The Association of Choroidal Thickening by Atropine With Treatment Effects for Myopia: Two-Year Clinical Trial of the Low-concentration Atropine for Myopia Progression (LAMP) Study

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• PURPOSE: To evaluate longitudinal changes in subfoveal choroidal thickness (SFChT) among children receiving atropine 0.05%, 0.025%, or 0.01% over 2 years and their associations with treatment outcomes in myopia control.

• DESIGN: Double-blinded randomized controlled trial.

• METHODS: SFChT was measured at 4-month intervals using spectral domain optical coherence tomography. Cycloplegic spherical equivalent (SE), axial length (AL), best-corrected visual acuity, parental SE, outdoor time, near work diopter hours, and treatment compliance were also measured.

• RESULTS: 314 children were included with qualified choroidal data. The 2-year changes in SFChT from baseline were 21.15 ± 32.99 μm, 3.34 ± 25.30 μm, and −0.30 ± 27.15 μm for the atropine 0.05%, 0.025%, and 0.01% groups, respectively ($P < .001$). A concentration-dependent response was observed, with thicker choroids at higher atropine concentrations ($\beta = 0.89$, $P < .001$). Mean SFChT thickness significantly increased at 4 months in the atropine 0.025% ($P = .001$) and 0.05% groups ($P < .001$) and then remained stable until the end of the second year ($P > .05$ for all groups). Over 2 years, an increase in SFChT was associated with slower SE progression ($\beta = 0.074$, $P < .001$) and reduced AL elongation ($\beta = -0.045$, $P < .001$). In the mediation analysis, 18.45% of the effect on SE progression from atropine 0.05% was mediated via its choroidal thickening.

• CONCLUSIONS: Low concentration atropine induced a choroidal thickening effect along a concentration-dependent response throughout the treatment period. The choroidal thickening was associated with a slower SE progression and AL elongation among all the treatment groups. Choroidal response can be used for assessment of long-term treatment outcomes and as a guide for concentration titrations of atropine. (Am J Ophthalmol 2022;237: 130–138. © 2021 Elsevier Inc. All rights reserved.)

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MYOPIA IS THE MOST COMMON OCULAR DISORDER worldwide, with an especially high prevalence in East Asia.[1-3] It is associated with excessive eyeball growth leading to sight-threatening complications.[4] Studies conducted in different countries have found low-concentration atropine eye drops to be effective in slowing myopia progression among children.[5-12] However, treatment responses to atropine vary widely among individuals.[13,14]

The Low-concentration Atropine for Myopia Progression (LAMP) study demonstrated a concentration-dependent response for low-concentration atropine drops from 0.01% to 0.05%, with 0.05% conferring highest efficacy among the studied concentrations of up to 67% compared with the placebo group.[8] Furthermore, young age is significantly associated with poor treatment efficacy for low-concentration atropine.[15] Younger children therefore require higher concentrations of atropine for better treatment outcomes.[15] However, at the same concentration and within the same age group, there are still variations in treatment responses. It is crucial to find a potential biomarker for individualized treatment strategies.

The choroid has been found to play a role in the regulation of eye growth and refractive error developments

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from animal studies. In young chicks, choroidal thickness changed rapidly and predictably in response to modifications in the focus of retinal images.[16] A negative association between the changes in choroidal thickness and axial length (AL) has also been reported for macaque monkeys wearing defocus lenses.[17] Among human studies, choroidal thickening was also observed in healthy children treated with atropine 1% for 1 week[18,19] and in children with myopia treated with atropine 0.01% for less than 8 weeks.[20-22] A recent study explored choroidal changes in children receiving atropine 1% or 0.01% for 6 months. It reported atropine 1% increased choroidal thickness, which was associated with the 6-month AL change.[23]

Based on these previous reports, we hypothesize that the choroidal-thickening effect of atropine is associated with its treatment effect. Choroidal thickness (ChT) is a potential biomarker and mediator for long-term treatment outcomes. In this study, we evaluated longitudinal changes in subfoveal choroidal thickness (SFChT) among children receiving low concentrations of atropine at 0.05%, 0.025%, and 0.01%. There was also a "switch-over" placebo group in which the participants switched over to atropine 0.05% in the second year. The study was for 2 years, along with the LAMP study. We also evaluated the associations between SFChT changes and atropine treatment responses, and tested whether changes of SFChT could mediate the atropine effect on SE progression.

METHODS

Previous reports have described the LAMP study design.[24] LAMP was a randomized, double-blinded, placebo-controlled trial that studied the efficacy and safety of daily topical atropine eye drops at 0.05%, 0.025%, and 0.01% concentrations in preventing myopia progression among 438 children aged 4 to 12 years. The recruited children had myopic refractions of at least −1.0 diopters (D) and astigmatism of less than 2.5 D in both eyes. Children with systemic diseases or ocular diseases, previous experiences with myopia control therapy (eg, atropine, pirenzepine, orthokeratology lenses, or other optical methods), or a history of allergies to atropine (eg, a cardiac or respiratory illness) were all excluded.

At the beginning of the study, the children were randomized to 4 treatment groups (atropine 0.05%, 0.025%, 0.01%, and placebo) for treatment, with follow-up at 2 weeks and at 4, 8, and 12 months.[24] In the second year, participants in the placebo group were switched to the atropine 0.05% group, while participants in the other 3 treatment groups were maintained at the initial regimens initially prescribed for the first year. The study conformed to the tenets of the Declaration of Helsinki and was approved by the Hong Kong Eye Hospital Ethics Committee, with all procedures conducted in accordance with the former. Written informed consents were obtained from parents or guardians, and verbal consent from the study participants. The study is registered at www.chictr.org.cn, identifier: ChiCTR-TRC-13004032, and www2.ccrb.cuhk.edu.hk/registry/public/, identifier: CUHK_CCT00383.

• **REFRACTION AND OCULAR BIOMETRIC PARAMETERS MEASUREMENT:** Previous reports have described the examinations conducted as part of the LAMP study.[24] The ocular biometrics of each participant were obtained after complete cycloplegia, which comprised at least 2 cycles of eye drops. During the first cycle, 2 separate eye drops of cyclopentolate 1% (Cyclogyl; Alcon-Convreur) and tropicamide 1% (Santen) were administered to both eyes 5 minutes apart. A second cycle of the same cycloplegic drops was administered 10 minutes after the first cycle. Cycloplegic autorefraction was performed by an autorefractor (Nidek ARK-510A). Five readings, all of which were <0.25 D apart, were obtained and averaged. Spherical equivalent (SE) refraction was calculated as spherical power plus half of the cylinder power. Axial length (AL) was measured using a Zeiss IOL Master unit (Carl Zeiss Meditec Inc). All measurements were performed for both eyes during the initial visit, 2 weeks later, and at follow-up every 4 months throughout the next 2 years.

• **CHOROIDAL THICKNESS MEASUREMENT:** Spectral-domain optical coherence tomography (SD-OCT) (Heidelberg Engineering) was used for choroidal imaging. The system adopted a volume scan pattern (25° × 30°; 32 total B-scans) centered on the fovea. Each B-scan in the volume was a composite average of 35 individual line-scan images, and the 45° cross-line scan pattern was used. With the enhanced depth imaging (EDI) protocol, contrast of the choroid was enhanced. All images were inspected, and the choroidal layer was manually segmented using a MATLAB software (MathWorks) by 2 well-trained examiners (S.L. and J.L.) independently.[25] In the segmentation for each radial scan, the fovea was denoted by a dot, and 31 points were plotted for both the upper and lower boundaries of choroidal layer (Supplemental Figure).[26] The average SFChT across the 4 scan lines was calculated for use in the final analysis.[27]

Reliability tests for inter-investigator agreement of SFChT measurements were performed using images of 36 participants (10%). The intraclass correlation coefficients were 0.918 ($P < .001$), 0.995 ($P < .001$), 0.992 ($P < .001$), and 0.896 ($P < .001$) for the atropine 0.05%, 0.025%, 0.01%, and placebo groups, respectively. Choroidal thickness was measured at baseline and during follow-up visits at 4, 8, 12, 16, 20, and 24 months. All measurements were conducted between 3:00 PM and 5:00 PM to minimize the effects of diurnal variations.

• **QUESTIONNAIRES ON PARENTAL MYOPIA, OUTDOORS TIME, NEAR WORK ACTIVITY, AND TREATMENT COMPLI-**

ANCE: The validated questionnaires used in the current study were mainly derived from Chinese translated versions that had been used in the Sydney Myopia Study and adopted in the Hong Kong Children Eye Study.[3,28] Questionnaires were administered at baseline and follow-up, surveying the time children spent on outdoors, screens, and total near work. The detailed definitions and calculations have been described in previous reports.[3]

• STATISTICAL ANALYSIS: The analysis included data from both eyes of all participants. SFChT changes were calculated according to differences between baseline and designated follow-up visits. The χ^2 test and Fisher exact test were used to analyze group differences in categorical data, whereas analysis of variance was used to analyze group differences of continuous data; Bonferroni correction was used for multiple comparisons. Analysis of variance with repeated measures was used to compare 3 or more group means where the participants were the same in each group. Generalized estimating equations with robust standard errors for longitudinal data analysis were used to adjust the correlation between eyes and to incorporate all valuable data. To visualize the results, 10-μm change of choroidal thickening has been considered as a 1-unit change in all regression models. Two models were used to detect the factors associated with SE/AL progression. Model 1 included the SFChT changes, age, sex, baseline AL, outdoor time, near work diopter-hour, parental myopia, and treatment compliance, and model 2 included atropine treatment in addition to the factors of model 1. To evaluate the potential for confounding, analyses were repeated adjusting for age, sex, baseline AL, time spent outdoors and on near work, status of parental myopia, and treatment compliance. Interaction analysis was used to test whether baseline SFChT is a moderator for the SE progression. The mediation analysis was used to test whether change of SFChT is a mediator for the SE progression. Statistical analyses were performed using SPSS Statistics 24.0 software (IBM Corp) and R 4.0.3 software (R Foundation for Statistical Computing). *P* values <.05 were considered statistically significant.

RESULTS

Of the 438 children recruited for the LAMP study, 350 completed all second-year follow-up visits and were included in this study. However, 18 children were subsequently excluded due to unavailable baseline choroidal data. Another 16 were excluded due to suboptimal image quality. Finally, 316 children were examined, with 81, 80, 86, and 69 children allocated to the atropine 0.05%, 0.025%, 0.01%, and switch-over groups, respectively. Among groups, there were no significant differences in demographic features and baseline SFChT, refractive errors, AL, times for near work and outdoor activities, and parental SE (Supplemental Table 1). Similarly, there were no significant differences in baseline characteristics between included and excluded children (Supplemental Table 2).

• LONGITUDINAL CHANGES IN SFCHT: After the first year, changes in SFChT relative to baseline were 21.20 ± 29.84 μm, 6.24 ± 24.81 μm, −3.96 ± 23.11 μm, and −4.50 ± 21.48 μm for the atropine 0.05%, 0.025%, 0.01%, and placebo groups, respectively (Table 1 and Figure 1). SFChT significantly increased in the atropine 0.025% and 0.05% groups, whereas no significant changes occurred in atropine 0.01% and placebo group (Table 1). Changes in SFChT over 2 years were similar to those in the first year, at 21.15 ± 32.99 μm, 3.34 ± 25.30 μm, and −0.30 ± 27.15 μm for the atropine 0.05%, 0.025%, and 0.01% groups, respectively. The exception was the placebo group which had switched to atropine 0.05%, having a significant increase in SFChT in the second year at 13.97 ± 31.56 μm. In general, mean SFChT thickness significantly increased at 4 months after baseline for the atropine 0.05% ($P < .001$) and 0.025% groups ($P = .001$), and then remained stable until the end of the second year ($P > .05$ for all groups) (Table 1). The changes in SFChT (10-μm changes as a 1-unit change) followed a concentration-dependent response, with thicker choroids at higher atropine concentrations ($\beta = 0.89$, $P < .001$) (Table 2).

• ASSOCIATIONS BETWEEN CHANGES IN SFCHT WITH SE PROGRESSION AND AL ELONGATION: Changes in SFChT, atropine concentration, and age were associated with both SE progression (Table 3) and AL elongation (Supplemental Table 3) over 2 years. An increase in SFChT was associated with slower SE progression ($\beta = 0.074$, $P < .001$) and reduced AL elongation ($\beta = -0.045$, $P < .001$). In subgroup analysis, greater SFChT thickening and age remained significantly associated with both SE progression (Supplemental Table 4) and AL elongation (Supplemental Table 5) for each treatment group over 2 years. Seemingly unrelated regression showed that the coefficients of change in SFChT were similar among all atropine groups at 24 months from baseline ($P = .72$).

• INTERACTION AND MEDIATION ANALYSIS BETWEEN ATROPINE CONCENTRATION AND CHOROIDAL THICKNESS ON SE PROGRESSION: There was no interaction between atropine concentration and baseline choroidal thickness on SE progression over 2 years ($P > .05$ for all treatment groups). In the mediation analysis, the atropine concentration was treated as both a categorical and ordinal variable to test the mediation effect. Using atropine 0.01% as the reference group, 18.45% of the effect ($P < .001$) on SE progression from atropine 0.05% and 5.08% of the effect ($P = .54$) on SE progression from atropine 0.025% was mediated via choroidal thickening (Figure 2). When the atropine concentration was treated as an ordinal variable, the

TABLE 1. Comparisons of Changes in Subfoveal Choroidal Thickness Over Two Years Among Different Atropine Groups

Variable	(4) Atropine 0.05% ($n = 81$)	(3) Atropine 0.025% ($n = 80$)	(2) Atropine 0.01% ($n = 86$)	(1) Switch-Over Group[a] ($n = 69$)	*P* Values for					
					4 vs 3	4 vs 2	4 vs 1	3 vs 2	3 vs 1	2 vs 1
Baseline to (μm)										
4 months	18.48 (29.46)	6.11 (21.31)	−0.09 (22.88)	−2.90 (23.92)	<.001[b]	<.001[b]	<.001[b]	.03[b]	.003[b]	.35
8 months	23.27 (31.89)	9.40 (24.38)	−1.39 (23.30)	−3.12 (22.41)	<.001[b]	<.001[b]	<.001[b]	<.001[b]	<.001[b]	.59
12 months	21.20 (29.84)	6.24 (24.81)	−3.96 (23.11)	−4.50 (21.48)	<.001[b]	<.001[b]	<.001[b]	.001[b]	.001[b]	.86
16 months	19.74 (34.90)	1.10 (20.26)	−2.69 (14.91)	9.62 (29.28)	<.001[b]	<.001[b]	—	.17	—	—
20 months	18.32 (34.21)	3.38 (25.83)	0.50 (26.36)	10.78 (30.75)	<.001[b]	<.001[b]	—	.48	—	—
24 months	21.15 (32.99)	3.34 (25.30)	−0.30 (27.15)	13.97 (31.56)	<.001[b]	<.001[b]	—	.39	—	—

Note: Data are shown as mean (SD).

[a]Placebo in the first year and switched over to atropine 0.05% group in the second year.

[b]Significance level set at $P < .05$.

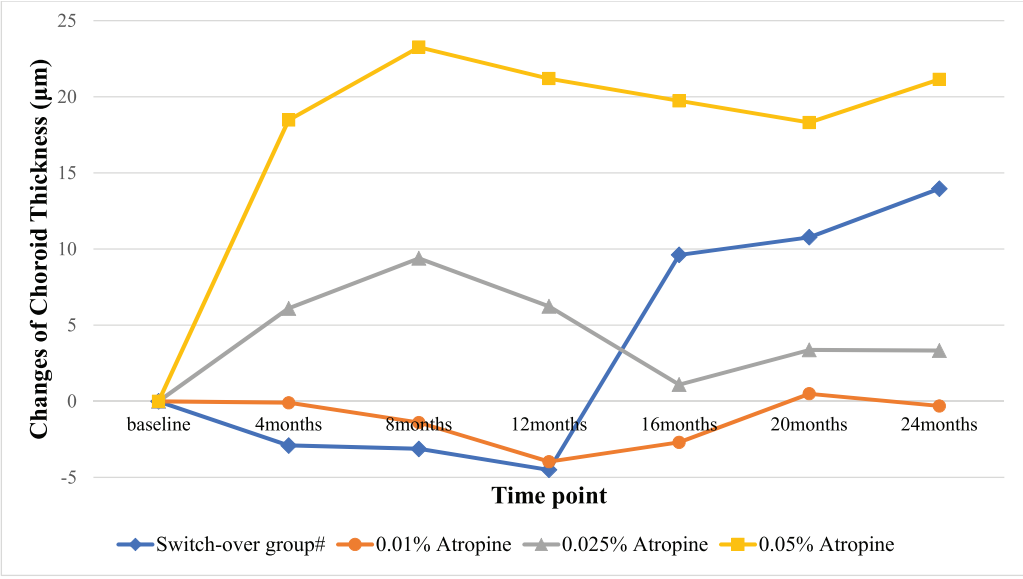


FIGURE 1. Changes of subfoveal choroidal thickness against different time points among different groups. #Switch-over group: placebo in the first year and switched over to 0.05% atropine group in the second year.

TABLE 2. Factors Associated with Changes in Subfoveal Choroidal Thickness Over Two Years

Factor	β (95% CI)	*P* Value
Treatment group	0.890 (0.470 to 1.310)	<.001[a]
Age (y)	0.009 (−0.227 to 0.245)	.94
Sex		
Male	Reference	
Female	−0.059 (−0.784 to 0.665)	.87
Baseline axial length (mm)	0.257 (−0.163 to 0.677)	.23
Outdoor activity (h/d)	0.158 (−0.169 to 0.484)	.34
Near work (diopter h/d)	0.025 (−0.067 to 0.118)	.59
Parental myopia		
≤1 with moderate or high myopia	Reference	
Both with moderate or high myopia	0.340 (−0.369 to 1.050)	.35
Treatment compliance (d/wk)	0.160 (−0.137 to 0.457)	.29

Note: Generalized estimating equations were used to adjust the correlation between eyes.
[a]Significance level set at $P < .05$.

mediation effect for choroidal thickening remained significant (15.50%, $P < .001$).

DISCUSSION

Given the variable response to atropine treatment, finding the indicators of treatment response is clinically valuable to individualize treatment strategies, such as adjustment of concentration or switching over to alternative or combination therapies. In this study we have, for the first time, found longitudinal changes in SFChT among children receiving daily atropine 0.05%, 0.025%, 0.01%, and placebo eye drops in a double-blinded randomized controlled trial. First, we found choroidal thickening followed a concentration-dependent manner over 2 years. Significantly greater choroidal thickening was detected in the atropine 0.05% and 0.025% groups, but not in the atropine 0.01% and placebo groups. In the switch-over group, SFChT increased after children were switched over to the atropine 0.05% group in the second year.

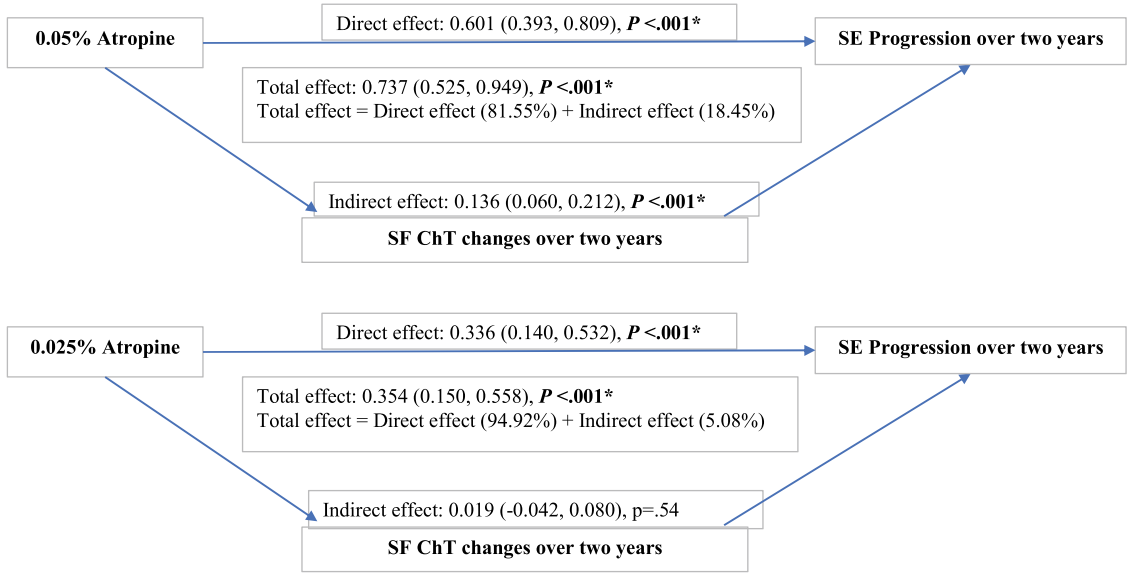
Second, the choroidal-thickening effect of low-concentration atropine was maintained throughout the period of treatment.

Third, choroidal thickening effects were quantitatively correlated with treatment responses, in which every 10-μm of thickening was associated with SE progression by 0.074 D or AL elongation by 0.045 mm (Table 3, Supple-

TABLE 3. Factors Associated With Spherical Equivalent Progression Over Two Years

Factor	Model 1		Model 2	
	β (95% CI)	*P* Value	β (95% CI)	*P* Value
SFChT changes over 2 years	0.072 (0.049 to 0.096)	<.001[a]	0.074 (0.045 to 0.103)	<.001[a]
Age (y)	0.173 (0.113 to 0.234)	<.001[a]	0.153 (0.091 to 0.216)	<.001[a]
Sex				
Male	Reference	—	Reference	—
Female	−0.141 (−0.328 to 0.047)	.14	−0.128 (−0.324 to 0.067)	.20
Baseline axial length (mm)	−0.014 (−0.118 to 0.089)	.79	0.002 (−0.107 to 0.111)	.97
Outdoor activity (h/d)	0.043 (−0.040 to 0.126)	.31	0.046 (−0.043 to 0.135)	.31
Near work (diopter h/d)	0.008 (−0.012 to 0.028)	.42	0.014 (−0.008 to 0.037)	.21
Parental myopia				
≤1 with moderate or high myopia	Reference	—	Reference	—
Both with moderate or high myopia	−0.124 (−0.304 to 0.057)	.18	−0.180 (−0.379 to 0.018)	.08
Treatment compliance (d/wk)	−0.017 (−0.096 to 0.063)	.68	0.016 (−0.084 to 0.115)	.76
Atropine treatment				
Atropine 0.01%	—	—	Reference	—
Atropine 0.025%	—	—	0.336 (0.124 to 0.547)	.002[a]
Atropine 0.05%	—	—	0.601 (0.091 to 0.216)	<.001[a]

SFChT = subfoveal choroidal thickness.
Note: Generalized estimating equations were used to adjust the correlation between eyes.
[a]Significance level set at P < .05.



SE = spherical equivalent; SFChT = subfoveal choroidal thickness
* Significant level set at P<.05.

FIGURE 2. Mediation analysis. *Significance level set at *P* < .05. SE = spherical equivalent; SFChT = subfoveal choroidal thickness.

mental Table 3). This relationship was similar across all groups.

Fourth, the effect of atropine 0.05% to slow SE progression was partially mediated via its choroidal thickening.

Taken together, our data provide evidence that the choroidal-thickening effect is a potential biomarker and mediator for myopia progression. Choroidal thickening could be considered as a reference for adjusting atropine concentrations during treatment.

Changes in SFChT have been evaluated in atropine studies. Among 30 healthy children, the administration of atropine 1% twice daily for 1 week led to 15-μm choroidal

thickening.[18] Another study among 20 young adults with myopia found an average of 6-μm choroidal thickening 60 minutes after instilling atropine 0.01% eye drops.[29] In the current study, we found choroidal thickening in an atropine concentration-dependent manner for the atropine 0.025% and 0.05% groups, but no significant thickening for the atropine 0.01% and placebo groups.

In another recent study, significant increases in SFChT were observed (26 ± 14 μm) after 1-week loading of atropine 1%, whereas there were decreases (−5 ± 17 μm) in the atropine 0.01% group after 6 months.[23] Interestingly, in this study, the SFChT thickening (21.15 ± 32.99 μm) in atropine 0.05% was similar to the SFChT thickening (26 ± 14 μm) in a study by Ye and associates, using a much higher concentration of atropine 1%.[22]

One notable finding of this study is the association of choroidal thickening with treatment efficacy. Notably, the factor most strongly associated with treatment efficacy was concentration level ($\beta = 0.601$), followed by age ($\beta = 0.153$) and then choroidal thickening effect ($\beta = 0.074$). Consistent with our previous reports, atropine treatment efficacy is concentration dependent[8]—the higher the concentration, the greater the response—and is also age dependent—the younger the patient's age, the lower the response.[15] Young children therefore require a higher concentration of atropine for better treatment responses. For those patients already using higher-concentration atropine, choroidal thickening effects are also of clinical relevance. A greater choroidal thickening is associated with a greater response, and vice versa. Accordingly, we advise that children who exhibit no choroidal thickening effect should be considered for higher atropine concentrations or for switching over to alternative or combined treatment.

There was no interaction between atropine concentration and baseline choroidal thickness on SE progression, indicating no differential effect by atropine treatment on SE progression with regard to baseline choroidal thickness. On the other hand, mediation analysis revealed that change in choroidal thickness is a partial mediator of atropine 0.05% effect on SE progression. It is noted that this mediation effect only accounts for 18.45%. There are other direct and mediated effects of atropine through pathways not evaluated in this study.

First, atropine may induce choroidal thickening through stimulation of release of dopamine, which thickens the choroid.[30,31] Second, the antagonistic action of atropine on muscarinic receptors may block the contraction of the choroidal smooth muscle, which in turn regulates choroidal thickness.[32] Third, atropine may mediate choroidal blood vessel relaxation as it reportedly relaxed mesenteric and renal arteries in rats.[33] This could increase capillary permeability, which causes choroidal thickening.[34]

Fourth, atropine may also reduce the progression of myopia through potentiating the synthesis and release of intraocular nitric oxide (NO). In chicks, NO plays a role in inhibiting form-deprivation myopia;[35] conversely, inhibition of NO or its synthesis prevented amelioration of myopia by atropine[35] or removal of form deprivation.[36]

Reduced axial elongation due to atropine has also been attributed to its choroidal thickening effect.[37] As the choroid thickens, it moves the retinal pigment epithelium forward, causing the measured AL to shorten. However, our data suggest this mechanical effect is small. In phase 1 of the LAMP study, AL elongation was 0.41 mm in the placebo group and 0.20 mm in the atropine 0.05% group, a difference of 0.21 mm.[8] The mean choroidal thickening of 22.7 μm in the atropine 0.05% group only accounted for 10.8% of the reduced AL progressions in this group compared with placebo. Therefore, our results suggest that choroidal thickening from atropine has an additional effect of slowing the AL elongation in addition to its mechanical shortening effect on AL.[34]

This is one of the first studies to report the long-term choroidal thickening effect of low-concentration atropine drops. We found that SFChT significantly increased at 4 months after baseline and then remained stable over the 2 years of the study. Because choroidal thickening is associated with treatment efficacy, early-stage choroidal thickening effects could predict treatment response in 2 years time. Thus, it becomes possible to optimize concentration levels for individual children early during treatment based on early changes in choroidal thickness. A previous study suggested that choroidal thickening response occurred 1 week after the application of atropine[18]; it is therefore possible that choroidal thickening effects occur even earlier than 4 months after application. Further studies on early-stage choroidal changes are hence warranted.

Another strength of this study is its randomized controlled design with various concentrations of atropine. The presence of the placebo group allowed direct comparison with natural SFChT changes over a 1-year period. Furthermore, all SFChT measurements were conducted after full cycloplegia to achieve retinal images of high quality. The application of mydriatic eye drops removes the effect of accommodation, which has been shown to cause choroidal thinning. We also specifically measured SFChT in the afternoons to minimize variations due to diurnal variation.

There were limitations to this study. The placebo group had to be switched over to atropine 0.05% treatment during the second year due to ethical considerations against leaving the children untreated. Nevertheless, the second-year results are valuable in confirming the association of SFChT thickening with decreased myopia progression.

In addition, the current report only encompasses 2 years. Changes beyond this study duration, including time points after the cessation of treatment, will be presented in subsequent reports. Furthermore, choroidal imaging in our study involved manual measurements, which might introduce interobserver variations. In view of this, measurements were

conducted by 2 independent investigators to obtain good reliability scores.

Lastly, recent animal and clinical studies have shown that muscarinic antagonists may affect the choroidal thickness.[18,38-40] Nevertheless, all participants in all 4 groups in this study were administered the same mydriatic agents at baseline and at every visit, using a standardized protocol. Thus, the change in choroidal thickness from each visit compared with baseline, as well as difference between groups, should not be affected by the use of mydriatic agents.

In conclusion, low-concentration atropine induced choroidal thickening along a concentration-dependent response throughout the treatment period of 2 years. The thickening was associated with slower SE progression and AL elongation. The anti-myopia effect from atropine 0.05% was partly mediated via choroidal thickening. Choroidal response can be used as a biomarker for assessment of long-term treatment outcomes and as a guide for concentration titrations of atropine.

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