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Effectiveness of repeated low-level red light in myopia prevention and myopia control

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ABSTRACT

Background/aims To compare the effects of repeated low-level red light (RLRL) treatment on axial length growth and refractive error changes in myopic and premyopic children.

Methods Subjects were assigned randomly to four subgroups: myopia-RLRL group (M-RL), myopia-control group (M-C), premyopia-RLRL group (PM-RL) and premyopia-control group (PM-C). Subjects in the RLRL group completed a 12-month treatment composed of a 3 min RLRL treatment session twice daily, with an interval of at least 4 hours, for 7 days per week. Visits were scheduled before and at 1-month, 3-month, 6-month, 9-month and 12-month follow-up after the treatment. Repeated-measures analysis of variance was used to compare the spherical equivalent refractive errors (SE) and axial length (AL) changes between the groups across the treatment period.

Results After 12 months of treatment, in the myopia group, SE and AL changes were −0.078±0.375 D and 0.033±0.123 mm for M-RL and −0.861±0.556 D and 0.415±0.171 mm for M-C; in the premyopia group, the progression of SE and AL was −0.181±0.417 D and 0.145±0.175 mm for PM-RL and −0.521±0.436 D and 0.292±0.128 mm for PM-C. PM-RL indicated a lower myopia incidence than PM-C (2.5% vs 19.4%). Additionally, the percentage of AL shortening in the M-RL was higher than that in the PM-RL before the 9-month follow-up.

Conclusion RLRL effectively delayed myopia progression in children with myopia and reduced the incidence of myopia in premyopic children. Moreover, RLRL exhibited a stronger impact on myopic children compared with premyopic individuals.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Growing evidence indicates that repeated low-level red light (RLRL) is a novel intervention for myopia. However, the myopia prevention and control effects in different populations, such as myopia and premyopia remain unknown.

WHAT THIS STUDY ADDS

⇒ This study demonstrated that using RLRL presented a better effect on retarding axial length and spherical equivalent refractive errors in myopic children than premyopic individuals.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ RLRL has been proven to prevent and control myopia, while this research further put forward the different effects among myopia and premyopia. We speculated that the homoeostatic effect of axial elongation and shortening is bidirectional.

INTRODUCTION

Myopia is a global public health concern and one of the significant factors of visual impairment.[1] It increases the incidence of eye diseases such as cataracts, glaucoma and myopic retinopathy and causes a severe social and economic burden.[2 3] A total of 49.8% of the world population, approximately 4758 million, will be affected by myopia by the year 2050.[1] Therefore, exploring intervention methods for myopia control and prevention is urgent.

Various methods, including low-concentrate atropine, orthokeratology (OK), spectacles and contact lenses that modify peripheral defocus, have been studied to slow down the axial length growth in children with myopia.[4–7] More recently, the use of repeated low-level red light (RLRL) treatment to retard the myopia progress in myopic children has been reported.[8 9] RLRL treatment of 3 min twice a day has been demonstrated to slow the progress of myopia successfully. While it is important to search for ways to retard myopia progress, it is also critical to find methods to prevent myopia from developing. However, the methods that worked in retarding myopia progress may not work in myopia prevention because premyopic and myopic eyes may belong to two fundamentally different populations.[10 11] According to the haemostasis theory proposed by Filcroft *et al*, the premyopic eye successfully maintains the emmetropisation progress.[10] Refractive errors result when either this process fails (a primary homoeostatic failure) or when an emmetropic eye fails to remain so during subsequent years (a secondary homoeostatic failure). The frequency distributions of refractive errors at any age group can be approximated by a Bi-Gaussian model with one narrow Gaussian representing a population that maintains emmetropisation (premyopic) and the other broader Gaussian indicating a myopic population.[12] It has been suggested that the 'dysregulated' population (myopia) has higher variability than the 'regulated' population (premyopic).[10 12]

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Low-concentrate atropine has been reported to reduce the incidence of myopia and myopic progression.[5 13 14] Increasing outdoor activities is effective in myopia prevention but has little effect on myopia retardation.[11 15 16] It is currently unknown whether there are differences in the effectiveness of RLRL treatment between premyopic and myopic children. Therefore, we designed this study to compare the effects of RLRL treatment on axial length growth and refractive error changes in premyopic and myopic children.

MATERIALS AND METHODS

Subjects

This prospective, randomised, parallel-control study was conducted at the Tianjin Medical University Eye Hospital (Tianjin, China) between March 2022 and May 2023. Written informed consent was obtained from all enrolled participants or their parents or guardians. All procedures adhered to the tenets of the Declaration of Helsinki and were approved by the Tianjin Medical University Eye Hospital ethics committee. The trial has been registered with the Chinese Clinical Trial Registry (ChiCTR2200062028).

The subjects were divided into two groups (myopia group and premyopia group) based on their spherical equivalent refractive errors (SE). In the myopia group, eligible participants were children 8–13 years of age with SE of −6.00 to −1.00 D, astigmatism of 1.50 D or less, anisometropia of 1.50 D or less and best-corrected visual acuity (BCVA) of 20/20 or more in either eye. In the premyopia group, eligible participants were children with SE of ≤+0.75 D and >−0.50 D,[17] having at least one parent with an SE in either eye of −3.00 D or less and meeting the other criteria for the myopia group. The exclusion criteria included acute and subacute inflammations or infection of the anterior chamber of the eye, history of surgery or myopia prevention and control methods such as contact lenses (including OK lenses and peripheral defocus contact lenses), peripheral defocus glasses, atropine, etc, severe insufficiency of tears, corneal hypoesthesia, allergic eye diseases, retinal diseases and any significant systemic illness. Eligible subjects were randomly allocated to either the RLRL or the control group according to a randomisation list pre-generated by a computer programme. Finally, all participants were divided into four subgroups: myopia-RLRL group (M-RL), myopia-control group (M-C), premyopia-RLRL group (PM-RL) and premyopia-control group (PM-C).

Repeated low-level red light therapy

A low-level red light therapy device (Eyerising; Suzhou Xuanjia Optoelectronics Technology, Suzhou, China) was used in this study. It consists of semiconductor laser diodes, which deliver low-level red light with a wavelength of 650±10 nm at an illuminance level of approximately 1600 lux through the pupil to the fundus. Subjects in the RLRL group took the device home, where they were instructed to complete treatment twice daily with an interval of at least 4 hours, with each treatment lasting 3 min, for 7 days per week. Subjects were asked to adjust the best position and wear refractive correction spectacles before use to ensure the light entered the eyes properly. To ensure an accurate measure of compliance, the date and time of treatment sessions were automatically captured by the device and transferred to the server through the internet. On noticing that the subject had not logged into the system for 2 days consecutively, a reminder message was sent to both the supervisor and the subject to guarantee 75% treatment rate. Besides, the server also monitored the power of the device, and if the unforeseen fluctuation occurred, the device was remotely shut down. The supervisor would confirm with the subjects to ensure the minimum number of treatments required by the test (5 days a week). During the treatment period, if SE changed by −0.50 D in myopia group, or pre-myopes became myopes, new appropriate spectacles were provided to the subjects.[8 18 19] After 12 months of treatment, subjects with a treatment compliance rate of ≥75% were included for further analysis.

Measurement

Subjects underwent a complete ophthalmic examination, including visual acuity, intraocular pressure, slit-lamp ophthalmic examination and fundus examination. In addition to the items mentioned above, axial length and cycloplegic refractive error were measured before and 1, 3, 6, 9 and 12 months after the treatment. After their last exposure to RLRL, we reminded them to ensure that they were back at the hospital for examination within a week. All evaluations were performed from 09:00 to 11:00 to avoid diurnal variation.[20]

Spherical equivalent refractive errors

Cycloplegia was conducted with 1% cyclopentolate (Alcon, Geneva, Switzerland) 5 min apart, three times. Pupil diameter and reactivity were checked to confirm full cycloplegia after an additional 30 min. Full cycloplegia was considered adequate if the pupils did not react to light and pupil size was more than 6.0 mm. After full cycloplegia was achieved, refraction was measured using an autorefractor (KR-800, Topcon, Tokyo, Japan). At least three consistent readings of cycloplegic refractive error were recorded. The difference in spherical or cylindrical power among the three readings was required to be within 0.25 D, and the average of these three readings was used in the analysis. The SE was calculated using the sum of the spherical power and half of the cylindrical power.

Axial length

Axial length (AL) was measured before cycloplegia with a non-contact optical low-coherence reflectometry device (Lenstar LS-900; Haag-Streit AG, Berne, Switzerland). Subjects were advised to fixate on the target during the measurements and blink several times for an intact tear film. Only the intrasession differences of three repeated measures ≤0.02 mm were kept on each measurement occasion. The average was used as a representative value for further analysis.

Sample size

Based on existing publications, we estimated that the progression of AL would be 0.08 mm, 0.40 mm, 0.16 mm and 0.30 mm per year with a pooled SD of 0.18 mm in M-RL, M-C, PM-RL and PM-C, respectively.[8 21–23] During the design phase of this study, there was no relevant study on the changes in AL of premyopic children treated with RLRL, so the estimated value for this group came from the results of our pre-experiments. With an α level of 0.05 and 80% power, the sample size required was 26 subjects per group or 104 participants in total. Adjusting for a 20% loss to follow-up yielded a total sample size of 132 participants.

Statistics

All statistical analyses were performed using SPSS statistical package V.25 (SPSS, IBM, Chicago, Illinois, USA). Data were first tested for normality using the sample Shapiro-Wilk test. The means and SDs of measured parameters were

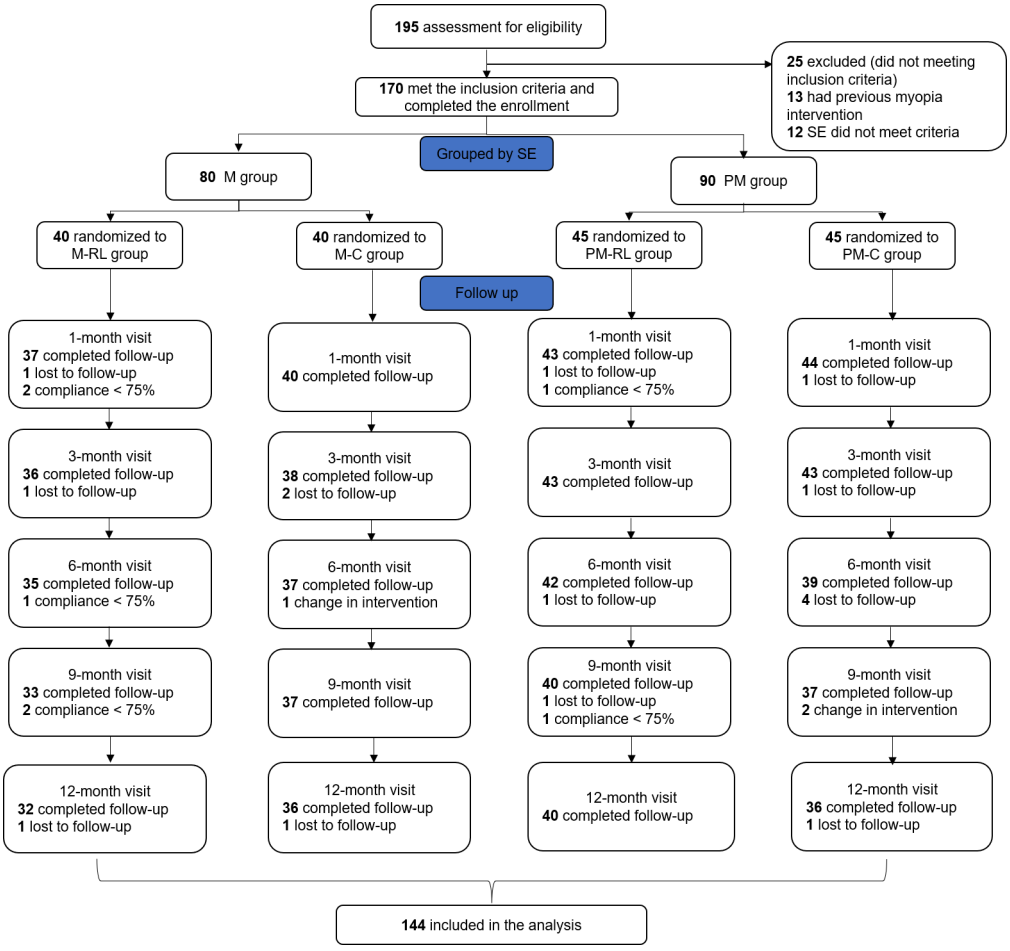

Figure 1 Flow diagram of the study. M-C, myopia-control group; M-RL, myopia RLRL group; PM-C, premyopia-control group; PM-RL, premyopia RLRL group; SE, spherical equivalent refractive errors; RLRL, repeated low-level red light.

computed for descriptive purposes. Independent samples t-tests were used to compare the statistical differences in baseline data between M-RL and M-C and between PM-RL and PM-C, including age, AL, BCVA and SE. The χ^2 test was used to compare gender distribution differences. Repeated-measures analysis of variance (ANOVA) was used to compare the AL and SE changes between the groups across the treatment period. Independent samples t-tests were used to compare compliance between the two groups of RLRL subjects, and linear regression analysis was used to examine the correlation between the changes in AL at 12 months and the baseline AL, age and compliance. For all subjects, only right-eye data were included in the analysis. A p value$<$0.05 was considered statistically significant.

RESULTS

A total of 170 subjects were enrolled in this study, including 40 in the M-RL group, 40 in the M-C group, 45 in the PM-RL group and 45 in the PM-C group. Among those, 144 completed all follow-up visits, including 32 in the M-RL group, 36 in the M-C group, 40 in the PM-RL group and 36 in the PM-C group. Seven subjects dropped out due to RLRL compliance below 75%, 3 subjects dropped out due to choosing other myopia control methods (1 with OK lenses, 2 with atropine) and 16 subjects lost to follow-up, as detailed in figure 1.

The mean age at baseline was 9.19±1.23 years, and 50% were men. The baseline demographic and ocular characteristics of the subjects in the four groups are presented in table 1. There were

Table 1 Demographics and baseline data among the groups (mean±SD)

	M-RL (n=32)	M-C (n=36)	P value	PM-RL (n=40)	PM-C (n=36)	P value
Sex (M/F)	16/16	17/19	0.819	22/18	17/19	0.498
Age (y)	9.37±1.69	9.55±1.13	0.604	8.95±0.87	8.94±1.09	0.980
BCVA (logMAR)	−0.011±0.036	−0.007±0.022	0.592	−0.010±0.034	−0.014±0.044	0.670
SE (D)	−2.91±1.27	−2.61±0.98	0.292	0.36±0.32	0.37±0.30	0.893
AL (mm)	24.71±0.92	24.58±0.64	0.512	23.40±0.63	23.30±0.78	0.570

AL, axial length; F, female; M, male; M-C, myopia-control group; M-RL, myopia RLRL group; PM-C, premyopia-control group; PM-RL, premyopia RLRL group; RLRL, repeated low-level red light ; SE, spherical equivalent refraction.

no statistically significant differences in age, sex, baseline BCVA, baseline SE and baseline AL between the two subgroups in the myopia group (all p>0.05). The two subgroups in the premyopia group had similar results (table 1).

Baseline BCVA (logMAR) is shown in table 1. After 12-month treatment, BCVA (logMAR) in each group was: −0.007±0.023 in M-RL group, −0.009±0.025 in M-C group, −0.016±0.039 in PM-RL group, −0.009±0.026 in PM-C group, respectively. Repeated-measures ANOVA indicated that there was no statistical difference in BCVA before and after the treatment in each group (all p>0.05).

Change in SE

After 12 months, the SE change in the M-RL group was −0.078±0.375 D, while that of the M-C group was −0.861±0.556 D (p<0.001), indicating a 90.9% difference in SE change between the two groups. For the premyopic group, after 12 months, the average SE change of the PM-RL group was −0.181±0.417 D, while that of the PM-C group was −0.521±0.436 D (p=0.001), indicating a 65.3% difference in SE change between the two groups. The detailed changes of SE in the four groups at each follow-up time point are shown in figure 2A. In the RLRL group, the myopia group had an average SE change of 0.103 D less than that of the premyopic group after 12 months of treatment. However, the two groups had no statistical difference (p=0.28).

Change in AL

After 12 months, the average AL change of the M-RL group was 0.033±0.123 mm, while that of the M-C group was 0.415±0.171 mm (p<0.001), indicating a 92.0% difference in AL change between the two groups. After 12-month treatment in the premyopia group, the average AL change of the PM-RL group was 0.145±0.175 mm, while that of the PM-C group was 0.292±0.128 mm (p<0.001), indicating a 50.3% difference in AL change between the two groups. The detailed changes of AL in the four groups at each follow-up time point are shown in figure 2B. In the RLRL group, the myopia group had an average AL change of 0.112 mm less than that of the premyopia group after 12 months of treatment (p=0.003). This suggests that RLRL showed a higher degree of delay in AL in the myopic population compared with premyopic patients.

To look at AL changes in all subjects after 12 months, AL changes are presented in a histogram (figure 3). In the control group, the myopic group (B) showed a broader distribution range of AL changes and greater variability than the premyopic group (A). In the RLRL group, the overall AL change shifted to the left (C and D), especially in the myopia group, which showed a more concentrated distribution.

AL shortening in RLRL

An AL shortening greater than 0.05 mm is defined as significant shortening,[8 24] and the percentage of subjects who achieve significant shortening is summarised in figure 4. In the M-RL group, the time point with the maximum AL shortening percentage was at 3 months after treatment, which was 53.1%. Additionally, 21.9% of the subjects still had a significant shortening in AL after 12 months of treatment. In the PM-RL group, the maximum AL reduction percentage was also at 3 months, which was 22.5% and there were still 12.5% of subjects with significant AL reduction at 12-month follow-up. It is worth noting that the percentage of AL reduction in the M-RL group was higher than that in the PM-RL group, and the difference was not statistically significant until 9 months of treatment (figure 4).

Myopia incidence in premyopia

In the PM-RL group, the incidence rate of myopia, defined as myopia detected who did not have myopia at baseline, was 2.5% at the 12-month follow-up. In contrast, in the PM-C group, myopia occurred as early as 6 months after treatment and myopia incidence increased to 19.4% over 12 months, which was 16.9% higher than that of the PM-RL group (χ^2=5.776, p=0.042) (online supplemental figure 1).

Compliance, baseline parameters and treatment effects

The average compliance rates in the myopia and premyopia groups were 86.2% and 83.5% (p=0.540), respectively. The compliance rate was not significantly correlated with 12-month AL change in both RLRL groups (p=0.053, p=0.131, respectively). Additionally, age, baseline AL and baseline SE were analysed to determine their effects on AL changes after 12 months of treatment. The results indicated that only the M-C group showed a negative correlation between age and AL change (r=−0.452,

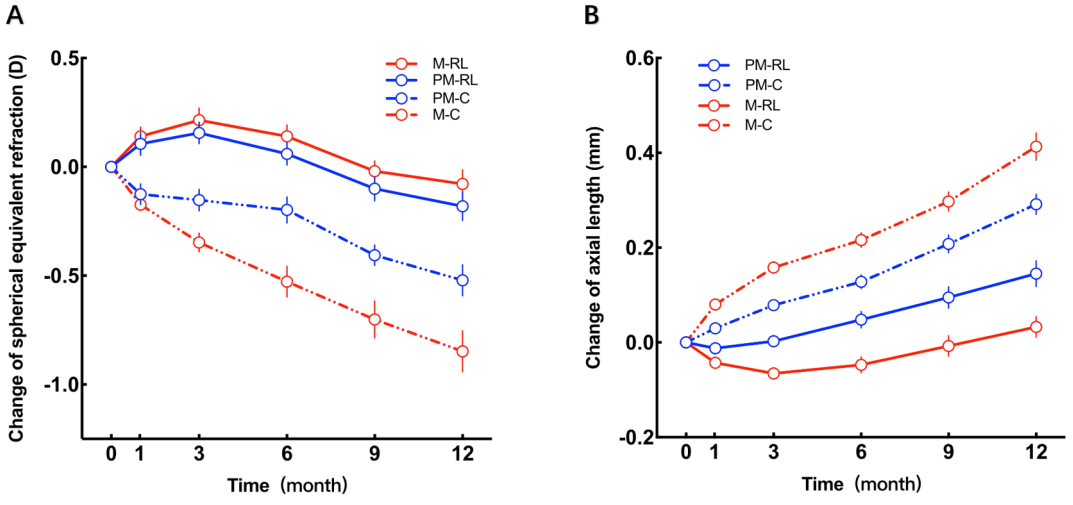

Figure 2 Time courses of change of spherical equivalent refraction (A) and axial length (B) in the four groups. Data was showed by mean±1 SE. M-C, myopia-control group; M-RL, myopia RLRL group; PM-C, premyopia-control group; PM-RL, premyopia RLRL group; RLRL, repeated low-level red light.

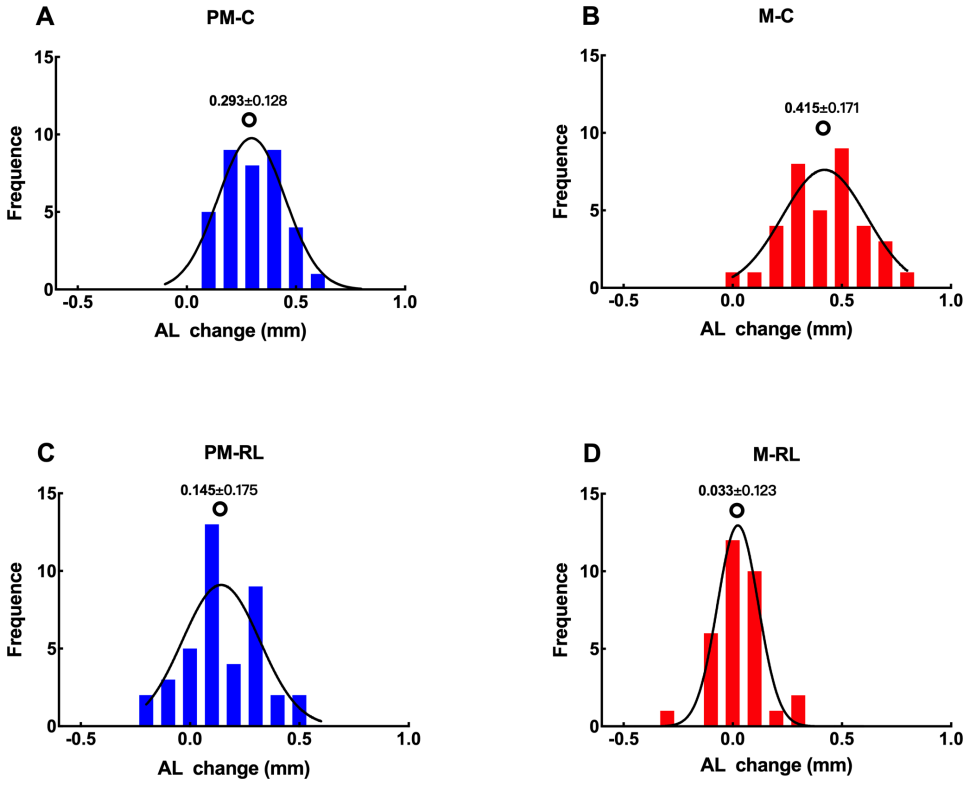

Figure 3 The distribution frequency of AL changes in four groups after 12 months of follow-up. A Gaussian curve is fitted to the distribution map (black line). AL, axial length; M-C, myopia-control group; M-RL, myopia RLRL group; PM-C, premyopia-control group; PM-RL, premyopia RLRL group; RLRL, repeated low-level red light.

p=0.006), and none of the other parameters or groups had statistically significant effects on AL change (all p>0.05).

DISCUSSION

This study found that RLRL could not only effectively delay myopia progression in children with myopia but also lower the incidence of myopia in premyopic children. Moreover, compared with premyopic children, RLRL showed better AL and SE control effects in children with myopia.

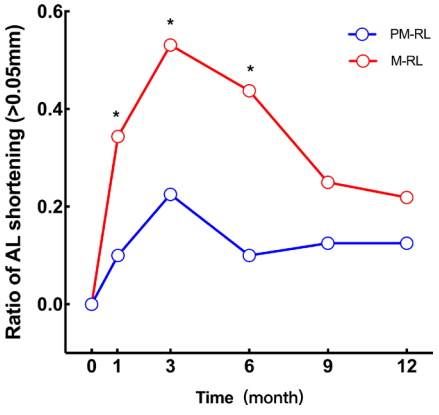

Figure 4 The percentage of subjects showing significant AL shortening during the treatment. Axial length (AL) shortening (>0.05 mm) was defined as a significant shortening. A *indicated that there was a statistical difference between the two groups in the χ^2 test (p<0.05). M-RL, myopia-RLRL group; PM-RL, premyopia-RLRL group; RLRL, repeated low-level red light.

Myopia control and RLRL

A recent meta-analysis revealed that RLRL could slow the elongation of AL by an average of 0.29 mm per year compared with the control group wearing single-vision spectacles.[25] Previous studies evaluated 16 intervention methods for myopia control.[4] It was found that high concentrate atropine (1% or 0.5%) was the most effective strategy, which can delay the increase in AL by an average of 0.21 mm compared with the placebo. Gong *et al*'s meta-analysis on the efficacy of different concentrations of atropine for myopia control showed that high concentrate atropine (1% or 0.5%) delayed the AL elongation by an average of 0.27 mm per year.[26] This suggests that RLRL may have a higher potential as an intervention to control myopia.

In this study, the change in AL in the M-RL group was 0.033±0.123 mm after 12 months of treatment and was delayed by an average of 0.38 mm compared with the control group (0.413±0.176 mm). This result is similar to Chen's study, with an average change in AL of 0.01 mm in 12-month treatment,[9] but different from Jiang *et al*'s study with an AL change of 0.13 mm in 12 months.[8] This difference may be related to the compliance and dose-response of RLRL treatment. Jiang *et al*'s study indicated that compliance was related to myopia progression, and the group with compliance >75% had a lower change in AL than the group with compliance <50% (0.088 mm vs 0.210 mm). Although there was no correlation between compliance and AL change in this study, the compliance of the study subjects was all above 75%. On the other hand, in Jiang *et al*'s study, the protocol was 5 days a week, while this study was designed for 7 days per week, which may also be a reason for the less AL growth in this study. Future research could focus on the difference in myopia control effect with different treatment frequencies.

Myopia prevention and RLRL

Reported methods for myopia prevention include outdoors, reducing near-work and low-concentration atropine.[13–16 27–31] RLRL treatment's effectiveness, intervention method and convenience (twice daily for 3 min each time) make it a promising emerging myopia prevention method likely to be accepted by many participants and their families. In this study, after 1 year of RLRL treatment in premyopia, AL and SE progress was significantly slower compared with the control group (0.128 mm vs 0.292 mm, −0.181 D vs −0.521 D). The incidence of myopia in the PM-RL group was significantly lower than that in the PM-C group. Another study on RLRL for premyopic children found that the myopia incidence rates of the intervention group and the control group were 40.8% and 61.3%, respectively.[24] Both results were significantly higher than those of this study. First, the study by He *et al* was conducted during the severe outbreak of COVID-19, when children were almost always doing near-work indoors, which increased the risk of myopia progression. Furthermore, He *et al*'s study found that the RLRL treatment was more effective in children with a baseline SE between 0.01 D and 0.50 D than for those with an SE between −0.5 D and 0 D, with an incidence rate of myopia as high as 83.1%. In their study, this subgroup accounted for 39.4%, while in this study, it only accounted for 27.5%. In addition, due to the impact of the pandemic, there were cases of intervention interruption among some participants in He *et al*'s study, which led to a decrease in the effectiveness of the intervention. Meanwhile, all participants who completed the 12-month follow-up in this study had a compliance of over 75%. Finally, considering the dose-response effect of RLRL in myopic children (7 days/week vs 5 days/week), this may also be a reason for the difference between our study and the study from He's group.[8 24] There is limited research on using RLRL for myopia prevention in premyopic children, and more long-term studies are needed to support the therapeutic effect.

The difference in myopia and premyopia after RLRL

In this study, the M-C group showed higher AL elongation and SE progression compared with the PM-C group, but in the RLRL group, the myopic subgroup showed a greater delay in AL and SE changes. Additionally, we found that both RLRL subgroups showed AL shortening. However, the amplitude of AL shortening was greater in the myopic subgroup than in the premyopic subgroup.

There is ample evidence for homoeostatic mechanisms in early life.[10 32] During the first few years of life, the eye grows toward emmetropia, a process called emmetropisation. In this theory, the homoeostatic effect could keep eye growth from changing too fast.[10] On the other hand, myopia might be considered a surrogate variable for the failure of regulated growth to achieve or maintain an emmetropia.[10 12] Due to the disruption of the homoeostatic effect, the myopic population exhibited faster eye growth development than the non-myopic population. Previous studies have shown that myopic children have more rapid AL and SE development than non-myopic children.[22 23] In this study, after RLRL treatment, the premyopic children had lower efficacy than the myopic children. We speculate that myopia prevention and control interventions may interfere with homoeostasis. Based on this assumption, the homoeostatic effect could develop in two ways, which holds both axial elongation and shortening amplitude from changing too much. It is worth noting that previous studies on atropine had also reported similar differences in efficacy between myopic and non-myopic populations.[5 13 14 26 27 33]

Previous studies showed that choroid thickens after RLRL treatment, and such change at 3 months could predict 12-month myopia control efficacy.[25 34] This suggested that although changes in choroidal thickness cannot fully explain the phenomenon of AL shortening after RLRL treatment, there was a significant correlation with the treatment effect. In addition, previous studies indicated that choroidal thickness in myopic children was thinner than in non-myopic children, and as myopia progressed, choroidal thickness also decreased.[35 36] We suppose that myopic children may have a higher degree of improvement in choroidal thickness compared with non-myopic children, which might also be a reason for the lower AL and SE changes in the myopic subgroup.

Adverse events

In this study, no patients experienced any severe adverse reactions or issues. Only three participants reported about the light being too intense in the early stage. Still, their subjective assessment indicated that the after-image was less than 4 min, and there were no abnormal changes in follow-up visits. No such issues were reported in the follow-up visits 1 month after treatment. Tang *et al*'s meta-analysis indicated that none of the studies reported vision-threatening events such as glare, flash blindness, or afterimages after treatment and no structural damage was observed on the photosensory layer from optical coherence tomography (OCT) images.[25] However, a recent case reported bilateral vision loss lasting 2 weeks after a 5-month RLRL treatment. The child reported of abnormally bright light and prolonged afterimages after exposure to light. Fortunately, the bilateral outer retinal damage partially recovered, and the visual acuity improved to 20/25 OU 3 months after stopping the RLRL therapy.[37] Although a case like this is rare, more caution is needed because the most extended duration of the RLRL studies so far has been 2 years and longer-term effects are still unknown.

Our research indicates that RLRL could be beneficial to prevent myopia and delay the myopia onset. Only 6 min of treatment is convenient for regions with a high prevalence of myopia or lack of sufficient outdoor activities.[38] Previous studies have shown that OK lenses were not effective to all myopia due to the problem of cost, comfort, corneal staining or other complications.[39] For patients with high myopia, high astigmatism or flat corneas, it was also difficult to fit OK lenses.[40] In comparison, the advantage of RLRL therapy is its effect on both premyopes and myopes with no astigmatism limit. Recent studies investigated that 0.01% atropine has no significant effect on myopia control,[13] and the side effects aggravated with increasing concentration.[26] Therefore, for patients who were suffering ineffectual myopia control with OK lenses or low-dose atropine, RLRL treatment can be provided as an alternative or combined method for myopia control. In the future, it is necessary to evaluate the safety and effectiveness of RLRL combined with other myopia control methods.

There are several limitations to this study. First, there was no appropriate sham equipment for the control groups. Second, this study did not include choroid-related data, which may have a role in explaining the differences in treatment effects between the myopic and premyopic subgroups. In addition, this study did not evaluate the time course of a short-term rebound in AL after treatment discontinuation. Previous studies have reported AL rebound and choroidal thinning after RLRL discontinuation at 3 months, but the early stage and more detailed patterns of change are not yet known.

In conclusion, this study evaluated the effectiveness of RLRL in myopia prevention and myopia control. We found that RLRL cannot only effectively delay myopia progression in myopic children but also reduce the incidence of myopia in premyopic children. In addition, the effect of using RLRL in myopic children is higher than in premyopic individuals, and the specific reasons need further research.

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Contributors GL: Interpretation, methodology and manuscript drafting; HR: Data analysis and methodology; YL: Investigation and data acquisition; BW: data acquisition; BD: supervision; DS: data analysis; RW: Funding acquisition, study design and guarantor.

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Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval Written informed consent was obtained from all enrolled participants or their parents or guardians. All procedures adhered to the tenets of the Declaration of Helsinki and were approved by the Tianjin Medical University Eye Hospital ethics committee. The trial has been registered with the Chinese Clinical Trial Registry (ChiCTR2200062028).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. Data and materials are available upon request from the corresponding author at rwei@tmu.edu.cn.

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