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Atropine and Spectacle lens Combination Treatment (ASPECT): 12-month results of a randomised controlled trial for myopia control using a combination of Defocus Incorporated Multiple Segments (DIMS) lenses and 0.025% atropine

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ABSTRACT

Aim To evaluate and compare the efficacy of combination treatment using 0.025% atropine and Defocus Incorporated Multiple Segments (DIMS) spectacle lenses to 0.025% atropine and single vision (SV) spectacle lenses in slowing myopia progression in children with myopia.

Methods Randomised controlled trial conducted on children aged 4–16 years with myopia between −1.00D and −6.00D and astigmatism ≤2.00D. Children were randomly allocated into two groups: 0.025% atropine and SV spectacle lenses treatment group (group A), and 0.025% atropine and DIMS spectacle lenses treatment group (group B). Cycloplegic spherical equivalent refraction (SER) and axial length were measured at baseline, 6 and 12 months.

Results 102 patients completed the 12-month follow-up: n=49 in group A, mean age 9.50±2.78 years and n=53 in group B, mean age 9.90±2.47 years. At 12 months, the mean AL±SD change was 0.18±0.16 mm in group A and 0.07±0.16 mm in group B (mean difference: 0.11, 95% CI: 0.05 to 0.17; p≤0.001). Mean SER±SD progression at 12 months was −0.19±0.42D and −0.09±0.35D in groups A and B, respectively (p=0.13). 39.6% of children in group B had no axial elongation over 12 months compared with 12.2% of the children in group A (p=0.002).

Conclusions Combination treatment with 0.025% atropine and DIMS spectacle lenses is more effective in controlling axial elongation than 0.025% atropine with SV lenses. Although not significant, SER differences between groups were lower in group B. These findings support a potential additive effect of the two treatments.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Defocus Incorporated Multiple Segments (DIMS) spectacle lenses and atropine have proven effectiveness as stand-alone treatments in controlling myopia progression in children. However, there is a scarcity of evidence of their efficacy when used in combination. This is the first randomised controlled trial to assess and report on the efficacy of 0.025% atropine plus DIMS spectacle lenses.

WHAT THIS STUDY ADDS

⇒ Children with myopia treated with combination therapy achieved emmetropic age-matched axial length growth over 12 months, and approximately 4 out of 10 children had no axial elongation over 12 months.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Combination therapy is a promising intervention for myopia management, as it appears to be more effective than monotherapy.

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INTRODUCTION

Myopia has become a major global public health problem, recently classified as a disease by the National Academies of Sciences, Engineering, and Medicine.[1] According to this report, the increasing prevalence and severity of this condition worldwide requires that myopia is recognised as a disease and that the impact of its complications is taken seriously, such that timely and collaborative measures may be implemented to ensure its prevention and management.

Currently, myopia management includes interventions such as lifestyle changes, pharmacological treatment, mainly with atropine eye drops, optical interventions and, more recently, light-based approaches such as low-level red-light therapy.[2–6] The application of atropine for myopia management is currently 'off-label' in Europe, the United States and many other countries. However, several

studies have widely documented their efficacy and safety over the last decades.[5 7] On the contrary, a new generation of spectacle lenses with an optical design specifically intended for myopia control has been developed in recent years. These spectacle lenses have evidenced stand-alone efficacy in controlling myopia progression and axial elongation.[6 8 9] However, there is limited scientific evidence on their efficacy and safety when combined with another myopia management intervention.

This is the first randomised controlled trial (RCT) to assess the efficacy and safety of combined treatment with atropine eye drops and Defocus Incorporated Multiple Segments (DIMS) spectacle lenses in Europe and, to the best of our knowledge, worldwide. Previous retrospective and nonrandomised studies have published promising effectiveness of combined treatment with 0.01% atropine and DIMS spectacle lenses, showing less myopia progression and axial elongation with combination treatment compared with monotherapy with either atropine or DIMS spectacle lenses individually.[10 11] Nonetheless, atropine is known to have dose-dependent effectiveness and furthermore the efficacy of atropine at doses of 0.01% has been questioned, so it is of particular interest to analyse the efficacy of combined treatment with higher atropine concentrations in a controlled and randomised setting.[7 12] The aim of this RCT is to evaluate and compare the efficacy of combination treatment using 0.025% atropine and DIMS spectacle lenses compared with 0.025% atropine and single vision (SV) spectacle lenses in slowing myopia progression in children with myopia.

MATERIALS AND METHODS

Study design

This is an RCT that included children aged 4–16 years with myopia with SER between −1.00 and −6.00 dioptres (D) and astigmatism ≤2.00D. The study was conducted at the Ophthalmology Service of Hospital Clinico San Carlos, Madrid, Spain, a public metropolitan tertiary referral hospital. Participants in this study were randomised to receive 0.025% atropine eye drops and SV spectacle lenses (group A) or 0.025% atropine eye drops and DIMS spectacle lenses (group B) at an allocation ratio of 1:1 in blocks of six using the automatic randomisation module of Research Electronic Data Capture. The allocation sequence was concealed from those assigning participants to intervention groups until participants were enrolled and allocated to interventions. The trial is registered in the European Union Clinical Trials Register (EudraCT number 2021-003373-64 and ClinicalTrials.gov ID NCT06431841). This study adhered to the tenets of the Declaration of Helsinki and was approved by the ethics committee of Hospital Clinico San Carlos (21/522-EC_M). Written informed consent was obtained from parents or guardians, written assent from those 12 years and older and verbal consent from all other participants. Participants were unmasked due to the study design including an active control group. However, participants and parents/caregivers were unaware of their group allocation and unaware of which spectacle lenses (SV, group A or DIMS, group B) they were wearing. Outcome measurements were performed by clinicians who were unaware of the treatment each participant was receiving.

Inclusion and exclusion criteria

Inclusion criteria were as follows: (1) age 4–16 years; (2) SER between −1.00 and −6.00D; (3) astigmatism ≤2.00D and anisometropia ≤1.50D; (4) monocular best-corrected visual acuity (BCVA) 0.02 logMAR (6/9) or better; (5) myopia progression of >−0.50D SER in either eye in the preceding year and (6) acceptance of the study design and written informed consent and assent if 12 years of age or older. Exclusion criteria were as follows: (1) strabismus and binocular vision abnormalities; (2) ocular and systemic abnormalities or baseline condition of the patient that do not allow the examination to be performed (eg, mental or psychomotor retardation); (3) prior ocular surgery and (4) history of myopia control treatments.

Interventions

0.025% atropine eye drops were supplied by the same authorised compounding pharmacy to ensure uniformity and consistency in the preparation of all eye drops. The compounding process is regulated by Spanish legislation (Royal Decree 175/2001), which establishes the rules for elaborating any compounding process and the Good Manufacturing Practice. All participants were asked to instil one drop every night in both eyes. Atropine eye drops were packaged in 5 mL bottles without preservatives, and the expiration date of 1 month was labelled on each bottle. Eye drops were prescribed by electronic health prescription, and each bottle's pickup date at the pharmacy could be tracked to monitor compliance. Atropine and spectacle lens compliance were also assessed by questionnaire and monitored by telephone visits at 3-month intervals.

DIMS spectacle lenses (MiYOSMART, HOYA, Japan) consist of a central optical zone (9.4 mm diameter) for distance prescription and a multiple annular focal zone with multiple segments (33 mm diameter) having a relative positive power (+3.5D). The diameter of each segment is 1.03 mm.[6] Single-vision spectacle lenses were provided by HOYA (Lens 1.67 EYNOA). All lenses in the study were custom-made and made of plastic material. Nano-Vista Group donated frames for both groups. All patients attending the myopia unit where the study was conducted receive a booklet about myopia and its risk factors such as environmental and lifestyle factors. The research team did not provide any additional material or advice on lifestyle changes to the study participants, as they would have received this in any case.

Procedures

All participants were followed up according to the same schedule and examination protocol: baseline visit, 3 months (telephone visit), 6 months and 12 months after the baseline visit.

At each visit, distant BCVA in the logarithm of the minimum angle of resolution (logMAR) was assessed using the Early Treatment Diabetic Retinopathy Study chart. Near visual acuity was evaluated using best-corrected distance refraction with a reduced logMAR reading chart at 40 cm. Cycloplegic and noncycloplegic refraction were performed using Huvitz autorefractor and keratometer (HRK-7000A Huvitz Co., Ltd., Gunpo, Republic of Korea); cycloplegic refraction was performed according to the following schedule: three cycles of one eye drop of 1% cyclopentolate (Novartis, Basel, Switzerland) administered to both eyes 5 min apart. Cycloplegic autorefraction was performed 30 min after the last eye drop. Additional eye drops were administered before cycloplegic refraction if the pupils were not fully dilated or reacted to light after the complete regimen. Axial length (AL) was measured with an optical biometer (Lenstar LS 900, Haag-Streit, Koeniz, Switzerland). The average of five autorefractors and AL measurements for each eye were used for analysis. Mesopic and photopic pupil sizes were measured with the wave-front analyser (KR-1W, Topcon, Tokyo, Japan). The complete ocular examination included accommodation and binocular vision assessment, stereopsis, slit lamp exam of the anterior segment, intraocular pressure, corneal endothelial

cell density (ECD) with specular microscopy using EM-4000 (Tomey, Nagoya, Japan), fundus examination and optical coherence tomography (OCT) of the macula and optic nerve using enhanced depth imaging EDI-OCT (Heidelberg Spectralis, Heidelberg Engineering, Heidelberg, Germany). All participants initiated both treatments (atropine and SV or DIMS spectacle lenses) simultaneously, 2 weeks after the baseline visit, to allow for customised lens fitting.

Outcome variables

Spherical equivalent refraction (SER) and AL under cycloplegia were measured at baseline and at 6 months and 12 months. The primary outcomes were myopia progression, which was the difference between the mean cycloplegic SER at the baseline and subsequent visits and the change of AL, which was the difference between the mean AL at the baseline and subsequent visits.

Sample size calculation

To achieve 90% power to detect a difference of 0.50D (0.70D SD) in myopia progression between the two groups at the 0.05 significance level (two-tailed),[5 8] and assuming a dropout rate of approximately 15%, the minimum number of subjects required in each group was 49.

Statistical analysis

Descriptive data are presented as the mean and SD for continuous variables and as absolute and relative frequencies for categorical variables.

Depending on the data distribution, differences between the two eyes were assessed using either a paired sample t-test or the Wilcoxon signed-rank test.

Differences between the two groups in demographic and baseline characteristics were evaluated using an independent sample t-test or the nonparametric Mann-Whitney U test, as appropriate.

Factors associated with outcomes (AL and SER at 6 or 12 months) were analysed using a linear regression model, adjusted both in univariate and multivariate analyses for the baseline value. The results are expressed as beta coefficients with standard errors, along with the corresponding p-values.

RESULTS

Study participants

A total of 392 children with myopia were examined for eligibility, and subsequently, 111 children were enrolled in the trial. Participants were randomly allocated to groups A (n=55) and B (n=56). At the 12-month visit, 9 participants did not attend the follow-up (figure 1): 6 (10.9%) children from group A and 3 (5.4%) children from group B (p=0.31). 102 subjects successfully completed the 12-month visit: 49 (48.03%) children in group A and 53 (51.96%) children in group B. There was no significant difference among group demographics. Baseline characteristics are shown in table 1.

Baseline differences between the right and left eyes were not statistically significant for the primary outcome variables (AL: p=0.18; SER: p=0.64). Therefore, only the right eye was considered for statistical analysis.

Primary outcomes: AL and SER changes

As for AL, at 12 months, the mean AL±SD change was 0.18±0.16 mm in group A and 0.07±0.16 mm in group B (mean difference: 0.11, 95% CI: 0.05 to 0.17; p≤0.001). Group B showed significantly less axial elongation than group A over time. Additionally, 21 out of 53 (39.6%) of the children in group B had no axial elongation over 12 months compared with 6 out of 49 (12.2%) of the children in group A (p=0.002). Table 2 shows AL and SER changes at 6 and 12 months.

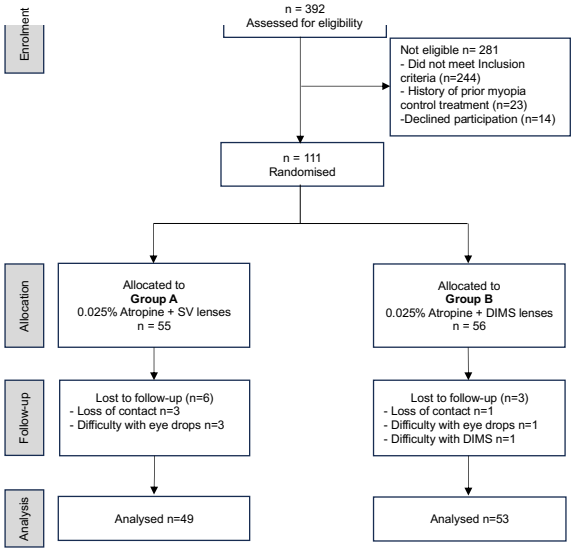

Figure 1 Consolidated Standards of Reporting Trials of the study. DIMS, Defocus Incorporated Multiple Segments; SV, single vision.

For SER changes, the mean SER±SD change over 12 months was −0.19±0.42D and −0.09±0.35D for groups A and B, respectively (p=0.13). Changes in AL and SER over time are shown in figure 2. In addition, the proportion of children progressing by 0.2 mm or more in AL and 0.5 D or more in SER over 12 months was also compared between the two groups. For AL, 40.8% of children in group A progressed by 0.2 mm or more, as opposed to only 20.8% of children in group B (p=0.027). For SER, 20.4% of children in group A progressed 0.5D or more compared with 18.9% of children in group B (p=0.844).

Factors associated with AL and SER progression

At 12 months, the age group (11–15 years, β=−0.094, p=0.025) and group B (β=−0.100, p=0.004) were associated with reduced axial elongation in the multivariate analysis, indicating that older children and those in group B had slower AL change (online supplemental table 1). Baseline AL was a highly significant predictor of AL progression in both the univariate (β=0.982, p<0.001) and multivariate models (β=1.010, p<0.001).

For SER, the univariate analysis indicated that Hispanic ethnicity (β=0.194, p=0.012) and 'other' ethnic groups (β=0.345, p=0.012) were associated with slower myopia progression at 12 months. Parental myopia (both parents) was significantly associated with faster SER progression (β=−0.297, p=0.003). However, all these variables lost significance in the multivariate model. Baseline SER was a significant predictor of change in SER (β=1.000, p<0.0019) in both univariate and multivariate models (online supplemental table 2).

The mean increase in photopic and mesopic pupil size at 12 months was 1.3±1.02 mm and 1.4±1.0 mm (p=0.70), and 0.8±0.9 mm and 0.5±0.84 mm (p=0.26) in groups A and B, respectively. 0.025% atropine eye drops were overall well-tolerated by children in both groups. Two children in group

Table 1 Demographic and baseline characteristics of the study participants

		Total	Group A	Group B	P value
Gender	Female	51 (50.0%)	25 (51.0%)	26 (49.1%)	0.84
	Male	51 (50.0%)	24 (49.0%)	27 (50.9%)	
Age		9.70±2.62	9.50±2.78	9.90±2.47	0.53
Ethnicity	Caucasian	42 (41.2%)	19 (38.8%)	23 (43.4%)	Caucasian vs other: 0.17
	Hispanic	51 (50.0%)	28 (57.1%)	23 (43.4%)	
	Arabic	8 (7.8%)	2 (4.1%)	6 (11.3%)	
	African	1 (1.0%)	0 (0.0%)	1 (1.9%)	
Age at myopia onset		7.60±2.61	7.30±2.57	7.80±2.65	0.33
Parental myopia	None	42 (43.3%)	20 (42.6%)	22 (44.0%)	0.64
	Only one	34 (35.1%)	15 (31.9%)	19 (38.0%)	
	Both	21 (21.6%)	12 (25.5%)	9 (18.0%)	
SER (D)		−2.3±1.20	−2.4±1.19	−2.2±1.21	0.14
AL (mm)		24.4±0.88	24.2±0.93	24.6±0.80	0.028
Photopic pupil size (mm)		3.6±0.71	3.5±0.70	3.8±0.70	0.09
Mesopic pupil size (mm)		6.6±0.91	6.3±0.96	6.8±0.82	0.010
Corneal ECD		3021.7±319.95	3022.5±346.58	3020.8±295.14	0.82
IOP		16.2±2.21	16.4±1.98	16.0±2.44	0.50
K1		43.1±1.29	43.5±1.32	42.8±1.17	0.008
K2		44.2±1.36	44.6±1.37	43.8±1.23	0.002

AL, axial length; ECD, endothelial cell density; IOP, intraocular pressure; K1, flat keratometry; K2, steep keratometry; SER, spherical equivalent refraction.

A dropped out secondary to atropine adverse effects, and two children in group B required photochromatic DIMS spectacle lenses in the 6-month visit as proposed to researchers to alleviate symptoms. In univariate and multivariate analyses, photopic and mesopic pupil size were not associated with SER and AL change at 12 months (online supplemental tables 1 and 2).

DISCUSSION

Children with myopia who received combination treatment with 0.025% atropine eye drops and DIMS spectacle lenses had less axial elongation over 12 months than those who received 0.025% atropine and SV spectacle lenses. This is the first RCT to evaluate the efficacy and safety of combination treatment using 0.025% atropine eye drops and DIMS spectacle lenses.

DIMS spectacle lenses have proven stand-alone efficacy in controlling SER and AL progression.[6 8 9] Lam *et al* reported a mean AL progression of 0.11±0.02 mm and 0.21±0.02 mm at 12 and 24 months, respectively, in Asian children.[6] McCullough *et al* evaluated the effectiveness of DIMS spectacle lenses in UK children, reporting axial elongation of 0.18±0.20 mm at 12 months.[13] Present trial results showed an AL change of 0.07±0.16 mm over 12 months in children with myopia using DIMS spectacle lenses plus 0.025% atropine eye drops. Therefore, children with combined intervention appear to have less axial elongation than DIMS spectacle lenses used as monotherapy in both Asian and European children with myopia. It is noteworthy that the mean age±SD of our study participants in group B was 9.90±2.47 years compared with 10.19±1.46 years and 10.3±2.4 years in the Asian and European studies, respectively.[8 13]

As for SER change, children with myopia using DIMS spectacle lenses showed a progression of SER of −0.17±0.05D and −0.36±0.42D over the 1 year in Asian and European populations, respectively.[10 13] The present study found a SER change of

Table 2 AL and SER changes over 6 and 12 months in groups A and B

	Group A (n=49)	Group B (n=53)	Mean difference, 95% CI	P value
Time/visit	Mean AL±SD (mm)			
$\Delta_{6\text{-}0}$ (Baseline to 6 months)	0.08±0.10	0.02±0.14	0.06 95% CI: 0.01 to 0.11	p=0.002*
$\Delta_{12\text{-}6}$ (6 months to 12 months)	0.10±0.08	0.04±0.07	0.06 95% CI: 0.03 to 0.09	p≤0.001*
$\Delta_{12\text{-}0}$ (Baseline to 12 months)	0.18±0.16	0.07±0.16	0.11 95% CI: 0.05 to 0.17	p≤0.001*
Time/visit	Mean SER±SD (D)			
$\Delta_{6\text{-}0}$ (Baseline to 6 months)	−0.06±0.26	0.02±0.21	−0.08 95% CI: −0.18 to 0.01	p=0.06
$\Delta_{12\text{-}6}$ (6 months to 12 months)	−0.13±0.30	−0.10±0.32	−0.03 95% CI: −0.16 to 0.09	p=0.46
$\Delta_{12\text{-}0}$ (Baseline to 12 months)	−0.19±0.42	−0.09±0.35	−0.10 95% CI: −0.26 to 0.05	p=0.13

*Statistically significant difference.
AL, axial length; SER, spherical equivalent refraction.

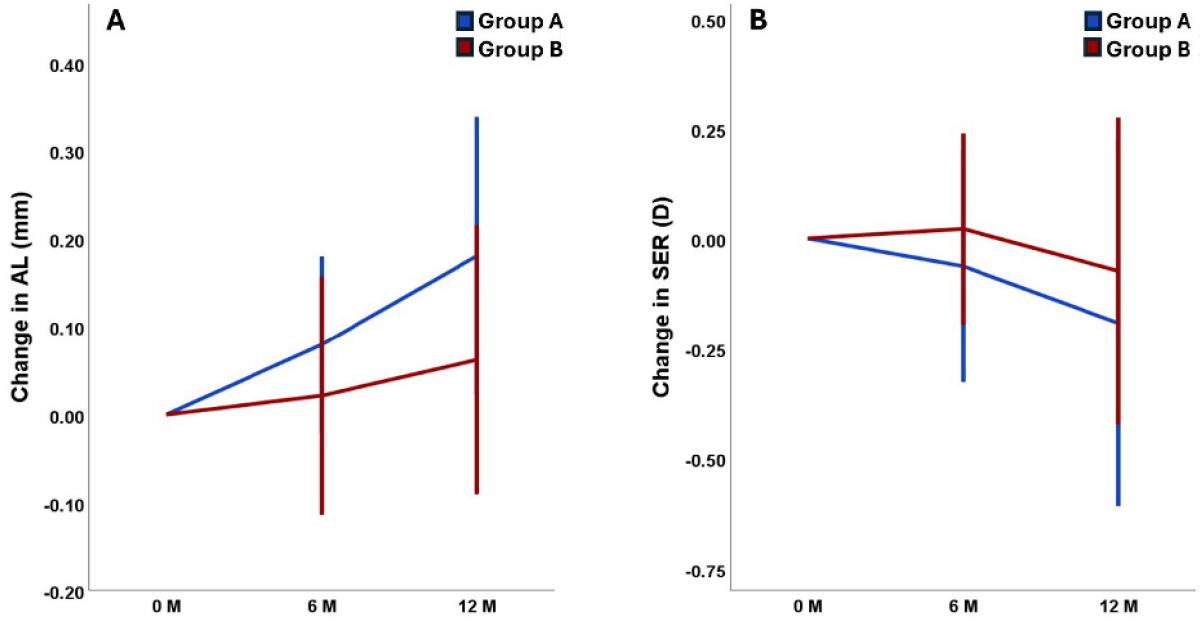

Figure 2 Changes in AL and SER over 1 year in group A (blue) and group B (red). Al, axial length; SER, spherical equivalent refraction.

−0.19±0.42D and −0.09±0.35D in groups A and B, respectively. Although SER changes between our treatment groups at 6 and 12 months were not statistically significant, combined therapy appears to have less SER progression than previous findings with DIMS spectacle lenses alone. Interestingly, and contrary to expectations, the change in AL and SER found in the European study was greater than the studies on the Asian population.[10 13 14] However, the former was an observational study, and the latter was an RCT like the current trial.

In the LAMP study, the change in SER at 1 year was −0.27±0.61D, −0.46±0.45D, −0.59±0.61D and −0.81±0.53D in the 0.05%, 0.025% and 0.01% atropine and placebo groups, respectively, with significant differences between groups ($p<0.001$).[5] In addition, the change in AL at 1 year was more significant in the placebo group (0.41±0.22 mm) than in the 0.05% (0.20±0.25 mm), 0.025% (0.29±0.20 mm) and 0.01% (0.36±0.29 mm) atropine groups ($p<0.001$). Thus, 0.025% atropine concentration significantly reduced myopia progression compared with placebo. Participants in group A (0.025% atropine+SV spectacle lenses) had a change in SER of −0.19±0.42D and AL of 0.18±0.16 mm. Further studies in non-Asian populations are needed to evaluate and compare the efficacy of 0.01% and 0.025% atropine for myopia management.

The scientific evidence on combined treatment with atropine eye drops and DIMS spectacle lenses is scarce. A retrospective study on Asian children with myopia reported improved effectiveness in controlling myopia progression and axial elongation in participants who received a combination of 0.01% atropine and DIMS compared with those who received DIMS or SV alone, with the authors suggesting a possible additive effect of the combination treatment.[11] In particular, SER and AL change over 12 months was −0.49±0.66D and 0.28±0.24 mm, respectively, in the atropine 0.01%+DIMS group. These findings are greater than those found in the present study, possibly because the study was conducted in Asian children and they used atropine concentrations of 0.01% instead of 0.025%. A nonrandomised, experimenter-masked prospective study in Italy investigated the effectiveness of 0.01% atropine+DIMS spectacle lenses in children of European ethnicity.[10] At 12 months, the 0.01% atropine+DIMS group showed a significant reduction in SER compared with DIMS or atropine alone. For AL change, all three treatment groups showed significantly less axial elongation (0.09±0.11 mm in the atropine group, 0.07±0.07 mm in the DIMS group and 0.06±0.08 mm in the DIMS+atropine group) than the control group (0.22±0.14 mm). However, the differences between the three treatment groups were not statistically significant.

The literature on myopia management often uses the percentage reduction in progression as an index to describe the treatment effect.[6 15 16] However, this index can be misleading, according to recent reports.[17] Considering the percentage reductions in this study, children in group B had 61.1% less axial elongation and myopia progressed 54.7% slower than those in group A.

The possible underlying mechanism behind the potential additive effect of combining atropine eye drops with DIMS spectacle lenses is currently unknown. However, it is hypothesised that the increased pupil size resulting from atropine may enhance the impact of DIMS spectacle lenses. In this sense, other studies with combination treatment of atropine and orthokeratology have suggested that pupils may hold the key to why a combined therapy of atropine and orthokeratology works better than either treatment alone.[18 19] In the present study, we analysed whether pupil size (photopic and mesopic) was associated with outcomes for both SER and AL and found no significant association.

Determining the contribution of age-normal physiological growth to axial elongation in myopic eyes is a complex but essential issue for evaluating the efficacy of myopia control interventions. Chamberlain *et al* suggested that the success of myopia progression control should be measured by how much axial elongation can be slowed to match the normal emmetropic eye growth of a child of the same age.[20] Hence, most myopia control interventions aim to achieve emmetropic eye growth. Axial elongation in 9-year-old European children is 0.34 mm/year (myopes) and 0.19 mm/year (emmetropes).[4] The Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error found that emmetropic eyes have an AL progression of 0.16 mm/year for 6–9-year-olds, 0.08 mm/year for 9–12-year-olds and

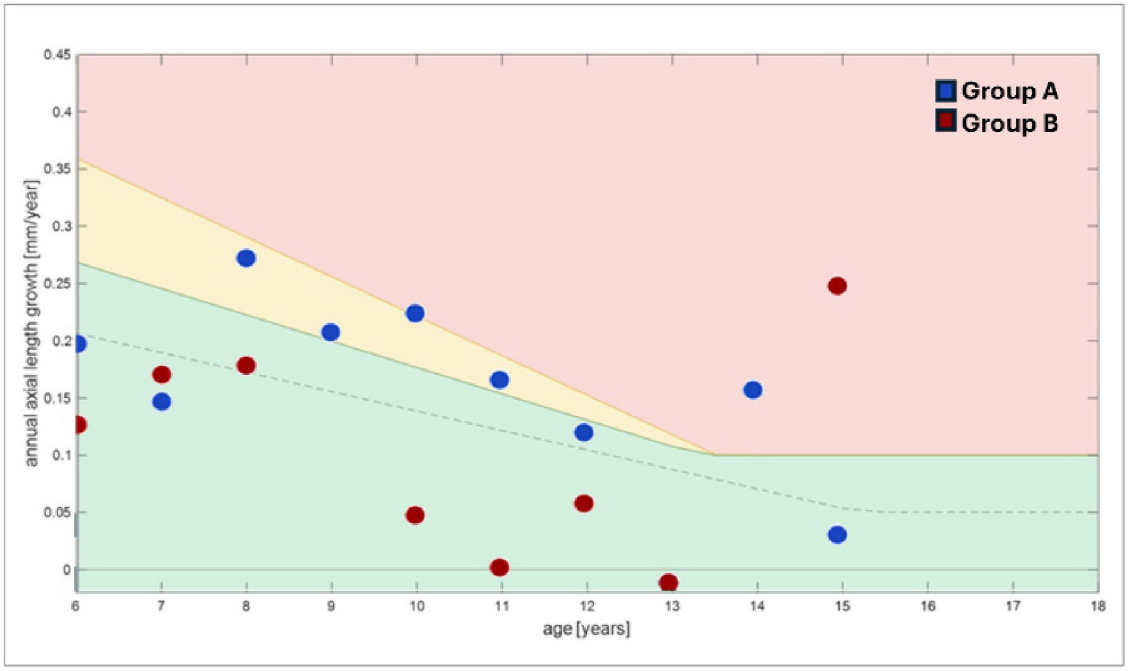

Figure 3 Axial length (AL) growth in groups A and B, plotted in the age-matched myopia control (AMMC) system.[22] For each age, the mean annual AL growth value is plotted within the colour-coded zones: 'green' corresponds to the physiological AL growth rate; 'yellow' corresponds to a moderately excessive AL growth rate (+25% but less than+50% of the average physiological AL growth rate) and 'red' reflects a highly excessive AL growth rate (more than 50% above the physiological AL growth rate). Each point represents the mean AL value for a given age. Note: This study included children aged 4–16 years, and the AMMC data included children aged 7–16 years; thus, children who did not meet the latter age were excluded.

0.02 mm/ year for 11–14-year-olds.[21] Our study found an axial elongation of 0.18 mm/year for group A (mean age 9.5 years) and 0.07 mm/year for group B (mean age 9.9 years). Recently, the Age-Matched Myopia Control system has developed a method to compare a patient's actual annual AL growth rate with the average physiological AL growth rate of an age-matched cohort of emmetropic children.[22] We use this approach to plot our findings (figure 3). According to these data, most patients treated with a combination of 0.025% atropine eye drops and DIMS spectacle lenses achieve comparable axial elongation to age-matched emmetropes during the first year of treatment. This suggests that combined therapy is a promising management strategy, especially for younger children with increased AL.

Additionally, 39.6% of participants in group B and 12.2% of participants in group A showed no increase in AL from baseline to 12 months. Nucci *et al* reported that 10% of the children in the DIMS group, 15% in the atropine group and 18% in the atropine+DIMS group had no axial elongation over 12 months.[10] Similarly, Lam and colleagues found that 14% of children wearing DIMS showed no increase in AL over 2 years.[6] We can, therefore, conclude that approximately 4 out of 10 children treated with combination therapy in our RCT did not experience axial elongation throughout the 12 months of treatment.

Study strengths and limitations

This is the first RCT to evaluate the efficacy of a combination treatment of 0.025% atropine eye drops and DIMS spectacle lenses in children with myopia. This study includes different ethnicities, reflecting the diversity of the world's major capitals, particularly in Europe. We evaluated and compared the progression of SER and AL in different ethnic groups. Although univariate analysis indicated that Hispanic and Arab (North African) ethnic groups were associated with slower progression of myopia at 12 months and a trend in AL change compared with Caucasians, multivariate analysis did not confirm these data. Combination therapy appears to be effective regardless of ethnicity, which is of particular value for clinical practice. One limitation of any study that uses atropine eye drops is compliance. Compliance has a direct impact on efficacy, regardless of the treatment modality.[23 24] This may affect one and/or both interventions and atropine eye drops and spectacle lenses. However, we did not find significant differences regarding compliance between the two treatment groups.

Finally, these are 12-month results from a 24-month RCT. It will be very valuable to know the longer-term efficacy of combined therapy for myopia control.

CONCLUSIONS

Combination treatment with atropine 0.025% and DIMS spectacle lenses is more effective in controlling axial elongation than atropine 0.025% with SV spectacle lenses. Children with myopia treated with combination therapy achieved emmetropic age-matched AL growth over 12 months, suggesting a promising approach for myopia management.

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