 dp al año
- La mayoría de los estudios son en **población asiática**
- Las **concentraciones altas** tienen mayor eficacia, pero también mayor efecto rebote tras la suspensión del tratamiento
- Las **concentraciones bajas** son más tolerables dado sus mínimos efectos secundarios, con efecto más mantenido a largo plazo.
- La concentración **0.01%** parece la dosis más indicada para ralentizar la progresión de la miopía en la infancia.
- Aún quedan muchos interrogantes ¿cuándo iniciar? ¿Cuándo suspender? etc...
- ¿Tratamiento combinado?
- ¿Otros fármacos?



Update in myopia and treatment strategy of atropine use in myopia control

Pei-Chang Wu¹ · Meng-Ni Chuang¹ · Jessy Choi² · Huan Chen³ · Grace Wu⁴ · Kyoko Ohno-Matsui⁵ · Jost B Jonas⁶ · Chui Ming Gemmy Cheung⁴

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one of the mechanisms leading to the uncontrolled axial elongation of the globe. Atropine is currently the most effective therapy for myopia control. Recent clinical trials demonstrated low-dose atropine eye drops such as 0.01% resulted in retardation of myopia progression with significantly less side effects compared to higher concentration preparation

Rationale for use of atropine

To date, atropine is the only medication that has been demonstrated to be consistently effective in slowing myopic progression [17, 18]. Once myopia has developed in a child, the rate of progression is estimated to be around -1 D per

ATROPINA



Update in myopia and treatment strategy of atropine use in myopia control

Pei-Chang Wu¹ · Meng-Ni Chuang¹ · Jessy Choi² · Huan Chen³ · Grace Wu¹ · Kyoko Ohno-Matsui⁴ · Jost B Jonas⁵ · Chui Ming Gemmy Cheung³

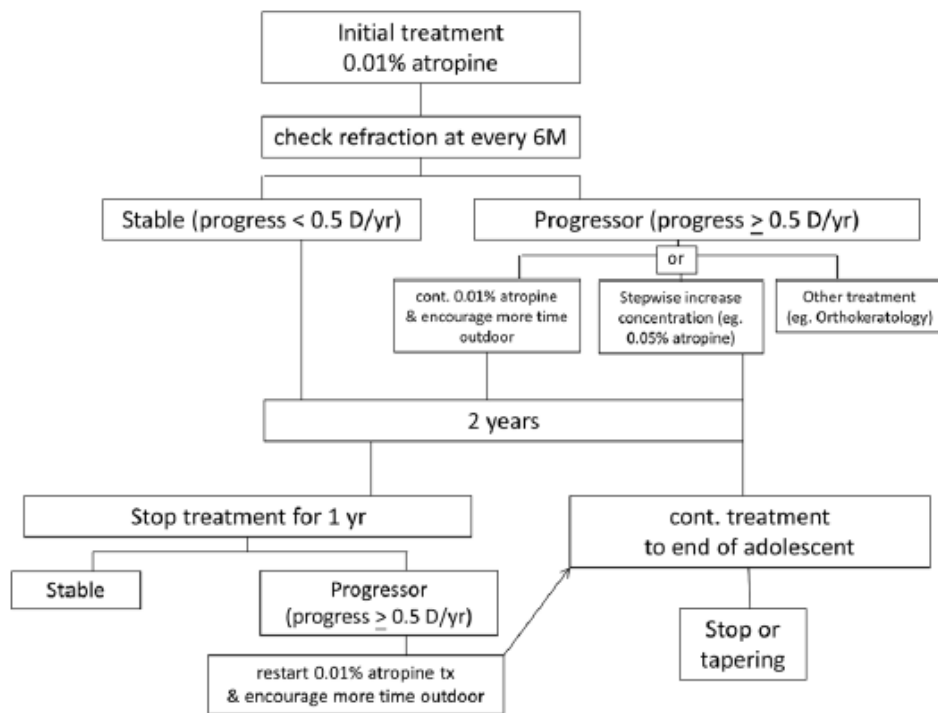


Fig. 1 The proposed strategy of atropine treatment for myopia control in clinical implementation

RESEARCH ARTICLE

Open Access

Efficacy and safety of interventions to control myopia progression in children: an overview of systematic reviews and meta-analyses



- La **atropina** es la intervención que actualmente ha demostrado ser más eficaz en el control de la progresión de la miopía
- El tratamiento debe durar al menos **2 años** y posteriormente debe valorarse según la tasa de progresión miópica en esos 2 años
- Hay un porcentaje no despreciable de **no respondedores**
- Otras intervenciones que han demostrado ser eficaces son:
 - ❖ La **ortoqueratología** (con riesgo de queratitis microbiana)
 - ❖ Las **LC multifocales** (con menor riesgo de queratitis infecciosa)
 - ❖ El aumento del **tiempo al aire libre**

Ophthalmology. 2019 Jan;126(1):113-124. doi: 10.1016/j.ophtha.2018.05.029. Epub 2018 Jul 6.

Low-Concentration Atropine for Myopia Progression (LAMP) Study: A Randomized, Double-Blinded, Placebo-Controlled Trial of 0.05%, 0.025%, and 0.01% Atropine Eye Drops in Myopia Control.

Yam JC¹, Jianq Y², Tanq SM², Law AKP², Chan JJ², Wong E², Ko ST³, Young AL⁴, Tham CC², Chen LJ⁴, Panq CP².

- Dosis **0.05%** máxima eficacia con buena tolerancia
- Sólo **1 año** de seguimiento
- Pendientes de mayor tiempo de evolución + resultado de **ATOM₃**

ATROPINA - GUÍA DE ACTUACIÓN

- Edad diana **5-14 años**, aunque tampoco hay contraindicación en $<5 / >14$
- Indicado en aquellos niños con **progresión > 0.50 dp al año**
- Concentración **0.01%** 1 gota diaria antes de dormir
- **Consentimiento informado** con padres o tutores
- Graduación bajo **cicloplejia + LA previo al tratamiento**
- Revisiones **cada 6 meses**
- **Respondedores:** tratamiento al menos 2 años o continuado hasta los 16 años
- **No respondedores:** al menos 1 año de tratamiento:
 - aumentar dosis
 - ofrecer otra alternativa de tratamiento

NUESTROS RESULTADOS

- **40** niños sanos y sin otra patología oftalmológica
- Al menos progresión de **0.5dp** en el año previo a iniciar tratamiento
- Edad **10.8 ± 2.5** (6-16 años)
- **35%** varones
- EE **-3.5±1.6dp** (-0.75 / -9.25)
- 1 gota de **atropina 0.01%** todas las noches antes de acostarse en cada ojo
- Revisión oftalmológica completa cada **6 meses**

NUESTROS RESULTADOS

Atropina 0.01%	Pretratamiento	12 meses
EE (dp)	-0.84 ± 0,37 (n=80)	-0.33 ± 0.48 (n=50)
LA (mm)	-	0.22 ± 0.24 (n=50)

- **4 niños NO RESPONDEDORES**
- **1 PÉRDIDA**

Atropina 0.01%	Pretratamiento	12 meses
EE (dp)	-0.84 ± 0,37 (n=80)	-0.14 ± 0.20 (n=40)
LA (mm)	-	0.16 ± 0.23 (n=40)

ARMAS FARMACOLÓGICAS

- **Agentes antimuscarínicos**
 - Atropina
 - Pirenzepina
 - Otros (tropicamida / escopolamina)
- **Hipotensores**
- **Metilxantina 7-MX**
- Análogos colinérgicos nicotínicos
- Inhibidores de acetilcolinesterasa
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- Otros factores de crecimiento

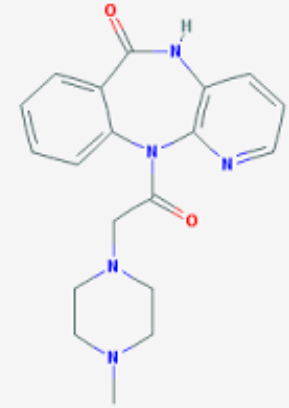


Ganesan P. Pharmaceutical intervention for myopia control. Expert Rev Ophthalmol 2010 Dec;5:759-787.

PIRENZEPINA

- Menor efecto midriático
- Menor parálisis de la acomodación
- Gel 2% cada 12 horas

- Menor eficacia que atropina
- Posología más incómoda



*Bartlett JD, et al. J Ocul Pharmacol Ther 2003;19:271-9.
Tan DT. Ophthalmology 2005;112:84-91.*

OTROS ANTIMUSCARÍNICOS

➤ TROPICAMIDA

Aplicación nocturna

Efecto corta duración

No estudios randomizados

➤ ESCOPOLAMINA

Farmacocinética muy similar a atropina



HIPOTENSORES OCULARES

BETA BLOQUEANTES (maleato de timolol)

- 159 niños aleatorizado
- ↓PIO 3 mm Hg
- no efecto sobre miopía

Jensen H. Myopia progression in young school children. A prospective study of myopia progression and the effect of a trial with bifocal lenses and β blocker eye drops. Acta Ophthalmol. Suppl. 1991;200:1-79.

METILXANTINA 7-MX

- Efecto en remodelación y crecimiento ocular en conejos
- Oral
- Seguro
- Mínimo efecto sobre miopía (ensayo piloto 36 m)



Trier K, Munk Ribel-Madsen S, Cui D, Brogger Christensen S. Systemic 7-methylxanthine in retarding axial eye growth and myopia progression: a 36-month pilot study. J. Ocul. Biol. Dis. Infor. 2008;1(2-4):85-93..

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