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Original Article

Therapeutic Effect of Topical 0.125% Atropine in South Korean Myopic Children: A Real-World Experience

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Purpose: To evaluate the effectiveness of 0.125% atropine eye drops in controlling myopia progression by analyzing 1-year follow-up data through a multicenter retrospective study in South Korea.

Methods: A retrospective chart review was conducted across five centers, including 121 myopic children (aged 4–11 years) treated with 0.125% atropine between January 2021 and December 2023. An equal number of age-, sex-, axial length (AL)-, and spherical equivalent (SE)-matched untreated individuals (control group) were included. Baseline and follow-up data at 6 and 12 months included visual acuity, autorefraction, AL measurement (IOLMaster 700), and fundus examination. The primary outcome measures were changes in SE and AL compared to controls.

Results: Age, SE, and AL in the treatment group at baseline were 7.5 ± 1.5 years (range, 4 to 11), –3.07 ± 1.65 diopters (D; range, –0.25 to –5.88 D), and 24.39 ± 0.85 mm (range, 22.19 to 26.94 mm), respectively, and these parameters showed no statistical differences compared to the matched controls. SE after 1-year treatment was less myopic in the treatment group (–3.42 ± 1.72 D vs. –3.94 ± 1.92 D, $p = 0.019$). Similarly, AL was significantly shorter in treatment group compared to the control group (24.65 ± 0.88 mm vs. 24.88 ± 0.80 mm, $p = 0.031$). The SE change from baseline was –0.33 ± 0.73 D in the treatment group versus –0.91 ± 1.01 D in the control group ($p < 0.001$). AL increased by 0.25 ± 0.32 mm in the treatment group, significantly less than 0.49 ± 0.24 mm increase in the control group ($p < 0.001$). Baseline AL and mean keratometry showed no correlation with AL progression (all $p > 0.05$).

Conclusions: The use of 0.125% atropine eye drops significantly reduced myopia progression, with approximately 50% reduction in AL elongation compared to controls. Given its effectiveness and variable compliance, 0.125% atropine eye drops may serve as a viable alternative to low-dose atropine for myopia control.

Key Words: Atropine, Axial length, Myopia

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Myopia has become a growing global health concern, with its prevalence rising significantly in recent years [1]. In East Asia, the prevalence of myopia among individuals under the age of 19 years is approximately 60% to 80% [2,3], with high myopia affecting 10% to 20% of this age group [4], whereas the prevalence of myopia is estimated to be approximately 30% in the global population [1,5]. Myopia typically develops in childhood and is primarily characterized by excessive axial elongation, known as axial myopia. As axial length (AL) increases, the risks of myopic macular degeneration, retinal detachment, cataracts, and glaucoma rise proportionally [6], leading to substantial socioeconomic burdens [7]. Consequently, controlling myopia progression has become a critical focus in ophthalmology.

Over the past decade, various interventions have been explored to slow myopia progression [8–10], with low-dose atropine emerging as one of the most effective and widely used treatments [11,12]. Compared to higher concentrations, low-dose atropine eye drops are associated with fewer side effects, such as near vision impairment and photophobia. The Atropine for the Treatment of Myopia 2 (ATOM2) study demonstrated that 0.01% atropine effectively slowed myopia progression with minimal rebound effects [11], while the recent Low-Concentration Atropine for Myopia Progression (LAMP) study suggest that 0.05% atropine may offer greater efficacy [12]. A recent study has shown that long-term treatment with 0.05% atropine is effective in prevent AL elongation [13]. However, prospective studies in the Unites States found the effect of 0.01% or 0.02% atropine is controversial in children [14]. In clinical practice, atropine eye drops are prescribed in various concentrations, creating uncertainty among clinicians regarding their comparative effectiveness and optimal recommendations for caregivers. Although atropine has been studied extensively worldwide, there are relatively few studies evaluating its efficacy in South Korea [15–18]. This study aims to evaluate the efficacy of 0.125% atropine over a one-year follow-up period through a multicenter retrospective study in Korea. By analyzing its impact on AL and refractive errors, this study seeks to provide clinical insights into the use of medium-dose atropine for myopia control.

Materials and Methods

Ethics statement

This retrospective study was approved by the Institutional Review Board of Gangnam Severance Hospital (No. 3-2024-0288). Informed consent was waived because the study was a retrospective chart review. The study adhered to the principles of the Declaration of Helsinki and all data collection complied with the Health Insurance Portability and Accountability Act.

Study design and setting

A multicenter retrospective study from five centers included 121 myopic children (aged 4–11 years) who received 0.125% atropine eye drops treatment during January 2021 and December 2023. The inclusion criteria included a spherical equivalent (SE) of 0.00 to –6.50 D. Exclusion criteria were a history of ocular disease, ocular surgery, previous history of treatment to slow myopic progression, and ocular trauma. If both eyes met the inclusion criteria, data from the right eye were selected. An equal number of untreated individuals, matched for age, sex, AL, and SE, were included for comparison. The data from untreated historical controls were collected from a large cohort data between 2010 and 2024 only in one of the centers (Kim's Eye Hospital, Seoul, Korea).

All subjects underwent a comprehensive ophthalmological examination before treatment with atropine eye drops, including visual acuity assessment, cycloplegic auto refraction, AL measurement, slit-lamp examination, and fundus examination. At initial examination, cycloplegic refraction was performed, and subsequent examinations were done with noncycloplegic autorefraction under the effect of 0.125% atropine. The cycloplegic autorefraction involved administering three drops of cyclopentolate hydrochloride (Ocucyclo, Samil) at approximately 10-minute intervals, with measurements conducted at 1 hour after first drops of cyclopentolate instillation. Autorefraction was performed using the Topcon KR-800 (Topcon Medical Systems), except at Gangnam Severance Hospital (Seoul, Korea), where the Topcon KR-1 (Topcon Medical Systems) was used. AL was measured by ocular biometry (IOLMaster 700, Carl Zeiss Meditec).

Single-use preservative-free formulation of atropine

0.125% (Myoguard, LitePharmTech) was also used for the treatment. Subjects were instructed to administer atropine eye drops to both eyes once nightly before bedtime. All measurements were performed every 6 months following atropine treatment. In each patient, same dose-formulation was used throughout the follow-up periods. Treatment efficacy was calculated as the difference between SE or AL values in the treatment group and those in the matched control group.

Statistical analysis

Statistical analysis was performed using Python ver. 3.12.7 (Python Software Foundation), SciPy statistics function ver. 1.13.1 (SciPy), and pandas ver. 2.2.3 (Pandas). For categorical variables, chi-square test was conducted for ratio difference. For SE and AL comparison between treatment group and matched controls, the independent *t*-test was used. The correlations between baseline mean keratometry reading or baseline AL and treatment efficacy were conducted with Pearson correlation analysis. Statistical significance was set at $p < 0.05$.

Results

This study included 121 atropine-treated patients (treatment group) and 121 matched individuals (control group). The male to female ratio was 63:58 in both groups (chi-square test, $p > 0.999$). In the treatment group, baseline age, SE, and AL were 7.5 ± 1.5 years (range, 4 to 11 years), –3.07 ± 1.65 diopters (D; range, –0.25 to –5.88 D), and 24.39 ± 0.85 mm (range, 22.19 to 26.94 mm), respectively, which showed no statistical differences in comparison with the control group (Table 1).

The SE in the treatment group changed to –3.16 ± 1.66 D at 6 months but showed no statistical difference with the SE in the control group (–3.57 ± 1.77 D; $p = 0.065$, independent *t*-test). At 12 months, SE changed to –3.42 ± 1.72 D in the treatment group, which was significantly less myopic than the control group (–3.94 ± 1.92 D, $p = 0.019$). AL showed similar patterns with the SE change. At 6 months, AL was not different between groups (24.50 ± 0.85 mm vs. 24.67 ± 0.79 mm, $p = 0.112$). However, at 12 months, AL was statistically different between groups (24.65 ± 0.88 mm vs. 24.88 ± 0.81 mm, $p = 0.031$) (Table 1 and Fig. 1A, 1B).

Table 1. Baseline characteristics, and SE and AL change at 6 and 12 months

Characteristic	Treatment group (n = 121)	Control group (n = 121)	*p*-value
Baseline			
Sex			>0.999*
Male	63	63	
Female	58	58	
Age (yr)	7.5 ± 1.5 (4 to 11)	7.6 ± 1.5 (4 to 11)	0.965†
SE (D)	–3.07 ± 1.65 (–0.25 to –5.88)	–3.04 +1.61 (–0.25 to –6.38)	0.868†
AL (mm)	24.39 ± 0.85 (22.19 to 26.94)	24.39 ± 0.82 (22.47 to 26.66)	0.982†
At 6 mon			
SE (D)	–3.16 ± 1.66	–3.57 ± 1.77	0.065†
SE difference (D)	–0.06 ± 0.59	–0.49 ± 0.67	<0.001†
AL (mm)	24.50 ± 0.85	24.67 ± 0.79	0.112†
AL difference (mm)	0.11 ± 0.20	0.28 ± 0.16	<0.001†
At 12 mon			
SE (D)	–3.42 ± 1.72	–3.94 ± 1.92	0.019†
SE difference (D)	–0.33 ± 0.73	–0.92 ± 1.01	<0.001†
AL (mm)	24.65 ± 0.88	24.88 ± 0.81	0.031†
AL diff (mm)	0.25 ± 0.32	0.49 ± 0.24	<0.001†

Values are presented as number only, mean ± standard deviation (range), or mean ± standard deviation.
SE = spherical equivalent; AL = axial length; D = diopters.
*Chi-square test; †Independent *t*-test.

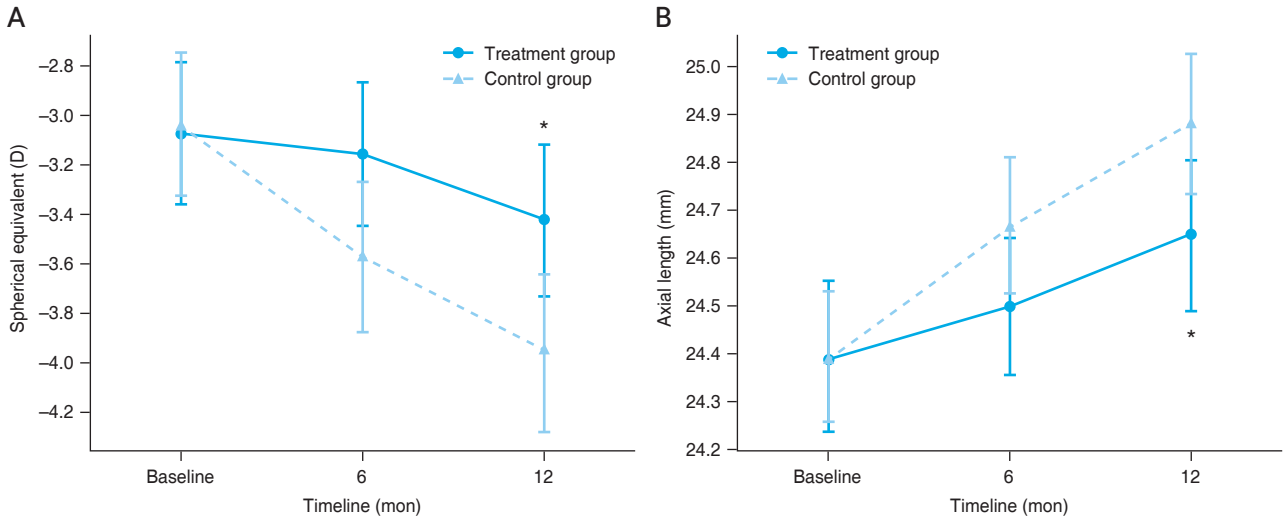

Fig. 1. Changes of (A) spherical equivalent and (B) axial length over time in 0.125% atropine treatment group and age-, sex-, axial length-, and spherical equivalent-matched control group. D = diopters. *Statistically significant ($p < 0.05$, independent *t*-test).

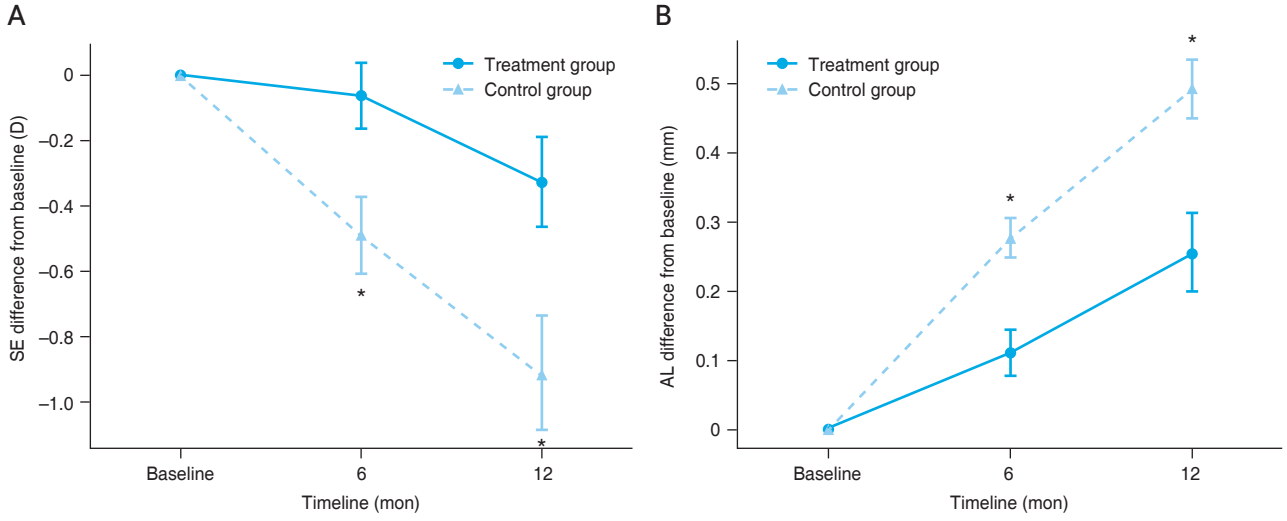

Fig. 2. Difference from baseline of (A) spherical equivalents (SE) and (B) axial length (AL) over time in 0.125% atropine treatment group and matched control group. D = diopters. *Statistically significant ($p < 0.05$, independent *t*-test).

SE differences from baseline to 6 months were –0.06 ± 0.59 D in the treatment group and –0.49 ± 0.67 D in the control group, which was statistically different ($p < 0.001$). AL changes were also different during the same timeline (0.11 ± 0.20 mm vs. 0.28 ± 0.16 mm, $p < 0.001$). From baseline to 12 months, SE differences were –0.33 ± 0.73 D in the treatment group and –0.92 ± 1.01 D in the control group, which was statistically different ($p < 0.001$). AL changes for the same timeline also showed statistical differences (0.25 ± 0.32 mm vs. 0.49 ± 0.24 mm, $p < 0.001$) (Table 1 and Fig. 2A, 2B).

To determine factors related to treatment efficacy, correlations of baseline mean keratometry and AL with 1-year changes of SE and AL differences were investigated. Mean keratometry was not significantly correlated with 1-year AL difference (Pearson rho = 0.072; $p = 0.435$) and SE difference (Pearson rho = 0.031; $p = 0.733$). Similarly, baseline AL showed no significant correlation with 1-year AL difference (Pearson rho = –0.090; $p = 0.327$) and SE difference (Pearson rho = 0.050; $p = 0.586$) (Fig. 3A–3D).

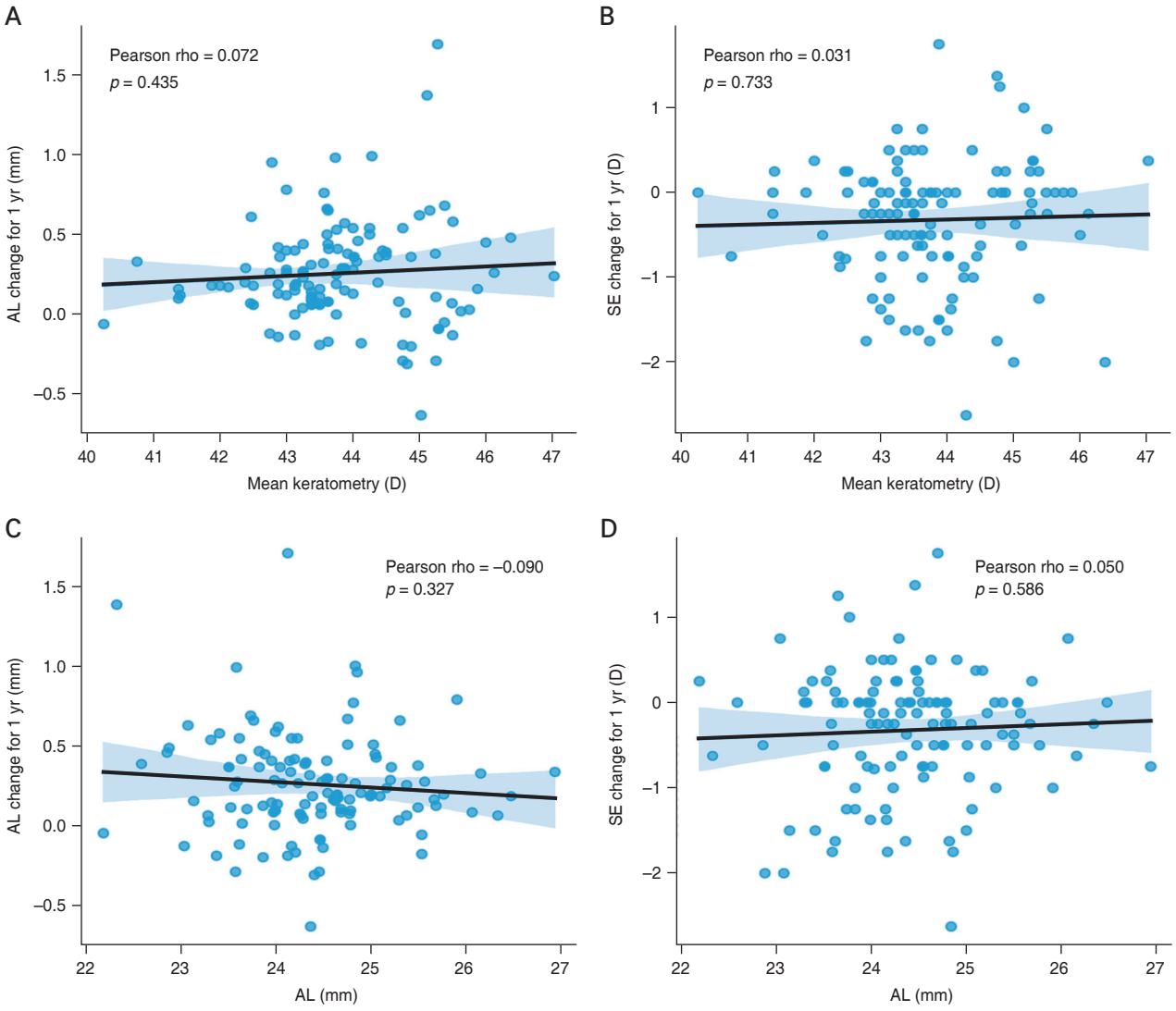

Fig. 3. Correlation scatter plots of (A, B) baseline mean keratometry and (C, D) axial length (AL) with 1-year (A, C) AL and (B, D) spherical equivalent (SE) differences. D = diopters.

Discussion

This study demonstrated that 0.125% atropine eye drops showed a significant reduction of SE progression and AL elongation compared to controls. In this study, the SE at 1 year was approximately 64% less progressive compared to the control group, while AL change was reduced by about 50% compared to controls. Given the high prevalence of myopia and high myopia in South Korea [5], interventions to slow myopia progression should be considered in pediatric ophthalmology clinics. To use low-dose atropine, it must either be compounded directly or prepared by the hospital pharmacy, which poses a practical inconvenience. Additionally, mixing with artificial tears introduces uncertainty regarding the final concentration and incurs extra cost. Although numerous studies have been conducted to date, there is still ongoing debate about what constitutes the optimal concentration. Since 0.01% and 0.05% atropine formulations are not currently available on the market in South Korea, 0.125% atropine could serve as a viable alternative for myopia control.

According to the LAMP study, over 1 year, the SE changed by –0.27 D in the 0.05% atropine group, whereas the control group showed a change of –0.81 D [12]. Additionally, AL increased by 0.20 mm in the 0.05% atropine group, compared to an increase of 0.41 mm in the control

group [12]. The efficacy of 0.05% atropine in the LAMP study was comparable to our study. This might be related with poor compliance of 0.125% atropine in the real-world setting compared to well-controlled randomized clinical trials. However, a study conducted in Denmark reported that a group receiving a loading dose of 0.1% atropine for 6 months followed by 0.01% atropine for another 6 months showed a significantly greater reduction in AL progression compared to the group that used only 0.01% atropine for 1 year [19]. Other studies demonstrated that 0.125% atropine instillation every other night showed similar efficacy to daily 0.125% atropine instillation [20]. Therefore, optimal dose and frequency in medium-dose atropine should be investigated in further studies.

AL gradually increases with age, with the most rapid elongation occurring between ages 4 and 8 years, followed by a slower annual growth rate between ages 9 and 12 years [21–23]. In this study, baseline AL showed no significant correlation with 1-year changes of the AL and SE. Baseline mean keratometry also showed no statistically meaningful correlations with the same parameters. These findings suggested that the baseline AL and keratometry readings may have no prognostic values for atropine treatment. However, prognostic values of ocular biometric profiles need more specific subgroup analysis with large sample sizes. For example, even in those with the same SE, patients with lower keratometry values tend to have longer AL and their AL elongation could be different compared to those with higher keratometry values. Future studies comparing the treatment response across different clinical settings, such as subgroups defined by age, AL, or keratometry readings could provide valuable insights into predicting treatment efficacy.

This study has several limitations. First, as a retrospective study, many cases lacked recorded information on the myopia status of the parents, making it impossible to include this factor in the analysis. Additionally, patients who discontinued the medication due to side effects and subsequently did not return for follow-up may not have been accounted for. Second, cycloplegic refraction was not performed at 6- and 12-month follow-up visits. Although cycloplegic refraction was not performed at subsequent visits, it was the same for both treatment and control groups. Therefore, even if autorefraction slightly overestimated myopia, it can still be used to compare the differences between the two groups. Third, the adherence and compliance of 0.125% atropine eye drops was not assessed accurately. Given the challenge in clinical practice of verifying whether patients consistently use atropine eye drops as prescribed, we believe that our study reflects real-world experience. Finally, the control group data may still be subject to selection bias—for instance, including intentionally untreated or slow-progressing patients—even if the selection was performed randomly from a large cohort dataset by a program. Additionally, the control group data were collected during a different period from the patients treated with atropine, who were recruited from a secondary hospital rather than a tertiary hospital. Considering that many of the patients in the atropine group were recruited during the COVID-19 pandemic, this difference may also reflect a selection bias. However, since many studies have reported greater progression of myopia during the COVID-19 period, it is also possible that this study may have slightly underestimated the treatment effect of atropine.

In conclusion, this multicenter study demonstrated the effectiveness of 0.125% atropine eye drops in myopic children. The estimated efficacy was approximately 50% reduction in ALs compared to controls. Our study suggests that 0.125% atropine could be a good option for prescriptions, considering various levels of adherence and compliance. A prospective study comparing the effectiveness of 0.05% atropine with 0.125% atropine will be needed in the future.

Conflicts of Interest: None.
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