Clinical science

Two-year outcomes of repeated red light therapy in premyopic children: sustained efficacy and rebound effects

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► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/bjo-2025-327600).

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Received 26 March 2025
Accepted 23 September 2025

To cite: Liu G, Li N, Rong H, *et al*. *Br J Ophthalmol* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/bjo-2025-327600

ABSTRACT

Background To evaluate the long-term prevention effectiveness and rebound effect of repeated red light therapy (RRLT) in children with premyopia over 2 years.

Methods A total of 108 premyopic children (cycloplegia spherical equivalent refraction (SER): −0.50 to +0.75 D) were enrolled and followed for 24 months. Participants were randomly assigned to the RRLT or control groups. The RRLT was administered two times per day for 3 min per session, with at least 4-hour interval. At the beginning of the second year, participants receiving RRLT were further randomised into continued treatment and washout subgroups. Axial length (AL), SER and subfoveal choroidal thickness (SChT) were measured.

Results Over 2 years, the RRLT group showed significantly smaller AL elongation (0.26 mm; 95% CI 0.18 to 0.35 mm) and SER progression (−0.21 D; 95% CI −0.35 to −0.08 D) compared with the controls (AL: 0.43 mm; 95% CI 0.36 to 0.49 mm; SER: −0.66 D; 95% CI −0.79 to −0.52 D). The RRLT group also demonstrated significantly less SChT thinning (−2.44 µm; 95% CI −16.11 to 11.23 µm) than the controls (−44.12 µm; 95% CI −53.05 to −35.19 µm). After RRLT cessation in the second year, the washout subgroup exhibited significantly faster AL elongation and more SChT thinning than the controls, with no significant difference in SER progression.

Conclusions The 2-year RRLT intervention effectively retarded AL elongation and SER progression in premyopic children by 0.17 mm and −0.45 D, respectively. Notably, a significant rebound effect was observed in AL growth following 1-year RRLT cessation.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Although repeated red light therapy (RRLT) has been proposed as an effective myopia control intervention, reports on its efficacy in preventing myopia are limited, and its rebound effect after 1-year treatment cessation remains unknown.

WHAT THIS STUDY ADDS

⇒ This study firstly reported that 2-year RRLT significantly slowed axial elongation and spherical equivalent refraction (SER) progression in premyopic children by 0.17 mm and −0.45 D, respectively. However, a notable rebound in axial elongation was observed during the 1-year discontinuation period.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ RRLT effectively and safely prevented myopia over a 2-year period, but the significant rebound effect in axial growth following a 1-year discontinuation of therapy highlighted the need to explore viable discontinuation strategies that can minimise this effect and sustain long-term benefits.

BACKGROUND

Myopia has become a global public health challenge, with its prevalence and severity increasing dramatically worldwide, particularly in East Asia.[1] Early-onset myopia poses an even greater concern, as it substantially increases the risk of progressing to high myopia,[2 3] which is associated with vision-threatening complications such as glaucoma, myopic maculopathy and choroidal neovascularisation.[4] These complications can lead to irreversible vision loss and place a heavy burden on healthcare systems and societies. Consequently, delaying the onset of myopia or slowing its progression is critical to mitigating the associated risks and reducing the long-term impact on visual health.

Currently, interventions for preventing the onset of myopia remain limited. Evidence suggests that increasing outdoor exposure,[5–8] reducing near-work activities,[9] using low-dose atropine[10] and wearing spectacle lenses with highly aspherical lenslets[11 12] can reduce the incidence of myopia in emmetropic or hyperopic children by 11–46.4% over 2 years.[5 6 10] The International Myopia Institute introduced the concept of premyopia, a refractive state of an eye of ≤ +0.75 D and > −0.50 D in children.[13] This premyopia condition serves as a warning that myopia may develop in the coming year.[14] Therefore, it is crucial to implement effective and safe interventions during this stage to prevent or postpone the onset of myopia.

Repeated red light therapy (RRLT) has emerged as a promising intervention for myopia control, using a device that emits 650 nm visible red light. Recent studies have demonstrated that its significant inhibitory effect on myopia progression[15–17] is potentially linked to sustained choroidal thickening.[17–19]

Reported reductions in myopia incidence following 12-month RRLT intervention range from 45% to 87% among premyopic children, making it a novel and effective way for myopia prevention.[15 16 19 20] Our prior research confirmed that 1-year RRLT significantly slowed axial length (AL) elongation and spherical equivalent refraction (SER) progression, effectively delaying myopia onset in premyopic children.[16]

Building on our previous findings that demonstrated the effectiveness of 1-year RRLT in significantly reducing AL and SER progression in premyopic children, this study extends the investigation to the second year to provide deeper insights into its long-term efficacy and safety. Key questions addressed include the sustainability of the preventive effects observed during the second year, the potential for rebound effect (defined as a faster axial elongation upon treatment cessation than that expected in a matched and untreated group[21]), and the impact of prolonged use on choroidal thickness (ChT). This 2-year prospective randomised study evaluates these aspects to offer a comprehensive understanding of the extended use of RRLT and its implications for clinical practice.

METHODS

Study design and setting

The study design has been reported previously for the first year study.[16] This was the extended second year phase of the prospective, parallel-group, randomised clinical trial. Participants were enrolled at Tianjin Medical University Eye Hospital (Tianjin, China) from July 2022 to December 2022. The 2-year follow-up was completed in December 2024. Before the study commenced, all personnel and investigators underwent comprehensive training on the study procedures. The study was registered with the Chinese Clinical Trial Registry (identifier: ChiCTR2200062028).

Eligibility criteria

Eligible participants were aged 8–13 years and had cycloplegic SER ≤ +0.75 D and > −0.50 D in both eyes,[16] astigmatism ≤1.50 D, anisometropia ≤1.50 D, and best-corrected visual acuity (BCVA, LogMAR) of 0.0 or better in both eyes and at least one parent with a SER ≥ −3.00 D in either eye. Participants were excluded if they had a history or presence of strabismus, other ocular abnormalities, ocular surgery, contact lens use, any systemic diseases or previous experiences with any myopia interventions.

Intervention

In the first year, eligible premyopic children were randomly assigned to either the RRLT group receiving RRLT or the control group with no intervention at an allocation ratio 1:1.[16] At the start of the second year, children in the RRLT group were randomly assigned in a 1:1 ratio to either a continued therapy subgroup or a washout subgroup. Children in the control group received no intervention throughout the entire 2-year study period.

Children in the RRLT group were given the RRLT device (Eyerising; Suzhou Xuanjia Optoelectronics Technology, Suzhou, China), consisting of semiconductor laser diodes capable of emitting low-level red light with a wavelength of 650±10 nm.[16] The RRLT was administered at home and scheduled two times per day for 3 min per session, with at least a 4-hour interval between sessions, and 7 days per week, under the supervision of parents/guardians. Follow-up examinations were conducted in the first month and third month after the baseline evaluation and once every 3 months thereafter. During the 2-year study period, if premyopic children became myopes with SER ≤ −0.50 D,[13] they would be provided with single-vision spectacles.

Intervention compliance monitoring

The RRLT device automatically recorded the exact date and time of each treatment session and transmitted these data seamlessly to the server via the internet. If the system detected two consecutive days of inactivity in participant logins, an automated reminder was sent to the parent or legal guardian to encourage better treatment compliance and ensure adherence to the required minimum treatment frequency (two sessions per day, 5 days per week). Participants with a treatment compliance rate exceeding 75% were selected for further analysis during the entire treatment period.

Randomisation and masking

After eligibility criteria were verified, treatment assignments were allocated with concealment based on a pregenerated randomisation list by a computer program (R software, V.4.2.0). The participants had an equal probability of assignment to either receiving RRLT or no RRLT intervention. Due to the nature of the intervention, it was not feasible to mask the children or their parents/guardians. Nevertheless, all study examiners and statisticians were masked to the treatment assignment.

Study outcomes

At baseline and follow-up visits, all participants underwent a complete ophthalmic examination, including BCVA, intraocular pressure, slit-lamp ophthalmic examination, SER, AL and fundus examination. All examinations were conducted from 9 to 11 AM to avoid diurnal variation.

The primary outcome was the change in AL at 24 months relative to baseline. Before cycloplegia, AL was measured using a non-contact optical biometer (Lenstar LS-900; Haag-Streit AG, Berne, Switzerland). At each visit, three consecutive measurements, with a between-measurement difference of 0.02 mm or less, were collected and then averaged as the representative value for each eye.

An important secondary outcome was the SER change at 24 months relative to baseline. Cycloplegia was administered semiannually using three drops of 1% cyclopentolate (Alcon, Geneva, Switzerland) in each eye, with a 5 min interval between drops; refraction measurements were taken at least 30 min after the final drop. SER was calculated as the sum of the sphere plus one-half of the cylindrical power.

Other secondary outcomes included the 24-month cumulative incidence rate of myopia (defined as cycloplegic SER of −0.50 D or less in the enrolled eye),[13] and the change in subfoveal choroidal thickness (SChT). SChT was assessed using a swept-source optical coherence tomography (OCT) (VG200, Svision Imaging, Ltd., Luoyang, China), which has a scanning speed of 200 000 A-scans/s with a light source of 1050 nm in wavelength. The device boasts a full-width at half-maximum axial resolution of approximately 5 µm within tissues and an estimated lateral resolution of roughly 15 µm at the retinal surface. OCT imaging was performed in a dark room after full cycloplegia to eliminate the influence of accommodation on SChT and maximise the image quality. SChT was defined as the vertical distance between Bruch's membrane and the choroid−sclera interface and was automatically segmented using the OCT built-in software. The same operator carried out every scanning operation, and all images were checked to have a signal strength of more than 7.

Sample size

The sample size estimation was based on a two-sided α-level of 0.05, 90% power, a 24-month axial elongation of 0.70 mm with a SD of 0.38 mm,[10] and a 50% treatment effect (reducing axial elongation by 0.35 mm). A sample size of 60 participants (20 per group) would achieve 90% power at a 0.05 significance level. Accounting for a 20% annual dropout rate, a total sample size of 96 participants (32 per group) was required.

Statistics

Data collected from the subjects' right eye were included in this analysis. Baseline continuous and categorical data were respectively represented by means±SDs and numbers (N) with percentages (%). The normality of continuous data was examined through the Kolmogorov-Smirnov test. Independent sample t-tests were conducted to compare differences in baseline parameters between the RRLT and control groups, and differences in 12-month follow-up parameters between the continued RRLT and washout subgroups. The χ^2 test was used to compare the distributional differences for categorical variables.

Outcomes were analysed by means of intention-to-treat (ITT). Participants who attended at least one subsequent follow-up visit were included in the ITT and the missing data were not imputed. For some participants with interrupted treatment, only the data before the interruption were calculated for ITT statistical analysis.

Mixed-effects linear models were developed to compare 1-year and 2-year changes in AL, SER and SChT between the RRLT and control groups, and changes in AL, SER and SChT between the continued RRLT and washout groups at each follow-up point from the 12-month mark onward, relative to the 12-month follow-up values. AL, SER and SChT were described using mean differences and 95% CIs.

Subgroup analyses were performed to compare the myopia control effect, including AL elongation and SER progression, among participants with varying baseline SER values (−0.50 to 0.00 D vs 0.01 to +0.75 D) and different age stratification (8–10 years vs 11–13 years).

All statistical tests were two-sided, and a p value <0.05 was considered statistically significant. All analyses were performed using R software (V.4.2.0).

RESULTS

Children with premyopia (n=126) were recruited and assessed for eligibility. A total of 108 subjects were enrolled for this study, with 58 and 50 subjects allocated into the RRLT and control groups, respectively. Among them, 93 (86.1%) completed the first-year follow-up visits, including 53 (91.4%) in the RRLT group and 40 (80%) in the control group. At baseline, no significant differences were observed between the two groups regarding age, sex distribution, BCVA (LogMAR), AL, SER and SChT (all p>0.05, table 1). At the beginning of the second year, 53 subjects in the RRLT group were randomised into a continued therapy subgroup (27) and a washout subgroup (26), and 40 subjects continued the trial in the control group. Among those, 25 (92.6%), 23 (88.5%) and 33 (82.5%) subjects in the RRLT continued therapy subgroup, washout subgroup and control group, respectively, finished the second-year follow-up visits. At the entry of the second year, the demographic characteristics of the subjects in the continued therapy and washout groups were of no significance (all p>0.05, table 2). Over 2 years, 27 subjects could not continue with the study due to various reasons. 3 subjects dropped out due to RRLT compliance below 75%, 5 subjects dropped out due to their preference to choose other myopia control treatments and 19 subjects were lost to follow-up, as detailed in figure 1.

Table 1 Demographics and characteristics at baseline between the RRLT and control groups

Parameter	RRLT (58)	Control (50)	P
Age (year)	10.14±1.56	9.98±1.58	0.604
Gender (M/F)	31/27	26/24	0.710
BCVA (LogMAR)	−0.01±0.03	−0.01±0.04	0.617
AL (mm)	23.31±0.69	23.31±0.58	0.996
SER (D)	0.20±0.40	0.21±0.32	0.910
SChT (μm)	360.72±60.92	361.34±60.19	0.958

AL, axial length; BCVA, best-corrected visual acuity; F, female; M, male; RRLT, repeated red light therapy; SChT, subfoveal choroidal thickness; SER, spherical equivalent refraction.

Changes in AL and SER over 2 years

Over the 2 years of continuous RRLT, the cumulative mean AL elongation was 0.26 mm (95% CI 0.18 to 0.35 mm), significantly smaller than that (0.43 mm, 95% CI 0.36 to 0.49 mm) in the control group (p<0.001; figure 2A). The respective cumulative mean SER progressions were −0.21 D (95% CI −0.35 to −0.08 D) and −0.66 D (95% CI −0.79 to −0.52 D) (p<0.001; figure 2B). The changing trend of AL and SER from baseline to 24-month follow-up is shown in figure 2.

Changes in AL and SER in the first year versus second year

In the first year, the AL elongation was 0.09 mm (95% CI 0.05 to 0.14 mm) for the RRLT group and 0.18 mm (95% CI 0.15 to 0.21 mm) for the control group (p<0.001), and the corresponding SER progression was −0.02 D (95% CI −0.10 to 0.06 D) and −0.22 D (95% CI −0.31 to −0.13 D), respectively (p<0.001). During the second year, the AL elongations for the continued therapy subgroup, washout subgroup and control group were 0.15 mm (95% CI 0.12 to 0.18 mm), 0.32 mm (95% CI 0.27 to 0.37 mm) and 0.24 mm (95% CI 0.19 to 0.28 mm), respectively. The respective SER progressions were −0.22 D (95% CI −0.31 to −0.13 D), −0.59 D (95% CI −0.76 to −0.43 D) and −0.46 D (95% CI −0.60 to −0.32 D). The AL elongation and SER progression in the second year for subjects receiving RRLT were significantly less than those in the control group (AL elongation: p=0.002, SER progression: p=0.025). Compared with the control group, RRLT reduced AL elongation by −0.09 mm (95% CI −0.14 to −0.04 mm) in the first year

Table 2 Demographics and characteristics at 12 months between the continued RRLT and washout groups

	RRLT (53)		
Parameter	Continue (27)	Washout (26)	P
Age (year)	10.63±1.18	11.27±1.69	0.118
Gender (M/F)	13/14	13/13	0.889
BCVA (LogMAR)	−0.01±0.03	−0.01±0.04	0.660
AL (mm)	23.41±0.74	23.42±0.72	0.954
SER (D)	0.11±0.58	0.21±0.42	0.496
SChT (μm)	378.37±60.40	372.69±59.18	0.731

AL, axial length; BCVA, best-corrected visual acuity; F, female; M, male; RRLT, repeated red light therapy; SChT, subfoveal choroidal thickness; SER, spherical equivalent refraction.

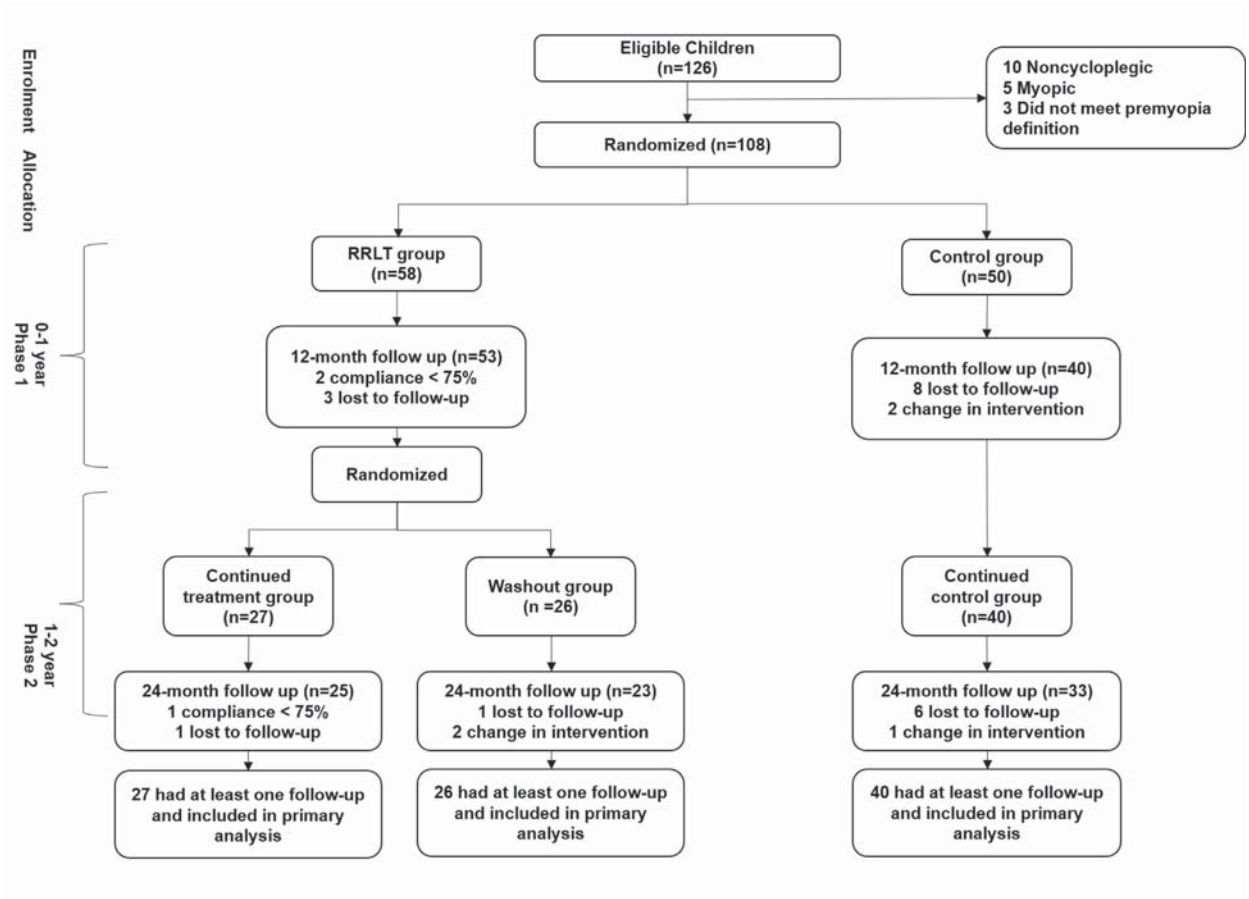

Figure 1 Flow diagram of the study. RRLT, repeated red light therapy.

and −0.09 mm (95% CI −0.17 to −0.01 mm) in the second year (p>0.999), meanwhile the relative reduction in SER progression was −0.20 D (95% CI −0.31 to 0.09 D) in the first year and −0.24 D (95% CI −0.46 to −0.02 D) in the second year (p=0.797). After RRLT cessation, significantly faster AL elongation was found in the washout subgroup when compared with those in the control group in the 1-year discontinuation period (p=0.012). No significant differences in SER progression were observed between the washout subgroup and the control group in the second year (p=0.130).

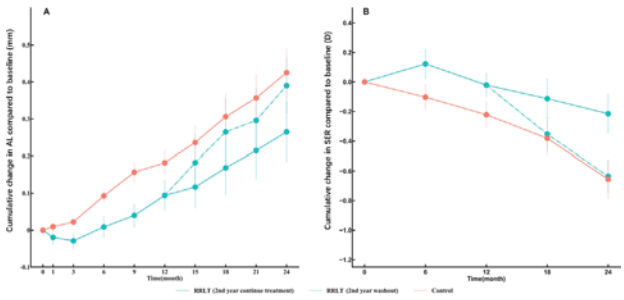

Figure 2 Changes in AL and SER for groups over time. The RRLT group was randomised into a continued therapy subgroup and a washout subgroup at the entry of the second year. Data were shown by mean±95% CI. AL: axial length; SER: spherical equivalent refraction; RRLT: repeated red light therapy.

Myopia incidence

In the first year, the myopia incidence rate in the RRLT group was 5.7% (3 of 53), while in the control group it was 22.5% (9 of 40), showing a statistically significant difference (p=0.026). The 2-year cumulative incidence rates of myopia were 24.0% (6 of 25) in the RRLT group and 39.4% (13 of 33) in the control group. The absolute mean difference between the two groups was 15.4% (95% CI −8.2% to 39.0%; p=0.266).

Changes in SChT during treatment and cessation

Over the course of 2 years, SChT significantly increased at 1 month with RRLT, continued to thicken and peaked at the third month, with a change of 19.98 µm (95% CI 16.36 to 23.60 µm). Subsequently, the extent of thickening gradually decreased until the end of the observation period. The 24-month change in SChT of the RRLT group was −2.44 µm (95% CI −16.11 to 11.23 µm). Conversely, SChT in the control group showed a continuous thinning over the 2-year period, with a reduction of −44.12 µm (95% CI −53.05 to −35.19 µm) (figure 3). The mean changes in SChT in the RRLT group and control group were 12.40 µm (95% CI 4.94 to 19.86 µm) and −29.78 µm (95% CI −36.83 to −22.72 µm) in the first year, respectively (p<0.001), and −13.84 µm (95% CI −20.68 to −7.00 µm) and −12.94 µm (95% CI −18.53 to −7.35 µm) during the second year, respectively (p=0.824). After stopping RRLT, SChT in the washout group significantly decreased by −33.92 µm (95% CI −42.42 to −25.42 µm) in the first 3 months compared with the control group (−5.98 µm, 95% CI −10.1 to −1.85 µm; p<0.001), and continued to thin until the end of the observation period. During the second year, the SChT change in the washout group was

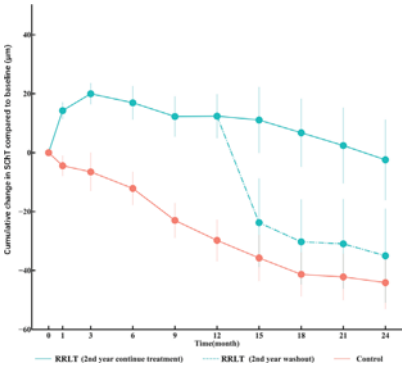

Figure 3 Changes in SChT for groups over time. The RRLT group was randomised into a continued therapy subgroup and a washout subgroup at the entry of the second year. Data were shown by mean±95% CI. SChT: subfoveal choroidal thickness; RRLT: repeated red light therapy.

−41.91 µm (95% CI −52.58 to −31.25 µm), which was significantly more than that in the control group (−12.94 µm, 95% CI −18.53 to −7.35 µm; p<0.001).

Subgroup analyses

Subgroup analyses were performed to compare the myopia control effect, including AL elongation and SER progression, among participants with varying baseline SER values (online supplemental table 1) and different age stratification (online supplemental table 2). The treatment effect did not show significant variation by baseline SER (−0.50 to 0.00 D vs 0.01 to +0.75 D), whether in the first year or across the entire 2-year period. Regarding age, participants aged 11–13 years exhibited less AL elongation and SER progression compared with those aged 8–10 years in the first year; however, children of different age groups did not show significant differences in the progression of AL and SER over the entire 2-year period.

Safety

The BCVA (LogMAR) in the RRLT group and control group were −0.01±0.03 and −0.01±0.03 at the 12-month visit, respectively, and −0.02±0.04 and −0.01±0.03 at the 24-month visit, respectively. The longitudinal mixed model analysis indicated that there was no statistically significant difference in BCVA before and after 1-year or 2-year RRLT (baseline vs 1-year visit, p=0.989; baseline vs 2-year visit, p=0.331).

Throughout the study, there were no significant changes observed in fundus structure, and none of the participants reported experiencing adverse effects such as glare, flickering, afterimages lasting longer than 6 min or any reduction in BCVA.

DISCUSSION

To our knowledge, this is the first trial to evaluate the long-term efficacy of RRLT for myopia prevention in premyopic children over a 2-year period, while also assessing the rebound effect following treatment cessation. This study demonstrated that RRLT significantly slowed axial elongation and SER progression in premyopic children by 0.17 mm and −0.45 D, respectively. However, a notable rebound in axial elongation was observed during the 1-year discontinuation period, emphasising the need to explore viable discontinuation strategies that can minimise this effect and sustain long-term benefits.

Two-year efficacy of RRLT on myopia prevention

Although RRLT has been proposed as an alternative myopia control intervention,[15] reports on its efficacy in preventing myopia are limited. A 12-month randomised clinical trial including school-aged children with premyopia found that, when compared with the control group, RRLT intervention significantly reduced AL elongation by 0.17 mm and slowed SER progression by −0.41 D in the absence of interruption from the COVID-19 pandemic.[20] Another randomised clinical trial consistently found a significant reduction in AL change of 0.19 mm and SER change of −0.31 D after 1-year RRLT in premyopes.[19] In the present study, 2 years of RRLT retarded AL elongation by 0.17 mm and reduced SER progression by −0.45 D compared with the control group. These findings highlight the sustained efficacy of continuous RRLT for myopia prevention over 2 years.

Although the 2-year incidence of myopia in the RRLT group (24.0%) was lower than that (39.4%) in the control group, the difference was not statistically significant. This finding contrasts with previous studies, which demonstrated that 1 year of RRLT significantly reduced the incidence of myopia in premyopic children.[16 19 20] In this study, however, the lack of a significant effect over 2 years may be attributed to the increase of those whose SER was very close to −0.50 D (the cut-off for myopia) at the entry of the second year. Of course, this finding requires validation through long-term, large-scale clinical studies.

To date, only increasing outdoor time and low-concentration atropine have been evaluated in 2-year randomised clinical trials as preventive interventions for myopia.[5 6 10] For example, 0.01% atropine[10] and increasing outdoor time during recess (approximately 40 or 80 min/day) for premyopic children[5] have shown limited effects, reducing AL elongation by 0.07–0.10 mm and SER progression by −0.20 to −0.13 D compared with controls. In contrast, the 2-year effects of RRLT observed in this study appear stronger. Besides, the Low-Concentration Atropine for Myopia Prevention (LAMP2) trial demonstrated that 0.05% atropine drops reduced SER progression by −0.54 D and slowed AL growth of 0.22 mm over 2 years,[10] slightly greater than our findings (SER reduction: −0.45 D; AL elongation reduction: 0.17 mm). This discrepancy may be attributed to the differences in study populations. While LAMP2 included children without myopia (SER: 0.00 D to +1.00 D), our study focused on children with premyopia (SER: −0.50 D to +0.75 D), who are at higher risk of myopia progressing.

Continuing RRLT in the second year

Previous pooled analyses of various myopia control interventions have revealed that most interventions experience a decline in efficacy during the second year, particularly in controlling axial elongation.[22] For example, both 1% atropine and orthokeratology have demonstrated stronger myopia control effects during the first year compared with the second year.[23 24] Similarly, a recent 2-year post-trial follow-up study evaluating RRLT in myopic children reported that while RRLT maintained its efficacy in the second year, its relative effect declined by 22–32% compared with the first year.[25]

In contrast, our study found that in premyopic children, AL elongation and SER progression in the second year of RRLT remained significantly less than those in the control group, confirming the sustained effectiveness of RRLT. Notably, the relative reductions in AL elongation and SER progression in the RRLT group were similar between the first and second years. This indicates that the efficacy of RRLT in premyopic children

during the second year was comparable to its efficacy in the first year, without the decline observed in myopic populations.[25]

The differences in findings may be attributed to variations in eye growth patterns between myopic and non-myopic populations.[26] Premyopic children typically have less pronounced axial elongation compared with their myopic counterparts, which could contribute to the sustained efficacy of RRLT observed in this study. Further research is needed to explore these differences and their implications for long-term treatment strategies.

Rebound effect after cessation of RRLT

Rebound is characterised by a greater myopic progression following the cessation of treatment than would have been expected in untreated children of the same age.[22 27] Previous studies have reported varying degrees of rebound effects after discontinuing myopia control methods, such as orthokeratology and atropine.[27 28] The average annualised rebound has been estimated as +0.05 ± 0.10 mm for AL elongation and −0.09±0.24 D for refractive error progression.[21]

In the present study, cessation of RRLT resulted in significantly faster AL elongation in the washout subgroup compared with the control group during the 1-year discontinuation period, with a mean difference of 0.08 mm, indicating a rebound effect in terms of AL growth. Compared with findings in children with mild to moderate myopia, where rebound effects included a −0.37 D difference in SER progression and a 0.14 mm difference in AL elongation relative to controls,[25] the rebound effect in premyopic children appeared to be less pronounced. Nonetheless, over the entire 2-year study period, the AL elongation in the washout group was similar to that of the control group, suggesting that the impact of RRLT on AL elongation in premyopic eyes was almost completely reversed within 1 year of treatment cessation.

This finding warns us that RRLT should not be abruptly discontinued after 1 year, as doing so may negate the early benefits of the intervention. To optimise the sustained efficacy of RRLT, further research is needed to examine the rebound effect in children with different refractive statuses and those who have participated in treatments of varying durations, and to determine the most appropriate discontinuation strategy, addressing the timing of discontinuation and whether it should be tapered.

Choroidal thickness (ChT) changes during treatment and cessation

ChT is negatively correlated with AL and plays a key role in myopia progression.[29] In the present study, premyopic children without intervention exhibited continuous SChT thinning over 2 years, consistent with patterns reported in both myopic and emmetropic children.[30 31] In contrast, RRLT induced significant SChT thickening during the first year, peaking at 3 months (19.98 µm), while the more rapid thickening was observed in myopic children (peaking at 1 month, 14.76–17.4 µm).[18 32 33] This difference may reflect variations in choroidal characteristics between different refractive groups.

In the second year, SChT changes in the RRLT group were positive for the first 9 months, with slight thinning observed by the end of the study. Notably, SChT in the RRLT group remained significantly thicker than that in the control group throughout the 2 years, suggesting that choroidal thickening induced by RRLT may help slow axial elongation. However, SChT thinning alone could not fully explain AL changes, as AL elongation in the RRLT group was still significantly less than in the control group despite similar SChT thinning during the second year. This suggests that RRLT's effects on AL may involve mechanisms beyond ChT changes, such as retinal vasculature changes, and scleral hypoxia and remodelling.

Studies suggest that the choroidal thickening dissipates within months following discontinuation of myopia intervention.[25 34] Similarly, the present study found that, after RRLT cessation, the washout group experienced significantly greater SChT thinning (−41.91 µm) compared with the control group (−12.94 µm) over the 1-year discontinuation period, indicating abrupt discontinuation of RRLT may disrupt normal ChT regulation in premyopic children. Notwithstanding a difference of 28.97 µm in SChT thinning, the washout group only showed an increase of 0.08 mm more in AL compared with the control group. It seems that the relationship between SChT thinning and AL elongation was weaker than expected (20–39 µm ChT thinning corresponding to a 1 mm increase of AL in children[35]), highlighting the need for further research to identify other ocular structures or mechanisms involved in the rebound effect following RRLT cessation.

Adverse events

As research advances in the field of RRLT for myopia management, it is essential to closely monitor the safety of treatments. After this 24-month RRLT intervention, no participants experienced any adverse reactions or issues in the present study. Additionally, a separate 2-year study by Xiong *et al*[25] found that prolonged RRLT was well tolerated among children with myopia. Despite this, during RRLT intervention, clinicians must supervise participants in the proper use of the instruments, encourage regular follow-ups and pay special attention to any adverse events that may arise during monitoring. If any adverse reactions occur, RRLT should be stopped immediately, and appropriate treatment should be administered. Given the current regulatory changes of RRLT in China, future larger and longer-term real-world studies are essential to gain a better understanding of the long-term safety of RRLT.

Limitations

The current study had some limitations. First, the absence of sham equipment for the control group may have introduced potential bias, as participants and their guardians were aware of their treatment assignments, which could have influenced adherence or reporting of outcomes. Second, the participant dropout rate in the control group, for those who completed the 2-year follow-up, was higher than anticipated. This could potentially hamper the statistical power and introduce bias into the results. Third, although we observed significant changes in AL, SER and SChT, we did not evaluate changes in choroidal and retinal vasculature.[19] Fourth, the efficacy and safety observed in this study are specific to the RRLT device used, which emits a specific wavelength (650±10 nm) and intensity. It remains unclear whether different power intensities, wavelengths or treatment frequencies might yield similar or even superior outcomes. Future studies should explore the effects of varying these parameters to optimise the intervention. Fifth, while the 2-year follow-up period provides valuable insights into the efficacy and rebound effects of RRLT, longer-term studies are necessary to evaluate whether the benefits persist beyond this period and to better understand potential long-term adverse effects. Sixth, this study focused exclusively on premyopic children aged 8–13 years, limiting the generalisability of the findings to other age groups or refractive states, such as myopic children or younger age groups at risk of myopia onset. Finally, external validation for subgroup analysis

that included greater sample sizes could be warranted in the future studies.

CONCLUSIONS

This study demonstrated that RRLT effectively and safely prevented myopia over a 2-year period, with sustained efficacy in slowing axial elongation and refractive progression. However, a significant rebound effect in axial growth was observed following a 1-year discontinuation of therapy, highlighting the need for careful management of treatment cessation. Future clinical research should focus on optimising treatment and discontinuation protocols to maximise long-term benefits while minimising rebound effects.

Acknowledgements The authors would like to thank all the participants involved in the study.

Contributors GL: conception and design, data collection and manuscript drafting; NL: conception and design, methodology and manuscript drafting; HR: methodology and data analysis; JH and EP: data collection; EEP: language polishing; BD: conception and design, and supervision; RW: funding acquisition, conception and design, and overall responsibility. All authors are guarantors of this work.

Funding National Natural Science Foundation of China (No. 82070929), Tianjin Key Medical Discipline (Specialty) Construction Project (TJYXZDXK-037A).

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants. The study was reviewed and approved by the ethics committee of Tianjin Medical University Eye Hospital (ethics approval ID: 2021KY-11) and was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all parents/guardians, and verbal assent was provided by the participants.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The datasets generated/analyzed during the current study are available from the corresponding author on reasonable request.

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