Prevention of Myopia Progression with 0.05% Topical Atropine: 2-Year Results in a Portuguese Cohort

Prevenção de Progressão da Miopia com Atropina Tópica 0,05%: Resultados de 2 Anos numa Coorte Portuguesa

Madalena Sousa Gonçalves [1], Margarida Brízido [2], Florence Aerts [1], Filipa Ching [3], Ana Rita Azevedo [1], Ana C. Almeida [1]

[1] Ophthalmology Department, ULS Loures Odivelas, Hospital Beatriz Ângelo, Loures, Portugal
[2] Ophthalmology Department, ULS Almada Seixal, Hospital Garcia de Orta, Almada, Portugal
[3] Pharmacy Department, ULS Loures Odivelas Hospital Beatriz Ângelo, Loures, Portugal

Recebido/Received: 2024-11-11 | **Aceite/Accepted:** 2025-04-16 | **Published online/Publicado online:** 2025-06-04

DOI: https://doi.org/10.48560/rspo.38890

ABSTRACT

INTRODUCTION: Myopia is considered by many an emerging public health challenge. Different forms of treatment have been proposed to treat myopia progression, one of them being topical atropine. The purpose of our study was to evaluate the efficacy and safety of 0.05% atropine eyedrops in controlling myopia progression in a cohort of Portuguese children over 2 years.

METHODS: Children aged 4 to 16 years old with myopic refraction of at least -1.00 dioptre (D) and myopia progression of ≥ -0.50 D/year were enrolled in this prospective non-randomized interventional single-center study. Patients were prescribed 0.05% atropine eye drops to be applied once nightly to both eyes over a period of 2 years. Outcome measures were change in spherical equivalent (SE) and axial length (AL) over 2 years.

RESULTS: Of the 55 children enrolled in the study, 24 children have completed 2 years of treatment (12 female). At the 2-year follow-up, mean SE was -5.76 (±2.36) D and mean AL was 25.27 (±1.08) mm. Change of SE from baseline was -0.47 (±0.50) D and AL change from baseline was 0.31 (±0.27) mm. After 2 years of treatment, 5 children showed no progression on SE and AL and discontinued treatment, with a mean change of SE of 0.175 D and AL of 0.10 mm. None of the patients who completed the 2-year follow-up reported adverse effects.

CONCLUSION: In this cohort, 0.05% atropine eye drops were safe, well-tolerated and effectively retarded progression of SE and AL.

KEYWORDS: Administration, Topical; Atropine/administration & dosage; Child; Myopia/drug therapy.

RESUMO

INTRODUÇÃO: O A miopia atinge atualmente proporções epidémicas e é considerada um desafio de saúde pública. Neste sentido, têm surgido várias formas de terapêutica para controlo da progressão da miopia, sendo uma delas a atropina tópica. O objetivo deste estudo é avaliar a eficácia e segurança de atropina 0,05% tópica no controlo da progressão da miopia numa coorte

de crianças portuguesas ao longo de 2 anos de tratamento.

MÉTODOS: Crianças com idades compreendidas entre 4 e 16 anos, com refração miópica de pelo menos -1,00 D e progressão da miopia de ≥ -0,50 D/ano aceitaram participar neste estudo prospetivo não-randomizado intervencional. Foi prescrita atropina 0,05% tópica para aplicar uma vez à noite nos dois olhos ao longo de 2 anos. Os objetivos foram avaliar a progressão da miopia em termos de alterações no equivalente esférico (EE) e comprimento axial (CA).

RESULTADOS: Um total de 55 crianças foram inscritas no estudo e dessas 24 completaram os 2 anos de seguimento (12 do sexo feminino). Aos 2 anos de seguimento, a média de EE era -5,76 (±2,36) D e de CA era 25,27 (±1,08) mm. A variação registada após 2 anos de tratamento no EE foi de -0,47 (±0,50) D e no CA foi de 0,31 (±0,27) mm. Cinco crianças mostraram ausência de progressão da miopia e o tratamento foi descontinuado, com uma média de diferença de EE de 0,175 D e de CA 0,10 mm. Nenhuma das crianças que completou os 2 anos de seguimento reportou qualquer efeito adverso.

CONCLUSÃO: Em crianças portuguesas, o uso de atropina 0,05% tópica foi seguro, bem tolerado e eficaz no controlo da progressão do EE e CA.

PALAVRAS-CHAVE: Administração tópica; Atropina/administração e dosagem; Criança; Miopia/tratamento farmacológico.

INTRODUCTION

With projections indicating that nearly half of the world's population may be affected by 2050, myopia is reaching epidemic proportions and constitutes an emerging public health challenge.[1,2] Axial myopia occurs due to excessive elongation of the eye, which causes images from distant objects coming into focus in front of the retina, leading to blurred distance vision.[1] According to the World Health Organization (WHO) classification myopia is characterized by a spherical equivalent (SE) objective refractive error of less than -0.50 dioptres (D) oftentimes correlated with an increase in axial length (AL).[3]

Changes in AL are more commonly associated with refractive error during childhood and puberty, which places early childhood as the optimal period for prevention and therapy of myopia, reducing myopia-related complications such as myopic macular degeneration and retinal detachment.[4] Pathologic myopia carries huge treatment costs; studies have shown that the cost increment is over 100% if myopia progresses to the pathologic state (US$ 166 to US$ 1,210) and a further 100% increment when pathologic myopia progresses to blindness (US$ 1,210 to US$ 2,420).[5] Screening 100 000 children and providing myopia progression treatment could avoid 816 cases of high myopia, 462 cases of pathologic myopia, and 7 cases of blindness.[5]

Several new forms of treatment have been proposed to treat myopia progression, such as defocus incorporated multiple segments (DIMS) spectacle lenses, highly aspherical lenslet target (HALT) lenses, orthokeratology and topical atropine.[1,6] Atropine is a non-selective muscarinic antagonist that has proven efficacy in myopia progression control in various concentrations, the most common being 1%, 0.5%, 0.1%, 0.05% and 0.01%.[7] The pathological mechanism of myopia and the pathways involved in the anti-myopic effects of atropine are still largely unknown. However, some evidence on the matter does exist.[6,8] Pharmacologically, atropine acts in different ocular tissues such as cornea, iris, ciliary body and muscles, lens' epithelium, retina, choroid and sclera, with good bioavailability. Non-accommodative mechanisms for developing myopia may be influenced by atropine, namely by increasing scleral fibrous layer and choroid thickness and modulating expression and activity levels of several retinal growth factors.[6,8]

A meta-analysis of 19 studies suggested a concentration-independent mechanism for atropine efficacy in myopia progression control, whereas the adverse effects are concentration-dependent.[9] Recent data from low-concentration atropine for myopia progression (LAMP) have proposed the dose of 0.05% for maximum efficacy with minimal side effects.[6,7,9] The purpose of our study was to evaluate the efficacy and safety of 0.05% atropine eye drops in controlling myopia progression in a cohort of Portuguese children over 2 years.

MATERIAL AND METHODS

This study was conducted from August 2021 to August 2023 at Hospital Beatriz Ângelo in Lisboa, Portugal. Children aged 4 to 16 years with myopic refraction of at least -1.00 D and myopia progression of ≥ -0.50 D/year were enrolled in this prospective non-randomized interventional single-center study. Children with ocular diseases (e.g., cataract, congenital retinal diseases, amblyopia and strabismus), previous or current use of other optical methods for myopia control (e.g., DIMS spectacle lens) were excluded. Written informed consent was obtained from parents or guardians. The study was approved by the Ethics Committee of Hospital Beatriz Ângelo. All procedures were conducted according to the tenets of the Declaration of Helsinki.

Participants were prescribed 0.05% atropine eye drops, applied once nightly to both eyes. Eye drops were prepared by the hospital's pharmacy. Cycloplegic refraction, axial length, and best-corrected visual acuity (BCVA) were measured at baseline and every six months thereafter. Cycloplegic autorefraction was performed using an autorefractor and confirmed by retinoscopy after a cycloplegia regimen (two drops of cyclopentolate 1%, 10 minutes apart, applied 60 minutes before the exam). SE was calculated as spherical power plus half of the cylinder power. Ocular AL was measured on Zeiss IOL Master (Carl Zeiss Meditec Inc, Dublin, CA). The primary outcome was myopia progression in terms of SE change over 2 years. Secondary outcomes included AL change at 2 years. The primary safety outcome measure was the occurrence of adverse events, which were actively monitored at each visit.

Statistical data analysis was performed using SPSS statistical software version 9.

RESULTS

A total of 55 children (110 eyes) were recruited. Of these, 24 children completed 2 years follow-up, 15 completed 1 year of follow-up, 10 completed 6 months of follow-up, and 6 have less than 6 months of follow-up. Seven children opted out of the study (dropout rate of 12.73%): 3 for lack of compliance, 2 for inability to collect the eye drops and 2 due to adverse effects (headache (1) and reduced near visual acuity (1)). Our current analysis focuses on the 24 children (12 female) who have completed the 2-year follow-up.

The mean age at the start of treatment was 10.83 years of age (range 6-16). At baseline, mean SE was -5.39 (±2.37) D, and mean AL was 25.21 (±1.45) mm. At the 2-year follow-up, mean SE was -5.76 (±2.36) D and mean AL was 25.27 (±1.08) mm. Change of SE from baseline was -0.47 (±0.50) D and AL change from baseline was 0.31 (±0.27) mm. All data from SE and AL parameters at 6, 12 and 24 months of follow-up, as well as changes of SE and AL, are summarized in Table 1.

After 2 years of treatment, 5 children showed no progression on SE and AL and opted to discontinue treatment, with a mean change of SE of 0.175 D and AL of 0.10 mm. None of the patients who completed the 2-year follow-up reported adverse effects.

DISCUSSION

In the present study, we investigated the effect of 0.05% atropine eye drops on myopia progression in a real-world setting among children aged 4 to 16 years old with SE of at least -1.00 D and myopia progression of ≥0.50 D/year. Over a 24-month period, there was a clear stabilization of myopia progression in children who were progressing at least -0.50 D per year and 5 children opted to suspend treatment due to no progression.

The first large-scale study investigating topical atropine efficacy was Atropine for the Treatment of Myopia (ATOM) 1, a randomized placebo-controlled clinical trial in an Asian population, that concluded atropine 1% eyedrops were effective, but with significant visual side effects, which led to a high dropout rate.[10] The ATOM2 trial included Asian children aged 6-12 years with myopia of at least -2.00 D and were randomly assigned to 0.5%, 0.1%, and 0.01% atropine, with a 2-year follow-up.[10] The mean SE change at 2-year was more significant in the 0.5% (-0.30±0.60 D) compared to 0.1% and 0.01% groups (-0.38±0.60 and -0.49±0.63 D, respectively).[10] The mean increase in AL was 0.27±0.25, 0.28±0.28, and 0.41±0.32 mm in the 0.5%, 0.1%, and 0.01% groups, respectively.[10] In our study 0.05% atropine performed very similarly to the obtained results with 0.1% in terms of SE and AL mean changes over a 2-year follow-up. This was also observed in other clinical trials and could be explained by the fact that efficacy of atropine is dose-independent, and side effects are dose-dependent.[9,11-13]

In the Childhood Atropine for Myopia Progression (CHAMP) randomized clinical trial, performed in a mainly non-Asian population aged from 6 to 10 years, participants were randomly assigned with 0.01% or 0.02% atropine eye drops or placebo, over a 36-month follow-up.[14] Atropine, 0.01%, was associated with significantly higher responder rates than placebo at all time points, whereas atropine, 0.02%, was associated with a higher responder rate *vs* placebo only at month 12.[14] In the 0.01% atropine group change in SE from baseline was -1.04 D and change in AL from baseline was 0.68 mm, with a significant difference *vs* placebo ($p < 0.001$).[14] In our study, atropine 0.05% revealed a more significant mean change in SE and AL at 24-month (-0.47 D and 0.31 mm, respectively, versus -0.79 D and 0.51 mm in CHAMP).[14]

More recently, the LAMP trial, a randomized placebo-controlled clinical trial, included Asian children aged 4 to

Table 1. Ophthalmic Parameters at Follow-Up Visits (baseline and at 6, 12 and 24 months).

	Baseline		6 months		12 months		24 months	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
SE (D)	-5.39	2.37	-5.64	2.53	-5.70	2.38	-5.76	2.36
AL (mm)	25.21	1.45	25.04	1.00	25.05	1.08	25.27	1.08
Mean change SE			-0.22	0.44	-0.27	0.44	-0.47	0.5
Mean change AL			0.056	0.072	0.16	0.13	0.31	0.27

SE – spherical equivalent; D – diopters; mm – millimeters; AL – axial length; SD – standard deviation.

12 years old that were randomly assigned to 0.05%, 0.025% and 0.01% atropine and placebo.[11] At 2-year follow-up, mean change in SE in the 0.05% and 0.01% atropine groups and placebo were -0.46 D, -0.84 D and -1.01 D, respectively,[11] whereas mean change in AL in the 0.05% and 0.01% atropine groups and placebo were 0.48, 0.63 and 0.70 mm, respectively.[11] In our study, mean SE change was similar to the LAMP study, whereas mean AL change over 2 years was inferior (0.31 mm vs 0.48 mm in LAMP2).

Patients from our sample are older than cohorts from previous studies (mean age at the start of the treatment of 10.83 years *vs* 8.45 years in LAMP1) and also had higher grades of baseline myopia (mean baseline SE of -5.91 D *vs* -3.98 D, -3.93 D, -4.49 D and -4.50 D, and mean baseline AL of 25.21 mm *vs* 24.85 mm, 24.88 mm, 25.13 mm and 25.07 mm, in LAMP1, LAMP2, LAMP3 and LAMP4, respectively).[11-13] This, in addition to the small sample size and different population, might help to explain the differences found in the current study.[11-13]

Contrary to previous studies, Repka *et al*[15] in a randomized clinical trial including 187 children aged 5 to 12 years in the US, concluded that atropine, 0.01%, eye drops delivered nightly over 2 years did not slow myopia progression or axial elongation. The lack of benefit from atropine, 0.01%, in their study differs from the results of at least 5 clinical trials in East Asian and South Asian populations with similar age and refractive error eligibility criteria.[15] This difference might partly be explained due to differences in follow-up, ethnicity with different myopia progression rates or different atropine 0.01%, eye drop formulation. This study highlights the inconsistent results of various studies of low-dose atropine for myopia control published over the last few years and the importance of validating results in different populations.

In the MOSAIC study, a 2024 randomized clinical trial performed in a European population with 2-year follow-up, the authors concluded that 0.01% atropine treatment efficacy was greater during the second year.[16] Given recent evidence from the LAMP study that 0.05% atropine is the best dosage balancing efficacy with side effects, the second phase of the MOSAIC will cross over the placebo-assigned patients to 0.05% atropine for a 12-month period,[16] which will be interesting to compare with our findings. This was also verified by Ha *et al* in a recent meta-analysis in which atropine at 0.05% concentration ranked as the most beneficial.[9]

As no single treatment has 100% efficacy in all patients, there is increasing interest in combined treatment for its add-on effect,[17,18] although randomized clinical trials are still needed to understand treatment sustainability over longer periods of follow-up.

A 2022 systematic review comparing 0.01% topical atropine and orthokeratology (OK lens) showed that combined use of OK lens and 0.01% atropine was more effective than monotherapy with OK lens or 0.01% atropine.[17] When it was further compared with other atropine dosages, the combined treatment had a similar efficacy to high-dose atropine.[17] Longer follow-up periods are needed to evaluate treatment sustainability and compliance over time.

Relatively to the DIMS lens, a recent 2-year double-masked randomized controlled experiment revealed that myopia progression was 52% slower in the DIMS group than in the single vision (SV) group, and axial elongation was 62% less in the DIMS group than in the SV group.[19] This proved that DIMS lenses are an effective and safe treatment for myopia progression control.

In a systematic review, when comparing results at 1-year from studies using 0.05% atropine or DIMS or HALT lenses, it was noted a reduction in SE progression of 67%, 87% and 67% respectively, and a reduction on axial elongation of 51%, 61% and 64% respectively.[20]

Huang *et al* studied the efficacy of 0.01% atropine and DIMS lenses combined or DIMS lenses alone or SV lenses alone, in myopia control in Chinese children aged 7 to 12 years old.[21] This study revealed that combined treatment was the most effective in slowing myopia progression, with a mean SE change of -0.49 ± 0.66 D and a mean AL change of 0.28 ± 0.24 mm, at 1-year follow-up.[21]

Another retrospective study analysed Chinese myopic children who received 3 different optical treatments combined with 0.01% atropine: one group with SV lenses (SV + AT), another with DIMS lenses (DIMS + AT) and another with OK lenses (OK + AT).[22] At 12 months, DIMS + AT was the group with the most significant results in slowing myopia progression.[22] Similarly, Nucci P *et al* compared 0.01% atropine, DIMS lens and combined treatment in a European population, and concluded that combined treatment was the most effective.[18]

Contrary to this results, in a retrospective comparative study conducted in Portuguese children in 2023, Guimarães *et al* compared 0.01% atropine and DIMS lens.[23] The authors concluded DIMS lens were superior to atropine in preventing AL elongation at 6 months (p = 0.038).[23] However, there was no statistically significant difference on SE variation between groups at 6 months (p = 0.302).[23] Confronted with our results, the different atropine concentration, along with the fact shorter follow-up period, may explain the different results.

Also, even results from similar study protocols are heterogeneous. Several clinical and demographic factors may influence myopia progression, such as baseline rates of progression, degree of myopia, age at presentation and ethnicity,[9,10] and even the stability of the atropine solution, which may explain the different obtained results. That being said, randomized clinical trials are needed to confirm the various treatments' efficacy in head-to-head comparative studies, conducted in different populations, and adjusted to age and myopia degree.

Considering different topical atropine dosages, a meta-analysis by Ha *et al* and the LAMP study, have proposed that the optimal atropine concentra¬tion should be the one with the best balance between efficacy and safety.[6,9,10] Atropine at a concentration of 0.05% demonstrated superior performance in balancing efficacy and safety in a Chinese cohort of children.[9,11-13] In the present cohort, only 2 children reported mild treatment-related adverse effects.

In a recent meta-analysis comparing optical, pharma-

cological and environmental interventions for myopia control, it was also pointed out that unwanted effects related to myopia control interventions were not consistently reported, and emphasized the need for improved methods to monitor adverse effects,[20] highlighting the need to better standardize and actively question adverse effects during follow-up visits.

Myopia is a rising global public health problem that requires lifetime interventions, from prevention of myopia progression and correction of refractive error to treatment of pathologic myopia.[19] There are still various questions that remain unanswered related to myopia control. We still lack evidence on the best timing to initiate and suspend treatment, optimal atropine dosage, possible rebound effect and efficacy of combined treatments. It is important to perform head-to-head large-scale comparative studies to best understand the most effective treatment, considering different populations, ages and other characteristics (e.g., iris colour). The predominance of the Asian population in large clinical studies limits generalizability of the findings.[9]

As no direct comparisons have been made between all the different treatment modalities, we are still unable to establish a specific treatment order, such as designating one as the first-choice or second-choice therapy.[24] More studies are needed with direct comparisons between the different treatment modalities.

A key strength of our study is that it only included non-Asian children, contrarily to most studies with low-concentration atropine that involve almost exclusively Asian children. The broad age range of children recruited can be a strength and a limitation, since statistical analysis was not adjusted to those parameters.

A major limitation of our study is the lack of a control group, which hinders comparative statistical analysis, as well as the small sample size.

CONCLUSION

In summary, our study demonstrated that 0.05% atropine may effectively delay progression of SE and elongation of AL in Portuguese children, without significant side effects.

Further studies are needed to evaluate long-term efficacy of 0.05% atropine on myopia progression, as well as determine optimal timing for treatment suspension, monitor possible rebound effect and compare with other types of treatment, including combined modalities.

CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO

MSG, MB, FA, ARA and ACA: Drafting of the text, sourcing and editing of investigation results, and critical revision for important intellectual content.

All authors approved the final version to be published.

MSG, MB, FA, ARA e ACA: Redação do texto, obtenção e edição dos resultados da investigação e revisão crítica do conteúdo intelectual importante.

Todos os autores aprovaram a versão final a ser publicada.

RESPONSABILIDADES ÉTICAS

Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.

Fontes de Financiamento: Não existiram fontes externas de financiamento para a realização deste artigo.

Confidencialidade dos Dados: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.

Proteção de Pessoas e Animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pela Comissão de Ética responsável e de acordo com a Declaração de Helsínquia revista em 2024 e da Associação Médica Mundial.

Proveniência e Revisão por Pares: Não comissionado; revisão externa por pares.

ETHICAL DISCLOSURES

Conflicts of Interest: The authors have no conflicts of interest to declare.

Financing Support: This work has not received any contribution, grant or scholarship

Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of patient data.

Protection of Human and Animal Subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and those of the Code of Ethics of the World Medical Association (Declaration of Helsinki as revised in 2024).

Provenance and Peer Review: Not commissioned; externally peer-reviewed.

REFERENCES

1. Zhu Q, Tang GY, Hua ZJ, Xue LP, Zhou Y, Zhang JY, et al. 0.05% atropine on control of myopia progression in Chinese school children: a randomized 3-year clinical trial. Int J Ophthalmol. 2023;16:939-46. doi: 10.18240/ijo.2023.06.17.
2. Holden BA, Fricke TR, Wilson DA, Jong M, Naidoo KS, Sankaridurg P, et al. Global Prevalence of Myopia and High Myopia and Temporal Trends from 2000 through 2050. Ophthalmology. 2016;123:1036-42. doi: 10.1016/j.ophtha.2016.01.006.
3. World Health Organization The Impact of Myopia and High Myopia In: Myopia. WHO Library. Geneve: WHO;2016;
4. Kleinstein RN, Jones LA, Hullett S, Kwon S, Lee RJ, Friedman NE, et al. Refractive error and ethnicity in children. Arch Oph-

thalmol. 2003;121:1141-7. doi: 10.1001/archopht.121.8.1141.
5. Agyekum S, Chan PP, Zhang Y, Huo Z, Yip BH, Ip P, et al. Cost-effectiveness analysis of myopia management: A systematic review. Front Public Health. 2023;11:1093836. doi: 10.3389/fpubh.2023.1093836.
6. Yam JC, Jiang Y, Tang SM, Law AK, Chan JJ, Wong E, et al. 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. Ophthalmology. 2019;126:113-24. doi: 10.1016/j.ophtha.2018.05.029.
7. Li FF, Kam KW, Zhang Y, Tang SM, Young AL, Chen LJ, et al. Differential Effects on Ocular Biometrics by 0.05%, 0.025%, and 0.01% Atropine: Low-Concentration Atropine for Myopia Progression Study. Ophthalmology. 2020;127:1603-11. doi: 10.1016/j.ophtha.2020.06.004.
8. Chierigo A, Ferro Desideri L, Traverso CE, Vagge A. The Role of Atropine in Preventing Myopia Progression: An Update. Pharmaceutics. 2022;14:900. doi: 10.3390/pharmaceutics14050900.
9. Ha A, Kim SJ, Shim SR, Kim YK, Jung JH. Efficacy and Safety of 8 Atropine Concentrations for Myopia Control in Children: A Network Meta-Analysis. Ophthalmology. 2022;129:322-33. doi: 10.1016/j.ophtha.2021.10.016.
10. Chia A, Chua WH, Cheung YB, Wong WL, Lingham A, Fong A, et al. 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). Ophthalmology. 2012;119:347-54. doi: 10.1016/j.ophtha.2011.07.031.
11. Yam JC, Zhang XJ, Zhang Y, Yip BH, Tang F, Wong ES, et al. Effect of Low-Concentration Atropine Eyedrops vs Placebo on Myopia Incidence in Children: The LAMP2 Randomized Clinical Trial. JAMA. 2023;329:472-81. doi: 10.1001/jama.2022.24162. Erratum in: JAMA. 2023;329:1123. doi: 10.1001/jama.2023.3989.
12. Yam JC, Zhang XJ, Zhang Y, Wang YM, Tang SM, Li FF, et al. Three-Year Clinical Trial of Low-Concentration Atropine for Myopia Progression (LAMP) Study: Continued Versus Washout: Phase 3 Report. Ophthalmology. 2022;129:308-21. doi: 10.1016/j.ophtha.2021.10.002.
13. Zhang XJ, Zhang Y, Yip BH, Kam KW, Tang F, Ling X, et al. Five-Year Clinical Trial of the Low-Concentration Atropine for Myopia Progression (LAMP) Study: Phase 4 Report. Ophthalmology. 2024;131:1011-20. doi: 10.1016/j.ophtha.2024.03.013.
14. Zadnik K, Schulman E, Flitcroft I, Fogt JS, Blumenfeld LC, et al; CHAMP Trial Group Investigators. Efficacy and Safety of 0.01% and 0.02% Atropine for the Treatment of Pediatric Myopia Progression Over 3 Years: A Randomized Clinical Trial. JAMA Ophthalmol. 2023;141:990-9. doi: 10.1001/jamaophthalmol.2023.2097. Erratum in: JAMA Ophthalmol. 2023;141:1005. doi: 10.1001/jamaophthalmol.2023.4206.
15. Repka MX, Weise KK, Chandler DL, Wu R, Melia BM, Manny RE, et al. Low-Dose 0.01% Atropine Eye Drops vs Placebo for Myopia Control: A Randomized Clinical Trial. JAMA Ophthalmol. 2023;141:756-65. doi: 10.1001/jamaophthalmol.2023.2855.
16. Loughman J, Kobia-Acquah E, Lingham G, Butler J, Loskutova E, Mackey DA, et al. Myopia outcome study of atropine in children: Two-year result of daily 0.01% atropine in a European population. Acta Ophthalmol. 2024;102:e245-56. doi: 10.1111/aos.15761.
17. Tsai HR, Wang JH, Huang HK, Chen TL, Chen PW, Chiu CJ. Efficacy of atropine, orthokeratology, and combined atropine with orthokeratology for childhood myopia: A systematic review and network meta-analysis. J Formos Med Assoc. 2022;121:2490-500. doi: 10.1016/j.jfma.2022.05.005.
18. Nucci P, Lembo A, Schiavetti I, Shah R, Edgar DF, Evans BJ. A comparison of myopia control in European children and adolescents with defocus incorporated multiple segments (DIMS) spectacles, atropine, and combined DIMS/atropine. PLoS One. 2023;18:e0281816. doi: 10.1371/journal.pone.0281816.
19. Lam CS, Tang WC, Tse DY, Lee RP, Chun RK, Hasegawa K, et al. Defocus Incorporated Multiple Segments (DIMS) spectacle lenses slow myopia progression: a 2-year randomised clinical trial. Br J Ophthalmol. 2020;104:363-8. doi: 10.1136/bjophthalmol-2018-313739.
20. Lanca C, Pang CP, Grzybowski A. Effectiveness of myopia control interventions: A systematic review of 12 randomized control trials published between 2019 and 2021. Front Public Health. 2024;12:1460156. doi: 10.3389/fpubh.2024.1460156.
21. Huang Z, Chen XF, He T, Tang Y, Du CX. Synergistic effects of defocus-incorporated multiple segments and atropine in slowing the progression of myopia. Sci Rep. 2022;12:22311. doi: 10.1038/s41598-022-25599-z. Erratum in: Sci Rep. 2023;13:9650. doi: 10.1038/s41598-023-36663-7
22. Cao X, Guo Z, Wei Z, Ming H, Ma B, Zhao Y,et al. Effect of 0.01% atropine eye drops combined with different optical treatments to control low myopia in Chinese children. Cont Lens Anterior Eye. 2025;48:102317. doi: 10.1016/j.clae.2024.102317.
23. Guimarães S, Barros da Silva P, Oliveiros B, Silva E. Myopia control: short-term effect of 0.01% atropine vs. defocus incorporated multiple segment lenses-a retrospective study in European children. Int Ophthalmol. 2023;43:3777-84. doi: 10.1007/s10792-023-02788-x.
24. Tariq F, Mobeen R, Wang X, Lin X, Bao Q, Liu J, et al. Advances in myopia prevention strategies for school-aged children: a comprehensive review. Front Public Health. 2023;11:1226438. doi: 10.3389/fpubh.2023.1226438.

Corresponding Author/
Autor Correspondente:

Madalena Sousa Gonçalves
Rua Padre António Vieira, nº1 1º Frente,
Porto Salvo
2740-113 Oeiras, Portugal
E-mail: madalena.tssg@gmail.com

ORCID: 0000-0002-1313-4847