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The effect of atropine 0.025% on optical quality, corneal tomography, and binocular vision

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HIGHLIGHTS

The instillation of atropine 0.025% affects certain binocular vision indices, such as heterophoria, near point of convergence, near point of accommodation, and accommodative lag. Among biometric indices, only pupil size exhibited a statistically significant change following the instillation of atropine 0.025%.

ABSTRACT

Purpose: Our study pointed to evaluate the effect of atropine eye drop at 0.025% on optical quality, corneal tomography, and binocular vision.

Methods: A total of 51 university students received 0.025% atropine eye drops, once nightly to both eyes for 5 nights. Refraction, visual acuity (VA), accommodation facility, accommodation lag, near point of convergence (NPC), near point of accommodation (NPA), heterophoria, and corneal topography were measured before and after instillation.

Results: After using 0.025% atropine eye drops, the far and near heterophoria changed from -1.73 (±0.415) to -0.82 (±0.267) ($p = 0.005$) and -3.69 (±0.823) to 0.018 (±0.726) ($p < 0.001$), NPC increased from 4.573 (±0.4763) to 6.625 (±0.8328) ($p = 0.002$), NPA increased from OD (right eye) = 11.014 (±0.4059) to 17.635 (±1.0303) ($p < 0.001$), and OS (left eye) = 10.867 (±0.4394) to 17.110 (±0.9679) ($p < 0.001$), Monocular estimated method (MEM) retinoscopy increased from OD = 0.848 (±0.0415) to 1.137 (±0.0570) ($p < 0.001$), and OS = 0.892 (±0.0439) to 1.196 (±0.0570) ($p < 0.001$), accommodation facility decreased from OD = 9.69 (±0.827) to 8.44 (±0.878) ($p = 0.119$), and OS = 11.01 (±0.983) to 8.69 (±0.899) ($p = 0.005$), near VA decreased from OD = 0.992 (±0.0055) to 0.937 (±0.0170) ($p = 0.004$), and OS = 0.992 (±0.0055) to 0.927 (±0.0219) ($p = 0.005$), pupil diameter increased from OD = 3.043 (±0.0783) to 5.121 (±0.1314) ($p < 0.001$), and OS = 3.059 (±0.0714) to 5.253 (±0.1412) ($p < 0.001$), far VA, central corneal thickness (CCT), corneal densitometry, corneal curvature, ocular and corneal higher order aberration (HOA) and lower order aberration (LOA) remained unchanged (all $p > 0.05$).

Conclusions: The far and near VA, monocular accommodation facility, spherical refraction, corneal densitometry, corneal curvature, CCT, ocular and corneal HOA and LOA did not change significantly, but heterophoria, NPC, NPA, accommodative lag and pupil size changed significantly after instillation.

Key words: low-concentration atropine eyedrops, myopia, optical quality

INTRODUCTION

Myopia is the most common ocular disorder worldwide with increasing prevalence over the past decade [1, 2], particularly myopic shift increases in children aged 6–8 years follow by decrease in time spent outdoor activities during home quarantine for the coronavirus disease 2019 (COVID-19) pandemic [3]. It affects almost ⅓ of the US population, but the incidence ranges from 3% for Sherpa in Nepal to over 90% in Taiwan University students [4]. In general, Asians have significantly higher prevalence of myopia [5]. It is predicted that by 2050, approximately half of the world population will be myopic [1, 3, 6–8]. Which is expected about 10% of the cases will be of high myopia [1, 6, 8]. High myopia increases the risk of ocular complications such as: macular degeneration, macular hemorrhage, retinal detachment, choroidal neovascularization, cataracts, and glaucoma [1, 7, 9, 10]. Thus, myopia has become a serious global public health and socioeconomic issue. Finding an effective and safe method to prevent progression of myopia is important.

Several studies have shown that various concentration of low-concentration atropine eye drop is effective on controlling myopia progression [6, 9, 11]. Many studies have revealed that 0.01%, 0.025%, 0.05%, and 0.1% atropine could control myopia progression in children with reasonable efficacy but negligible side effects [11]. But, there is no study of the efficacy and side effect of atropine in young adult. Whereas, myopia onset and progression can arise in adulthood [12]. Thus, this study evaluates the effects of atropine 0.025% on refraction, visual acuity (VA), accommodation facility, accommodation lag, near point of convergence (NPC), near point of accommodation (NPA), horizontal heterophoria, and corneal topography on university students.

METHODS

The research protocol was reviewed and approved by the Research Ethics Committee, and the study was performed in accordance with the Declaration of Helsinki. Written informed agreement was obtained from patients of all participants. All procedures were based on the intention-to-treat principle.

57 university students (114 eyes), aged 19–26 years, with spherical power between +0.50 D and -5.25 D in at least one eye, astigmatism ≤4.00 D, and best corrected visual acuity (BCVA), expressed as decimal, no worse than 9/10 were enrolled in this trial. The average age of all students was 22.0 (±1.65) years. The exclusion criteria were ocular diseases (e.g. cataracts, risk of angle closure glaucoma, amblyopia, and strabismus), previous regular use of atropine or other optical methods for myopia control or amblyopia treatment, allergies to atropine, or systemic diseases (e.g. endocrine, cardiac, respiratory, and convulsion diseases).

The patients in this study were examined and their sex, age, spherical power, BCVA, far and near heterophoria, NPC, NPA, monocular accommodation facility, lag of accommodation, ocular aberrometer, pupil size, and corneal topography were recorded on the first visit to our clinic. Patients used atropine eye drops (once nightly). All examinations were repeated after 5 days of use. Refraction and ocular aberrometer was measured with an autorefractometer (HR-K8000A, Hovitz, Korea). The MEM retinoscopy was measured with a retinoscope (Beta200, HEINE, Germany) and a target at distance 40 cm. NPA was measured monocularly with push up technique. The students wore their fully corrected spectacle prescription and focused on the previous line of BCVA with the right eye while the left eye was occluded. The students were instructed to concentrate on a letter as the near chart was moved nearer. They were told to keep the letter as clear as possible until first sustain blur occur. The final distance in centemeter was recorded as the student's NPA. NPA was recorded three times and the average taken. NPC was measured with push up technique. The students wore their fully corrected spectacle and focused on the previous line of BCVA. They were instructed to concentrate on a letter as the near chart was moved nearer. They were told to keep the letter as single as possible until first double vision occur or the examiner see one eye has been deviated. The final distance in centemeter was recorded as the student's NPC. NPC was recorded 3 times and the average taken. Heterophoria was measured with cover test technique at distance (6 m) and near (40 cm) with prism bar (Oculus, Germany). The accommodation facility was measured monocularly. The students wore their fully corrected spectacle prescription. It was measured with fliper lens (±2.00 D), and looked at the near chart at 40 cm (the upper line of BCVA), and first place +2.00 D in front of an eye random, while the

other eye was ocluded. It was reported immediately when the reader read clearly, and immediately reversed to -2.00 D, until the font was clear and then reversed again. Finaly, the numbers of cycles completed within 1 min were recorded. Corneal topography and pupil size were measured with pentacam (HR, Oculus, Germany).

Statistical analysis

All statistical analyses were performed using SPSS software (ver. 22). After entering the data into the SPSS software and refining them, first, using descriptive methods, descriptive indices have been calculated for all the quantitative variables under study, as well as frequency distribution tables and descriptive graphs of the data. Then, the normality of the data distribution has been investigated with the Kolmogorov-Smirnov test, skewness and kurtosis indices. Then paired t-test, independent t-test and analysis of variance as well as chi-square test and Pearson's correlation coefficient were used. The significance level of the study was $p < 0.05$.

RESULT

A total of 57 university students (114 eyes) were enrolled in this study. And 6 students were lost to follow-up. In total, 51 university students (102 eyes) used atropine 0.025% eye drops. Table 1 shows the changes in binocular vision parameters before and after use of 0.025% atropine eye drop.

TABLE 1

Binocular vision before and after atropine instillation.

Parameters	Before	After	P-value
Far cover test	-1.73 (±0.415)	-0.82 (±0.267)	0.005
Near cover test	-3.69 (±0.823)	0.18 (±0.726)	<0.001
NPC	4.573 (±0.4763)	6.625 (±0.8328)	0.002

NPC – near point of convergence.

Table 2 shows the changes in accommodative parameters before and after use of 0.025% atropine eye drops.

TABLE 2

Accommodative parameter before and after atropine instillation.

Parameter	Before	After	P-value
NPA (OD)	11.014 (±0.4059)	17.635 (±1.0303)	<0.001
NPA (OS)	10.867 (±0.4394)	17.110 (±0.9679)	<0.001
MEM (OD)	0.848 (±0.0415)	1.137 (±0.0570)	<0.001
MEM (OS)	0.892 (±0.0439)	1.196 (±0.0570)	<0.001
Accommodation facility (OD)	9.69 (±0.827)	8.44 (±0.878)	0.119
Accommodation facility (OS)	11.01 (±0.983)	8.69 (±0.899)	0.005

MEM – monocular estimated method; NPA – near point of accommodation; OD – right eye; OS – left eye.

Table 3 shows the changes in refraction and VA before and after use of 0.025% atropine eye drops.

TABLE 3

Refraction and visual acuity before and after atropine instillation.

Parameter	Before	After	P-value
Spherical RE (OD)	-1.206 (±0.1987)	-1.108 (±0.2082)	0.070
Spherical RE (OS)	-1.147 (±0.1983)	-0.980 (±0.2085)	<0.001
Far VA (OD)	1.320 (±0.0279)	1.331 (±0.0301)	0.629
Far VA (OS)	1.343 (±0.0269)	1.324 (±0.0298)	0.446
Near VA (OD)	0.992 (±0.0055)	0.937 (±0.0170)	0.004
Near VA (OS)	0.992 (±0.0055)	0.927 (±0.0219)	0.005

OD – right eye; OS – left eye; RE – refractive error; VA – visual acuity.

Table 4 shows the changes in corneal topography and pupil diameter before and after use of 0.025% atropine eye drops.

TABLE 4

Corneal topography and pupil diameter before and after atropine instillation.

Parameter	Before	After	P-value
CCT (OD)	554.44 (±4.823)	554.67 (±4.874)	0.700
CCT (OS)	554.92 (±4.823)	554.79 (±4.763)	0.857
CC max (OD)	43.573 (±0.1908)	43.581 (±0.1895)	0.675
CC min (OD)	42.586 (±0.1998)	42.565 (±0.1982)	0.140
CC max (OS)	43.618 (±0.1892)	43.622 (±0.1914)	0.860
CC min (OS)	42.632 (±0.1988)	42.635 (±0.1995)	0.876
CD (OD)	15.90 (±0.145)	15.95 (±0.135)	0.561
CD (OS)	16.28 (±0.145)	16.36 (±0.146)	0.515
Pupil diameter (OD)	3.043 (±0.0783)	5.121 (±0.1314)	<0.001
Pupil diameter (OS)	3.059 (±0.0714)	5.253 (±0.1412)	<0.001

CC – corneal curvature; CCT – central corneal thickness; CD – corneal densitometry; OD – right eye; OS – left eye.

Table 5 shows the changes in ocular and corneal aberrometer before and after use of 0.025% atropine eye drops. All remained unchanged ($P > 0.05$).

TABLE 5

Ocular and corneal aberrometer before and after atropine instillation.

Parameter	Before	After	P-value
OLOA (OD)	0.4904 (±0.05987)	0.4809 (±0.05992)	0.799
OLOA (OS)	0.4768 (±0.05943)	0.4681 (±0.05879)	0.701
OHOA (OD)	0.0790 (±0.00384)	0.0766 (±0.00344)	0.479
OHOA (OS)	0.0955 (±0.01867)	0.0739 (±0.00348)	0.265
CLOA (OD)	0.2813 (±0.07394)	0.2789 (±0.08170)	0.934
CLOA (OS)	1.1945 (±0.07381)	1.1938 (±0.07384)	0.981
CHOA (OD)	0.3505 (±0.00812)	0.3544 (±0.01019)	0.535
CHOA (OS)	0.3396 (±0.00993)	0.3327 (±0.01098)	0.423

CHOA – corneal higher order aberration; CLOA – corneal lower order aberration; OD – right eye; OHOA – ocular higher order aberration; OLOA – ocular lower order aberration; OS – left eye.

DISCUSSION

The results indicate that the horizontal phoria particularly, near heterophoria had an esophoric shift significantly after 5 days use of atropine 0.025%.

There has been one previous study regarding the changes in heterophoria after treatment with low-concentration atropine eye drops. In 2023 Jiang [13], reported that heterophoria didn't change significantly after atropine 0.01% instillation.

By changing viewing from a distance to a near object, the near-reflex response (near-triad) comprising of ocular accommodation, convergence and pupil miosis is elicited to achieve and maintain clear and single binocular vision [14] according to partial paralysis of ciliary muscle, caused by 0.025% atropine, more nervous impulses are needed to compensate the accommodation, thus esophoric shift would be expected following to near-triad reflex. Esophoric shift in low-concentration atropine eye drops would be a method for treatment of decompensated exophoria.

NPA and NPC had decreased significantly after 5 days of instillation. There has been no previous study regarding the changes in NPC. According to near-triad reflex growth, decrease in NPC would be expected. Many studies showed significantly decrease in NPA [1, 7, 11, 15, 16], except two [8, 17], that remained unchanged.

Lag of accommodation increased significantly. There have been two previous studies regarding the changes in lag of accommodation. In 2023 Jiang [13], reported atropine 0.01% had no significantly effect on accommodative lag. But, in 2022 Liang [18], reported a significantly increase in lag of accommodation occurred after 7 days of 0.05% atropine use. According to partial paralysis of ciliary muscle, arising from atropine instillation and accommodation amplitude deduction, it would be predictable that accommodative lag increases after the instillation. But the changes would be less in lower dose of atropine. Monocular accommodation facility decreased slightly in the right eye, and decreased significantly in the left eye. The differences between two eyes would be because of monocular accommodative spasm. Although both right and left eye showed degrees of decrease, but the changes aren't clinically significant. Jiang [13], reported that binocular accommodation facility remained unchanged in 0.01% atropine instillation, and Wang [17], reported that both monocular and binocular accommodation facility improved significantly over time in both atropine 0.01% and control group. However. The accommodation facility measurement is subjective, depending on the speed of the response. Therefore, there is no guarantee that different participants use the same criteria of clarity or the same response speed to initiate the alternation of the lens. Thus, using simple clinical measurement of subjective accommodation facility as an indicator of accommodation status may be misleading [17, 19].

Spherical refraction showed a slightly hyperopic shift, but remained unchanged clinically. In 2013 Hiraoka [20], reported that cycloplegia with topical atropine significantly increased spherical equivalent refraction. In low-dose atropine only a slight hyperopic shift would be reasonable.

Far VA remained unchanged. Near VA reduced slightly, but not clinically significant. Considering that the spherical refractive error has not changed significantly, it is reasonable that far VA remains unchanged. Other studies reported the same, far VA didn't change after low-dose atropine instillation [1, 17]. Near VA showed no significantly changes in other studies with low-dose atropine instillation [1, 15, 17].

Pupils were dilated after atropine application. All other studies showed degrees of pupil dilation after atropine application [1, 11, 12, 15–18, 21]. Corneal densitometry, flattest and steepest corneal curvature, and CCT remained unchanged. There has been no previous study regarding the changes in corneal densitometry after atropine application. Corneal curvature remained stable in one other previous study [9], CCT has been reported unchanged in some studies [8, 21], but a trend for thicker CCT was reported in one study [18].

Ocular and corneal HOA and LOA remained stable. There has been one study regarding the changes in ocular and corneal HOA before and after atropine instillation, which reported no changes in corneal HOA, but an increase in ocular HOA [20].

This study has some limitations. First, our follow up period was short and we could not determine the changes after long-term use of 0.025% atropine eye drops. Second, we had only objective measurement.

CONCLUSION

In summary, use of atropine 0.025% had no clinically significant effect on far and near VA, monocular accommodation facility, spherical refraction, corneal densitometry, flattest and steepest corneal curvature, and central corneal thickness, and ocular and corneal HOA and LOA. but heterophoria had a significantly esophoric shift, NPC and NPA decreased significantly, and accommodative lag and pupil size increased significantly after atropine application.

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Authors' contributions:
Amir Asharlous: design and conduct of the study, preparation, review, and approval of the manuscript.
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Asgar Doostdar: collection, management of the data, preparation, review, and approval of the manuscript.
Mahdi Mahmoodi: analysis, and interpretation of the data, preparation, review, and approval of the manuscript.
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None.

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Ethics:
The content presented in the article complies with the principles of the Helsinki Declaration, EU directives and harmonized requirements for biomedical journals.