Short-term effect of atropine on higher-order aberrations in myopic children

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Abstract

Background: This study aimed to investigate the short-term effect of cycloplegia on higher-order aberrations (HOAs) in school-age myopic children who received 0.25% atropine for cycloplegic refraction.

Methods: We performed a retrospective chart review of 24 myopic children between the ages of 5 and 15 years, who had received one topical drop of 0.25% atropine for three consecutive nights before undergoing cycloplegic refraction. Auto-refraction, visual acuity, and HOAs measured with the iTrace aberrometer were compared before and after atropine use. To account for the effect of cycloplegia, the amount of HOAs under matching scanning sizes was compared.

Results: There were statistically significant differences in the spherical equivalent, with a hyperopic shift after atropine use ($p < 0.001$). Corrected visual acuity and spherical aberrations showed no significant change under the respective pupil and scanning sizes before and after atropine use. Under identical scanning sizes, there was a significant change in total spherical aberration (from 0.03 to 0.06 μm, $p = 0.044$) and internal spherical aberration (from –0.10 to –0.05 μm, $p = 0.049$) after atropine use. Differences in corneal spherical aberration were insignificant.

Conclusion: The positive shift of spherical aberration induced by the inhibition of accommodation in myopic children may have a possible effect against myopic progression. Future studies can focus on the long-term effect on HOAs and impact on visual quality with lower concentrations of atropine.

Keywords: Atropine; Cycloplegia; Higher-order aberrations; Myopia; Spherical aberration.

1. INTRODUCTION

The ideal formation of optical images involves a perfect focus on the retina of a spherically shaped wavefront from light rays at any given point. Optical aberrations are deviations of light rays from their aimed route.[1] The difference measured between the wavefront of light from the desired path and the actual wavefront is termed wavefront aberration, which is often expressed by orthogonal Zernike polynomials, representing the root mean square (RMS) of wavefront errors for each mode.[2,3] The lower-order aberrations, defocus and astigmatism, constitute around 80% of wavefront aberrations in the normal eye and can be corrected by eyeglasses.[4] However, after correction of lower-order aberrations (ie, refractive error) with spectacles, higher-order aberrations (HOAs) of Zernike polynomials remain. Though often of very low value, HOAs still affect the optical quality of the eye.[5] Coma, trefoil, and spherical aberrations play dominating roles amongst HOAs.[6]

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Myopia is a worldwide health issue with growing prevalence over the past decades.[7,8] Higher degrees of myopia may lead to pathologic change in the retina and even blindness from cataracts, maculopathy, and retinopathy.[9,10] This has led to rising concern for the prevention of myopia progression over the past years. Donders published the first reports suggesting atropine for myopia control in the 19th century.[11] Numerous studies from varying countries and populations have shown atropine to be effective on myopia retardation in the past 20 years.[12–16] Atropine is thus frequently used for extended periods in children of school age for myopia treatment in ophthalmologic clinics, particularly in Asian countries. Owing to high amplitudes of accommodation in children, atropine may also be utilized in cycloplegia for accurate measurement of the refractive status.[17] However, there is limited information on how atropine may affect HOAs in this population.

The following two main factors alter wavefront aberrations in the eye: the pupil diameter and accommodation. Atropine may impact the HOAs of the eye through a combined effect of decreasing the accommodation while increasing the pupil size. The pupil controls the amount of light reaching the retina, serving as the aperture of the eye, and it has already been established that the RMSs of wavefront aberrations are correlated with the second order of the pupil diameter.[18,19] To evaluate the amount of HOAs attributed to accommodation, we compared the results of HOAs at the same scanning diameter before and after atropine use.

2. METHODS

We performed a retrospective chart review on subjects visiting our ophthalmology clinic for cycloplegic refractive status

evaluation between September 2014 and August 2015 at the Taipei Veterans General Hospital, Taiwan, where 0.25% atropine had been used for cycloplegia in children during that period. Children aged 5 to 15 years were included in this review. At that time, atropine eye drops were prescribed at the initial visit, with instructions for administration on three consecutive nights before the return visit to achieve complete cycloplegia. Aberrometry examination before cycloplegia and at the return visit was offered if the parents and child wished for further evaluation. Cases with documentation of partial cycloplegia with pupillary light response noted on slit lamp examination, who did not complete the two aberrometry examinations, or with ocular pathologies apart from refractive error were excluded from data analysis.

Autorefraction had been performed with an autorefractor autokeratometer (KR-8900; Topcon Medical Systems, Tokyo, Japan), and the patient's refractive status was recorded as the average of three reliable readings. Myopia was defined as a spherical equivalent (SE) of less than –0.5 diopters (D) according to the refractive error acquired on the patient's return visit after cycloplegia. The wavefront scanning size and total RMS of HOAs from the third- to sixth-order Zernike coefficients were acquired by the built-in program of the iTrace aberrometer (Tracey Technologies, Houston, TX, USA). The RMSs of individual HOAs, including coma, trefoil, spherical aberration, and secondary astigmatism, were also analyzed. Data before and after administration of 0.25% atropine were included, and only results of the right eye were used for comparison.

To correct for the effect of pupil enlargement on HOAs, results of post-atropine iTrace aberrometer wavefront analysis were also acquired after adjusting to the same scanning diameter as before atropine use. Total HOAs and HOAs from the anterior corneal surface were analyzed on the iTrace aberrometer, and the internal HOAs were calculated by the difference in between. We chose the results of coma, spherical aberration, secondary astigmatism, and trefoil to represent the amount of HOAs.

The difference before and after atropine administration was analyzed using the paired *t*-test or the Wilcoxon signed-rank test according to the normality of data distribution as analyzed by the Shapiro-Wilk test. A two-tailed *p*-value <0.05 was used to determine statistical significance. All analyses were conducted using SPSS statistical software (version 22.0.0; SPSS, Inc., Chicago, IL, USA). The study followed the tenets of the Declaration of Helsinki, and approval was obtained from the institutional review board of Taipei Veterans General Hospital, Taiwan.

Table 1

Demographic, refractive, and HOA data of 24 eyes

Age, y, mean (SD)	9.58 (2.32)		
Gender	Number of cases		
Boys	9		
Girls	15		
	Preatropine	Postatropine	*p* value
Spherical equivalence, D, mean (SD)	–3.21 (2.81)	–2.79 (1.57)	0.009*
Scanning size, mm, mean (SD)	4.75 (1.07)	5.71 (0.97)	<0.001*
LogMAR VA, mean (SD)	0.05 (0.16)	0.05 (0.12)	0.56
RMSs of HOAs			
Total	0.22 (0.15)	0.41 (0.18)	<0.001*
Coma	0.1 (0.08)	0.22 (0.028)	0.005*
Spherical aberration	0.03 (0.07)	0.07 (0.16)	0.35
Secondary astigmatism	0.05 (0.04)	0.09 (0.07)	0.001*
Trefoil	0.12 (0.13)	0.21 (0.13)	0.003*

HOAs = higher-order aberrations; LogMAR = log of the minimum angle of resolution; RMSs = root mean squares; SD = standard deviation; VA = visual acuity.*Statistically significant.

Table 2

Results of HOAs before and after atropine use under same scanning sizes (preatropine pupil diameter in each eye)

	Pre-atropine	Post-atropine	*p*
Total eye, μm (SD)			
RMSs of HOAs	0.22 (0.15)	0.25 (0.17)	0.21
Coma	0.1 (0.08)	0.12 (0.09)	0.37
Spherical aberration	0.03 (0.07)	0.06 (0.1)	0.044*
Secondary astigmatism	0.05 (0.04)	0.06 (0.07)	0.16
Trefoil	0.12 (0.13)	0.12 (0.12)	0.69
Internal, μm (SD)			
RMSs of HOAs	0.26 (0.19)	0.27 (0.18)	0.83
Coma	0.14 (0.07)	0.16 (0.13)	0.81
Spherical aberration	–0.1 (0.11)	–0.05 (0.1)	0.049*
Secondary astigmatism	0.05 (0.04)	0.06 (0.07)	0.96
Trefoil	0.13 (0.14)	0.12 (0.11)	0.88
Corneal, μm (SD)			
RMSs of HOAs	0.23 (0.13)	0.23 (0.14)	0.73
Coma	0.14 (0.09)	0.14 (0.1)	0.82
Spherical aberration	0.12 (0.09)	0.11 (0.07)	0.67
Secondary astigmatism	0.04 (0.03)	0.04 (0.04)	0.64
Trefoil	0.09 (0.06)	0.08 (0.09)	0.53

The scanning size was defined as the pre-atropine pupil diameter in each eye.HOAs = higher-order aberrations; RMSs = root mean squares; SD = standard deviation.*Statistically significant difference of pre- and postatropine aberrations compared with results under the same scanning size.

3. RESULTS

A total of 24 patients were included, with a mean age of 9.58 ± 2.32 years (range, 5-15 years). The average cycloplegic SE was –2.79 ± 1.57 D (range, –5.75 to –0.75 D). The mean scanning diameters before and after atropine are shown in Table 1, with a mean difference of 0.95 ± 0.75 mm (range, –0.2 to 2.4 mm). The mean hyperopic shift noted after atropine use was 0.41 ± 2.05 D (range, –5.13 to 5.75 D), which was statistically significant ($p = 0.009$). The RMSs of total HOAs, coma, secondary astigmatism, and trefoil showed significant increases under the same scanning size after atropine use, but there was no significant change in spherical aberration (Table 1).

At identical scan sizes, using the pre-atropine pupil diameter in each eye for both calculations before and after application of atropine, there was a significant positive shift in total spherical aberration (0.03 ± 0.07 to 0.06 ± 0.10 μm; $p = 0.044$) and internal spherical aberration (–0.10 ± 0.11 to –0.05 ± 0.10 μm; $p = 0.049$) after atropine use. Changes in corneal spherical aberration and other HOAs were insignificant under the same scanning diameter (Table 2). RMSs of HOAs before and after atropine with and without identical scanning sizes are shown in Fig. 1. With the iTrace simulated Snellen E display, we demonstrate the change in internal aberrations after short-term use of 0.25% atropine despite correction of refractive error and under the same scanning size, which shows the effect of accommodation inhibition on total HOAs, coma, spherical aberration, secondary astigmatism, and trefoil (Fig. 2). Changes in spherical aberration after short-term use of 0.25% atropine in patients with varying scanning sizes are demonstrated in Fig. 3.

4. DISCUSSION

As expected, significant hyperopic shift around 0.50 D after 0.25% atropine use was noted in our study group, explained by the paralysis of physiologic tonic accommodation after cycloplegia and decreased lens thickness after loss of accommodation.[20] Similar findings were observed by Hiraoka et al,[21,22] who

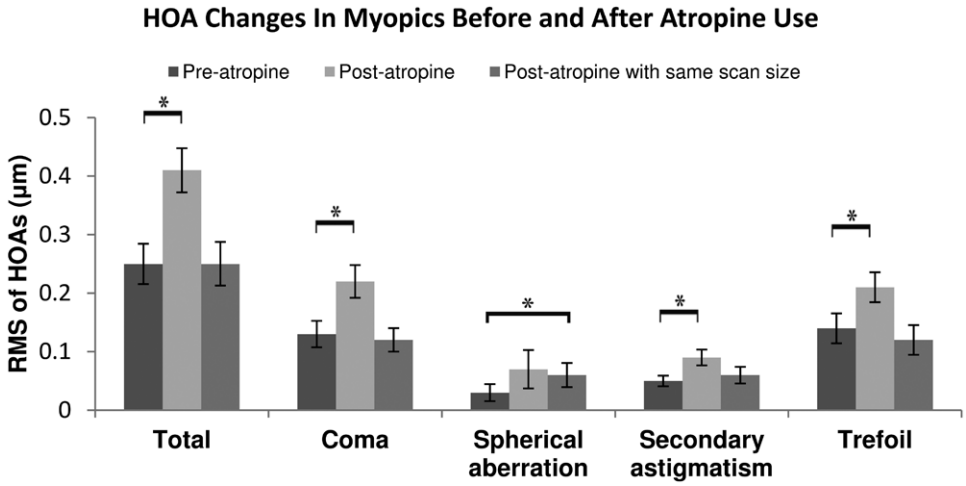

Fig. 1 Root mean squares of higher-order aberrations (HOAs) before and after 0.25% atropine use. *Significance at $p < 0.05$. Error bars represent standard error of the means. RMS = root mean square.

reported shifts of SE from –3.07 to –2.57 D after 1% cyclopentolate administration in myopics, which is close to our results. The degree of hyperopic shift may vary among reported studies owing to the different concentrations or properties of the medication administered.

When light passes through, we can consider the eye as a compound lens structure consisting of the cornea with a tear film, pupil, and crystalline lens.[3] When accommodating, miosis increases the depth of focus and decreases HOAs.[3,23] Accommodation also changes the curvature of the anterior lens surface, affecting the amount of HOAs in the human eye.[23,24] Increase in HOAs after the inhibition of accommodation has been reported in several studies. Carkeet et al[25] measured the RMSs of HOAs at a 6-mm pupil using Hartman-Shack technology and noted a significant difference in RMSs of HOAs between 1% cyclopentolate hydrochloride (0.426 μm) and non-cycloplegic 2.5% phenylephrine hydrochloride (0.385 μm), concluding that cycloplegics agents caused a higher increase in HOAs compared with mydriatics without cycloplegic properties and thus demonstrating the effect of accommodation on wavefront aberrations. We also noted a significant change in total HOAs before and after atropine administration; however, this was no longer significant when the scanning diameters were identical. Our mean scan size was around 4.75 mm, which is smaller than the diameter by Carkeet et al[25] and may explain why the effect of cycloplegia was less significant.

Spherical aberration results in glare and a halo, affecting contrast sensitivity and the outcome of visual quality. Positive spherical aberration is when the peripheral rays are focused in front of central rays, and negative spherical aberration is when the focus is behind. The cornea induces positive spherical aberration,[26–28] while accommodation and the lens cause negative spherical aberration.[28,29] Li et al also used the iTrace aberrometer and demonstrated a negative shift in total and internal spherical aberrations after objective accommodation in healthy young emmetropic eyes at 3- and 5-mm pupil sizes.[30] Hiraoka et al[21] explored the effect of atropine on wavefront aberrations in hyperopic children with a Hartman-Shack aberrometer. They found a mean increase in total HOAs of 0.044 μm at a 6-mm pupil diameter after 1% atropine use in hyperopic children, including significant changes in coma-like aberrations (0.034 μm) and spherical aberrations (0.023 μm). They further reported

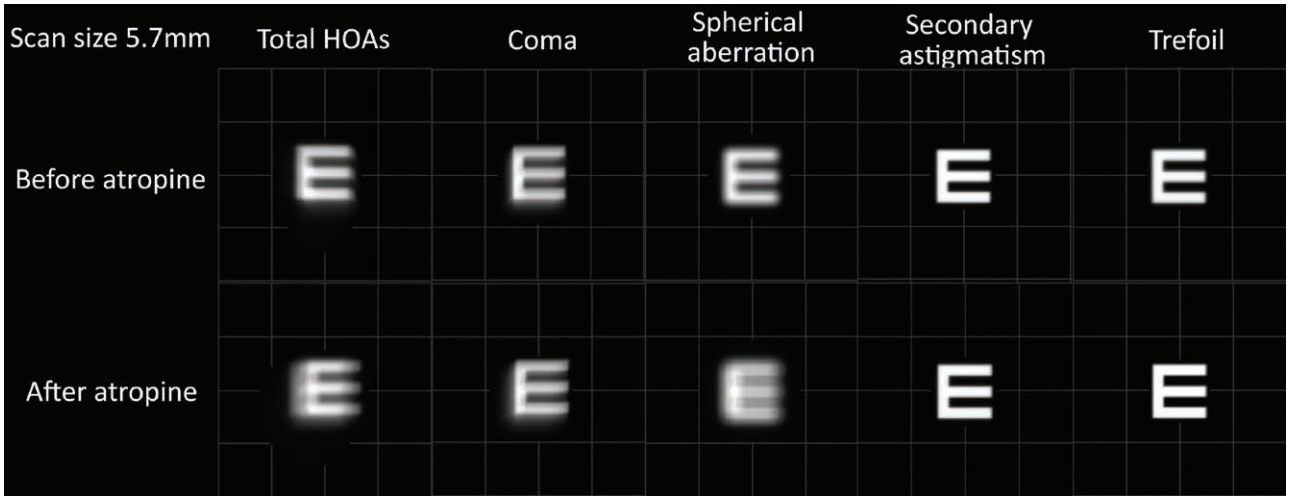

Fig. 2 Example of aberration changes before and after atropine use as depicted by the simulated E chart of a patient under the same scanning size of 5.7 mm. HOA = higher-order aberration

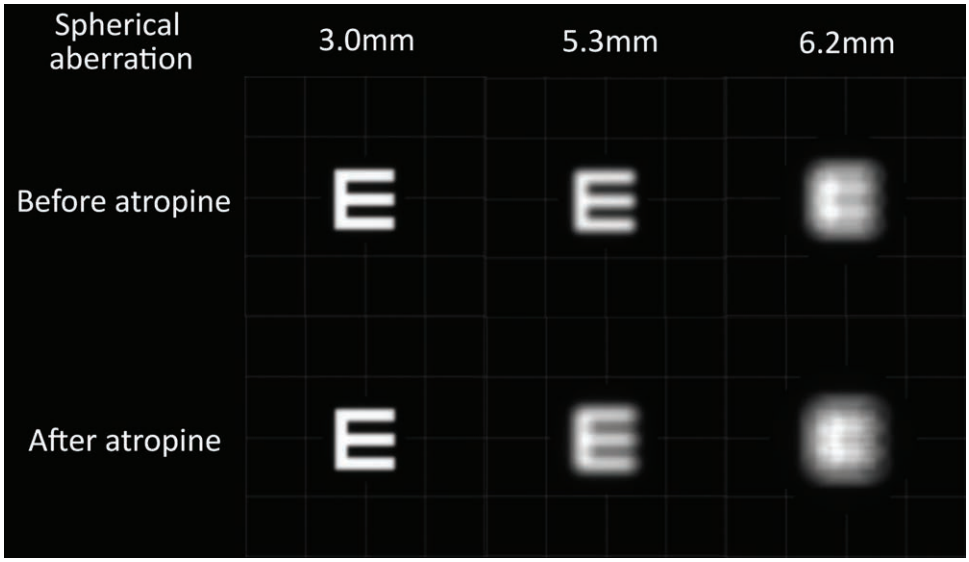

Fig. 3 Example of changes in spherical aberration before and after atropine use as depicted by the simulated E chart in patients with scanning sizes of 3.0, 5.3, and 6.2 mm.

results before and after 1% cyclopentolate hydrochloride eye drop instillations in myopic children, with similar findings of a significant positive shift of spherical-like aberrations (0.014 μm) and increased HOAs, but no statistically significant change in coma-like aberrations after cycloplegia.[22]

Atropine is the only medication proven to be effective for control of axial myopia progression; however, the precise mechanism is yet to be determined.[31] Current arguments include the possible involvement of retinal/scleral muscarinic receptors or scleral fibroblasts or that atropine may act through non-muscarinic or non-accommodation-related pathways.[32] Axial myopic eyes are elongated and thus relatively hyperopic in the periphery. The role of peripheral refraction in myopia control is also under debate. Studies from 1971 showed that pilots with peripheral farsightedness were more likely to develop myopia.[33] However, this has been challenged by many studies over the years. Relative peripheral refraction error was not found to be a significant risk factor when assessing the occurrence of myopia in 2043 non-myopic children by the Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error study group between 1995 and 2007.[34] Another large study of 1700 children concluded that relative peripheral hyperopia did not predict the occurrence or progression of myopia.[35] However, others have found that using special contact lenses to reduce peripheral hyperopia reduced progression of myopic refraction and axial elongation in children.[36] Positive spherical aberration contact lenses have also been reported to slow down axial growth of the eye.[37] Orthokeratology lenses, which induce positive spherical aberration and peripheral myopic defocus, are proven to be beneficial for myopia control.[37,38] Our finding of a positive shift of spherical aberration after cycloplegia agrees with previous literature that a significant negative shift of spherical aberration is noted during accommodation.[24,39] The positive shift of spherical aberration after atropine use may be a plausible mechanism for inhibiting myopia progression, but further research is needed.

HOA measurements were not obtained at a pre-determined pupil size in our study but were obtained by the largest scan size suitable according to the patient's physiologic pupil diameter before administration of atropine and then compared at identical sizes after atropine use. This may be a closer representation of the impact atropine has on the patient's visual quality in daily life. According to our knowledge, this is one of the few studies with direct measurement of the amplitude of HOAs under the patient's habitual pupil size.

Few studies have reported the effect of atropine use on HOAs in myopic children before this, despite being the main population under atropine treatment. Our findings may show that accommodation plays an important role among myopic children for improving retinal image quality.

The results of our study are limited by its retrospective nature, relatively short-term atropinization, and small number of cases included. Pupil centers may shift when obtaining different wavefront scans; thus, the same areas may not be included for analysis in a patient despite the same scanning size. Varying concentrations of atropine have been shown to effectively control myopia,[40] and our findings indicate that attention could be paid to future studies on the long-term effects of different concentrations of atropine on visual quality and HOAs in myopic children.

In conclusion, our study showed that short-term 0.25% atropine induces a significantly positive shift in spherical aberration among myopic school-age children, which may play a part in its role against myopic progression. Even after correction of refractive error, HOAs may affect the visual quality in those receiving atropine, and physiologic accommodation plays a role in improving retinal image quality. Future studies can focus on the long-term effect on HOAs, impact on the visual quality with lower concentrations of atropine, and role of positive spherical aberration in myopia control.

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