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Effects of low-concentration atropine eye drops on the optical quality of the eyes in myopic children

Weiran Li[1,2*], *Yiting Cao*[1,2*], *Jibo Zhou*[1,2]

Purpose: The present study was performed to compare the optical quality of the eyes of myopic children before and after treatment with atropine eye drops of different concentrations. **Methods:** In the study population of 71 patients (131 eyes), 34 patients (63 eyes) were given 0.01% atropine eye drops and 37 patients (68 eyes) were given 0.05% atropine eye drops. The modulation transfer function (MTF) cutoff frequency, Strehl ratio, objective scattering index (OSI), and predicted visual acuities (PVAs 100%, 20%, and 9%) under different lighting conditions were measured before and after two weeks of atropine treatment. **Results:** After using 0.05% atropine eye drops for two weeks, the Strehl ratio decreased from 0.27 ± 0.07 to 0.23 ± 0.07 (P = 0.0026), PVA 20% decreased from 1.15 ± 0.32 to 1.03 ± 0.36 (P = 0.0344), and PVA 9% decreased from 0.74 ± 0.23 to 0.64 ± 0.23 (P = 0.0073). The OSI was significantly higher after using 0.05% than 0.01% atropine eye drops (P = 0.0396), while both the Strehl ratio and PVA 20% were lower after using 0.05% than 0.01% atropine eye drops (P = 0.0087 and P = 0.0492, respectively). **Conclusion:** The children's optical quality did not change significantly after using 0.01% atropine eye drops, whereas it decreased after using 0.05% atropine eye drops.

Key words: Low-concentration atropine eyedrops, myopia, myopic children, optical quality analysis system (OQAS), optical quality

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Myopia is the most common ocular disorder worldwide and its prevalence has been increasing over the past several decades, especially in East Asia.[1–4] A number of methods are available to control the progression of myopia, including orthokeratology, peripheral defocus contact lenses, and increased outdoor activity.[5–8] Atropine eye drops have been shown to be an effective method to control the progression of myopia in children.[9–12] Atropine has a dose-related effect on the progression of myopia with greater effects and more obvious side effects, including photophobia, poor near vision, and rebound effects after withdrawal, observed at higher doses.[10] All of these risks seem to be mitigated by treatment with lower concentrations of atropine. Many studies have shown that moderate and low concentrations of atropine (e.g., 0.01%, 0.025%, 0.05%, and 0.1%) could control the progression of myopia in children with reasonable efficacy, minimal side effects, convenience of application, and slight rebound effects after discontinuation.[9–12] However, the efficacy and side effects (reduction in the degree of pupil dilation during accommodation and symptoms, such as photophobia and blurred near vision) of low-dose atropine differ according to the dose applied.[10,11,13] Yam *et al*.[11] and Moon and Shin[14] reported that different doses of atropine (0.01%, 0.025%, and 0.05%) exerted different effects on the progression of myopia, but only Yam *et al*.[11] reported the dose-dependent side effects.

This study was performed to determine whether there were differences in the optical quality of the eyes of myopic children after treatment with different doses of atropine (0.05% or 0.01%) administered as eye drops.

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 consent was obtained from the parents or guardians of all participants, and verbal consent was obtained from the participants. All procedures were based on the intention-to-treat principle.

Participants

71 children (131 eyes), aged 5–15 years, with spherical power between -0.50 and -6.00 diopters (D) in at least one eye, astigmatism ≤2.5 D, and best-corrected visual acuity (BCVA; expressed as the logarithm of the minimum angle of resolution, that is, log-MAR) no worse than 0.096 were enrolled in this trial. The average age of all children was 9.43 ± 2.03 years. The exclusion criteria were ocular diseases (e.g., cataracts, congenital retinal diseases, amblyopia, and strabismus), previous regular use of atropine or pirenzepine, or orthokeratology or other optical methods for myopia control, allergies to atropine, or systemic diseases

[1]Department of Ophthalmology, Ninth People's Hospital, Shanghai JiaoTong University School of Medicine, Shanghai, [2]Shanghai Key Laboratory of Orbital Diseases and Ocular Oncology, Shanghai, China

*Contribute equally to current study

Correspondence to: Dr. Jibo Zhou, Department of Ophthalmology, Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, 639 Zhizaoju Road, Shanghai - 200 011, China. E-mail: zhoujibo1000@aliyun.com

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(e.g., endocrine, cardiac, and respiratory diseases). The participants were randomized to receive 0.05% or 0.01% atropine eye drops, and both sex and age were balanced across the two groups.

Procedure

The patients in this study were examined and their sex, age, spherical power, cylinder power, and axial length (AL) were recorded on the first visit to our clinic. Myopic eyes were treated with 0.05% or 0.01% atropine eye drops (once nightly). All examinations were repeated after two weeks of treatment. The cycloplegia regimen was to apply one drop (six times, at five-minute intervals) of 0.5% tropicamide phenylephrine (Santen, Osaka, Japan) into both eyes. Refraction was measured with an autorefractor (RM-1; Topcon, Tokyo, Japan) ten minutes after applying the final drop. The mean spherical equivalent (SE) was calculated as spherical power plus half the cylinder power. The AL was measured by optical biometry (IOL Master 500; Carl Zeiss Meditec, Jena, Germany) and the intraocular pressure (IOP) was measured by tonometry (iCare IC100; iCare, Vantaa, Finland). Only treated eyes were recorded, while the healthy eyes were not. All examinations were performed and results were recorded by a technician blinded to the groups.

Optical quality measurement

The modulation transfer function (MTF) cutoff frequency, Strehl ratio, objective scattering index (OSI), and predicted visual acuities (PVAs 100%, 20%, and 9%) were measured under photopic lighting conditions using an Optical Quality Analysis System™ (OQAS; Visiometrics, Terrassa, Spain) preoperatively and after two weeks of atropine treatment. During measurement, the subjects placed their chin on the chinrest of the instrument tray and were asked to fix the center of a figure. With the exception of OSI where the system automatically set the pupil diameter to 4 mm, all other parameters were measured according to the corresponding pupil diameter of the patient. The OQAS system could automatically correct refractive errors from -8 D to +8 D.[15] To ensure the accuracy of the results, the measurements were repeated three times, and the average of the three results was calculated.

The OQAS system assesses optical quality in a completely objective manner. OSI objectively reflected the situation of scattered light in the eye, and its value was defined as the ratio of the peripheral light intensity of the dual-channel image to the central peak light intensity, with a higher OSI value indicating a higher level of intraocular scatter. The MTF cutoff value (i.e., the cutoff value of the MTF on the x-axis) represents the highest spatial frequency in a low-contrast environment in units of cycles per degree (cpd).[16,17] The MTF cutoff in the double-pass system was the frequency at which the MTF reached a value of 0.01. As the point spread function (PSF) images recorded by the double-pass system were disturbed by high-frequency signals and high-frequency signals inevitably appeared in the camera equipment, the frequency measurement may be unstable when the MTF is extremely small. To solve this problem, the system set the MTF threshold to 0.01, corresponding to 1% contrast. Therefore, the MTF cutoff value was equivalent to the highest frequency at which the optical system could focus an object on the retina under conditions of 1% contrast. The Strehl ratio reflected the influence of the wavefront aberration of the optical system on the light intensity at the imaged center point and was defined as the ratio of the measured PSF peak to the ideal perfect optical system (without aberrations). PVA 100%, 20%, and 9% only considered the optical system of the eye (i.e., predicted the best visual acuity of the patient at 100%, 20%, and 9% contrast based on the measured aberrations and intraocular scatter).

Statistical analysis

All statistical analyses were performed using StatView software (ver. 9.4; SAS, Cary, NC). Generalized estimating equations were used to compare the data before and after medication, and the data between different groups. The results are expressed as mean ± standard error. In all analyses, $P < 0.05$ was taken to indicate statistical significance.

Results

A total of 71 children (131 eyes) were enrolled in this study, and none were lost to follow-up. In total, 34 children (63 eyes) were treated with 0.01% atropine eye drops and 37 children (68 eyes) were treated with 0.05% atropine eye drops. There were no significant differences in demographic characteristics or optical quality before treatment between the two groups [Table 1].

Table 2 shows the changes in visual quality parameters before and after treatment with 0.01% and 0.05% atropine eye drops. After treatment with 0.05% atropine eye drops for two weeks, the Strehl ratio decreased from 0.27 ± 0.07 to 0.23 ± 0.07 ($P = 0.0026$), PVA 20% decreased from 1.15 ± 0.32 to 1.03 ± 0.36 ($P = 0.0344$), and PVA 9% decreased from 0.74 ± 0.23 to 0.64 ± 0.23 ($P = 0.0073$).

Table 3 shows the difference in optical quality between 0.01% and 0.05% atropine eye drops after two weeks of treatment. The OSI was significantly higher after using 0.05% than 0.01% atropine eye drops ($P = 0.0396$), whereas both the Strehl ratio and PVA 20% were lower after using 0.05% than 0.01% atropine eye drops ($P = 0.0087$ and $P = 0.0492$, respectively).

Discussion

The OQAS system was used to examine changes in objective optical quality in the eyes of myopic children after treatment

Table 1: Demographic characteristics and optical quality of the study population before treatment

	0.01%	0.05%	P
Age (years)	9.53±2.40	9.36±1.71	0.7394
Sex (male, %)	15 (44.12%)	19 (51.35)	0.5422
Spherical equivalent (D)	-1.61±1.12	-1.87±0.83	0.1415
LogMAR UDVA	0.45±0.30	0.53±0.28	0.1280
Axial length (mm)	24.20±0.75	24.09±0.73	0.3782
IOP (mmHg)	16.67±2.61	16.71±2.86	0.9349
OSI	0.38±0.30	0.41±0.31	0.7071
MTF cutoff frequency	46.15±9.35	44.56±10.74	0.4138
Strehl ratio	0.29±0.08	0.27±0.09	0.3368
PVA 100%	1.55±0.30	1.49±0.36	0.2893
PVA 20%	1.22±0.31	1.17±0.37	0.3833
PVA 9%	0.79±0.25	0.76±0.29	0.6209

IOP, intraocular pressure; LogMAR, the logarithm of the minimum angle of resolution; MTF, modulation transfer function; OSI, objective scattering index; PVA, predicted visual acuity; UDVA, uncorrected distance visual acuity. $P<0.05$ was considered statistically significant

Table 2: Optical quality before and after atropine treatment

	0.01%			0.05%		
	Before	2 weeks	*P*	Before	2 weeks	*P*
OSI	0.38±0.30	0.41±0.31	0.9351	0.38±0.24	0.53±0.53	0.1285
MTF cutoff frequency	46.15±9.35	44.56±10.74	0.1688	44.11±9.13	41.47±11.43	0.0885
Strehl ratio	0.29±0.08	0.27±0.09	0.1950	0.27±0.07	0.23±0.07	0.0026
PVA 100%	1.55±0.30	1.49±0.36	0.0671	1.44±0.33	1.39±0.38	0.1188
PVA 20%	1.22±0.31	1.17±0.37	0.2071	1.15±0.32	1.03±0.36	0.0344
PVA 9%	0.79±0.25	0.76±0.29	0.2671	0.74±0.23	0.64±0.23	0.0073

MTF, modulation transfer function; OSI, objective scattering index; PVA, predicted visual acuity. *P*<0.05 was considered statistically significant

Table 3: Comparison of the optical quality after 2 weeks of treatment with 0.01% and 0.05% atropine eye drops

	0.01%	0.05%	*P*
OSI	0.41±0.31	0.53±0.53	0.0396
MTF cutoff frequency	44.56±10.74	41.47±11.43	0.0955
Strehl ratio	0.27±0.09	0.23±0.07	0.0087
PVA 100%	1.49±0.36	1.39±0.38	0.1574
PVA 20%	1.17±0.37	1.03±0.36	0.0492
PVA 9%	0.76±0.24	0.64±0.23	0.0560

MTF, modulation transfer function; OSI, objective scattering index; PVA, predicted visual acuity. *P*<0.05 was considered statistically significant

with 0.05% or 0.01% atropine eye drops. The results indicate that the optical quality did not change significantly after two weeks of treatment with 0.01% atropine eye drops, but decreased after two weeks of treatment with 0.05% atropine eye drops.

There have been no previous studies regarding the changes in visual quality after treatment with low-concentration atropine eye drops. In 2019, Liu *et al*.[18] examined the changes in visual quality after orthokeratology in 35 myopic children with an average age of 11.46 ± 2.33 years, and found that the OSI value increased significantly after 1 month and then recovered slowly. Although orthokeratology and atropine both had an effect in controlling myopia, their mechanisms of action were different. The decrease in optical quality after orthokeratology was related to stray light, while that associated with atropine was related to changes in pupillary diameter and ciliary muscle adjustment function.

Kaymak *et al*.[19] reported that 24 h of using 0.01% atropine eye drops had a significant impact on pupil size and adaptability in young people, with a lower concentration of atropine in the eye drops showing a smaller effect on pupil size. In another study, Fu *et al*.[20] reported a stronger effect in eye drops containing 0.02% than 0.01% atropine in controlling the progression of myopia, but both 0.02% and 0.01% atropine eye drops increased the pupillary diameter after 1 year of treatment (all $P < 0.001$). Our results show that the optical quality decreased after two weeks of treatment with 0.05% atropine eye drops. Previous studies showed that pupil size showed different changes according to the concentration of atropine in the eye drops; thus, we propose that the optical quality may have decreased because of the change in pupil diameter.[21-23]

In the present study, the OSI was decreased in children treated with 0.05% atropine eye drops. This indicates that children treated with 0.05% atropine eye drops needed better refractive correction than those with normal eyesight. For example, some children with mild myopia did not need to wear glasses generally, but required glasses when they began using 0.05% atropine eye drops. The decreases in PVA 20% and PVA 9% indicate that children treated with 0.05% atropine eye drops had poorer vision than those with normal eyesight when reading materials with poor contrast. These observations suggest that reading materials with higher contrast should be provided to children using 0.05% atropine eye drops.

This study has some limitations. First, the follow-up period was short and we could not determine the changes in optical quality after long-term use of low-concentration atropine eye drops. Second, we had only objective examination results and did not use questionnaires to analyze subjective optical quality after using the atropine eye drops. Third, we compared only two atropine concentrations—0.05% and 0.01%—and therefore could not determine the optimal concentration with good therapeutic effects and minimal side effects. In addition, the measurement of OQAS can only subjectively reflect the changes of optical quality. Our further studies aim to assess the impact of atropine on visual quality subjectively by using or designing a formal questionnaire survey with a score grade. Finally, we only measured changes in visual quality in a bright environment, and did not compare the effects of different concentrations of eye drops on optical quality in bright and dark environments.

Conclusion

In summary, the optical quality of the eyes of myopic children did not change significantly after two weeks of treatment with 0.01% atropine eye drops, while the optical quality decreased after two weeks of treatment with 0.05% atropine eye drops. These results indicate that children using 0.05% atropine eye drops require better living and study environments.

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Conflicts of interest

There are no conflicts of interest.

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