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Short Term Effect of 0.02%/0.04% Atropine Sulfate Eye Drops on Choroid Thickness in Children with Myopia

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Abstract

Objective: Short-term effects of 0.02%/0.04% atropine sulfate eye drops on choroidal thickness in myopic children using optical coherence tomography angiography. **Methods:** Thirty-two children aged 6 - 12 years were selected and divided into 22 cases and 44 eyes in the 0.02%/0.04% atropine sulfate eye drops observation group and 10 cases and 20 eyes in the control group. The linear regression equation was used to evaluate the correlation among the spherical equivalent, the axial length and the subfoveal choroidal thickness, moreover, used to evaluate the correlation between the baseline and 6 months later. Independent samples T-test was used to detect whether there was any statistical difference between the nasal 1 mm subfoveal choroidal thickness and the temporal 1 mm subfoveal choroidal, meanwhile, compared with the baseline and 6 months later. $P < 0.05$ was considered statistically significant. **Results:** After 6 months follow-up, the axial length increased by 0.067 ± 0.199 mm in the atropine group, 0.201 ± 0.081 mm in the control group ($P < 0.05$); the spherical equivalent (all negative numbers, absolute values were taken) increased by 0.094 ± 0.239 D in the atropine group, 0.375 ± 0.268 D in the control group ($P < 0.05$); the subfoveal choroidal thicknesss increased by 27.023 ± 22.078 μm in the atropine group, −3.800 ± 8.177 μm in the control group ($P < 0.05$); the nasal 1 mm subfoveal choroidal thickness increased by 19.750 ± 18.022 μm in the atropine group, 0.050 ± 8.219 μm in the control group ($P < 0.05$); the temporal 1 mm subfoveal choroidal thickness increased by 22.091 ± 19.721 μm in the atropine group, −4.250 ± 6.339 μm in the control group ($P < 0.05$); the increment in thickness of the 1mm choroid in the nasal side of the submacular central recess was not statistically different from the temporal side at $P = 0.57$. The multiple linear regression analysis of baseline subfoveal choroidal thickness, axial length, and spherical equivalent had a R-squared of 0.011. The multiple linear regression analysis of the difference

in subfoveal choroidal thickness, axial length, and spherical equivalent was 0.269. **Conclusions:** 1) 0.02%/0.04% atropine sulfate eye drops can delay the growth of axial length and spherical equivalent; 2) 0.02%/0.04% atropine sulfate eye drops can thicken the choroid, and the thickness of the nasal side 1mm is the same as that of the temporal side 1 mm; 3) At baseline, the subfoveal choroidal thickness has no significant correlation with the axial length and spherical equivalent; 4) After 6 months, changes in axial length and spherical equivalent were negatively correlated with changes in subfoveal choroidal thickness.

Keywords

Myopia, Atropine, Optical Coherence Tomography Angiography, Choroid Thickness

1. Background

As early as the 19th century, atropine was found to inhibit the development of myopia in children, but the mechanisms and targets of its myopia control are still largely unknown, and its inhibitory effect is apparently not due to regulatory paralysis, as there are no muscarinic-like M3 receptors in the ciliary body, ciliary muscle, and iris of the chick, but formative deprivation myopia of the chick can be inhibited by atropine [1]. Retinal acetylcholine levels did not change from control levels during the development of experimental myopia in chicks and tree mice [2]. Fischer *et al.* found as early as 1998 that ablation of 90% of the cholinergic neurons in the chicken retina with the selective cholinergic toxin ethylcholine mustard did not abolish the inhibitory effect of atropine on myopia [3]. The above studies suggest that cholinergic stimulation may not be critical for the development of myopia.

Evidence-based medical studies have confirmed that effective myopia prevention and control methods such as atropine eye drops [4] and keratoplasty lenses [5] [6] exhibit choroidal thickening effects, suggesting that choroidal thickening is a protective factor for myopia control.

The choroid, located between the retina and the sclera, can influence the transmission of a series of chemical signals from the retina to the sclera, thus affecting the growth of the eye. These signals are essentially chemical substances (e.g., dopamine, nitric oxide, melatonin, etc. [7] [8] [9]) that can travel through the retina and choroid and affect the remodeling process of the sclera, thus influencing the process of myopia development. Choroidal thinning and reduced blood flow during the process of myopia development lead to scleral hypoxia, which in turn promotes scleral stromal remodeling, ultimately leading to eye axis elongation and promoting myopia development [10] [11].

In this experiment, OCTA was used to measure the choroidal thickness of the subject children to analyze the short-term effect of 0.02%/0.04% atropine sulfate

eye drops on the choroidal thickness in order to further explore the effect of 0.02%/0.04% atropine sulfate eye drops in controlling the development of myopia, and also to provide an experimental basis for the provision of effective concentrations of atropine eye drops.

2. Materials and Methods

2.1. Subjects

Forty-two children with myopia cases excluding organic eye disease were selected, and cases were included according to strict inclusion and exclusion criteria and divided into observation and control groups. All subjects were examined at baseline and followed up twice at 3 months and 6 months.

2.1.1. Inclusion Criteria

Subjects need to meet all of the following criteria to be included:

1) Written informed consent signed by the child and guardian has been obtained.

2) Children between the ages of 6 and 12 years (including the threshold).

3) Retinal banding optometry after ciliary muscle palsy, followed by primary optometric re-testing of spherical lenses in both eyes: −4.00 D ≤ spherical lenses ≤−1.00 D.

4) Retinal banding optometry after ciliary muscle paralysis, followed by primary optometric review with astigmatism ≤ 1.50 D in both eyes.

5) Refractive aberration (by SE) ≤ 1.50 D.

2.1.2. Exclusion Criteria

Subjects will not be enrolled if they meet any of the following criteria:

1) Subjects who may have an eye disease that affects vision or refractive error (e.g. cataract and other lens-damaging diseases, glaucoma, macular degeneration, keratoconus, uveitis, retinal detachment, severe vitreous opacities, etc.)

2) Subjects with a history of immune system disorders, central system disorders, Down's syndrome, asthma, severe cardiopulmonary dysfunction, severe liver and kidney dysfunction, etc. (except where the investigator determines that inclusion is possible).

3) Dominant strabismus or any other ocular pathology or acute inflammatory disease of the eye in both eyes.

4) Failure to correct distance vision to a logarithmic visual acuity of 4.9 in both eyes.

5) Have used or are using treatments to control myopia progression that the investigator assesses as affecting the evaluation of efficacy: e.g. atropine or pirenzepine; device treatments: optical methods such as keratoplasty lenses, multifocal contact lenses, multifocal myopic defocussing glasses; those with other prevention and control measures: e.g. auricular acupuncture, auricular acupuncture points, red light therapy devices, etc.

6) Drugs that have been used systemically or topically in the 3 months prior to

screening that affect the evaluation of efficacy, e.g. anticholinergics: atropine, tropicamide (except for dilated optometry), cyclopentetolide (except for dilated optometry), pirenzepine, etc.; cholinomimetics: trichothecene, etc.

7) Those allergic to atropine medication.

8) Those who have participated in clinical trials with other drugs or devices within 3 months prior to screening.

9) Other conditions deemed unsuitable by the investigator.

2.1.3. Criteria for Discontinuation/Disengagement

1) Poor adherence to the study intervention.

2) Serious adverse events, complications and specific physiological changes that make it inappropriate to continue with the trial.

3) Emergence of factors affecting the evaluation of efficacy.

4) Subjects who are lost to follow-up.

5) Other reasons for termination or discontinuation.

2.2. Experimental Equipment and Reagents

2.2.1. Main Experimental Reagents

Reagent name	Source
Atropine Sulfate Eye Drops (0.02%/0.04%)	Shenyang Xingqi Ophthalmic Co.

2.2.2. Experimental Apparatus

Instrument name	Specification	Equipment number	Manufacturer
Ophthalmic Optical Biometry	IOLMaster700	20172222323	Carl Zeiss (Germany)
Corneal topographer	TMS-4	07682210682010120001	TOMEY (Japan)
Laser scanning ophthalmoscope	Daytona (D2007)	20183162530	Shanghai Mingwang Medical Devices Co.
Slit Lamp Microscope	SL990N	20152220620	Shenzhen Koyukang Medical Equipment Co.
Pneumatic Intraocular Pressure Meter	TX-20	620322	Canon Corporation
Optical Coherence Tomography Angiography	RTVue XR 100	70054345001	OPTOVUE

2.3. Methods

2.3.1. Basic Examination

All subjects should undergo the following examinations:

Eye position, eye rotation: for strabismus and nystagmus.

Slit lamp microscopy: examination of the external eye, conjunctiva, cornea and lens to exclude anterior segment disease.

IOP: non-contact pneumatic IOP meter with three automatic measurements in the left and right eye respectively, system takes values automatically.

Biological measurements: AL, Anterior chamber depth (ACD), Central corneal thickness (CCT), corneal curvature, pupil diameter. The system automatically takes 5 measurements for the left and right eye respectively.

SE: retinal banding optometry after 6 consecutive doses of 0.5% compound tropicamide drops in both eyes following ciliary muscle paralysis. SE = spherical lens prescription + 1/2 column lens prescription (DS + 1/2 DC)

Fundus: laser scanning examiner to assess the fundus.

2.3.2. OCTA Examination

All subjects should undergo OCTA prior to pupil dilatation. In this study, an experienced operator uses OCTA to detect and measure SFCT, the nasal 1 mm subfoveal choroidal thickness, and the temporal 1 mm subfoveal choroidal thickness. After recording the subject's information, the mode is switched to Enhanced HD Line mode. The OCTA machine is adjusted to a comfortable height according to the subject's height and body type, and the subject is asked to remove the frame and place the chin on the jaw rest, with the forehead close to the forehead and the canthus at the level of the eye level, and look at the blue indicator in the lens, and scan through the central macular sulcus and optic disc.

Choroidal thickness measurement: Using the instrument's own measuring tool, the vertical distance from outside the hyperreflective line of the retinal pigment epithelium to the inner surface of the sclera is measured manually as the choroidal thickness. The choroidal thickness was measured at the central macular recess, 1 mm nasal and 1 mm temporal, respectively, and each value was averaged over three measurements by the same measurer.

2.3.3. Treatment Method

Experimental group: 0.02%/0.04% atropine sulphate eye drops, shake well before dropping, once daily, one drop in each eye at bedtime, and press the inner canthus tear sac area with your hand after dropping. Wear frame glasses during the day.

Control group: Refractive error correction with frame glasses only.

Follow-up: Both experimental and control groups should be followed up before, 12 weeks (±1 week) after and 24 weeks (±1 week) after the experiment. The above basic examination should be performed at each follow-up visit.

2.3.4. Statistical Treatment

Data were analysed using SPSS 27.0, with measures described using mean ± standard deviation ($\overline{X} \pm S$), and differences between groups for continuous data that met chi-squared were analysed by multiple-measures ANOVA, with differences considered statistically significant at $P < 0.05$. No statistically significant differences were found between the control and atropine groups at baseline for age, sex, AL, SE, SFCT, the nasal 1 mm subfoveal choroidal thickness, and the temporal 1 mm subfoveal choroidal thickness using independent samples t-tests, with differences considered statistically significant at $P < 0.05$. The correlation between equivalent spherical lens, eye axis length, and choroidal thickness under

the central macular recess at baseline was assessed by linear regression equation; the correlation between the difference in equivalent spherical lens, eye axis length, and choroidal thickness under the central macular recess after 6 months compared to baseline was assessed by linear regression equation. Independent samples T-test was used to detect whether there was any statistical difference between the nasal 1 mm subfoveal choroidal thickness and the temporal 1 mm subfoveal choroidal, meanwhile, compared with the baseline and 6 months later. $P < 0.05$ was considered statistically significant.

3. Results

A total of 42 children with myopia participated in this study, of which 10 were excluded due to loss of follow-up, substandard compliance and incomplete data collection, resulting in a total of 32 (17 males and 15 females, 64 eyes) being included in this study and data analysis.

Of the 32 children with myopia included in this study, 10 (6 males and 4 females) in the control group (myopia corrected with frame glasses only) had a total of 20 eyes and 22 (11 males and 11 females) in the atropine group (0.02%/0.04% atropine sulphate eye drops group) had a total of 44 eyes.

At baseline, there were no statistically significant differences in age, gender, AL, SE, SFCT, the nasal 1 mm subfoveal choroidal thickness or the temporal 1 mm subfoveal choroidal between the control and atropine groups ($P > 0.05$).

3.1. AL

At baseline, the AL in the control group was 24.7805 ± 0.59421 mm and in the atropine group was 24.6114 ± 0.69726 mm; in March, the AL in the control group was 24.893 ± 0.58979 mm and in the atropine group was 24.6443 ± 0.6938 mm; in June, the AL in the control group was 24.9815 ± 0.60552 mm and in the atropine group was 24.678 ± 0.6857 mm (Table 1). after six months of follow-up, the AL in the atropine group increased by 0.067 ± 0.199 mm and that in the control group by 0.201 ± 0.081 mm.

Table 1. Descriptive statistics of eye axis length (AL) change (mm).

	Group	$\bar{X}$	SD	N
AL at baseline	Atropine group	24.6114	0.69726	44
	Control group	24.7805	0.59421	20
	Total	24.6642	0.66675	64
AL at March	Atropine group	24.6443	0.6938	44
	Control group	24.893	0.58979	20
	Total	24.722	0.66855	64
AL at June	Atropine group	24.678	0.6857	44
	Control group	24.9815	0.60552	20
	Total	24.7728	0.67202	64

The multivariate test showed a time point effect P < 0.001, meaning that subjects showed significant changes in AL with changes in the number of follow-up visits. The interaction effect between time point and group P < 0.001 indicates that the change in AL in the control group with the change in follow-up time was significantly different from that in the atropine group (Table 2). Both the atropine and control groups showed an increasing trend in AL, but the degree of increase was more pronounced in the control group than in the atropine group (Figure 1).

3.2. SE

SE was negative in all subjects and absolute values were taken here for data analysis. At baseline, SE was 2.63750 ± 0.824082 D in the control group and 2.49148 ± 0.685925 D in the atropine group; at March, SE was 2.83125 ± 0.817444 D in the control group and 2.56250 ± 0.693355 D in the atropine group; at June, SE was 3.01250 ± 0.904030 D and 2.58523 ± 0.728257 D in the atropine group (Table 3); after six months of follow-up, the SE increased by approximately 0.094 ± 0.239D in the atropine group and 0.375 ± 0.268 D in the control group.

The multivariate test showed a time point effect P < 0.001, meaning that subjects' SE changed significantly with the number of follow-up visits. The P < 0.001 for the interaction effect between time point and group indicated that the change in SE in the control group with the change in follow-up time was significantly different from that in the atropine group (Table 4). SE tended to increase in both the atropine and control groups, but the degree of increase was more pronounced in the control group than in the atropine group (Figure 2).

Table 2. Multivariate test for eye axis length (AL).

Effect	Value	F	Assuming DF	Degrees DF	Sig.
Time point	1.079	32.898[a]	2.000	61.000	<0.001
Time point* Group	0.319	9.737[a]	2.000	61.000	<0.001

[a]: Accurate statistics.

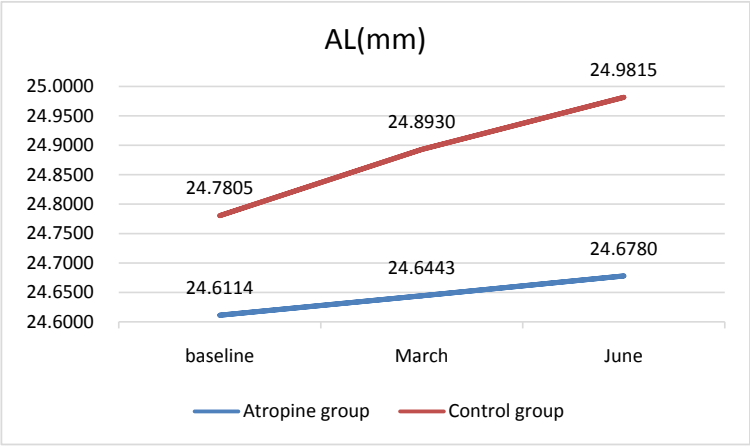

Figure 1. Folded graph of eye axis length (AL) change.

Table 3. Descriptive statistics for changes in equivalent sphericity (SE) (D).

	Group	$\bar{X}$	SD	N
SE at baseline	Atropine group	2.49148	0.685925	44
	Control group	2.63750	0.824082	20
	Total	2.53711	0.728420	64
SE at March	Atropine group	2.56250	0.693355	44
	Control group	2.83125	0.817444	20
	Total	2.53711	0.728420	64
SE at June	Atropine group	2.58523	0.728257	44
	Control group	3.01250	0.904030	20
	Total	2.71875	0.805179	64

Table 4. Equivalent sphericity (SE) multivariate test.

Effect	Value	F	Assuming DF	Degrees DF	Sig.
Time point	0.841	25.638[a]	2.000	61.000	<0.001
Time point* Group	0.319	8.468[a]	2.000	61.000	<0.001

[a]: Accurate statistics.

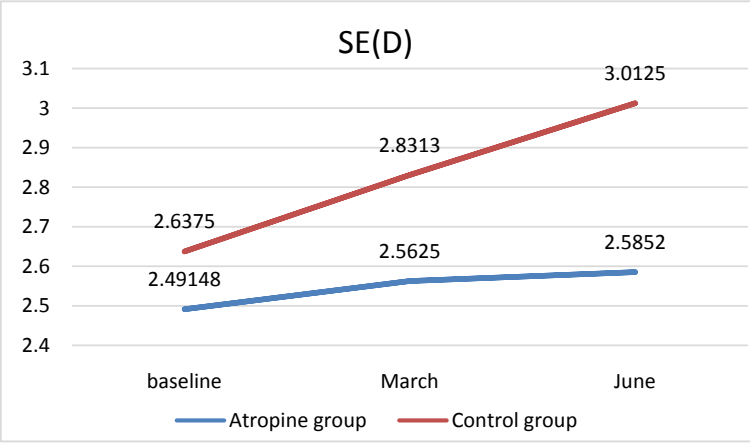

Figure 2. Folding graph of equivalent sphericity (SE) variation.

3.3. SFCT

At baseline, SFCT was 228.25000 ± 34.357984 μm in the control group and 225.09091 ± 55.111649 μm in the atropine group; in March, SFCT was 227.60000 ± 35.612535 μm in the control group and 243.38636 ± 58.305617 μm in the atropine group; In June, the SFCT was 224.65000 ± 34.919871 μm in the control group and 252.11364 ± 58.636133 μm in the atropine group (Table 5); after six months, the change in SFCT was 27.023 ± 22.078 μm in the atropine group and a slight thinning of SFCT in the control group, with a change of about −3.800 ± 8.177 μm.

The multivariate test showed a time point effect $P < 0.001$, meaning that subjects showed significant changes in SFCT as the number of follow-up visits

changed. The P < 0.001 for the interaction effect between time point and group indicated that the control group showed a significant difference in their SFCT changes with the change in follow-up time compared to the atropine group (Table 6). The SFCT in the atropine group showed a trend of thickening and a flattening of SFCT growth in the second three months compared to the first three months; the SFCT in the control group showed a trend of thinning as the follow-up time increased (Figure 3).

Table 5. Descriptive statistics of subcentral foveal choroidal thickness (SFCT) variation (μm).

	Group	$\bar{X}$	SD	N
SFCT at baseline	Atropine group	225.09091	55.111649	44
	Control group	228.25000	34.357984	20
	Total	226.14062	49.310763	64
SFCT at March	Atropine group	243.38636	58.305617	44
	Control group	227.60000	35.612535	20
	Total	238.45312	52.509086	64
SFCT at June	Atropine group	252.11364	58.636133	44
	Control group	224.65000	34.919871	20
	Total	243.53125	53.657044	64

Table 6. Multivariate test for subcentral fovea choroidal thickness (SFCT).

Effect	Value	F	Assuming DF	Degrees DF	Sig.
Time point	0.343	10.474[a]	2.000	61.000	<0.001
Time point* Group	0.795	24.594[a]	2.000	61.000	<0.001

[a]: Accurate statistics.

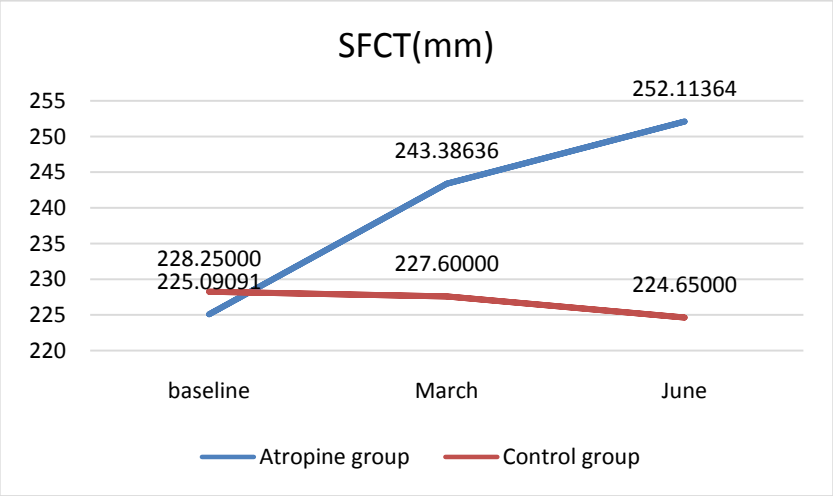

Figure 3. Folding graph of subcentral foveal choroidal thickness (SFCT) variation.

3.4. The Nasal 1 mm Subfoveal Choroidal Thickness

At baseline, the nasal 1 mm subfoveal choroidal thickness was 196.55000 ± 42.488977 μm in the control group and 199.45455 ± 60.484268 μm in the atropine group; in March, the nasal 1 mm subfoveal choroidal thickness was 197.05000 ± 42.213087 μm in the control group and 209.79545 ± 64.640897 μm in the atropine group; in June, the nasal 1 mm subfoveal choroidal thickness of the control group was 196.50000 ± 42.625084 μm and that of the atropine group was 219.20455 ± 66.567881 μm (Table 7); after six months, the nasal 1 mm subfoveal choroidal thickness of the atropine group increased by 19.750 ± 18.022 μm and that of the control group changed by −0.050 ± 8.219 μm.

In the multivariate test, a point-in-time effect of $P < 0.001$ was observed, meaning that subjects' the nasal 1 mm subfoveal choroidal thickness changed significantly with the number of follow-up visits. The interaction effect between time point and group was $P < 0.001$, indicating that there was a significant difference between the change in the nasal 1 mm subfoveal choroidal thickness in the control group and the atropine group with the change in follow-up time (Table 8). The nasal 1 mm subfoveal choroidal thickness in the atropine group all showed a trend towards thickening, with a flattening out of the nasal 1 mm subfoveal choroidal thickness growth in the second three months compared to the first three months; there was no significant change in the nasal 1 mm subfoveal choroidal thickness in the control group (Figure 4).

Table 7. Descriptive statistics of the nasal 1 mm subfoveal choroidal thickness (μm).

	Group	$\bar{X}$	SD	N
The nasal 1 mm subfoveal choroidal thickness at baseline	Atropine group	199.45455	60.484268	44
	Control group	196.55000	42.488977	20
	Total	198.54687	55.165819	64
The nasal 1 mm subfoveal choroidal thickness at March	Atropine group	209.79545	64.640897	44
	Control group	197.05000	42.213087	20
	Total	205.81250	58.521974	64
The nasal 1 mm subfoveal choroidal thickness at June	Atropine group	219.20455	66.567881	44
	Control group	196.50000	42.625084	20
	Total	212.10937	60.704101	64

Table 8. Multivariate test for the nasal 1 mm subfoveal choroidal thickness.

Effect	F	Assuming DF	Degrees DF	Sig.
Time point	11.457[a]	2.000	61.000	<0.001
Time point* Group	13.654[a]	2.000	61.000	<0.001

[a]: Accurate statistics.

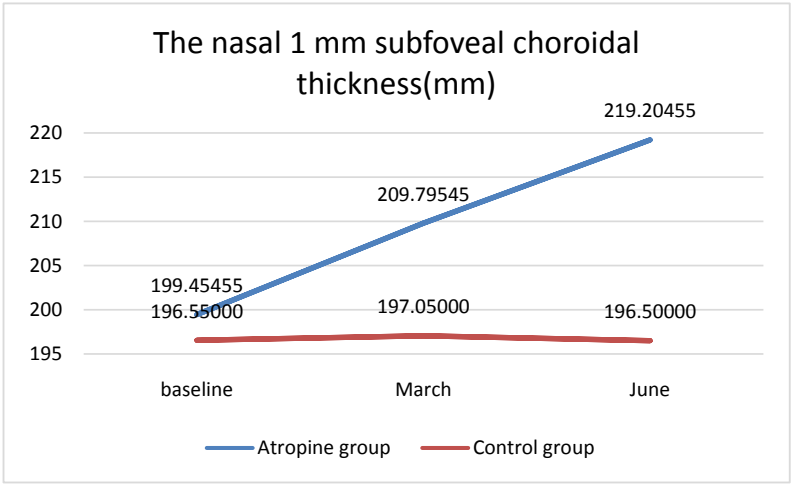

Figure 4. Folding diagram of the nasal 1 mm subfoveal choroidal thickness.

3.5. The Temporal 1 mm Subfoveal Choroidal Thickness

At baseline, the temporal 1 mm subfoveal choroidal thickness was 248.85000 ± 30.740467 μm in the control group and 238.95455 ± 54.633219 μm in the atropine group; in March, the temporal 1 mm subfoveal choroidal thickness was 248.60000 ± 34.077929 μm in the control group and 252.27273 ± 58.777611 μm in the atropine group; in June, the temporal 1 mm subfoveal choroidal thickness was 244.60000 ± 61.740934 μm in the control group and 261.04545 ± 60.607373 μm in the atropine group (Table 9). after six months, the temporal 1 mm subfoveal choroidal thickness increased by 22.091 ± 19.721 μm in the atropine group and the temporal 1 mm subfoveal choroidal thickness changed by −4.250 ± 6.339 μm in the control group.

In the multivariate test, $P = 0.001$ ($P < 0.05$) for the time point effect, meaning that subjects showed significant changes in the temporal 1 mm subfoveal choroidal thickness with the number of follow-up visits. The $P = 0.001$ ($P < 0.05$) interaction effect between time point and group indicates that the change in the temporal 1 mm subfoveal choroidal thickness in the control group with change in follow-up time was significantly different from that in the atropine group (Table 10). The temporal 1 mm subfoveal choroidal thickness in both the atropine and control groups tended to thicken, with a flattening of the temporal 1 mm subfoveal choroidal thickness growth in the second three months compared to the first three months; the temporal 1 mm subfoveal choroidal thickness in the control group thinned slightly (Figure 5).

3.6. Correlation of SFCT with AL and SE at Baseline

Multiple linear regression analysis of SFCT with AL and SE showed an R-squared of 0.011 (Table 11), meaning that AL and SE explained 1.1% of the variation in SFCT and the significance corresponding to AL and SE was much greater than 0.05 (Table 12). Therefore, SFCT was not significantly correlated with AL and SE at the subject's base.

Table 9. Descriptive statistics of the temporal 1 mm subfoveal choroidal thickness (μm).

	Group	$\bar{X}$	SD	N
The temporal 1 mm subfoveal choroidal thickness at baseline	Atropine group	238.95455	54.633219	44
	Control group	248.85000	30.740467	20
	Total	242.04688	48.410752	64
The temporal 1 mm subfoveal choroidal thickness at March	Atropine group	252.27273	58.777611	44
	Control group	248.60000	34.077929	20
	Total	251.12500	52.069398	64
The temporal 1 mm subfoveal choroidal thickness at June	Atropine group	261.04545	60.607373	44
	Control group	244.60000	31.094762	20
	Total	255.90625	53.458104	64

Table 10. Multivariate test for the temporal 1 mm subfoveal choroidal thickness.

Effect	F	Assuming DF	Degrees DF	Sig.	Effect
Time point	0.245	7.473[a]	2.000	61.000	0.001
Time point* Group	0.671	20.476[a]	2.000	61.000	<0.001

[a]: Accurate statistics.

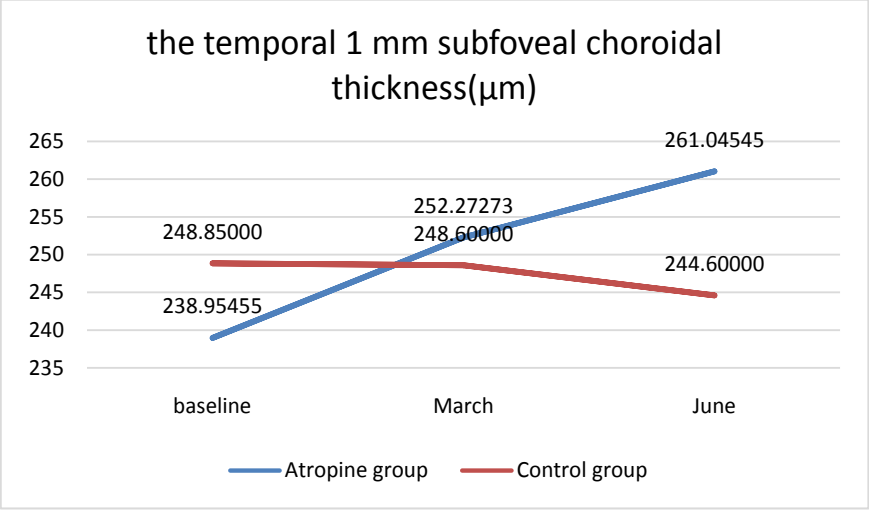

Figure 5. Folding diagram of the temporal 1 mm subfoveal choroidal thickness.

Table 11. Summary of linear regression analysis models for subcentral fovea choroidal thickness (SFCT), axial length (AL) and spherical equivalent (SE)[b].

R	R^2	Adjust R^2	Se	DW
0.107[a]	0.011	−0.021	49.82513	2.072

[a]: Predictor variable: (Constant), SE, AL; [b]: Dependent variable: SFCT.

3.7. Correlation of SFCT Difference with AL Difference and SE Difference

After 6 months of follow-up, multiple linear regression analysis of SFCT difference with AL difference and SE difference showed an R-square of 0.269 (Table 13), which means that AL difference and SE difference explained 26.9% of the variation in SFCT difference. The significance corresponding to AL difference was 0.018 ($P < 0.05$); the significance corresponding to SE difference was 0.005 ($P < 0.05$) (Table 14). Therefore, there was a significant correlation between SFCT difference and AL difference and SE difference in subjects after 6 months of follow-up.

The coefficient of influence of AL difference on SFCT difference was −36.861; the coefficient of influence of SE difference on SFCT difference was −29.142, that is, the changes in AL and SE were negatively correlated with the changes in SFCT, and the linear equation of the three can be expressed as SFCT difference = 26.687 − 36.861 * AL difference − 29.142 * SE difference (Table 14).

Table 12. Coefficients for linear regression analysis of subcentral foveal choroidal thickness (SFCT), axial length (AL) and spherical equivalent (SE)[a].

	Unstandardised coefficient		standardised coefficient	t	Sig.	Co-linear statistics
	B	Std.Error	Beta			VIF
(Constant)	31.835	232.333	-	0.137	0.891	-
AL	7.823	9.475	0.106	0.826	0.412	1.013
SE	0.539	8.673	0.008	0.062	0.951	1.013

[a]: Predictor variable: SFCT.

Table 13. Summary of the linear regression analysis model of the difference in subcentral foveal choroidal thickness (SFCT) with the difference in axial length (AL) and the difference in spherical equivalent (SE)[b].

R	R^2	Adjust R^2	Se	DW
0.518[a]	0.269	0.245	20.73160	1.648

[a]: Predictor variable:(Constant), Difference in SE, Difference in AL; [b]: Dependent variable: Difference in SFCT.

Table 14. Coefficient of linear regression analysis of the difference in subcentral foveal choroidal thickness (SFCT) on the difference in axial length (AL) and the difference in spherical equivalent (SE)[a].

	Unstandardised coefficient		standardised coefficient	t	Sig.	Co-linear statistics
	B	Std.Error	Beta			VIF
(Constant)	26.687	3.253	-	8.207	<0.001	-
difference in AL	−36.861	15.213	−0.284	−2.423	0.018	1.142
difference in SE	−29.142	9.880	−0.345	−2.949	0.005	1.142

[a]: Predictor variable: the difference in SFCT.

4. Discussion

The 0.01% to 0.05% atropine drops showed a concentration-dependent response to induce a choroidal thickening effect, and choroidal thickening was negatively correlated with SE progression and AL elongation in the treated group [12]. Jin's study of choroidal thickness in 86 children with low to moderate myopia showed results generally consistent with the present study, with an SFCT of (227 ± 61 μm) [13]. A European study analyzed baseline data from 250 myopic children aged 6 - 16 years using multiple linear regression and found that AL and SE at baseline were highly correlated with choroidal thickness [14]. There was no significant correlation between AL and SE and choroidal thickness at baseline in this experiment, which may be caused by ethnic differences and the small sample size in this study. A modest increase in ChT was observed in eyes given 0.01% atropine drops for 3 months, but was not statistically significant compared to controls [15]. Another study included 350 children between the ages of 4 and 12 years and found that younger age was associated with a poor response to treatment with lower concentrations of atropine (0.05%, 0.025%, and 0.01%). Of the three concentrations studied, younger children required the highest 0.05% concentration to achieve a similar reduction in myopic progression as older children receiving lower concentrations [16]. With a combination of efficacy and side effects, 0.05% atropine ophthalmic solution is the most beneficial atropine concentration for controlling myopia progression among the eight concentrations of atropine, 0.01%, 0.02%, 0.025%, 0.05%, 0.1%, 0.25%, 0.5%, and 1% [17]. However, 0.05% compared to lower concentrations of atropine eye drops leads to stronger side effects, such as blurred vision, fatigue, headache, eye pain, diplopia, difficulty concentrating, glare, etc. These side effects may affect patient acceptance and compliance, and their efficacy will be greatly reduced when used in the clinic [18] [19]. The concentration of atropine drops commonly available in the market today is 0.01%, and in order to achieve better therapeutic results, there is a need to find more effective and safe concentrations of atropine drops for clinical intervention in myopia development.

During the development of the visual system, a regular circadian rhythm is a prerequisite for normal eye growth [20]. The choroid is thicker at night while the AL is shorter at night, and the choroid is thinner during the day while the AL is longer during the day [21] [22]. A study observed diurnal variation in choroidal thickness in all quadrants of the 1 mm region of the central macular recess and the 3 and 6 mm rings, with mean amplitudes of 25.65 ± 2.01 μm in the central region and 23.47 ± 1.79 μm and 20.05 ± 1.3 μm in the 3 and 6 mm rings, respectively [21]. The daily rhythmic variation of the choroid in this study was comparable to the incremental choroidal thickness after 6 months of follow-up in the atropine group of this study (all choroidal thickness measurements performed in this study were at around 10:00 a.m.), which guides us to the need to pay attention to the circadian rhythmic variation of the eye when conducting clinical trials that require the collection of ocular-related data.

5. Conclusions

1) 0.02%/0.04% atropine sulfate eye drops can delay the growth of axial length and spherical equivalent.

2) 0.02%/0.04% atropine sulfate eye drops can thicken the choroid, and the thickness of the nasal side 1 mm is the same as that of the temporal side 1 mm.

3) At baseline, the subfoveal choroidal thickness has no significant correlation with the axial length and spherical equivalent.

4) After 6 months, changes in axial length and spherical equivalent were negatively correlated with changes in subfoveal choroidal thickness.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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Abbreviation/Symbol Description

Abbreviations	Full name
AL	Axial length
SE	Spherical equivalent
ACD	Anterior chamber depth
CCT	Central corneal thickness
IOP	Intraocular pressure
OCT	Optical coherence tomography
OCTA	Optical coherence tomography angiography
SFCT	Subfoveal choroidal thickness