Efficacy of Atropine Eye Drops for Suppressing Myopia Progression in Thai Children

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ABSTRACT

Objective: This retrospective cohort study aimed to assess the efficacy and safety of low-dose atropine eye drops in retarding myopic progression among school-age children at Siriraj Hospital.

Materials and Methods: The medical records of 247 myopia-diagnosed patients were reviewed. All patients were received low-dose atropine eye drops and had at least one follow-up visit within 1 year after the treatment initiation. Spherical equivalent (SE) measurements were collected at pre- and post-treatment visits, as well as any reported side effects. Comparing the SE changes observed between the pre- and post-treatment periods, as well as between the two different concentrations of atropine was analyzed.

Results: A total of 493 eyes were analyzed, with 461 eyes receiving 0.01% atropine eye drops and 32 eyes being administered 0.05%. The demographic data between two groups showed no significant difference. The comparison of SE change one year prior to and one year after treatment in the 0.01% and 0.05% group yielded a p-value of less than 0.001 and 0.003, respectively, (SE change were -0.38 D (-0.75-0.00 D) and -0.25 D (-0.72-(-0.25 D)) in the 0.01% and 0.05% group, respectively). However, the between-group comparison of SE change at 6 months and 1 year showed no significant difference. Regarding side effects, one-third of the eyes (12 eyes) in the 0.05% group (37.5%) experienced adverse effects while only eight eyes (1.7%) in the 0.01% group reported side effects.

Conclusion: This research contributes support to the effectiveness of employing low-dose atropine for the treatment of myopia in Thai children. However, the use of 0.05% atropine was associated with a higher incidence of side effects.

Keywords: Myopia; Atropine Eye Drops (Siriraj Med J 2023; 75: 794-799)

INTRODUCTION

Myopia, or nearsightedness, is a visual condition resulting in blurred distance vision. Holden and colleagues estimated a prevalence of myopia in 1.4 billion individuals worldwide in 2000 (22.9%), with a predicted increase to 4.8 billion by 2050.[1] The prevalence of myopia has been on the rise globally, particularly in Asian populations, and reportedly dramatically increased during the COVID-19 pandemic period.[2-6] Multiple factors have been attributed to the development of myopia, including genetic, environmental, and lifestyle factors, such as increased screen time on electronic devices, decreased outdoor exposure, and prolonged reading and studying.[7] Myopia usually occurs and progresses during the school-age period.[7] High myopia (-5.0 diopters or more), which can develop during the school-age period, can potentially extend beyond just affecting a person's daily activities and can lead to subsequent complications, such as retinal detachment, glaucoma, cataract, or macular pathologies.[8-10] Therefore, proactive practice to prevent and mitigate its progression should be taken into consideration.

The treatment approaches for myopia encompass

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various strategies, including environmental modifications, optical interventions, and medical treatment. Among the treatment options, atropine, which is a liquid medication that comes in the form of eye drops, has gained significant attention in recent years due to its ability to suppress the elongation of the eyeball and slow the progression of myopia.[11] Although the exact mechanism by which atropine slows myopia is not fully understood, it is believed to involve non-selective antimuscarinic, mydriatic, and cycloplegic effects, which block accommodation of the eye.[12] Other mechanisms, such as dopamine release, increased choroidal thickness, remodeling of scleral fibroblasts, and the inhibition of glycosaminoglycan in eye growth, are still not well elucidated.[12-16] However, the optimal concentration of atropine that strikes a balance between its efficacy and limiting its side effects remains uncertain. Several randomized controlled trials have been conducted to observe the outcomes and side effects of different atropine concentrations, ranging from 0.01% to 1%, in school-age children with myopia.

The ATOM 1[17] and ATOM 2[18] studies conducted in Singapore found that 0.01% atropine was the most effective concentration in suppressing axial length elongation with minimal side effects. Similarly, a retrospective study from Tiana et al.[19] and a prospective study in Japan[20] reported similar results. However, in a Hong Kong study, 0.05% was reported to be the most effective concentration among the 0.01%, 0.025%, 0.05% tested concentrations, and a placebo, with no serious side effects observed in any of the groups.[21,22] These results highlight the variability in the optimal concentration, even among school-age Asian populations.[23] Additionally, no study has yet been conducted in a Thai population to determine the appropriate concentration and potential side effects of atropine, despite started using 0.01% atropine since 2016 and 0.05% since 2019 in Siriraj Hospital in concentrations of 0.05% and. 0.01%. Therefore, we conducted this study to provide information specific to a Thai population to aid in clinical practice.

MATERIALS AND METHODS

This study was approved by the the International Review Board of Faculty of Medicine Siriraj Hospital (COA no. Si 650/2022). Following the approval, patients diagnosed with ICD-10 codes referring to myopia (H25.1) were identified. This retrospective comparative cohort study consisted of school-age patients aged 5–18 years old who were diagnosed with myopia with a spherical equivalent (SE) higher than -1.00 diopter (D) for more than 1 year. All the included patients were receiving atropine as the treatment at Department of Ophthalmology, Faculty of Medicine Siriraj Hospital, between January 2017 and December 2022. The inclusion criteria encompass the following conditions: individuals aged between 5 and 18 years old, myopic children with spherical equivalent (SE) greater than -1.0 D, who have been diagnosed with myopia for over one year and exhibit evidence of progression (indicated by changes in SE) and have not undergone any other forms of treatment aside from wearing eyeglasses prior to the prescription of atropine. Patients with concomitant ocular conditions that could potentially impact visual acuity, such as corneal pathologies, cataracts, and glaucoma, were excluded from the study. Additionally, individuals who were diagnosed with myopia subsequent to ophthalmic surgery or were lost to follow-up within the first year after initiating treatment were also excluded.

The required sample size was calculated with an alpha of 0.05, mean difference from a previous study of 0.220[21], power of 80%, and ratio of 6:1 between the 0.01% and 0.05% concentration atropine treatments. The required sample sizes according to the calculations were 71 and 426 in the 0.05% and 0.01% groups, respectively.

Evaluation method

The patient's demographic data, clinical features, and ocular examination data were retrospectively reviewed. Age at myopia diagnosis, age at starting atropine eye drops, sex, coexisting ocular diseases, best-corrected visual acuity (BCVA) before treatment, and autorefraction were recorded. At post-treatment visits, the spherical equivalent refractive errors were measured, and the side effects of the atropine eye drops at 6 months and 1 year were recorded.

Descriptive statistics were utilized to summarize the demographic data and clinical characteristics of the patients. Categorical data were presented as frequencies and percentages, while continuous variables were presented as median values and interquartile ranges (IQR) or as the mean and standard deviation (SD). Comparisons between the two groups were evaluated using Fisher exact or Mann–Whitney U test according to the distributive nature. The visual acuity data were transformed logarithmically to the minimum angle of resolution (logMAR) equivalents for statistical analysis. Changes in BCVA, spherical values, and spherical equivalent (SE) after treatment were evaluated using the Wilcoxon signed-rank test. A p-value of less than 0.05 was considered statistically significant. All the analyses were conducted using SPSS Statistics version 28.0 (SPSS, Inc, Chicago, IL, USA).

RESULTS

Overall, 247 cases (493 eyes) were enrolled in the study, among which 461 eyes received 0.01% atropine eye drops, while 32 eyes received 0.05% atropine eye drops. Table 1 presents all the relevant demographic data of the patients. The mean age of the patients in the 0.01% atropine group was 10.70 years old (SD ± 2.85), while in the 0.05% atropine group, the mean age was 10.06 years old (SD ± 3.67). No significant differences were observed in the demographic data between the patients receiving 0.01% atropine and those receiving 0.05% atropine.

Before treatment, myopic progression (spherical equivalent change) over one year in the 0.01% atropine group was -0.87 D (-1.37 to -0.5 D), while in the 0.05% atropine group, was -0.5 D (-1.09 to 0 D) (P-value 0.010). Following the initiation of atropine treatment, at the 6-month mark, myopic progression in the 0.01% atropine group (spherical equivalent) was -0.13 D (-0.38 to 0.13 D), whereas in the 0.05% atropine group was 0 D (-0.22 to 0.22 D) (P-value 0.053). After one year of treatment, myopic progression in the 0.01% atropine group (spherical equivalent) was -0.38 D (-0.75 to 0 D), and in the 0.05% atropine group, was -0.25 D (-0.75 to

TABLE 1. Demographic data and clinical findings.

	0.01% N = 461 (231 patients)	**0.05%** N = 32 (16 patients)	P-value
Study population			
Age at start treatment (years); mean (SD)	10.70 (± 2.85)	10.06 (± 3.67)	0.223†
Sex (Male/Female)	116/115	8/8	1.000*
Family History of myopia; n (%)			N/A
No	12 (2.6%)	4 (12.5%)	
Yes	122 (26.6%)	12 (37.5%)	
Unknown	325 (70.8%)	16 (50.0%)	
Study eyes			
Side (Right/Left)	231/230	16/16	N/A
BCVA at start treatment logMAR); median (IQR)	0.12 (0.04-0.30)	0.15 (0.05-0.30)	0.677#
Spherical change 1 year prior (D); median (IQR)	-0.75 (-1.25-(-0.5))	-0.38 (-1.00-0.00)	**0.007#**
SE change 1 year prior (D); median (IQR)	-0.87 (-1.37-(-0.5))	-0.50 (-1.09-0.00)	**0.010#**
At start treatment			
Spherical equivalent (SE) (D); median (IQR)	-5.37 (-7.25-(-4.13))	-5.31 (-8.00-(-4.66))	0.541#
Six months after treatment			
SE change (D); median (IQR)	-0.13 (-0.38-0.13)	0.00 (-0.22-0.22)	0.053#
BCVA at 6 months; median (IQR)	0.12 (0.04-0.20)	0.10 (0.04-0.28)	0.860#
Side effects; n (%)	8 (1.7%)	12 (37.5%)	0.001*
	Headache 2: Continue **Blurred near vision 4:** Stop **Irritation 2:** Continue	**Photophobia 4:** switch to 0.01% **Pupil sluggish react 2:** Continue. **Blurred near vision 6:** switch to 0.01%	
One year after treatment			
SE change (D); median (IQR)	-0.38 (-0.75-0.00)	-0.25 (-0.72-(-0.25))	0.799#
BCVA at 1 year; median (IQR)	0.10 (0.02-0.19)	0.12 (0.07-0.36)	0.066#

Abbreviations: IQR = interquartile range, SD = standard deviation, BCVA = Best-corrected visual acuity, logMAR = logarithmic minimum angle of resolution, SE = spherical equivalent.
*p-values were obtained by chi-square test.
†p-values were obtained by independent t test.
#p-values were obtained by Mann Whitney U test.

-0.25 D) (p-value 0.799). When comparing the efficacy within each atropine group before and after one year of treatment, both concentrations demonstrated a significant ability to slow myopic progression (p-value < 0.001 for the 0.01% atropine group and p-value = 0.003 for the 0.05% atropine group). However, when comparing the efficacy between the two groups at the one-year mark, no significant difference was observed (p-value = 0.799) (Fig 1).

In the 0.01% atropine group, four cases (8 eyes) (1.7%) experienced adverse drug reactions, with blurred near vision reported in two cases, headache in one case, and eye irritation in one case. Conversely, in the 0.05% atropine group, six cases (12 eyes) (37.5%) exhibited adverse drug reactions, including two cases of photophobia, one case of pupil dilatation, and three cases of blurred near vision (P-value 0.001).

DISCUSSION

Since 1966[24], atropine has been utilized as a mean to decelerate the progression of myopia and is widely regarded as the most effective medication available today.[11] Topical atropine, available in varying concentrations ranging from 0.01% to 1%, has been employed to effectively delay the progression of myopia[18,24-28] Numerous studies have indicated that 0.01% atropine may be the most suitable concentration for managing myopia progression.[17,18,29-33] However, it is important to note that no specific concentration of atropine has yet received approval from the US Food and Drug Administration (FDA) for the treatment of myopia.

At our institution, the hospital pharmacy unit has been preparing 0.01% atropine eye drops for clinical use since 2016, followed by the introduction of 0.05% atropine in 2019. Consequently, the sample size in our study consisted of more eyes in the 0.01% atropine group (461 eyes) than in the 0.05% atropine group (32 eyes), with the latter group number being lower than the expected sample size calculated statistically (71 eyes). Furthermore, in the 0.05% group, the change in spherical equivalent (SE) prior to treatment initiation showed a smaller shift. This observation might be attributed to the smaller sample size and a proclivity to prescribe a higher concentration of atropine, likely driven by the younger age of the participants and a higher incidence of family history of myopia (37.5% and 26.6% in the 0.05% and 0.01% groups, respectively). The results of our study demonstrated statistically significant efficacy in myopia retardation during the one-year follow-up period in both the 0.01% and 0.05% atropine groups, consistent with findings from similar studies conducted worldwide. However, although the 0.05% atropine group

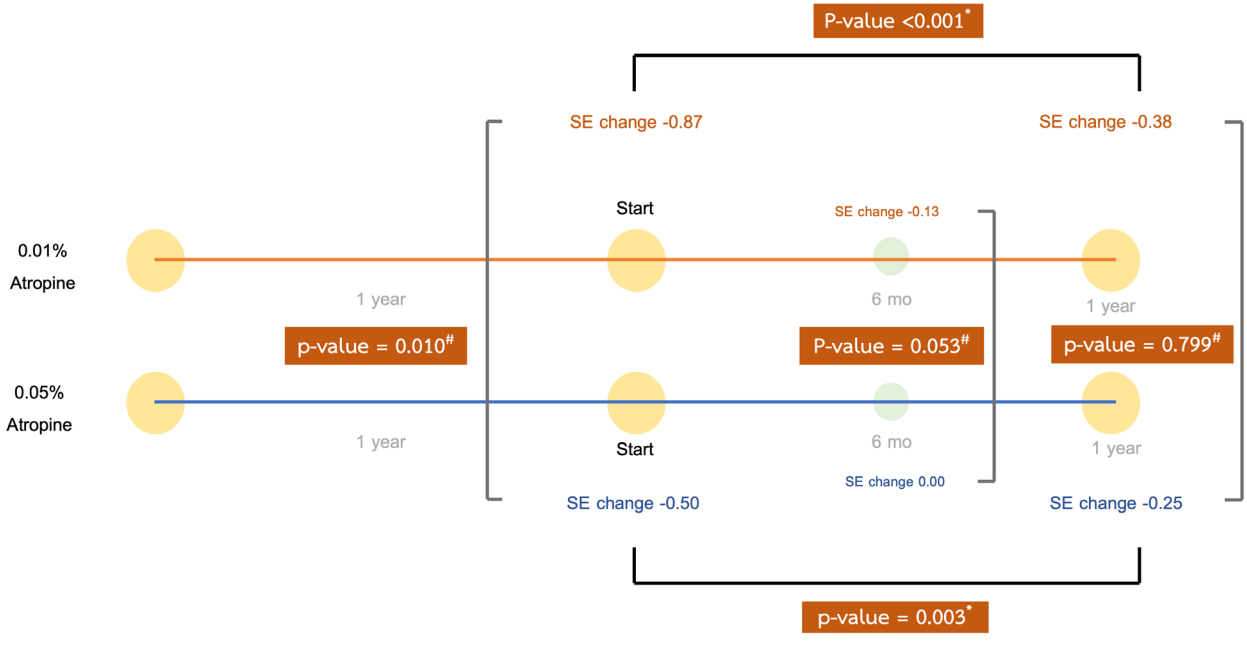


Fig 1. Comparison of SE change between before and after starting treatment and between atropine groups.
- 0.01% atropine group (N = 461): SE change -0.87 D (1-year before treatment), SE change -0.38 D (1-year after treatment) (p value < 0.001)
- 0.05% atropine group (N = 32): SE change -0.50 D (1-year before treatment), SE change -0.25 D (1-year after treatment) (p value = 0.003)
- Green circle = 6 months after treatment (SE change -0.13 D (0.01% atropine) vs 0.00 D (0.05% atropine) p value = 0.053)
- Yellow circle = 1 year after treatment (SE change -0.38 D (0.01% atropine) vs -0.25 D (0.05% atropine) p value = 0.799)

* = Comparison was done by using Wilcoxon signed-rank test.
# = Comparison was done by using Mann Whitney-U test.
Abbreviation: SE = spherical equivalent

exhibited a tendency toward a smaller change in spherical equivalent compared to the 0.01% atropine group, this difference did not reach statistical significance. This lack of statistical significance may be attributed to the discrepancy in the sample size between our two groups.

There are known to be some possible adverse drug reactions associated with topical atropine, which are dependent on its concentration[23], with higher concentrations being associated with an increased likelihood of side effects. In the present study, a small number of patients in the 0.01% atropine group (1.7%) reported experiencing side effects. These side effects included one case of headache, two cases of blurred near vision, and one case of eye irritation. Conversely, approximately one-third of the patients in the 0.05% atropine group experienced side effects. These side effects included two cases of photophobia, one case of pupil dilatation, and three cases of blurred near vision.

The present study has several limitations that need to be acknowledged. First, the small sample size, particularly within the 0.05% atropine group, restricted the statistical power and may have affected the ability to establish significant differences in clinical outcomes between the two atropine concentrations. Therefore, caution should be exercised when interpreting the results. Additionally, the relatively short one-year follow-up period may not have captured the long-term effects of atropine treatment for myopia management. The efficacy and safety profiles of 0.05% and 0.01% atropine concentrations may evolve over an extended period, highlighting the importance of conducting studies with longer follow-up durations. Furthermore, the present study only explored the comparative effectiveness of two atropine concentrations (0.05% and 0.01%).

To overcome these limitations and provide more robust and conclusive results, future studies should aim to include larger sample sizes to enhance the statistical power and improve the generalizability. Moreover, extending the follow-up period to multiple years would offer insights into the sustainability of the observed outcomes and potential long-term effects. Lastly, investigating additional concentrations of atropine would help elucidate the dose–response relationship and aid optimizing treatment strategies.

CONCLUSION

In conclusion, this preliminary study had shown that both 0.01% and 0.05% atropine concentrations are effective in delaying myopic progression among Thai school-age children. However, the higher incidence of adverse drug reactions in the 0.05% atropine group suggests the need for careful consideration when choosing the optimal concentration for myopia management in this specific population.

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