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ORIGINAL RESEARCH

Efficacy of Multifocal Soft Contact Lenses in Reducing Myopia Progression Among Taiwanese Schoolchildren: A Randomized Paired-Eye Clinical Trial

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ABSTRACT

Introduction: To evaluate the efficacy and safety of myopia control using a multifocal soft contact lens designed with high peripheral add power in schoolchildren.

Methods: This 1-year multi-center, prospective, randomized, double-blind, controlled study enrolled myopic schoolchildren aged 6–15 years with refractive errors between − 1.0 D and − 10.0 D. Each participant was randomly allocated to wear a daily disposable multifocal soft contact lens as the treatment in one eye and a single-vision soft contact lens as the control in the other eye. The primary endpoints were changes in the cycloplegic spherical equivalent (SE) and axial length at 1 year.

Results: Fifty-two of the 59 participants (88.1%) completed the study protocol. The mean change in SE was − 0.73 ± 0.40 D in the treatment group. and − 0.85 ± 0.51 D in

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the control group (mean difference: − 0.12 ± 0.34 D, $p = 0.012$). The mean change in axial length was 0.25 ± 0.14 mm in the treatment group, and 0.33 ± 0.17 mm in the control group (mean difference: 0.08 ± 0.10 mm, $p < 0.001$). The treatment was well tolerated, and no serious adverse events were observed.

Conclusions: Treatment with multifocal soft contact lenses with high peripheral add power was effective in controlling the progression of myopia and axial length elongation in myopic schoolchildren.

Keywords: Axial length; Children; Myopia control; Multifocal soft contact lens; Peripheral myopic defocus

Key Summary Points

Myopia represents a growing global health issue characterized by ongoing deterioration. The prevalence of myopia in East Asia is extremely high.

The utilization of a peripheral high-add-power design in multifocal soft contact lenses can induce peripheral myopic defocus, potentially altering abnormal eyeball growth and serving as a viable option for myopia control treatment.

In this 1-year randomized paired-eye clinical trial involving myopic schoolchildren, it was found that eyes fitted with multifocal soft contact lenses exhibited a substantial decrease in myopia progression and axial elongation compared to those wearing single vision contact lenses.

The use of multifocal soft contact lenses featuring a peripheral myopic defocus optical design is a safe and effective approach for myopia control in children.

INTRODUCTION

Myopia is an escalating global health concern, with persistent deterioration. By 2050, the global prevalence of myopia is projected to reach 54%, with a high prevalence of 10% [1]. This issue is particularly severe in Taiwan, where findings from a national survey in 2017 revealed a staggering 90% prevalence of myopia and 24.16% prevalence of high myopia among 18-year-old schoolchildren [2]. Given the association of myopia with various ocular diseases such as cataract, retinal detachment, glaucoma, and myopic macular degeneration, it is crucial to reduce the risk of related visual impairment in the future for a growing number of myopic children [3, 4]. As a result, myopia control therapies have garnered extensive attention and application in ophthalmology to mitigate myopia progression and its associated risks [5].

Presently, evidence-based strategies for myopia control primarily include pharmaceutical treatment, using atropine eye drops and optical interventions such as orthokeratology, soft multifocal contact lenses, and specially designed spectacles [6]. Clinical practitioners can inform parents about the potential adverse effects associated with different treatment options and guide them in selecting a suitable control method based on their child's unique circumstances. Currently, most optical interventions are based on the theoretical principle that inducing myopic defocus in the peripheral retina may modify abnormal eyeball growth and reduce axial elongation [7, 8]. This involves achieving foveal focus while maintaining myopic defocus in the peripheral retina. Recent studies have suggested that greater degrees of peripheral myopic defocus can lead to more effective control of axial elongation in the eye [9]. A high peripheral myopic defocus can be achieved using a high-add-power design in multifocal soft contact lenses.

The objective of this study was to assess the effectiveness and safety of a multifocal soft contact lens with a high peripheral add power design for myopia control in schoolchildren.

METHODS

Study Design

This prospective, randomized, double-blind, placebo-controlled study was conducted at three sites at two medical centers in Taiwan (National Taiwan University Hospital and Chang Gung Memorial Hospital, Linkou and Taipei branches). Eligible participants were randomly assigned to receive either the multifocal soft contact lens (test lens) or the single-vision soft contact lens (control lens), worn in the left or right eye. Such a paired-eye design could mitigate variations associated with myopia progression among participants, including differences in lifestyle or genetic susceptibility, leading to a balanced comparison between the treatment and control groups. The study spanned 50 weeks, encompassing a 2-week screening phase, followed by a 48-week treatment period involving ten visits. A schematic rendition of the study design is presented in Supplement Fig. S1.

Eligibility Criteria

The study recruited schoolchildren aged 6–-15 years, irrespective of sex, presenting with a spherical equivalent (SE) refractive error ranging from − 1.00 D to − 10.00 D in both eyes. Inclusion criteria encompassed a minimum visual acuity of 0.8 with contact lenses in each eye, astigmatism equal to or below 1.50 D, anisometropia less than or equal to 1.00 D, and willingness to adhere to the assigned contact lens usage and study protocol. Participants were excluded if they had amblyopia, strabismus, pathologically dry eyes, aphakia, ongoing ocular infections or inflammation, severe ocular allergies, anterior segment abnormalities, corneal vascularization exceeding 1 mm, or a history of herpetic keratitis. Additional exclusion conditions included the use of atropine, orthokeratology, or other myopia control treatments within the previous month; presence of systemic diseases affecting vision or contact lens wear; surgically altered eyes; and long-term use of certain medications that might disrupt contact lens wear, tear production, or refractive state (e.g., pseudoephedrine, antihistamine).

Randomization and Masking

A permuted block randomization approach with a 1:1 ratio was employed to allocate participants into two distinct arms, structured as follows: (A) left eye as treatment and right eye as control, or (B) left eye as control and right eye as treatment. The treatment group wore multifocal soft contact lenses, whereas the control group wore single-vision soft contact lenses in the opposite eye. Utilizing SAS 9.4 software, randomization code lists were produced at each study site by an independent code programmer. The randomized data remained inaccessible to all study personnel, preserving the integrity of the blinding process. The corresponding study group for each participant was securely documented within sealed envelopes, maintaining confidentiality until the data lock point.

Intervention and Control

Randomized participants were assigned to wear a multifocal soft contact lens (Largan Myopia Control Soft Lens) as the intervention in one eye, and a single-vision soft contact lens (Largan 1-Day Soft Contact Lens) as the control in the other eye. Before the formal study phase, eligible participants received Largan 1-Day Soft Contact Lens pairs during the screening visit to facilitate lens fitting and familiarity with wearing. The multifocal soft contact lens, the investigational product, had specific attributes including a composition of 45% HEMA copolymer, 55% water content, oxygen permeability of 18×10^{-11} (cm^2/s) ($mlO_2/ml \times mmHg$) @ 35 °C, a blue tint, UV blocking with Benzophenone UV absorbing monomer, diameter ranging from 10.0 to 16.0 mm, and base curve ranging from 6.5 to 10.8 mm. Being available in powers from − 10.00 D to + 0.00 D, it offered a peripheral progressive add power ranging from + 3.00 to + 5.50 D. The lenses were subjected to daily disposable wear. Both the intervention and control lenses were

supplied by Largan Medical Co., Ltd., and the study kits were prepared, packaged, and distributed by the same company. Lens power was prescribed based on the data of cycloplegic refraction and over-refraction. The participants were instructed to wear the lens for at least 8 h per day, 6 days a week. However, during the adaptation period, wearing them for less than 8 h per day was acceptable. The participants were also instructed to avoid overnight use, as this would increase the risk of complications. Lenses were re-prescribed during the study period if the subject's visual acuity with the contact lenses was < 20/25.

Participants were eligible for withdrawal from the study under various circumstances, including voluntary consent withdrawal, loss of interest in contact lens wear, inability to comply with the protocol (e.g., not wearing lenses for a cumulative 10 weeks), experiencing discomfort or unsatisfactory vision with the lenses, encountering adverse reactions that rendered them unfit for lens wear, facing persistent difficulties in lens handling despite training, and receiving other treatments affecting study efficacy, as decided by the investigator. In line with ethical considerations, participants displaying rapid myopia progression within the initial 6 months of the study (defined as an increase of 1.00 D accompanied by axial elongation) were also withdrawn. The participants were subsequently offered alternative myopic control treatments.

Outcomes (Primary and Secondary)

This study encompassed two primary outcomes: changes in cycloplegic spherical equivalent and changes in axial length between the two eyes over the entire study period (48 weeks). Cycloplegia was induced using three consecutive drops of 1.0% tropicamide separated by 5-min intervals. Measurements were taken 15 min after the third drop of tropicamide. The devices used to measure refraction and axial length at each study site are listed in Supplementary Table S1. The identical instruments were consistently used for all the initial assessment and follow-up visits for each study participant. Secondary outcomes included tracking these changes at 12, 24, and 36 weeks, treatment compliance rates, and participants' self-assessment of visual symptoms. The treatment compliance rate was calculated as the number of days of actual wearing hours of at least 8 h/288 days (6 days/week for 48 weeks).

Adverse Events

For the safety evaluation, adverse events (AEs) were reported with a detailed breakdown, including count and percentage metrics. These data included participants with AEs, total AE occurrences, AEs linked to the study product, and their severity. Serious AEs were defined as those resulting in fatality, life-threatening scenarios, a substantial decline in best-corrected visual acuity by two lines, or necessitating hospitalization. Severe AEs included incapacitating or sight-threatening occurrences, whereas moderate AEs included interference with daily activities and/or treatment with prescription medications.

Sample Size

The study's sample size determination was based on a two-sided alpha level of 0.05 for a superiority t test, a robust 90% power, and a mean change difference of -0.22 ± 0.36 D in cycloplegic refractive error at week 48 between treatment and control groups [10]. This translated into 47 eyes per arm (94 eyes in total). Factoring in an estimated 20% dropout rate, the adjusted enrolment was set at 59 eyes per arm (118 eyes in total). Similarly, an assumed -0.10 ± 0.13 mm difference in mean axial length change at week 48 between treatment and control groups [11], warranted 30 eyes per arm (60 eyes total) for 90% power at a two-sided alpha of 0.05. Accounting for a 20% dropout rate, the adjusted enrollment target was 38 eyes per arm (76 eyes in total). To ensure the robustness of both clinical parameters, 118 eyes (59 patients) were selected for enrollment.

Statistical Analysis

Paired *t* tests were used to demonstrate the primary outcome differences between the treated and control eyes. A two-sided significance level of 0.05 was considered as statistically significant. For other secondary outcomes, paired *t* test and McNemar's test were used for continuous and categorical variables, respectively. All statistical analyses and graph drawing were performed using SAS version 9.4 and R statistical software, version 4.1.2.

Ethics

This study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments. The study protocol was approved by the institutional review boards of both medical centers, and registered on ClinicalTrials.gov. (IRB approval No.: 201709029DSA [NTUH], 201701288A0D001 [CGMH]; Clinical trial registry No.: NCT03413085). Written informed consent was secured from parents or legal guardians, and participants provided written assent too.

RESULTS

Sixty-three participants provided informed consent, and four failed the initial screening for enrollment. A total of 59 participants were randomized to wear the control and test lenses in either eye. The mean age was 11.1 ± 1.96 years. Thirty-eight patients (64.4%) were female. The baseline characteristics of the treated and control eyes are shown in Table 1. Fifty-two participants (88.1%) completed the study protocol and were included in the treatment efficacy analysis (Fig. 1). Some participants did not complete the protocol due to early termination of contact lens use in both the treated and control eyes. The reasons for early termination were: no longer interested in wearing contact lenses (three participants), rapid myopia progression (myopia increased by 1.00 D or more within 6 months), seeking other myopia control treatments (three participants), and withdrawal of consent (one participant).

Primary Outcome

The mean change in SE from baseline at week 48 was − 0.73 ± 0.40 D in the treatment lens group and − 0.85 ± 0.51 D in the control lens group (mean difference:

− 0.12 ± 0.34 D, 95% confidence interval [CI] − 0.22, − 0.03, $p = 0.012$) (Fig. 2A). The treatment lens group demonstrated a 52.3% reduction in myopia progression compared with the control lens group. The mean change in axial length from baseline at week 48 was 0.25 ± 0.14 mm in the treatment lens group and 0.33 ± 0.17 mm in the control lens group (mean difference: 0.08 ± 0.10 mm, 95% CI 0.05, 0.11, $p < 0.001$) (Fig. 2B). The treatment lens group demonstrated a 25.1% reduction in axial length elongation compared with the control lens group.

Secondary Outcomes

The mean change in SE from baseline at week 12, week 24, and week 36 were − 0.35 ± 0.28 D, − 0.47 ± 0.29 D, and − 0.59 ± 0.33 D in the test lens group, and − 0.29 ± 0.28 D, − 0.48 ± 0.35 D, and − 0.60 ± 0.38 D in the control lens group, respectively. No significant differences were noted between the groups at these points in time (Fig. 2A). The mean change in axial length from baseline at week 12, week 24, and week 36 were 0.07 ± 0.07 mm, 0.13 ± 0.09 mm, and 0.20 ± 0.12 mm in the test lens group, and 0.10 ± 0.07 mm, 0.18 ± 0.11 mm, and 0.25 ± 0.16 mm in the control lens group, respectively. Significant differences were noted between the groups at these time points (all $p < 0.05$) (Fig. 2B).

The mean compliance rate to the protocol-specified wearing time was 95.0 ± 16.6%. Owing to the paired-eye design, the compliance rate remained consistent for both the treatment and control eyes within each participant. Supplement Table S2 presents the outcomes of the participants' self-assessments of visual symptoms. In summary, 96.1% of the participants

Table 1 Baseline clinical characteristics of the studied eyes

Clinical characteristics	Treatment lens (N = 59)	Control LENS (N = 59)	p value
Snellen visual acuity, unaided	0.2 ± 0.12	0.2 ± 0.16	0.426
Snellen visual acuity with contact lens	1.0 ± 0.11	1.0 ± 0.10	0.108
Spherical equivalent (D)	− 3.74 ± 1.49 (range − 7.40, − 1.40)	− 3.71 ± 1.65 (range − 8.25, − 1.35)	0.607
Axial length (mm)	24.85 ± 0.85 (range 22.90, 27.06)	24.83 ± 0.89 (range 23.02 to 27.27)	0.757
Horizontal corneal curvature (D)	43.00 ± 1.27	42.96 ± 1.31	0.646
Vertical corneal curvature (D)	44.15 ± 1.35	44.22 ± 1.41	0.077
Intraocular pressure (mmHg)	16.64 ± 2.69	16.43 ± 2.39	0.469
Conjunctiva papilla/follicles	1 (1.7)	1 (1.7)	NA
Abnormal tear film evaluation, n (%)	0 (0)	0 (0)	NA
Corneal fluorescein staining, n (%)	1 (1.7)	2 (3.4)	0.99
Abnormal fundus examination, n (%)	0 (0)	0 (0)	NA

D diopter, *NA* not available

expressed being either "very comfortable" or "comfortable" in their overall assessment of comfort of the treated eyes. Participants reported a modest occurrence of mild symptoms such as sensations of dryness, burning, itching, photophobia, tearing, and unstable vision (ranging from 1.9 to 13.5%). However, no substantial differences were observed between the treated and control eyes. Notably, none of the participants reported glare, halo, or reading difficulties with the treated eye.

Subgroup Analyses

The results of subgroup analyses for the two primary endpoints (differences of change in SE and axial elongation between treatment and control lens group at week 48) based on baseline age group (6–12 and 13–15 years), gender, baseline spherical equivalent (< − 3.00 D and ≥ − 3.00 D), the compliance rate (> 90% and ≤ 90%), and whether the treatment lens was applied on dominant eye (yes and no), are presented in Fig. 3. Statistical significance was observed in the difference in SE change among subgroups with younger age, female sex, higher baseline myopia, better compliance rates, and treatment lens assigned to dominant eye. Similarly, the difference in axial elongation was statistically significant within the subgroups of younger age, both male and female, low and high baseline myopia, better compliance rates, and treatment lens assigned to dominant and non-dominant eye.

Adverse Events

Throughout the study period, the average daily lens wearing hours was comparable between treatment and control eyes (11.50 ± 1.68 vs. 11.52 ± 1.68, p = 0.12). Eighteen of the 59 participants (30.5%) experienced at least one eye-related AE. All of them were mild. None of the participants experienced severe AE. The

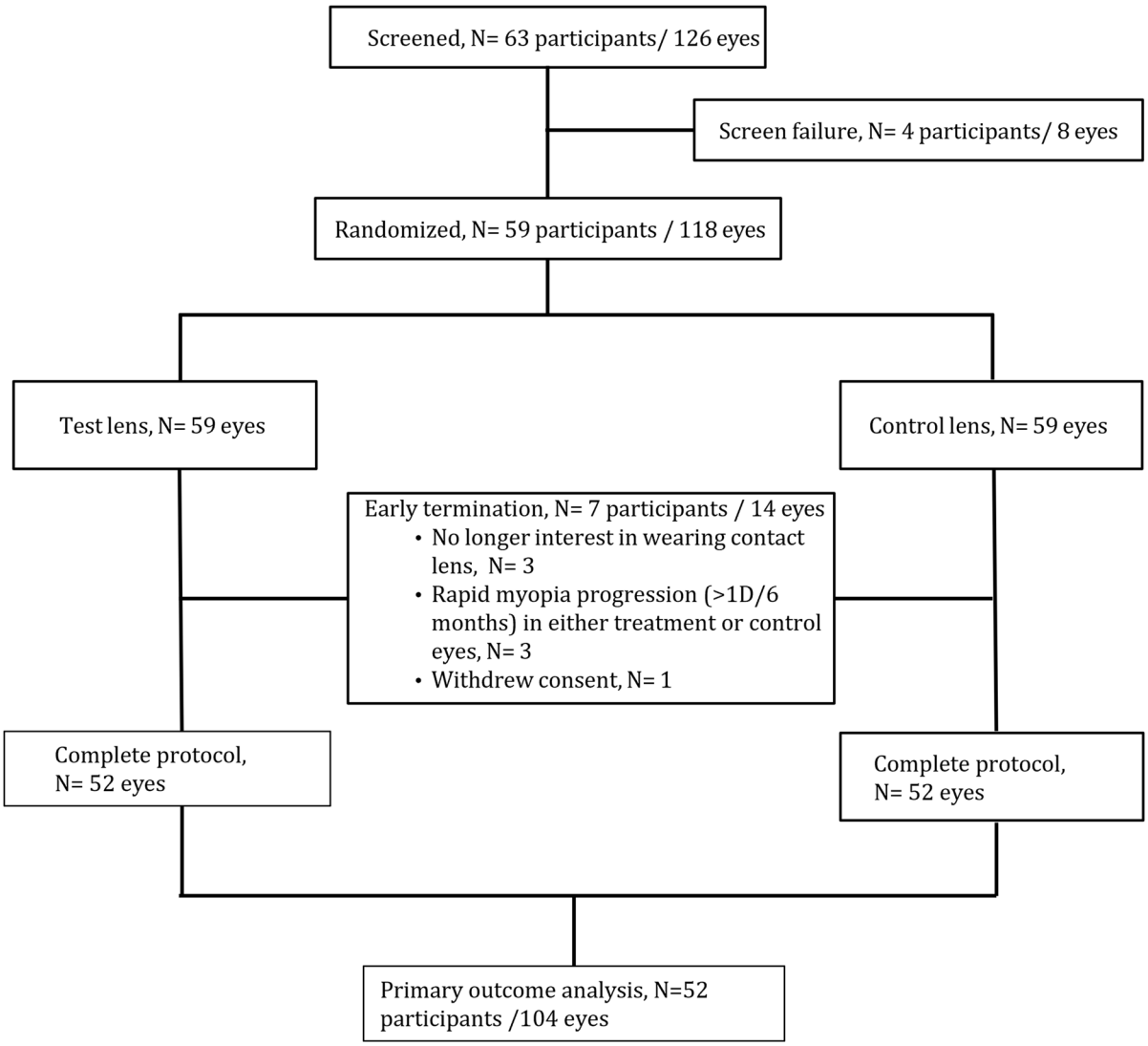

Fig. 1 Flowchart of participant enrollment

reported eye-related AEs in the test lens group were hordeolum (n = 5, 8.5%), allergic conjunctivitis (n = 4, 6.8%), acute conjunctivitis (n = 4, 6.8%), corneal epithelial defect (n = 2, 3.4%), chalazion (n = 1, 1.7%), and subjectively-reported unstable vision (n = 1, 1.7%). The most frequently reported eye-related AEs in the control lens group were acute conjunctivitis (n = 4, 6.8%), allergic conjunctivitis (n = 3, 5.1%), corneal epithelial defect (n = 2, 3.4%), hordeolum (n = 1, 1.7%), chalazion (n = 1, 1.7%), and subjectively reported unstable vision (n = 1, 1.7%). Among these, only five (8.5%) AE were judged to be treatment-related (one hordeolum, three allergic conjunctivitis, and one subjectively reported unstable vision). All patients recovered after receiving the corresponding ophthalmic treatment, with or without transient discontinuation of treatment lens or control lens wearing.

At week 48, three participants experienced anisomyopia greater than 1.00 D, but none exceeded 1.25 D. There was no significant difference between treatment and control eyes in the mean change of horizontal corneal curvature, intraocular pressure, and other ophthalmologic findings from baseline, except that the mean change of vertical corneal curvature in

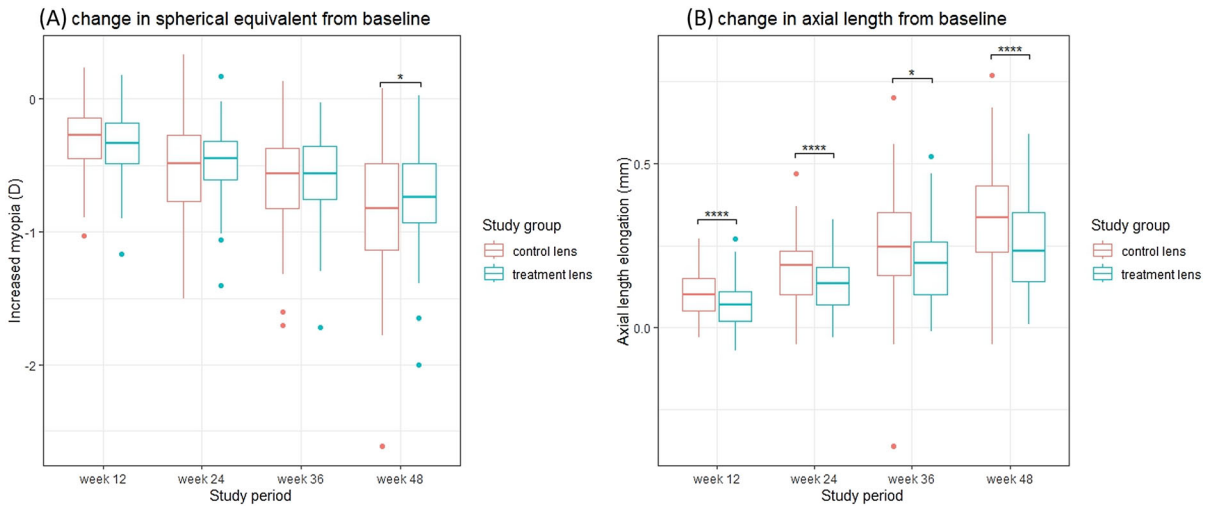

Fig. 2 Changes of cycloplegic refraction (**A**) and axial length (**B**) in the treatment and control groups during the study period. *$p < 0.05$; **** $p < 0.001$ by paired t test

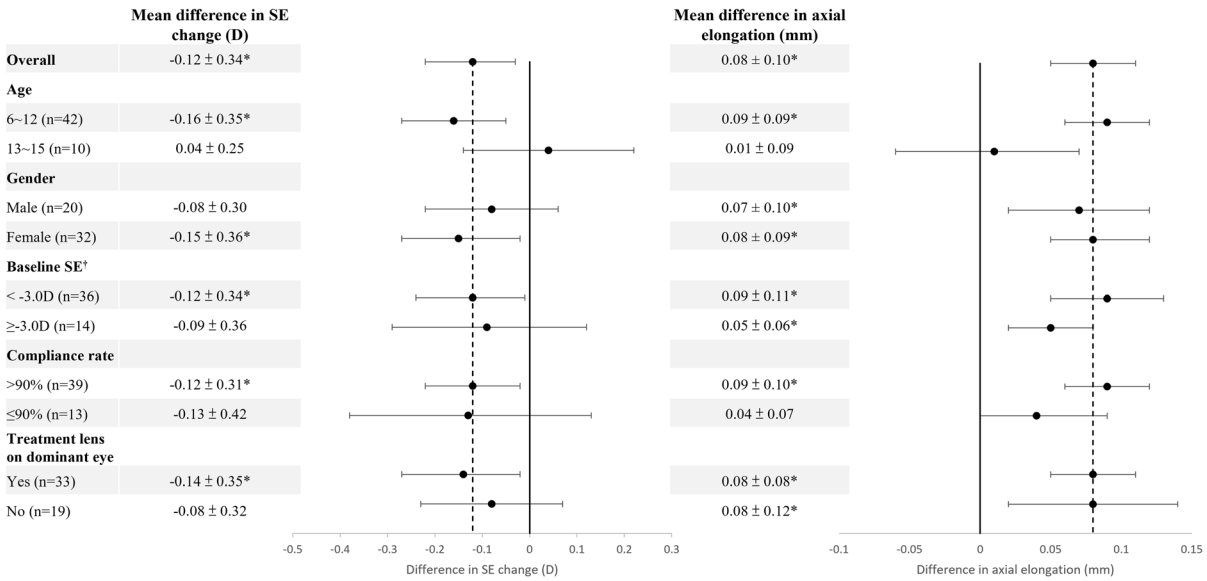

Fig. 3 Differences of change in spherical equivalent and axial length elongation between treatment and control lens group at week 48, stratified by baseline age, gender, baseline myopia, compliance rate, and dominant eye. *SE* spherical equivalent, *D* diopter. *Indicates $p < 0.05$ by paired t test.

†The summation of numbers within the subgroup based on baseline SE does not align with the total participant count, as two participants, whose treatment eye and control eye were placed in a different subgroup, were excluded from the analysis

the treatment eyes was significantly larger than the control eyes (0.17 ± 0.33 D vs. − 0.02 ± 0.37 D, $p < 0.001$) (Table 2). This was also observed at 12, 24, and 36 weeks. However, the mean vertical corneal curvature at each visit was comparable between the groups. Based on the final ophthalmological findings, these changes did not lead to corneal disorders and were not clinically significant.

Table 2 Change of ocular parameters and ophthalmologic findings in treatment and control eyes at week 48

Ocular parameters/ophthalmological findings	Treatment lens ($N = 52$)	Control lens ($N = 52$)	p value
Average daily lens wearing hours	11.50 ± 1.68	11.52 ± 1.68	0.12
Change in horizontal corneal curvature (D) from baseline	0.03 ± 0.20	0.03 ± 0.33	0.464
Change in vertical corneal curvature (D) from baseline	0.17 ± 0.33	− 0.02 ± 0.37	< 0.001
Change in intraocular pressure (mmHg) from baseline	− 0.24 ± 2.37	− 0.03 ± 2.37	0.469
Conjunctiva papilla/follicle, *n* (%)	0 (0)	0 (0)	NA
Abnormal tear film evaluation, *n* (%)	0 (0)	0 (0)	NA
Corneal fluorescein staining, *n* (%)	0 (0)	0 (0)	NA
Abnormal fundus examination, *n* (%)	0 (0)	0 (0)	NA

D diopter, *NA* not available

DISCUSSION

In this 1-year, multicenter, double-masked, randomized paired-eye comparison study, multifocal soft contact lens featuring peripheral add power demonstrated significant reduction in myopia progression by 0.12 D and in axial elongation by 0.08 mm compared to the single-vision soft contact lens in schoolchildren. The treatment was well tolerated, with no reported severe adverse events and no significant adverse changes in eye structure.

The average age of the children enrolled in this study was 11.1 years. Among them, the control group exhibited an average increase of 0.85 D in myopia progression within one year. These data align with the average rate of myopia progression among Taiwanese schoolchildren, as indicated by previous nationwide surveys [2, 12], implying that the study population was not significantly different from the general population.

In previous clinical trials, comparisons between multifocal soft contact lenses and single-vision soft contact lenses yielded varying effect sizes, ranging from insignificance to a reduction of 0.57 D in myopia progression and 0.19mm axial elongation over a 1-year period [9, 13–17]. A meta-analysis indicated a weighted mean difference of 0.22 D in myopia progression and 0.10 mm over the same duration [11]. Our study demonstrated a more modest effect size; nonetheless, a clinically meaningful reduction of 52.3% in myopia progression, as per the International Myopia Institute consensus, was observed [18, 19].

Subgroup analyses within this study revealed a more pronounced effect in younger children, those with lower baseline myopia, and those with higher compliance rates. These outcomes are consistent with a broader body of research [12, 20–22], which indicates that younger children with lower baseline myopia tend to exhibit greater progression, thus providing a clearer demonstration of the effectiveness of myopia control treatments.

A recent study indicated that multifocal soft contact lenses with + 2.5 D peripheral add power exhibited a more robust myopia control effect than those with + 1.5 D add power [9]. The former demonstrated a reduction of 0.24 D in myopia progression during the first year, whereas the latter exhibited a reduction of 0.08 D. This disparity could be attributed to the greater induction of peripheral myopic defocus. In our study, the multifocal soft contact lenses evaluated were designed with a higher peripheral add power range of + 3.00 to + 5.50 D; however, they did not exhibit a proportionally larger effect size. It is plausible that there is an upper threshold for the myopia control effect

when peripheral add power induces peripheral myopic defocus. Further investigations are warranted to test this hypothesis.

This study has several limitations. First, conventional myopia control treatments typically require several years of implementation because of the ongoing risk of myopia progression in the teenage years. However, this research spanned only one year, precluding a comprehensive assessment of the long-term effectiveness of myopia control and changes in myopia progression among children after treatment cessation. Second, the pre- and post-intervention accommodation lag, the corrected peripheral refraction, and the contrast sensitivity while wearing multifocal lenses with high add power were not assessed. However, no participants reported experiencing reading problems and visual symptoms of glare or halo in the treated eye, as indicated in their self-assessment reports (Supplement Table S2). Third, the primary population of this study consisted of East Asian children, rendering the results potentially less directly applicable to other ethnic groups.

CONCLUSIONS

In conclusion, the application of multifocal soft contact lenses in myopic schoolchildren led to a significant reduction in both myopia progression and axial elongation of the eyeball compared to single-vision soft contact lenses.

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Data Availability. The datasets generated during and analyzed during the current study are available from the corresponding author on reasonable request. Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Declarations

Conflict of Interest. Yao-Lin Liu, Ken-Kuo Lin, Chao-Wen Lin, Jiahn-Shing Lee, Chiun-Ho Hou, and Tzu-Hsun Tsai declare that they have no competing interests. Li-Sheng Cheng serves as a medical consultant for Largan Medical Co., Ltd.

Ethical Approval. This study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments. The study protocol was approved by the institutional review boards of both medical centers and registered on ClinicalTrials.gov. (IRB approval No.: 201709029DSA [NTUH], 201701288A0D001 [CGMH]; Clinical trial registry No.: NCT03413085).

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