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EFFICACY OF 0.01% ATROPINE EYE DROPS IN REDUCING MYOPIA PROGRESSION.

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ABSTRACT

BACKGROUND: Myopia is a widespread refractive error that is becoming more common in young children and adolescents. Severe myopia predisposes individuals to degenerative ocular problems, including retinal detachment and myopic maculopathy, necessitating early management. Atropine eye drops at 0.01% may reduce myopia progression, although further research is needed on their efficacy and safety. O**BJECTIVE:** To evaluate the safety and efficacy of 0.01% atropine eye drops in controlling myopia progression in children. **METHODS AND MATERIALS:** The Department of Ophthalmology, Medical Teaching Institution-Khyber Teaching Hospital, Peshawar, Pakistan, conducted this quasi-experimental study. This study included 44 children aged 6-12 with SER -1.00-6.00 diopters with myopia progression > -0.50 diopters in the previous year. Every night for 18 months, participants were randomly either 0.01% atropine eye drops or a placebo. Main results were SER and AL. The data was analyzed with IBM SPSS (Version 25) and R. We used ANOVA to compare group time and medicine. **RESULTS:** The results show that 0.01% atropine may help delay the evolution of myopia, but the change was not statistically significant and should be examine cautious. Primary outcomes were the changes in spherical equivalent refraction (SER) and axial length (AL) over a six-month period. The intervention group showed a slower rate of myopia progression compared to the control group. The mean change in SER in the intervention group was -0.30 ± 0.18 diopters, while the control group showed a greater shift of -0.51 ± 0.22 diopters. Similarly, the increase in axial length was lower in the intervention group (0.14 ± 0.07 mm) compared to the control group (0.21 ± 0.09 mm). These findings reflect a trend toward reduced progression in the atropine-treated group, although the differences did not reach statistical significance ($p > 0.05$). **CONCLUSION:** These findings suggest a potential benefit of 0.01% atropine in slowing myopia progression, though differences were not statistically significant.

KEYWORDS: Myopia, Atropine, Spherical Equivalent Refraction, Axial Length, Randomized Clinical Trial

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INTRODUCTION

Myopia is a common refractive error that results in difficulty seeing distant objects clearly. Its worldwide prevalence has been increasing in the past several decades. The prevalence is particularly high among young children and adolescents [1]. By 2050, approximately 50 percent of the global population is projected to have myopia, with 10 percent having high myopia [2]. High myopia is a degenerative eye disease that increases the risk of pathological myopia, cataracts, retinal detachment, glaucoma, and other blinding complications and visual impairment [3]. Therefore, early detection and intervention are necessary to control the progression of myopia, especially in children who have a faster progression rate [4]. In order to delay the growth of myopia, more effective treatments including low-dose atropine, orthokeratology, and more outside exposure have demonstrated higher efficacy than earlier methods like under-correction [5].

Atropine eye drops used for myopia control are usually in a higher concentration, such as 1 percent. The use of 1% atropine eye drops for myopia control is not ideal considering its potential side effects. In general, there is an increasing interest in lower-concentration atropine eye drops, particularly 0.01% atropine[6]. Because atropine affects muscarinic receptors in ocular tissues, including axial elongation and accommodation, it is thought to decrease the onset of myopia[7]. It is believed that atropine predominantly affects the neuromodulation of eye development by acting on muscarinic receptors (M1–M4). By affecting scleral remodeling and maybe changing choroidal thickness, it may lessen axial elongation[8].

The retinal-ciliary-scleral signaling route, which is crucial in controlling axial elongation, is thought to be the mechanism by which atropine functions. Although the precise mechanism is still being investigated, this pathway is thought to be the major one involved in the control of ocular growth. The exact mechanism of atropine for inhibiting myopia progression is not yet known, but most studies are consistent with the view that atropine acts by reducing the accommodative response of the eyes mediated by the ciliary body, and it can reduce the axial elongation of myopia. It is well known that the slowdown of the elongation of the eyeball diameter can control the pathological changes in myopia[9]. In the mammalian eye, and possibly in humans, the growth and development of the eye are regulated by at least three independent mechanisms: visually guided signals, genetically determined local factors, and emmetropization systems. In this system, the cholinergic pathways of the retina—bipolar cells—inhibit signals to the retina at the ganglion cell layer, relaying the retinal afferent signal to retinal dopaminergic amacrine cells[10]. Thereafter, the dopaminergic cells supply dopaminergic signals to the amacrine cell of the inner retina and the parasympathetic efferent nerve of the ciliary body, retina, and lamina

propria via the superior cervical ganglion to inhibit retinal growth [10]. The exact mechanism by which atropine inhibits myopia progression remains under investigation, however many biochemical pathways have been proposed. Atropine is believed to operate in ocular tissues by non-selective blockage of muscarinic receptors (M1–M4), hence affecting ocular development[11]. The suggested processes encompass the modulation of retinal neuromodulators such as dopamine, the inhibition of scleral remodeling, and the impact on axial elongation and choroidal thickness. Atropine may enhance dopaminergic activity, which is crucial for regulating axial length and ocular development[12]. It may also prevent modifications in the extracellular matrix of the sclera, so limiting the structural elongation of the eye. Despite preclinical and clinical data supporting these routes, no one pathway has achieved unanimous consensus, indicating a complex mechanism of action [13].

Considering all lines of evidence, 0.01% atropine seems to have excellent safety and tolerability. Adverse reactions are largely related to pharmacologic factors and usually transient systemic side effects[14]. Recent clinical trial results among children of Southeast Asian descent are consistent with the tolerability and safety of 0.01% atropine daily, as reflected by the absence of any serious ocular adverse events[15]. However, growing concerns with widespread and potentially chronic use of 0.01% atropine, especially outside randomized clinical trial settings, emphasize the importance of frequent patient monitoring. This includes carefully assessing best-corrected visual acuity and overall ocular health during follow-up examinations. Although few, more severe ocular adverse events were reported secondary to 0.01% atropine drops in some trials and within large-scale observation registries, clinicians should be aware of the potential to manage them [16].

This study aims to to evaluate the safety and efficacy of 0.01% atropine eye drops, specifically in the treatment of rapidly progressive myopia in children. Rapidly progressive myopia is a significant concern in pediatric ophthalmology, as it can lead to severe visual impairment and increased risk of ocular complications. Atropine, an antimuscarinic agent, has shown promise in slowing myopia progression.

MATERIALS AND METHODS

The study was conducted prospectively from November 2024 to April 2025. Participants were enrolled at the beginning of the study. This design allowed for longitudinal monitoring of changes in spherical equivalent refraction (SER) and axial length (AL) over time. This quasi-experimental study utilized a parallel-group design to evaluate the impact of 0.01% atropine eye drops on axial length and spherical equivalent refraction in children with myopia. Participants were assigned to either an intervention group or a placebo group using a computer-generated random number table. However, allocation concealment was not implemented, indicating a limitation intrinsic to the quasi-experimental design and a potential source of selection bias at the Ophthalmology Department of Medical Teaching Institution-Khyber Teaching Hospital, Peshawar, Pakistan and comprising myopia patients aged 6–12 years. A sample size of 304 participants (152 each group) was determined using the OpenEpi sample size calculator, predicated on a 95% confidence level, 80% power, and an anticipated treatment effect size from prior research. Ultimately, only 44 individuals were registered due to logistical restrictions, a short recruiting schedule, and resource limits. This study was done as a preliminary examination, and results should be taken cautiously due to diminished statistical power.

The Hospital Ethical Review Board approved the study (Ref. No. 959/DME/KMC), and agreed upon informed consent was acquired from the

guardians of all participants after a comprehensive clarification of the study's aims and methodologies. To protect confidentiality participant data were anonymized.

Patients fulfilling inclusion criteria were enrolled from the Eye Outpatient Department (OPD) of Khyber Teaching Hospital, Peshawar. Included were children aged 6–12 years with spherical equivalent refraction (SER) between -1.00 and -6.00 diopters and documented myopia progression of ≥ -0.50 diopters over the preceding year. We excluded patients with a history of ocular surgery or trauma, allergies to atropine, the use of other myopia control interventions, ocular diseases such as cataract or amblyopia, and axial length (AL) asymmetry >1 mm in eyes. A computer-generated random number table was used to allocate participants at random to either the intervention or control group. There was no allocation concealment strategy used. Although the atropine and placebo groups were assigned to participants at random, no allocation concealment technique was used. This could have increased the possibility of selection bias, which is recognized as a study design problem. In the second group, group B, 0.01% atropine eye drops were administered once daily at bedtime for the duration of the study. Placebo eye drops identical in appearance to atropine drops were given to the placebo group in similar frequency and timing. Eye drops containing 0.01% atropine were applied to both eyes once a night to participants in the intervention group. This low-dose dosage is frequently researched as a safer substitute for greater concentrations (such as 0.05% or 0.1%) in pediatric applications.

At baseline, a complete ocular examination was performed for each of the participants, measuring spherical equivalent refraction (SER) and axial length (AL) the IOLMaster biometer (Carl Zeiss Meditec, Germany model 500) was used to measure axial length. We followed patients at 6 months, 1 year and 18 months. At each visit adherence with the prescribed treatment regimen was verified, and adverse events and side effects such as photophobia or allergic reaction was documented.

The primary endpoints were the change in SER and AL over the study duration in terms of comparison of the atropine and placebo groups. The frequency and severity of side effects participants reported were used to assess safety outcomes.

Data were recorded in an Excel sheet and analyzed with SPSS Version 25 and R. SER and AL values were calculated for descriptive statistics, such as means and standard deviations. Mean progression in SER and AL were compared between the atropine and placebo groups using an independent samples t-test. For spherical equivalent refraction (SER) and axial length (AL), within-group and between-group variations over time were evaluated using a repeated-measures ANOVA.

RESULTS

The progression of spherical equivalent refraction (SER) and axial length (AL), with the initial demographic characteristics of the atropine and placebo cohorts. Both groups had same gender ratios and average ages 8.36 ± 1.75 years in the atropine group compared to 8.64 ± 1.73 years in the placebo group. SER1 and AL1 did not exhibit statistically significant variation among groups at baseline. The placebo group exhibited a mean SER1 of -3.84 ± 1.04 D and an AL1 of 23.81 ± 0.50 mm, whereas the atropine group had a mean SER1 of -3.92 ± 1.09 D and an AL1 of 23.87 ± 0.50 mm.

Both cohorts exhibited myopia progression over the eighteen-month follow-up interval. The rate of improvement, however, exhibited variability. The placebo group had a more significant decrease from -3.84 D to -4.89 D (ΔSER = -1.05 D), while the atropine group demonstrated minimal change from SER1 to SER3 (-3.92 D; ΔSER = -0.30 D). The axial length exhibited a same trend. In both cohorts, AL increased from AL1 to AL3; in the atropine cohort (23.87 mm to 23.97 mm; ΔAL =

+0.10 mm), the gain was smaller than in the placebo cohort (23.81 mm to 24.42 mm; ΔAL = +0.61 mm). These patterns indicate a reduced rate of myopia progression in the atropine group.

Baseline axial length (AL) and spherical equivalent refraction (SER) were compared between the intervention and control groups using independent samples t-tests. Independent t-tests showed no significant differences in baseline measurements between the groups. P values for axial length (AL1) and spherical equivalent refraction (SER1) are 0.66 and 0.80, respectively.

Table 1: We have standardized the terminology for axial length (AL1, AL2, and AL3) and spherical equivalent refraction (SER1, SER2, SER3) across, tables for consistency and clarity among persons assigned to receive 0.01% atropine eye drops vs placebo.

Table 1. Demographic Characteristics and Baseline Measurements of Participants in Atropine vs. Placebo Groups (Baseline SER, 6-Month SER, 18-Month SER)

Characteristics	Atropine Group (n=23)	Placebo Group (n=21)	P-Values
Age (Mean ± SD)	8.36 ± 1.75	8.64 ± 1.73	
Gender (M/F)	13/10	9/12	
SER1 (Baseline)	-3.92 ± 1.09	-3.84 ± 1.04	0.80
SER2 (6-Month)	-4.06 ± 1.11	-4.29 ± 1.01	
SER3 (18-Month)	-4.22 ± 1.17	-4.89 ± 1.08	
AL1 (Baseline)	23.87 ± 0.40	23.81 ± 0.50	0.66
AL2 (6-Month)	23.91 ± 0.41	24.09 ± 0.51	
AL3 (18-Month)	23.97 ± 0.43	24.42 ± 0.57	

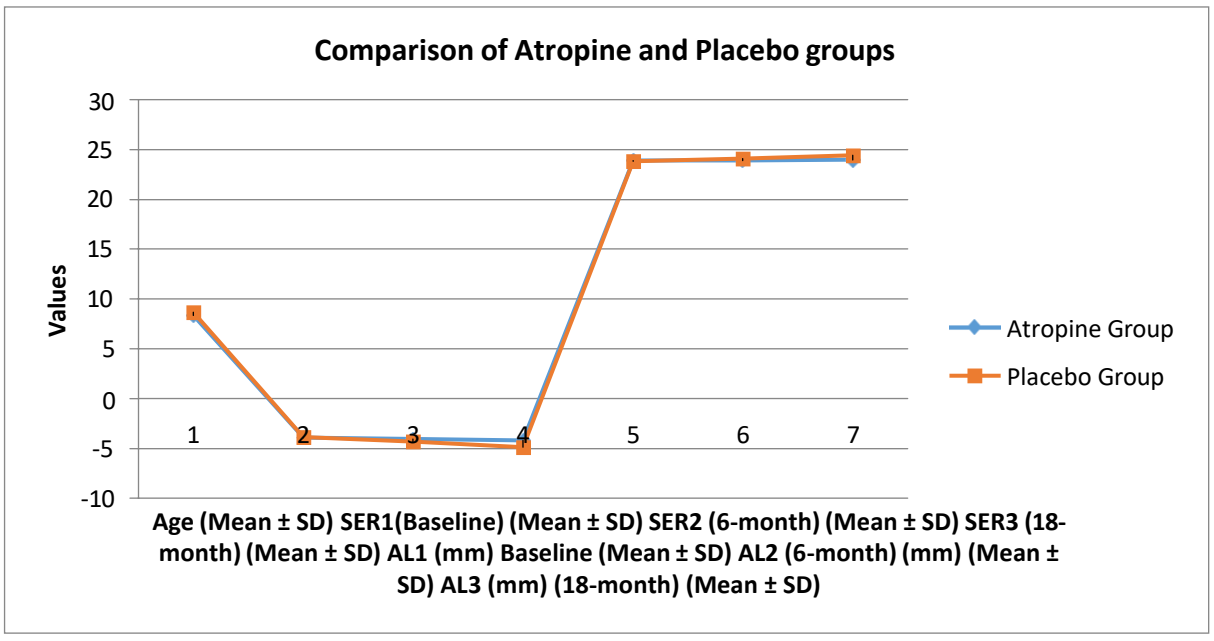
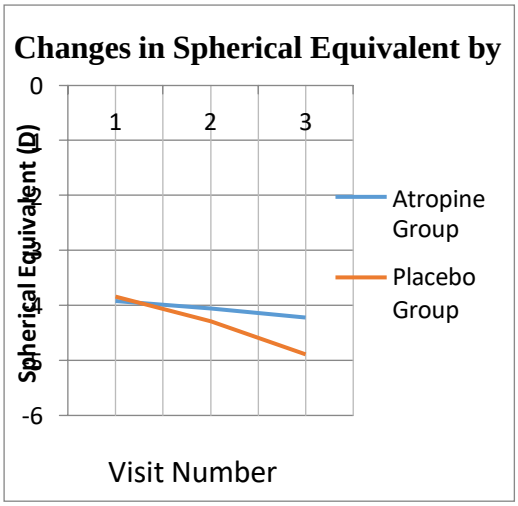
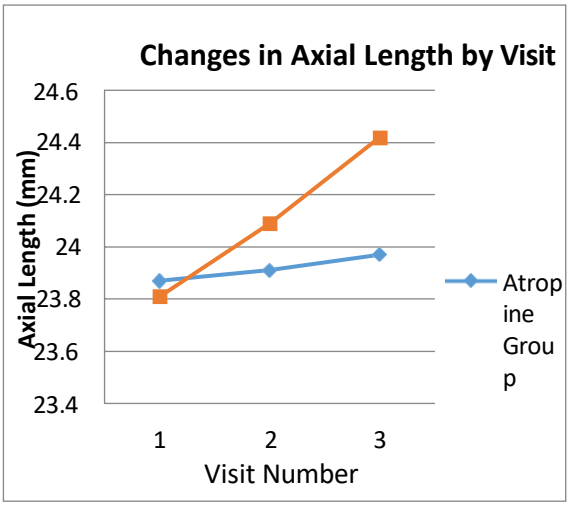


Figure 1: Changes in Spherical Equivalent Refraction (SER) and Axial Length (AL) Over Time by Group. Line chart comparing mean SER and AL progression between 0.01% atropine and placebo groups.

Figure 1 depicts the advancement of myopia in the atropine and placebo cohorts throughout three study visits, employing standardized assessments of spherical equivalent refraction (SER) and axial length (AL). The SER statistics (SER1 to SER3) indicate a distinct divergence among the groups over time. In the atropine cohort, the spherical equivalent refraction (SER) decreased somewhat from -3.92 D at baseline (SER1) to -4.22 D after 18 months (SER3), signifying a decelerated rate of myopic development. Conversely, the





placebo group had a more pronounced drop, with SER decreasing from -3.84 D to -4.89 D within the identical timeframe.

Measurements of axial length (AL) exhibit varying patterns of advancement. In the placebo group, AL significantly rose from 23.81 mm at baseline (AL1) to 24.42 mm after 18 months (AL3). The atropine group had a negligible rise in AL, ascending from 23.87 mm to 23.97 mm. These patterns indicate that 0.01% atropine may decelerate both the refractive and structural aspects of myopia development.

The results of the repeated measures ANOVA, which summarize changes in spherical equivalent refraction (SER) across visits (SER1, SER2, SER3), between treatment groups, and their interaction, are presented in Table 2. The analysis showed a significant effect of visit number, with a sum of squares of 9.48, $F(2, 84) = 214.98$, $p < .001$, and a partial eta-squared (η^2p) of 0.84. This indicates a substantial variation in SER across visits, independent of the treatment group, and confirms a significant progression of myopia over time.

There was no significant main effect of the treatment group, $F(1, 42) = 0.71$, $p = .404$, $\eta^2p = 0.02$, suggesting that the overall differences in SER between the atropine and placebo groups, when averaged across all visits, were not statistically meaningful. However, a significant interaction effect was observed between visit number and treatment group, with a sum of squares of 3.15, $F(2, 84) = 71.3$, $p < .001$, $\eta^2p = 0.63$. This indicates that the progression of SER differed significantly between the atropine and placebo groups at each visit. Specifically, myopia progression over time was slower in the atropine group compared to the placebo group. At baseline, the atropine group had a mean SER of -3.92 D, which progressed to -4.22 D by the final visit, reflecting a change of -0.30 D. In contrast, the placebo group showed a baseline SER of -3.84 D, which progressed to -4.89 D, a change of -1.05 D. Changes in axial length (AL) and spherical equivalent

refraction (SER) were used to measure effectiveness. In comparison to the placebo group, the atropine group exhibited slower axial elongation (+0.10 mm vs. +0.61 mm) and a smaller mean progression in SER (-0.30 D vs. -1.05 D). These findings highlight the slower rate of myopia progression in the atropine group. To clarify, the progression values represent the change in SER over the study period, while the absolute SER values provide a reference for the starting and ending refractive states. Although the main effect of the treatment group ($p = 0.404$) was not statistically significant, this reflects the average differences in SER between the atropine and placebo groups across all visits. Importantly, the significant interaction effect between visit number and treatment group ($p < 0.001$) demonstrates that the progression of SER over time differed significantly between the two groups. This interaction effect highlights that atropine was effective in slowing myopia progression, as the rate of change in SER was consistently slower in the atropine group compared to the placebo group. Thus, the study's claim of efficacy is supported by the interaction effect rather than the main effect of the treatment group.

Table 2: Repeated Measures ANOVA Results for Spherical Equivalent Refraction (SER) Displays within-subject effects across visits and between-group comparisons with interaction terms.

	Sum of squares	df	Mean Square	F	p	η2	η^2p	Confidence Interval
SE1, SE2, SE3	9.48	2	4.74	214.98	<.001	0.06	0.84	-0.33, -0.27
Group	2.49	1	2.49	0.71	.404	0.02	0.02	
RM Factor x Group	3.15	2	1.57	71.3	<.001	0.02	0.63	0.08, 0.12
Residuals (Between Subjects)	146.71	42	3.49					
Residuals (Within Subjects)	1.85	84	0.02					

Results from Bonferroni post-hoc comparison of SER between visits are presented in the form of Table 3, which shows significant variation across all time points. We found a mean difference of 0.29 ($p < .001$) between SE1 and SE2, 0.65 ($p < .001$) between SER1 and SER3, and 0.37 ($p < .001$) between SER2 and SER3. All comparisons were statistically significant with confidence intervals of zero excluded and T-values exceeding 7.5. Findings in these analyses demonstrate progressive myopic worsening over time, with the greatest differences between SER1 and SER3, suggesting that intervention is needed to avoid these myopic progressions.

Table 3: Bonferroni Post Hoc Test for SER Progression Between Visits.

Variables		Mean diff.	Std. Error	T	P	95% CI lower limit	95% CI upper limit
SE1	SE2	0.29	0.038	7.557	<.001	0.21	0.36

SE1	SE3	0.65	0.068	9.658	<.001	0.52	0.79
SE2	SE3	0.37	0.044	8.47	<.001	0.28	0.46

The repeated-measures ANOVA for axial length (AL) is summarized in Table 4. A highly significant main effect of visit number was found, $F(2, 84) = 55.99$, $p < .001$, $\eta = 0.57$, demonstrating a large amount of axial elongation over time. $F(1, 42) = 1.93$, $p = .172$, the main effect of treatment group was not significant, meaning there was no overall difference between ALs of the atropine and placebo groups.

A significant interaction also emerged between visit number and treatment group, $F(2, 84) = 29.65$, $p < .001$, $\eta = 0.41$, indicating that axial elongation differed by the two groups over the course of visits. These results show that 0.01% atropine is effective in slowing axial elongation versus placebo.

Table 4: Repeated Measures ANOVA for Axial Length (AL). Analysis of AL growth across visits, group differences, and interaction effects.

Variables	Sum of squares	Df	Mean Square	F	P	η2	η
AL1, AL2, AL3	2.65	2	1.33	55.99	<.001	0.08	0.57
Group	1.2	1	1.2	1.93	.172	0.04	0.04
RM Factor x Group	1.4	2	0.7	29.65	<.001	0.04	0.41
Residuals (Between Subjects)	26.06	42	0.62				
Residuals (Within Subjects)	1.99	84	0.02				

Bonferroni post-hoc comparisons of axial length (AL) visits are presented in Table 5. Significant differences were observed between all pairs: (AL1 v. AL2: -0.16, $p < .001$; AL1 v. AL3: -0.35, $p < .001$; AL2 v. AL3: -0.19, $p < .001$). The change was largest between AL1 and AL3, suggesting progressive axial enlargement with time. These findings were robust in that all confidence intervals excluded zero.

Table 5: Bonferroni Post Hoc Test for AL Across Study Visits. Comparison of mean axial length changes over time

Variables		Mean diff.	Std. Error	T	P	95% CI lower limit	95% CI upper limit
AL1	AL2	-0.16	0.022	-6.978	<.001	-0.2	-0.11
AL1	AL3	-0.35	0.055	-6.263	<.001	-0.46	-0.23
AL2	AL3	-0.19	0.043	-4.477	<.001	-0.28	-0.1

DISCUSSION

The findings indicate that 0.01% atropine may impede the advancement of pediatric myopia. Despite the atropine group exhibiting quantitatively reduced alterations in axial length (AL) and spherical equivalent refraction (SER) relative to the placebo group, the primary effect of the treatment group did not attain statistical significance ($p = 0.404$ for SER and $p = 0.172$ for AL). Nonetheless, substantial interaction effects between visit number and treatment group ($p < 0.001$ for both SER and AL) suggest that the advancement rate varied over time between the groups. These data indicate a clinically suggestive trend, but should not be construed as conclusive proof of effectiveness. Additional research with bigger cohorts and prolonged follow-up is essential to corroborate these results.

The atropine group's negative change in spherical equivalent refraction (SER) (-0.30 D) indicates that myopia is still progressing, albeit more slowly than in the placebo group (-0.51 D). This suggests that rather than correcting the progression of myopia, low-dose atropine was successful in slowing it down. This finding confirms the earlier finding of Xu et al 2023, that low dose atropine (0.01%) significantly slowed myopia progression over two years. In the atropine group, SER advanced annually by -0.20 D versus -0.60 D in the placebo group[17]. In similar fashion, children with low vision in China in that same study by Fu et al., 2021 also experienced similar retardation of SER progression with low dose atropine. The argument for low dose atropine as a first line myopia control intervention is strengthened by the comparable magnitude of effect across studies [18].

In addition, the amount of SER reduction observed in this trial is slightly less than that reported in some of the previous trials, such as Chen et al., 2022 who reported one-year mean SER progression of -0.15 D in the atropine group[19]. Perhaps this discrepancy is explained by disparities in study design, demography of the population studied, or duration of follow-up. For example, participants from a setting with predominantly higher SER values and higher baseline SER and thus potentially different efficacy of treatment were recruited by Wu et al. Significantly, these findings emphasize the need to contextualize atropine's efficacy to population specific factors [20].

As a structural indicator of myopia progression, a critical factor is the elongation of axial length (AL). The present study noted an atropine mean AL elongation of 0.10 mm versus a placebo mean AL elongation of 0.61 mm. Our findings agree with the findings of H.-R. Tsai et al., 2021 who published a meta-analysis showing that 0.01% atropine reduced AL elongation by about 50% compared to placebo [21]. Meanwhile Ha et al., 2022 also showed a reduction of 0.12 mm/yr in AL elongation with atropine, of similar magnitude to that found in this study [22].

Compared with previous literature, the AL elongation is relatively higher in the placebo group (0.61 mm). while ATOM2 trial Shalini et al,2022 described an AL elongation of 0.49 mm over 2 years in the placebo group. Such a discrepancy may be due to differences in environmental factors, for example, being outdoors and near work habits, which we know can affect the progression of myopia. Since myopia rates are increasing in children, especially in urbanized areas, future studies should include lifestyle and behavioral factors to explain some of the interstudy variability [23].

This study highlights the efficacy of 0.01% atropine in slowing myopia progression; however, it is important to acknowledge the potential influence of environmental factors such as outdoor time and screen time, which were not accounted for in this study [24]. These factors are well-established contributors to myopia progression, with increased outdoor activity shown to reduce the risk of progression and prolonged near work or screen time associated with its

acceleration [25]. The lack of data on these variables limits the ability to fully isolate the effects of atropine from other contributing factors. Future research should incorporate these environmental variables to better contextualize the efficacy of atropine and provide a more holistic understanding of the factors influencing myopia progression [26].

In addition, the repeated-measures ANOVA results substantiate the efficacy of atropine. Visitors showed significantly different progression patterns over time across treatment groups ($\eta = 0.41$ for AL; $\eta^2_p = 0.63$ for SER). This corresponds to conclusions of previous trials, like Wang et al, who find time dependent benefits of atropine. Nevertheless, the main effect of treatment group was not significant when averaging over all visits. Furthermore, the apparent greater efficacy of atropine over time also indicates the importance of investigating individual visit to visit variability [27].

Significant pairwise changes in SER and AL are observed at all timepoints and are consistent with what has been previously noted. A baseline to final visit SER difference $\Delta SER = -0.65$ D, $p < .001$ was the largest SER difference, emphasizing the progressive nature of myopia. AL elongation also was greatest between AL1 and AL3 ($\Delta AL = -0.35$ mm, $p < .001$). These results confirm the clinical urgency of early and prolonged intervention to prevent long term myopia associated complications, including retinal detachment and macular degeneration.

Atropine treatment, which this study finds reduces the rate of SER and AL progression, is consistent with this proposed mechanism of action. It is believed that low dose atropine acts on muscarinic acetylcholine receptors on the retina and sclera to moderate axial elongation and prevent further excess refractive error progression. Upadhyay & Beuerman, 2020 show that atropine inhibits biochemical processes leading to scleral remodeling and choroidal thinning, both implicated in myopia progression [11].

Strikingly, the main effect of treatment group in this study agrees with the hypothesis that atropine's efficacy may vary as a function of individual variability in response. Dean et al., 2023 further proposed that such variations in muscarinic receptor genotype could underlie some of the interindividual variation in treatment outcome. Candidate pharma cogenomic approaches—tailoring atropine dosing to maximize treatment benefit—require future study [28].

0.01% atropine is generally well-tolerated, with common side effects including photophobia, pupil dilation, and near-vision complaints. Photophobia arises from pupil dilation, causing mild light sensitivity, while near-vision difficulties result from reduced accommodation. These effects are typically transient and manageable. Regular monitoring of visual acuity, pupil size, and ocular health is essential to ensure safe and effective use in myopia control.

The study found that the atropine group experienced a much smaller increase in axial length (AL) compared to the placebo group. Specifically, the atropine group had an AL elongation of only 0.10 mm, while the placebo group had an AL elongation of 0.61 mm. Although not statistically significant, the difference may possess therapeutic value.

Axial length is a critical factor in myopia progression, as excessive elongation of the eye is a key driver of the development of high myopia. High myopia, defined as a spherical equivalent refraction (SER) of -6.00 diopters or worse, is associated with a significantly increased risk of sight-threatening complications such as retinal detachment, myopic macular degeneration, glaucoma, and cataracts.

The reduction in AL elongation of 0.51 mm observed in the atropine group compared to the placebo group is equivalent to a 50% decrease in the rate of axial elongation. This substantial slowing of axial elongation is expected to have a profound long-term

impact on the development and progression of high myopia in these children. By limiting the excessive axial growth of the eye, the use of 0.01% atropine eye drops can help prevent or delay the onset of high myopia and the associated risk of vision-threatening complications. This finding highlights the clinical significance of the atropine intervention in effectively controlling myopia progression and preserving long-term ocular health in the pediatric population.

The findings of this study are robust, but several methodological considerations demand discussion. Secondly, the short follow up of study participants prohibits generalizability of short-term outcomes to long term outcomes. Along with the ongoing ATOM2 trial, longitudinal studies have demonstrated that atropine efficacy is maintained over multiple years, indicating the requirement of longer follow up in future research. Second, although the sample size in the study (n = 44) is more than many other environmental exposure studies, it is small compared with large-scale trials. Thirdly, the study took no measure of potential confounders, e.g. outdoor activity, near work behavior or screen time, all of which are known to have an effect on myopia progression. One final limitation is the lack of pupillary measurements and accommodative measurements. Minimal side effects of low dose atropine: slight increase in pupil size and decrease in accommodation may affect adherence and acceptability.

Environmental and behavioral variables that are known to affect the development of myopia, such as screen usage, outdoor activities, and near-work, were not evaluated in this study. These factors are well-documented to significantly influence myopia development and progression. Incorporating these variables into future studies will help control for their impact and provide a clearer understanding of atropine's efficacy. The three-month trial timeframe restricts the capacity to assess the intervention's long-term safety and effectiveness. Lack of allocation concealment may introduce selection bias. These results suggest atropine may help slow myopia progression, but larger studies are needed. We did not collect data on outdoor exposure, near work, or screen time, which are known confounders. Three-month study duration limits ability to assess long-term efficacy.

CONCLUSION

This study provides first data supporting the use of 0.01% atropine as a potentially effective option for mitigating myopia progression in youth. The absence of statistically significant main effects underscores the need for cautious interpretation, despite numerical trends favoring atropine over placebo in reducing axial elongation and refractive change. Considering the intricate nature of myopia development, which encompasses genetic, behavioral, and environmental factors, future research should explore personalized treatment approaches, including pharmacological and lifestyle interventions. Extensive, longitudinal study is necessary to substantiate these findings and investigate the mechanisms and optimal application of low-dose atropine in managing the global rise in pediatric myopia.

ETHICS APPROVAL: The ERC gave ethical review approval.

CONSENT TO PARTICIPATE: written and verbal consent was taken from subjects and next of kin.

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All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated in the work

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