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ORIGINAL ARTICLE

High Myopia–Partial Reduction Ortho-k: A 2-Year Randomized Study

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ABSTRACT

Purpose. To investigate if the combination of partial reduction (PR) orthokeratology (ortho-k) and spectacles for residual refractive errors in the daytime was effective to slow myopic progression in high myopic children.

Methods. High myopic children (aged 8 to 11 years) with spherical equivalent refraction at least −5.75 diopters (D) and myopia −5.00 D or more myopic were recruited and randomly assigned into PR ortho-k and control groups. Subjects in the PR ortho-k group were fitted with custom made four-zone ortho-k lenses with target reduction of 4.00 D for both eyes, and the residual refractive errors were corrected with single-vision spectacles for clear vision in the daytime. Control subjects were fully corrected with single-vision spectacles. Axial length of each eye of all subjects was measured with the IOLMaster at 6-month intervals by a masked examiner. This study was registered at www.clinicaltrial.gov with the identifier NCT00977236.

Results. Fifty-two subjects were recruited and randomized to the PR ortho-k and control groups. Twelve PR ortho-k and 16 control subjects completed the study. Compared with the residual refractive errors at the 1-month visit (after stabilization of ortho-k treatment), the median increase in noncycloplegic residual myopia at the 24-month visit was 0.13 D. In the control group, the median increase in myopia was 1.00 D at the end of the study. The mean ± SD increases in axial length were 0.19 ± 0.21 mm in the PR ortho-k group and 0.51 ± 0.32 mm in the control group (95% confidence interval, −0.55 to −0.12; unpaired *t* test, p = 0.005).

Conclusions. This single-masked randomized study showed that PR ortho-k effectively slowed myopic progression in high myopes. Axial length elongation was 63% slower in PR ortho-k–treated children compared with children wearing spectacles. (Optom Vis Sci 2013;90:530–539)

Key Words: myopia control, orthokeratology, high myope, myopic progression, partial correction

Myopic progression in children is of great concern in Asian countries, such as Hong Kong, China, Japan, and Singapore, because of the high prevalence of myopia in these populations. Fan et al.[1] reported that the prevalence of severe myopia (spherical equivalent refraction of −6.00 diopters [D] or more myopic) was 1.19% in Hong Kong. The annual myopic shifts were −0.63 D and −0.71 D for low (−0.50 to −2.99 D)- and high myopic groups, respectively. High myopes have also been reported to show faster myopic progression.[1–3] Degenerative changes of the vitreous, glaucoma, and myopic degeneration are complications associated with high myopia,[4,5] and many researchers are still investigating ways to slow myopic progression.

Single-vision spectacles and contact lenses of conventional designs have been shown to be ineffective for myopic control,[6,7] and treatments using progressive spectacle lenses/bifocals had not been successful.[8,9] Pharmaceutical agents (atropine and pirenzepine) have been reported to reduce myopic progression,[10,11] but side effects such as accommodation insufficiency and dilated pupils can affect daily activities.[11]

Orthokeratology (ortho-k) was shown to have a potential to reduce myopic progression in a number of nonrandomized clinical studies.[12–15] The LORIC study[12] and CRAYON study[13] used A-scan biometry to measure axial length progression, whereas Santodomingo-Rubido et al.[14] and Kakita et al.[15] used the Zeiss IOLMaster (Carl Zeiss Meditec, Inc., Dublin, CA). These studies reported that axial length elongation in subjects wearing ortho-k lenses were 36 to 56% slower when compared with that of subjects wearing spectacles.[12–15] A recent randomized single-mask study has however confirmed the efficacy of ortho-k for myopic control

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in children.[16] This study reported a 43% slower increase in axial length in children wearing ortho-k lenses compared with those wearing single-vision glasses.

Most ortho-k lenses available commercially and used in published reports are for low to moderate myopes only. However, there is little information about the safety and success rate in correcting higher refractive errors. Clinically, attempts at high myopic reduction using commercially available ortho-k lenses could result in corneal staining, heavy lens binding, and lens decentration.[17] In view of these potential problems and until lenses designed for high myopes are available, a more conservative approach for high myopes is to target for 4.00 D reduction and to correct the residual refractive errors with single-vision spectacles to allow good visual acuity in the daytime.

OBJECTIVE

The objective of this study was to investigate the efficacy, based on axial length elongation, of a combination of partial reduction (PR) overnight ortho-k and single-vision spectacles to correct the residual refractive errors in the daytime on myopic control in high myopic children.

METHODS

This was an intervention study using a stratified, randomized, parallel-group, and single-masked design to investigate axial elongation of the eyeball in myopic children wearing ortho-k lenses overnight and single-vision spectacles for residual refractive error in the daytime (PR ortho-k group) and single-vision spectacles (control group) for a period of 2 years. The subjects were stratified by age and sex to minimize systematic bias. Randomization was performed in blocks of two using a commercial spreadsheet random number generator (Excel, Microsoft, Redmond, WA). The randomization list was generated and inspected by an independent project member who was not involved in subject recruitment or data collection to ensure equal numbers of subjects assigned to each group. This project member revealed the random allocation sequence to the unmasked examiner after eligibility of subjects was confirmed (by the unmasked examiner). The unmasked examiner would then proceed to prescribe the assigned treatment to the subjects accordingly.

Subjects were recruited via advertisements posted in local newspapers and leaflets in the Optometry Clinic of the School of Optometry, The Hong Kong Polytechnic University. Eligible subjects and guardians were informed verbally and in writing about the nature, benefits, and risks of the study. Ethics approval for this study was obtained from the Departmental Research Committee of the School of Optometry at The Hong Kong Polytechnic University. All procedures were performed following the tenets of the Declaration of Helsinki, as revised in 2002, and written informed consent was obtained from the subjects and parents (and/or guardians) before commencing the study.

Subjects who were lost to follow-up, noncompliant with test procedures/schedule, contraindicated to continue ortho-k treatment (PR ortho-k group) were excluded from the study. The first and last subjects were recruited in June 2008 and January 2010, respectively, and the last data collection visit was in January 2012.

This study was registered in clinical trial at www.clinicaltrial.gov with the identifier NCT00977236.

Inclusion Criteria

Table 1 lists the inclusion criteria for this study. Only children aged 8 to 11 years with spherical equivalent refraction of at least 5.75 D and myopia of −5.00 D or more myopic (cycloplegic subjective refraction) were recruited.

Sample Size

To estimate the sample size of this study, we aimed for 80% power based on the SDs reported in the LORIC study[12] and to detect a 0.3-mm (~0.75 D) difference in axial length between the two groups. With the significant level of 0.05 (two-tailed), the sample size calculated was 14 in each group. To allow for 30% dropouts, at least 40 subjects should be recruited in total.

Lenses and Solutions Used

For the PR ortho-k subjects, the lens parameters for each eye were determined using the manufacturer's computer software (EyeLite, Procornea Ltd, The Netherlands).

The initial target of all lenses was 4.00D to attempt 4.00D myopic reduction. Once stabilization was confirmed (i.e. when changes in myopia and corneal curvatures at two consecutive visits (one week apart) were not more than 0.50D), if the myopic reduction achieved was less than 3.25D, a lens with a higher target was ordered and fitted until there was no further improvement. The subject would then continue to wear the previous lens with the lower target (i.e. the lowest target lens which gave the maximum myopic reduction).

The lens specifications and solutions used are shown in Table 2. A second pair of lenses with the same parameters as the stabilized

TABLE 1.
Inclusion criteria

Age	8–11 yr of age on the date of recruitment
Refractive errors	Cycloplegic manifest ocular refraction in either eye Spherical equivalent refraction ≤−5.75 D AND Myopia −5.00 D or more myopic
Visual acuity	Monocular Snellen 6/7.5 or better
Ocular health	No binocular vision problems No ocular conditions that might affect vision or vision development No contraindications for overnight orthokeratology lens wear
General health	No systemic conditions that might affect vision or development of the refractive errors
Others	No previous experience in myopic treatment (e.g., refractive surgery) Willing to wear orthokeratology lenses in accordance with instructions if assigned to partial reduction orthokeratology group Available for monthly follow ups at the PolyU Optometry Clinic for 24 mo after treatment commences Willing to comply with the prescribed aftercare/data collection visits

TABLE 2.
Specifications of orthokeratology lens and solutions

Orthokeratology lens (Procornea Ltd., Netherlands)	
Material	Boston XO
Design	4-zone (BOZR, RC, AC, and PC) Spherical or toric (toric reverse curve and/or alignment curve), depending on corneal parameters
Jessen factor	0.75 D
Oxygen permeability	100 Barrer
Back optic zone radius	7.20–9.50 mm (0.05-mm step)
Optic zone diameter	6.0 mm
Total diameter	10.5 mm
Lens central thickness	0.22 mm
Wearing modality	Overnight orthokeratology
Replacement period	1 yr
Remarks	Manufacturer's recommendation for this lens design is for target up to 4.50 D myopia
Solution used (Menicon Co., Ltd., Japan)	
Soaking and disinfecting	MeniCare Plus
Daily cleaning	Menicon O_2 Care
Weekly enzymatic cleaning	Menicon Progent
Replacement period	1 month

lenses was ordered for each subject after the desired myopic reduction was achieved. This pair of lenses acted as a spare pair in case of damage or loss or as an annual replacement pair where appropriate. All subjects had to learn how to insert and remove their lenses using their fingers without the aid of a suction holder (lens remover) and without any assistance from their parents. All subjects were prescribed a pair of single-vision spectacles for the correction of residual refractive errors for daytime wear after stability of the ortho-k treatment.

Spectacles

For the control subjects, single-vision spectacles were prescribed with maximum plus, which gave maximum visual acuity, and subjects were asked to wear the spectacles in the daytime during waking hours.

For PR ortho-k subjects, residual refractive errors were corrected with a pair of single-vision spectacles to be worn during daytime.

After the commencement of the study, the spectacle prescription would be updated at any subsequent visit for either group of subjects if there was an increase of more than 0.50 D in refractive error (sphere or astigmatism) at that visit compared with the baseline (control group) or the stabilized refractive errors (PR ortho-k group).

Examination Schedules and Procedures

All subjects were required to attend noncycloplegic and cycloplegic examinations at the baseline and every 6-month visits for 2 years. Partial reduction ortho-k subjects had to attend three extra noncycloplegic visits (first morning after commencing lens wear [1-overnight], 1 week [1-week], and 1 month [1-month]) after lens delivery to assess/confirm lens performance (Fig. 1). Extra aftercare consultations were provided as required during the study period.

All measurements, excluding axial length measurements, were performed by the same examiner throughout the study. Axial length measurements were made by a masked examiner. All measurements were made on both eyes, but only data from the right eye were analyzed and presented in this report.

Masking

This study was a single-masked design to eliminate any examiner bias on myopic progression. The masked examiner (not involved in patient care) only measured and recorded the axial length.

Ophthalmic Examination

Cycloplegic assessments included objective and subjective refraction, axial length measurement, and fundus examination. These assessments were made at the baseline and at every 6-month visit following the noncycloplegic examination at each visit (Table 3). One drop of 0.5% proparacaine (Alcaine; Alcon-Couvreur, Puurs, Belgium) was first instilled, followed 1 minute later by one drop of 1.0% tropicamide (Mydriacyl; Alcon-Couvreur), and

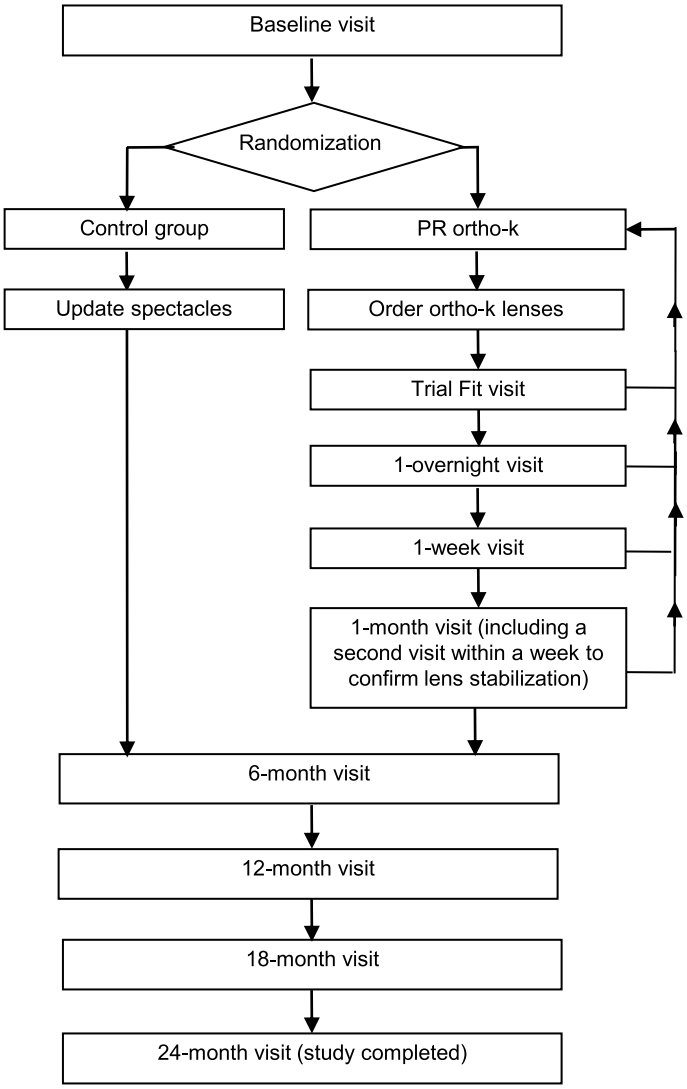

FIGURE 1.
Schedule of visits.

5 minutes later by one drop of 1.0% cyclopentolate (Cyclogy; Alcon-Couvreur). After 30 minutes, when no pupillary response was confirmed and the amplitude of accommodation was measured to be less than 2.00 D, cycloplegic measurements were made.

Objective refraction was performed with the Shin-Nippon Open field 5500K autorefractor (Ajinomoto Trading Inc., Japan). The autorefractor provided mean values of sphere and cylinder powers. Three measurements with any intermeasurement difference (of sphere and cylinder powers) of not more than 0.25 D were taken. The average value was calculated and used for analysis. Subjective refraction was measured in an examination room with lighting of 400 Lux, and the maximum plus maximum acuity was taken as the end point of refraction. Early Treatment Diabetic Retinopathy Study (ETDRS) chart series 2000 (Precision Vision, LaSalle, IL) were used to measure high (>90%) and low (10%) contrast visual acuity (VA). Three high-contrast (one for right eye, one for left eye, and one for binocular acuity) and one low-contrast charts were used. Both habitual VA and best-corrected VA (BCVA) were measured, with the high-contrast chart first, followed by the low-contrast chart. Habitual VA for the right eye was always assessed first, then the left eye, and finally both (binocular) eyes.

The anterior segment of the eyes of all subjects and lens-fitting evaluation of PR ortho-k subjects were performed using Topcon SL7 and Topcon IMAGEnet (Topcon Corporation, Japan). All corneal signs were graded using Efron grading scale where appropriate with photodocumentation.

Measurements of axial length were performed with Zeiss IOLMaster (Carl Zeiss Meditec, Inc.) by masked examiners after cycloplegia at baseline and at every 6-month visit. At each of these visits, the masked examiner was instructed to take the first five axial length readings with between-reading difference within 0.02 mm (as recommended by the manufacturer). The average data were used for analysis.

Corneal topography was performed with the Medmont E300 (Medmont International Pty Ltd, Australia) at baseline and at every 6-month visit for all subjects. Four corneal profiles, each with a score of 98 or above (as recommended by the manufacturer), were saved for each eye at each visit.

TABLE 3.
Data collection schedule

Data taking visits		Baseline	1-mo visit	Every 6 mo
Refraction (subjective and objective)	Precycloplegic	X	X	X
	Cycloplegic	X		X
BCVA (precycloplegic)	High contrast	X	X	X
	Low contrast	X	X	X
Photobiomicroscopy	Ocular health	X	X	X
	Lens assessment	-	X	X
Topography	Prefitting	X	-	-
	Postfitting	-	X	X
Corneal thickness	Precycloplegic	X	-	X
Pupillary response		X	-	X
Axial length	Postcycloplegic	X	-	X

Treatment of Data

Because data on age, pretreatment and posttreatment subjective spherical refractive error (myopia), and habitual VA were not normally distributed, nonparametric tests were used to analyze the data. Data for corneal thickness, axial length, flat K, and steep K were normally distributed, so parametric tests were used for analysis. The significance level was set at 0.05 with Bonferroni corrections, where multiple tests were performed. Medians and ranges were reported for data showing non-Gaussian distributions and mean ± SD for data that were normally distributed.

RESULTS

A total of 79 subjects were screened, and 52 eligible subjects were randomly assigned to the PR ortho-k (n = 26) and control (n = 26) groups at the baseline visit. After the first month of lens wear, only 19 subjects in each group continued in the study. At the end of the study, 16 control and 12 PR ortho-k subjects completed the study (Fig. 2).

No significant differences (Mann-Whitney *U* tests, $p > 0.05$) were found in the baseline demographic and ocular characteristics between subjects who completed the study and subjects who did not (Table 4).

Power of the Study

The power of this study, based on the sample size and axial length results, was 85% (95% confidence interval [CI], −0.55 to −0.12; unpaired *t* test, p = 0.005) (G*Power 3.0).

Baseline Data (of Completed Cases)

Table 4 also shows a summary of the baseline data of the two groups of subjects who completed the study. The median (range) age of the subjects was 10 (9 to 11) years and 10 (8 to 11) years in PR ortho-k and control groups, respectively. No significant differences in axial length, flat and steep K, and central corneal thickness were found between the two groups of subjects (unpaired *t* tests, $0.49 < p < 0.86$). Also, no significant between-group differences in age, precycloplegic subjective myopia and postcycloplegic subjective myopia and astigmatism, high- and low-contrast BCVA were found (Mann-Whitney *U* tests, $0.10 < p < 0.73$).

Ocular health presentation was comparable between the two groups (Table 5) (Fisher exact test, $0.175 < p < 1.000$). Corneal staining was found in four subjects (two in each group), but the severity was not more than grade 1.

Changes in Refractive Errors

Changes in myopia and astigmatism during the 2 years of monitoring are shown in Table 6 and Fig. 3. In the control group, five subjects were required to change their spectacles once during the study period (two at the 6-month visit, two at the 12-month visit, and one at the 18-month visit). In the PR ortho-k group, no change in lens target or daytime spectacles was necessary during the study period.

The myopia in the control group increased significantly over time (Friedman tests, $p < 0.001$). At the end of the study period, the median increase in myopia in the control group was −1.00 D (−2.50 to 0.50 D).

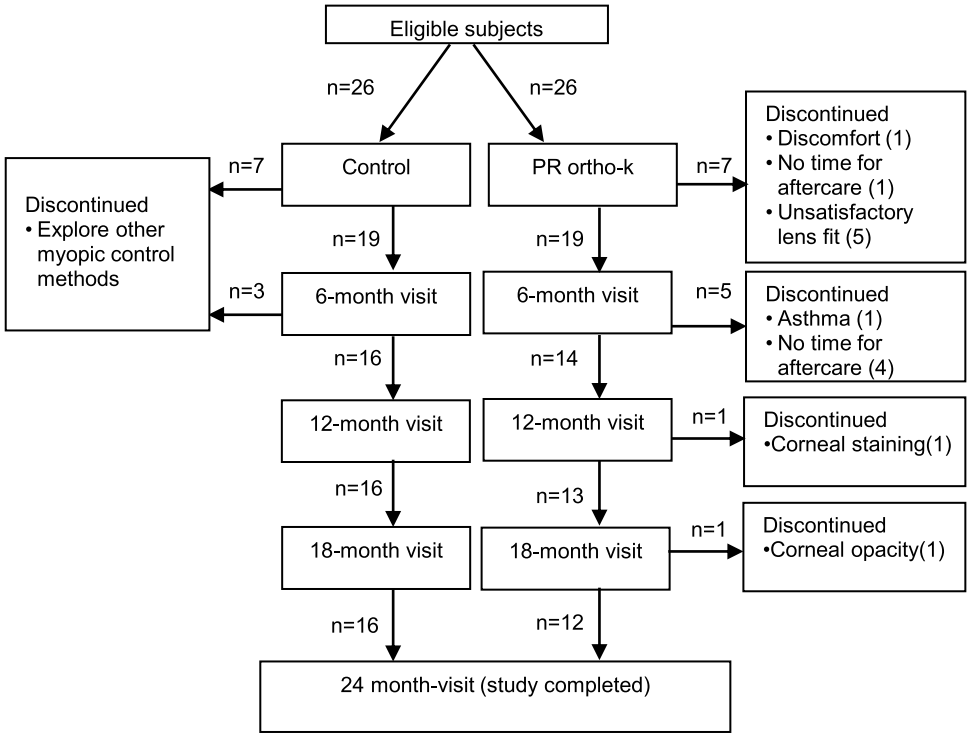

FIGURE 2.
Progression of subjects during the study period.

Compared with the residual refractive errors at the noncycloplegic 1-month visit (i.e., after stabilization of treatment), the median change (i.e., increase) in residual noncycloplegic myopia at the 24-month visit was −0.13 D (−0.75 to 1.00 D).

No significant increase in astigmatism in either group of subjects was observed during the 2-year study period (Mann-Whitney *U* tests with Bonferroni correction, $0.041 < p < 0.290$).

TABLE 4.
Baseline data of subjects who completed the study and those who did not

	All		Completed cases		Dropouts	
	PR ortho-k (n = 26)	Control (n = 26)	PR ortho-k (n = 12)	Control (n = 16)	PR ortho-k (n = 14)	Control (n = 10)
Age, yr	10 (8–11)	10 (8–11)	10 (9–11)	10 (8–11)	10 (8–11)	10 (8–11)
High-contrast BCVA (logMAR)	0.02 (−0.08 to 0.08)	0.04 (−0.10 to 0.16)	−0.04 (−0.08 to 0.06)	−0.05 (−0.20 to 0.14)	0.04 (−0.04 to 0.12)	0.04 (−0.08 to 0.18)
Low (10%)-contrast BCVA (logMAR)	0.25 (0.12–0.38)	0.22 (0.10–0.48)	0.25 (0.12–0.38)	0.17 (0.10–0.48)	0.36 (0.16–0.36)	0.22 (0.12–0.38)
Precycloplegic subjective Myopia, D	6.41 (5.00–8.00)	6.22 (5.00–8.00)	6.50 (6.00–8.30)	6.13 (5.00–8.30)	6.17 (5.25–7.50)	6.08 (5.25–9.00)
Postcycloplegic subjective Myopia, D	6.34 (5.00–8.00)	6.08 (5.00–8.00)	6.38 (5.75–8.25)	6.00 (5.50–8.00)	6.06 (5.00–7.50)	6.00 (5.25–9.00)
Postcycloplegic subjective Astigmatism, D	−0.68 (−1.75 to 0.00)	−1.09 (−2.00 to 0.00)	−0.63 (−1.50 to 0.00)	−1.00 (−1.50 to −1.00)	−0.69 (−2.00 to 0.00)	−1.10 (−1.75 to −0.50)
Axial length, mm	26.02 ± 0.57	25.93 ± 0.54	26.05 ± 0.80	25.97 ± 0.53	26.08 ± 0.64	25.73 ± 0.94
Flat corneal curvature, mm	7.78 ± 0.17	7.87 ± 0.16	7.78 ± 0.30	7.84 ± 0.13	7.82 ± 0.16	7.80 ± 0.31
Steep corneal curvature, mm	7.55 ± 0.18	7.60 ± 0.18	7.56 ± 0.29	7.58 ± 0.15	7.55 ± 0.16	7.51 ± 0.33
Central corneal thickness, μm	573 ± 46	573 ± 37	573 ± 56	581 ± 34	569 ± 35	560 ± 39

Values are presented as median (range) or mean ± SD.

TABLE 5.
Ocular signs (incidence [%]) observed in the two groups of subjects

		Baseline		6-mo		12-mo		18-mo		24-mo	
		PR ortho-k	Control	PR ortho-k	Control	PR ortho-k	Control	PR ortho-k	Control	PR ortho-k	Control
Corneal staining Grade 1 Efron Grading Scale	Central	0	0	16.7	0	16.7	8.3	0	16.7	8.3	0
	Inferior	16.7	12.5	8.3	18.8	25	16.7	25	25	16.7	25
	Nasal	0	6.3	8.3	0	8.3	16.7	6.3	8.3	16.7	6.3
	Superior	0	0	8.3	0	0	0	0	0	0	0
	Temporal	0	0	8.3	0	0	0	0	0	0	0
Pigmented arc	Inferior	0	0	92	0	100	0	100	0	100	0

No significant differences between the two groups of subjects at any visit (Fisher exact test, $0.175 < p < 1.000$), excluding pigmented arc.

High- and low-contrast BCVAs were not significantly different over time within-group (Friedman tests, $0.099 < p < 0.585$) or between groups at each visit (Mann-Whitney *U* tests, $0.093 < p < 0.586$).

Ocular Health

Corneal staining was observed in some subjects in both groups at each visit, but the incidence was generally higher in the PR ortho-k subjects (Table 5). However, all stainings observed were not significant (all were grade 1) between the two groups of subjects during the 2-year study (Fisher exact tests, $0.175 < p < 1.000$) (Table 5). No other adverse events were reported in either group of subjects who completed the study.

The incidence of pigmented arc among the PR ortho-k subjects at the 6-month visit was 92%. After 1 year of lens wear, the pigmented arc was found in all PR ortho-k subjects. The intensity of the pigmented arc increased with lens wear during the monitoring period.

Significant differences in central corneal thickness were found between the two groups at the 6-month, 18-month, and 24-month visits (Mann-Whitney *U* tests, $p = 0.011$, 0.026, and 0.026, respectively) (Fig. 4). No significant within-group differences were found at different visits during the study period (Friedman tests, $p = 0.359$ [PR ortho-k]; $p = 0.474$ [control]).

Len Binding and Lens Replacements

None of the PR ortho-k subjects reported lens binding at and after the 6-month visit. All subjects had a lens replacement at the 12-month visit (annual replacement) except for one subject who reported lens damage at the 6-month visit. Because a pair of spare lenses was ordered for each subject after the stabilization of treatment, this subject had an extra lens replacement (no change in lens parameters) during the study period without ceasing lens wear.

Axial Length Changes

Both groups of subjects showed increases in axial length during the 2-year monitoring period but at different rates (Fig. 5). Increases in axial length in the PR ortho-k group were significantly slower (by 63%) compared with increases in the control subjects (95% CI, −0.55 to −0.12; unpaired *t* test, $p = 0.005$). At the end of the 2-year monitoring period, the mean ± SD increases in axial length were 0.19 ± 0.21 mm in the PR ortho-k group and 0.51 ± 0.32 mm in the control group.

DISCUSSION

Compared with previous studies on low to moderate myopes[12–16] (Fig. 6), the current study showed the highest myopic retardation rate (63%). Although the number of subjects in each of group was small, this study has a power of 85% at 0.05% level of significance. To our knowledge, this study is the first randomized and single-blind study on the efficacy of PR ortho-k for myopic control in high myopic children. The high level of myopic control observed in this study may be caused by a relatively high magnitude of myopic reduction in PR ortho-k subjects, that is, the median myopic reduction in this group of subjects was about 4.00 D throughout the study period (Fig. 3).

It has been proposed that relative peripheral hyperopic defocus in myopes may trigger axial elongation.[18,19] The hypothesis is that, because peripheral retina shows greater relative hyperopia with respect to axial refraction in myopes (compared with emmetropes and hyperopes), this peripheral hyperopic defocus may promote axial myopia. In ortho-k, the central cornea is flattened, reducing the myopia, whereas the midperipheral cornea is steepened, leading to a ring of increased peripheral myopia in myopic eyes. The peripheral ring of myopia created on the corneal surface will lead to a reduction of peripheral hyperopic defocus, and this may reduce the visual feedback for eye elongation, leading to slower myopic progression.[18–23]

In the current study, all PR ortho-k subjects wore ortho-k lenses of target 4.00 D. Midperipheral corneal changes in these subjects were therefore more significant compared with low to moderate myopic subjects in previous studies[12–16] and the greater corneal

TABLE 6.
Changes (median [range]) in postcycloplegic subjective myopia and astigmatism (D) in the two groups of subjects at the end of the study

Change in	PR ortho-k (n = 12)	Control (n = 16)	p *
Myopia	4.50 (2.75–6.25)	−1.00 (−2.50 to 0.50)	<0.001
Astigmatism	−0.50 (−1.50 to 0.50)	0.00 (−0.75 to 0.75)	0.153

*Probability values for differences between groups using Mann-Whitney *U* tests (positive value indicates reduction in power; negative value indicates increase in power).

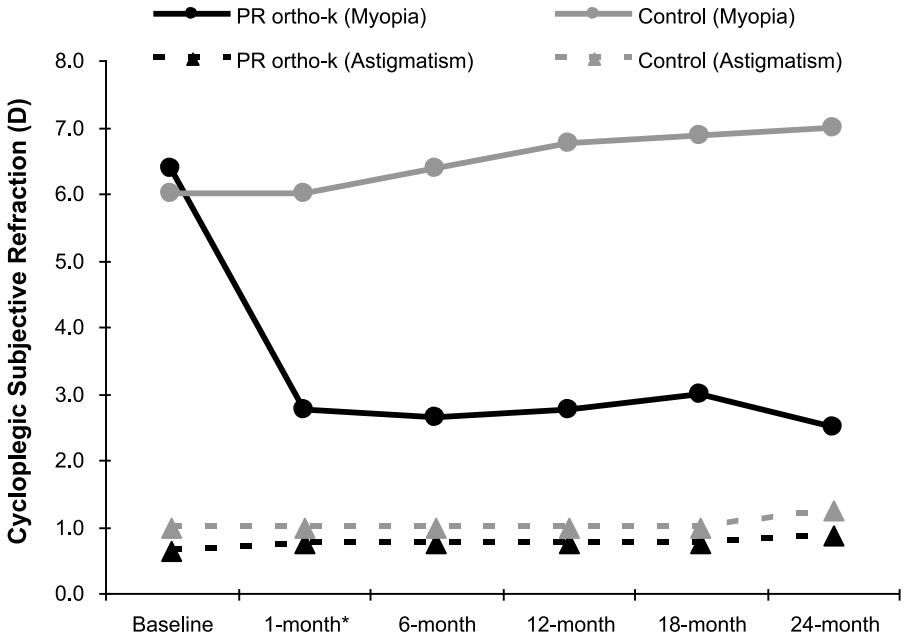

FIGURE 3.

Changes (median) in the refractive components of the subjects during the study period. *Noncycloplegic.

change (hence, greater increase in peripheral myopia) may have resulted in a better control of myopic progression. Further investigation in this area is warranted to confirm the role of peripheral refraction in myopic progression and in ortho-k.

The increase in axial length in the spectacle-wearing control subjects during the 2-year monitoring period was relatively small compared with that in control subjects in previous studies on myopic control in Chinese children.[12,15,16] This may be because the subjects in the current study were relatively older (mean age was 10 years).

In the LORIC study,[12] a weak relationship was reported between baseline spherical equivalent refraction and increases in vitreous chamber depth. The more myopic ortho-k subjects showed greater *slowing* in terms of changes in vitreous chamber depth (R^2 = 0.30), whereas the more myopic spectacle-wearing control subjects showed faster progression in terms of changes in vitreous chamber depth (R^2 = 0.34) after 2 years of lens wear. Kakita et al.[15] observed an association between changes in the axial length and the initial myopia only in higher myopic ortho-k subjects. Cho and Cheung,[16] however, reported no association between changes in the axial length and the initial myopia in the ROMIO study. In the current study, no relationships were observed between the baseline spherical equivalent refraction and increases in axial length in the control group (R^2 = 0.08) and the PR ortho-k (R^2 = 0.06). The amount of change in axial length cannot be predicted based on the individual's baseline spherical equivalent refraction.

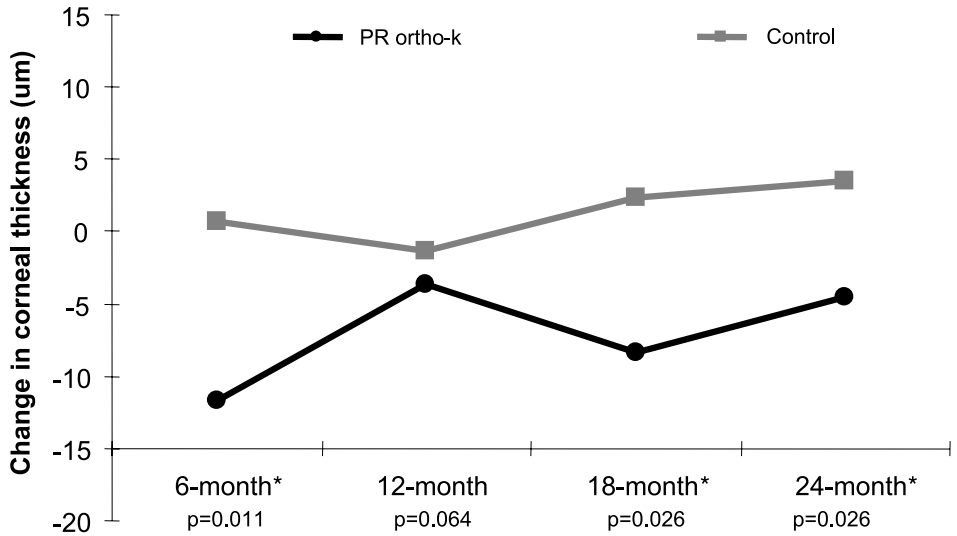

FIGURE 4.

Changes (median) in central corneal thickness between two groups during the study period. *Significant differences were found between the two groups of subjects.

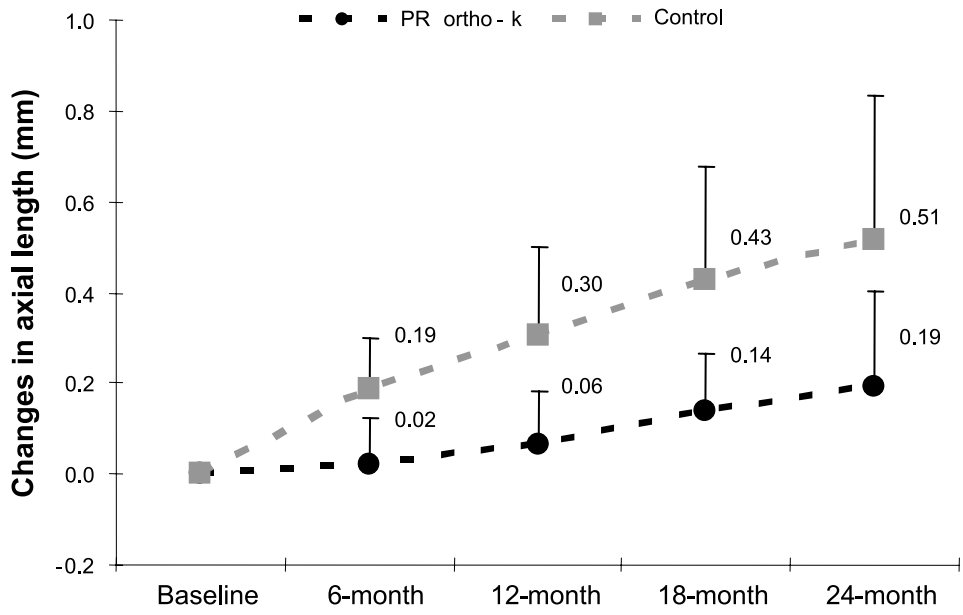

FIGURE 5.
Changes in axial length (mean ± SD) in the subjects.

After 1 month of lens wear, only 12 and 16 subjects in the PR ortho-k and control groups, respectively, completed the study. The dropout rates were 37% and 16% in the PR ortho-k and spectacle-wearing groups, respectively. There were no significant differences in the baseline parameters of those who completed the study and those who dropped out. The dropout rate in the study group was higher than those reported in other studies.[12,13,15,16] Cho et al.[12] reported complication (50%) such as corneal staining as the main reason for dropouts, whereas Walline et al.[13] reported that loss to follow-up contributed to 30% of the dropouts in their ortho-k group. Kakita et al.[15] reported only three dropouts in their study on 45 ortho-k subjects, and the reason for the dropout was caused by insufficient improvement in the uncorrected visual acuity and loss to follow-up in two subjects and one subject, respectively. Cho and Cheung[16] reported 27% dropout in their ortho-k group, and the main reason was lost to follow-up (10%). In the current study, the dropout in the PR ortho-k group was mainly caused by the inability of the subjects (parents) to comply with the intensive follow-up/data collection schedule. Because a higher frequency of corneal staining, although not clinically significant, was found in subjects undergoing ortho-k treatment, a number of unscheduled visits had to be arranged to ensure safe ortho-k lens wear. Four of these subjects withdrew as they were not able to attend the follow-up visits. The dropout subjects were offered extra visits to follow up the myopic progression after the completion of the study. However, all of them sought ortho-k from private practitioners and refused to attend the extra visits. A traditional intent-to-treat analysis was therefore not conducted.

During the study period, two subjects in the PR ortho-k group presented with undesired ocular signs, and they were withdrawn

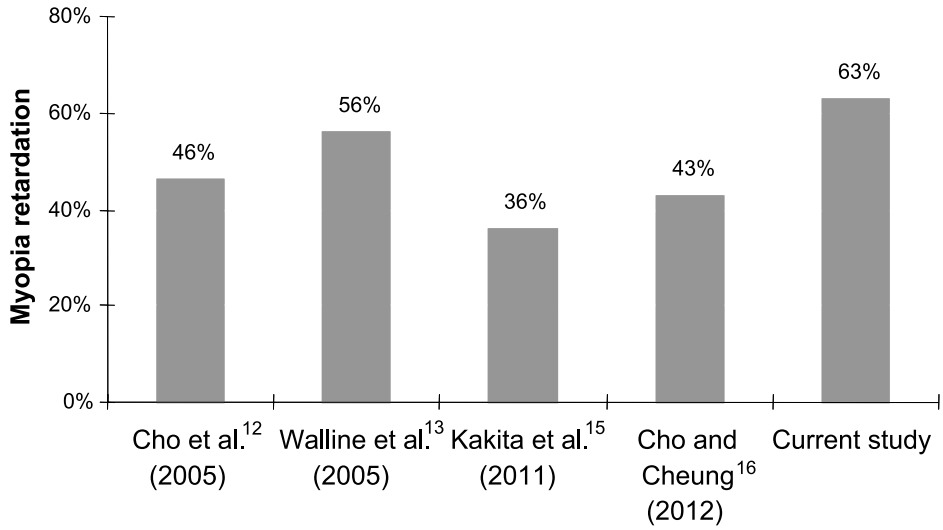

FIGURE 6.
Myopic retardation in orthokeratology subjects compared with those in the control groups in published myopic control studies and the current study.

from the study. One subject had grade 2 (coverage) peripheral corneal staining at the 12-month visit. The staining was epithelial, and the cornea recovered the next day. However, the parents were worried and decided to terminate participation in the study. Another subject was found to have corneal opacities in both eyes at the 18-month visit. He was referred for immediate medical consultation, but his parents were too busy to take him until about 2 months later. His ophthalmologist confirmed that the opacities were probably caused by allergy, which was not ortho-k related. During the 2 months before he consulted the ophthalmologist, his ocular health was monitored, and no changes (including the corneal opacities) were noted. Corneal curvatures returned to baseline values within 2 months, and there were no associated complications. Although the ophthalmologist advised that the subject may resume ortho-k treatment, the subject did not return and missed both 18- and 24-month data collection). Hence, he was excluded from the study.

Some studies have reported a tendency for increased corneal staining with increasing ortho-k lens wear in low to moderate myopes,[24–27] but the severity of the staining was mild (grade 1). Our results were in agreement with these reports[24–27] but only before lens stabilization. In contrast to these reports,[24–27] we found no significant differences in the incidences of staining between our ortho-k and control subjects in subsequent visits during the study period.

Pigmented arc was found in 32% of the PR ortho-k subjects at the 1-month visit and the incidences reached 92% and 100% after 6- and 12-month of lens wear respectively in the current study. Cho et al.[28] first reported the observation of pigmented arc in ortho-k Chinese children. They reported the presence of pigmented arcs in their subjects with high refractive errors after 1 week of lens wear. In a later study, Cho et al.[29] reported that the incidence of corneal pigmented arc was 27% after 3 months of lens wear in low myopic subjects. They reported that the incidence and the intensity of the arc were related to the baseline myopia, spherical equivalent refraction, the target myopia reduction, the amount of myopic reduction, and changes in central corneal curvatures. It was suggested that the pigmented arc was formed in the midperipheral cornea because the area of the reverse curve of the lens coincides with the area of abrupt corneal curvature change, where deep reservoirs of tears were formed under the lens.[29] In the current study, because all subjects were fitted with target 4.00 D lenses compared with lower targets for low myopes, a deeper tear reservoir was formed at the reverse curve region. This led to substantial steepening of the midperipheral cornea, giving a more significant change in topography within a relatively shorter period. This may explain the high incidence of pigmented arc found in the current study.

We found no significant differences in either high- or low-contrast BCVA between the two groups of subjects at any visit in this study. Previous ortho-k studies[30,31] have reported that unaided VA was significantly worse at the low-contrast level. The current study did not aim at complete reduction of the refractive errors of subjects randomized to wear ortho-k lenses, and all PR ortho-k subjects had to wear spectacles to correct their residual refractive errors in the daytime. Our results showed that both high- and low-contrast BCVAs were stable and comparable between visits after lens stabilization in these subjects, and VAs were comparable to those in the control group.

The combination of PR ortho-k and spectacles offered stable vision for the high myopic subjects throughout the 2 years of monitoring. Although we did not conduct a formal survey, all children and parents preferred to continue with this wearing mode at the end of the study. The parents appreciated the results of the study because they were not required to change the prescription of the ortho-k lenses and spectacles for 2 years, except for one subject who had to update his spectacle prescription at the 18-month visit (myopia increased by 0.75 D). All the ortho-k subjects in our study were required to handle the ortho-k lenses themselves, including insertion, removal, and cleaning, and all were capable and diligent in these respects, although there was one report of lens damage. This subject was not required to cease lens wear as a spare pair of lenses was ordered for each subject after stabilization for such incidents.

Limitations

A limitation of the current study was the relatively small sample size, leading to an apparently high dropout rate in the PR ortho-k group. Although run-in period and other incentives may be considered in future studies to minimize dropouts, they may not work as most of the subjects dropped out either because of adverse events and inability of the subjects (parents) to comply with the intensive follow-up/data collection schedule (PR ortho-k group) or parents seeking myopic control treatment for their children (control group). Notwithstanding this limitation, the result of this study supports the confirmation by Cho and Cheung[16] that ortho-k can control myopic progression. If a new ortho-k lens design for high myopes is available, full correction using ortho-k could be recommended because subjects will find it even more convenient if they do not have to wear spectacles in the day time.

CONCLUSIONS

The results of this randomized, single-masked study suggested that the combination of PR ortho-k and spectacles is a safe and feasible option for myopic reduction and control for high myopic children. Elongation of axial length compared with subjects wearing spectacles was slower by 63% during a 2-year monitoring period.

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