Retardation of Myopia in Orthokeratology (ROMIO) Study: A 2-Year Randomized Clinical Trial

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Purpose. This single-masked randomized clinical trial aimed to evaluate the effectiveness of orthokeratology (ortho-k) for myopic control.

Methods. A total of 102 eligible subjects, ranging in age from 6 to 10 years, with myopia between 0.50 and 4.00 diopters (D) and astigmatism not more than 1.25D, were randomly assigned to wear ortho-k lenses or single-vision glasses for a period of 2 years. Axial length was measured by intraocular lens calculation by a masked examiner and was performed at the baseline and every 6 months. This study was registered at ClinicalTrials.gov, number NCT00962208.

Results. In all, 78 subjects (37 in ortho-k group and 41 in control group) completed the study. The average axial elongation, at the end of 2 years, were 0.36 ± 0.24 and 0.63 ± 0.26 mm in the ortho-k and control groups, respectively, and were significantly slower in the ortho-k group ($P < 0.01$). Axial elongation was not correlated with the initial myopia ($P > 0.54$) but was correlated with the initial age of the subjects ($P < 0.001$). The percentages of subjects with fast myopic progression (>1.00D per year) were 65% and 13% in younger (age range: 7–8 years) and older (age range: 9–10 years) children, respectively, in the control group and were 20% and 9%, respectively, in the ortho-k group. Five subjects discontinued ortho-k treatment due to adverse events.

Conclusions. On average, subjects wearing ortho-k lenses had a slower increase in axial elongation by 43% compared with that of subjects wearing single-vision glasses. Younger children tended to have faster axial elongation and may benefit from early ortho-k treatment. (ClinicalTrials.gov number, NCT00962208.) (*Invest Ophthalmol Vis Sci.* 2012;53:7077–7085) DOI:10.1167/iovs.12-10565

The prevalence of myopia is high in Hong Kong and other East Asian countries.[1–9] It is well documented that significant axial elongation of the eyeball in high myopia can be associated with higher risk of sight-threatening complications such as maculopathy and retinal detachment.[10,11] Thus, early preventative treatment in children for retardation of axial elongation is important to prevent the development of high myopia.

Orthokeratology (ortho-k), an optical correction mainly for correcting low-to-moderate myopia, has been shown to have potential in slowing myopic progression in myopic children.[12–15] Lenses are worn during sleep and removed after waking up. Successful treatment allows users to see clearly in the daytime, provided that they continue to wear the lenses regularly at night to maintain the reshaping effect.

Five quasi-experimental studies using historical or self-selecting controls have reported slower myopic progression (by 32–55%) in low-to-moderately myopic children wearing ortho-k lenses compared with those wearing conventional eyeglasses[12,14–16] or single-vision soft contact lenses.[13] The treatment was well received by both children and parents, and there were no significant adverse effects reported with proper instruction and proper care given. The primary objective of the current study was to confirm if ortho-k can retard myopia in children with low-to-moderate myopia using a randomized clinical trial (ClinicalTrials.gov number, NCT00962208).

The importance of myopic control is to prevent the development of high myopia, that is, to reduce the number of children with fast progression in myopia. The average increase in myopia in myopic Chinese children in Hong Kong is approximately 0.50 diopter (D) per year.[17–19] Children with an average increase of more than 1.00D per year in myopia can therefore be regarded as fast progressors.[20–22] The secondary objective of this study was to determine and compare the percentages of subjects with slow, moderate, and fast progression of myopia in the two groups of subjects.

Methods

Study Design

This was an interventional 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 (study group) and single-vision spectacles (control group) for a period of 2 years. Subject recruitment was stratified by age, sex, and manifest refractive error 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 a project member who was not involved in subject recruitment or data collection, to ensure equal numbers of subjects assigned to each group. The random allocation sequence was revealed to the unmasked examiner who would proceed to prescribe the assigned treatment to the subjects accordingly.

Myopic progression was estimated from changes in axial length in both groups and the primary outcome measure (i.e., the axial length) was masked in the study. Double-masking could not be achieved because of the unique characteristics of the ortho-k treatment. Subjects in the study group knew that they were wearing ortho-k lenses because they needed to wear the lenses to sleep and had improved unaided

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Table 1. Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
• 6 to 10 years old (inclusive)	• Strabismus at distance or near
• Myopia: between 0.50D and 4.00D in at least 1 eye	• Previous experience in contact lens wear or myopia control treatment (e.g., refractive therapy or progressive spectacles)
• Astigmatism: <1.50D; with-the-rule astigmatism (axes 180 ± 30) ≤1.25D; astigmatism of other axes ≤0.50D in both eyes	• Contraindication for contact lens wear and orthokeratology (e.g., limbus to limbus corneal cylinder and dislocated corneal apex)
• Spherical equivalent (SE): >0.50D and ≤4.50D in both eyes	• Previous history of ocular surgery, trauma, or chronic ocular disease
• Anisometropia: ≤1.50D	• Concurrent use of medications that may affect tear quality
• Best-corrected logMAR visual acuity 0.10 or better in both eyes	• Systemic or ocular conditions that may affect tear quality or contact lens wear (e.g., allergy and concurrent medication) or that may affect refractive development (e.g., Down syndrome, ptosis)
• Symmetrical corneal topography with corneal toricity <2.00D in either eye	• Poor compliance to tests (e.g., poor fixation in noncontact tonometry or intolerance of lens wear)
• Agreed to randomization	• Not willing to comply with the allocated treatment and follow-up schedule

vision in the daytime. The unmasked examiners knew if a subject was on ortho-k treatment from the good unaided vision, the low (residual) refractive error, the typical topographic maps, and ocular signs (i.e., pigmented arc) observed in slit-lamp biomicroscopy. However, ortho-k did not present any particular identifying features during axial length measurement (IOLMaster; Zeiss Humphrey, Dublin, CA) and the examiner performing the measurement could be masked.

The study was approved by the Departmental Research Committee of the School of Optometry of The Hong Kong Polytechnic University. Written consent was obtained from both subjects and their parents before study participation. This study was registered at ClinicalTrials.gov, number NCT00962208.

Subjects

Subject recruitment was advertised in local newspapers and on the campus of The Hong Kong Polytechnic University from March 2008 to June 2009. Telephone interview was performed to screen out ineligible subjects using a checklist. Children, ranging in age from 6 to 10 years, with low-to-moderate myopia (0.50–4.00D) in at least one eye, and low refractive astigmatism (≤1.25D) and spherical equivalent not more than 4.50D in both eyes, and low anisometropia (≤1.50D) (based on manifest refraction), were recruited (Table 1). Ortho-k subjects were fitted with spherical 4-zone lenses (Menicon Z Night lenses; NKL Contactlenzen B.V., Emmen, The Netherlands) made of gas-permeable lens material (Menicon Z material, DK 163 ISO; central lens thickness: 0.24 mm). Lens fitting was performed according to the manufacturer's instructions (Easy Fit Software, v. 2006; NKL Contactlenzen B.V.) based on corneal topography, noncycloplegic manifest refraction, and the horizontal visible iris diameter. The use of a computer program helped to reduce subjective bias in lens selection. Complimentary lenses, solutions, and accessories were provided to facilitate compliance with regular replacement. Lenses were removed by manipulating the lens edge with the eyelid margins using fingers to reduce risk of contamination associated with the use of suction holder.[23] Control subjects were corrected with single-vision lenses made of plastic lens material, with refractive index of 1.56 (CR-39 material; Hong Kong Optical Lens Co., Hong Kong, China). They were given complimentary spectacle frames and lenses. Unless otherwise instructed, all subjects were required to wear the assigned treatment item on a daily basis. Full correction was targeted for all subjects. Habitual prescription was updated if the monocular VA was worse than 0.18 (logMAR) (Snellen 6/9) or residual myopia/astigmatism exceeded 0.50D at any visit after stabilization of treatment.

Subjects who were lost to follow-up, noncompliant with test procedures/schedule, contraindicated to continue ortho-k treatment (study group only), or could not achieve the desired myopic reduction (study group only) after modification of lens parameters were excluded from the study. The first and last subjects were recruited in March 2008 and November 2009, respectively, and the last data collection visit was in November 2011.

Procedures

All subjects were required to attend 6-monthly cycloplegic examinations (data collection visits) at the Optometry Clinic of the School of Optometry of The Hong Kong Polytechnic University after the initial visit for 2 years. Ortho-k subjects were also required to attend routine ortho-k aftercare visits (1 day, 1 week, 1 month, and every 3 months after lens delivery) and unscheduled visits where necessary, to ensure good ocular response and health. Clinical care was provided by the same practitioner throughout the study period.

At each data collection visit, habitual and best-corrected logMAR VA, manifest subjective refractive error (trial frame and trial lenses), anterior segment of the eye (TOPCON slit-lamp SL7 and TOPCON IMAGEnet system, ver. 2000; Topcon Corp., Tokyo, Japan), corneal topography (Medmont E300 topographer; Medmont Pty Ltd., Vermont, VIC, Australia), and intraocular pressure (NIDEK NT-2000; Nidek Co., Ltd., Aichi, Japan) were assessed by the unmasked examiner before cycloplegia. Maximum plus maximum VA was used in the assessment of subjective refraction. For corneal topography, at each data collection visit, the first four good corneal topographic maps with image score above 98 were saved. For ocular tonometry, the first three measurements (between measurement differences not more than 3 mm Hg) were saved.

Axial length measurement of the eyeball (IOLMaster) was performed by a masked examiner 30 minutes after cycloplegia with 1 drop of 0.5% proparacaine, followed by 1 drop of 1% tropicamide, and 1 drop of 1% cyclopentolate, administered 5 minutes apart. The first five axial length readings with signal-to-noise ratio above 3.5 and a maximum difference of 0.02 mm between any two readings were saved and the average was used for data analysis.

Subjects were classified into different myopic progression groups for further analysis. Those with myopic progression not exceeding the average annual growth (i.e., 0.50D per year or axial elongation ≤0.18 mm per year[24]) were regarded as slow progressors, whereas those showing myopic progression exceeding 1.00D per year (i.e., axial elongation >0.36 mm per year) were regarded as fast progressors. The remaining subjects who fell between the two categories (i.e., >0.50 and ≤1.00D per year or >0.18 and ≤0.36 mm per year) were regarded as moderate progressors.

Sample Size Calculation

The efficacy of myopic control of ortho-k was determined by dividing the difference in mean axial length changes in the two groups after 2

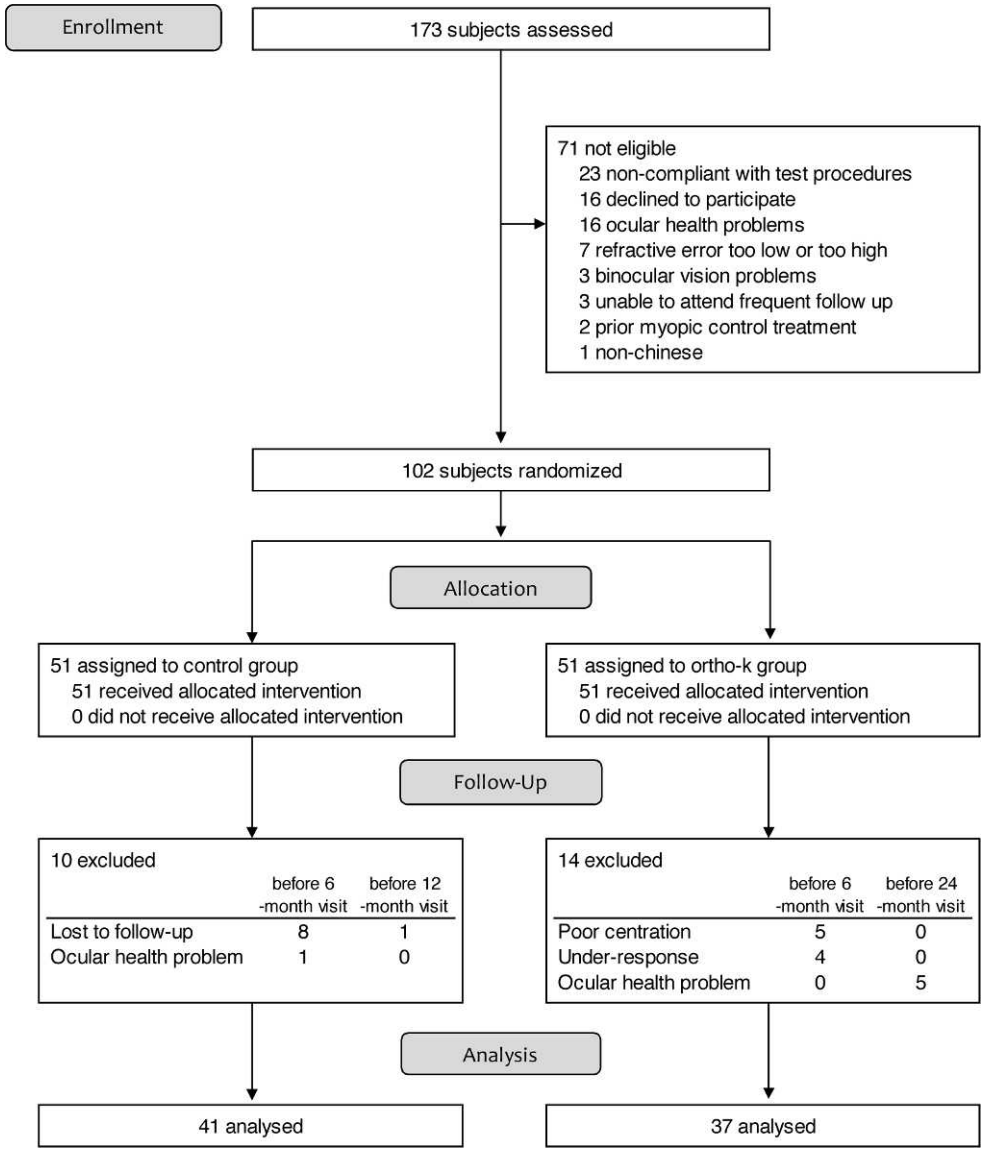


Figure 1. Study flow chart and dropouts.

years with the mean axial length change in the control subjects times 100%. We sought 80% power to detect a 0.18 mm (SD 0.27 mm)[12] (equivalent to 0.50D change in refraction)[24] difference in eye elongation between the two groups (over 2 years) with a significance level of 0.05 (two-tailed); the minimum number of subjects required to complete the study in each group was 20.

Statistical Analysis

Because all right eyes satisfied inclusion criteria, only data from the right eye were used for data analyses. Statistical analysis (SPSS software ver. 18.0; SPSS Inc., Chicago, IL) was performed by the principal investigator. Only completed cases were analyzed. Intention-to-treat analysis was not used in this study because subjects lost to follow-up in both groups and ortho-k subjects who were deemed not suitable to continue the treatment were not motivated or were reluctant to return for cycloplegic examinations. Mann–Whitney *U* tests and unpaired *t*-tests were used to compare the baseline characteristics between the two groups of subjects. Repeated-measures ANOVA tests (and paired *t*-tests with Bonferroni correction where appropriate) were used to compare changes in axial length during the study period. Since interim analyses (12- and 18-month axial length data between groups) on the primary outcome (i.e., axial elongation) were made during the study period, the level of significance used was adjusted accordingly where appropriate. Factors affecting axial elongation including age, sex, treatment, initial myopia, and initial corneal topography were investigated using stepwise multiple linear regression analysis. To obtain further insight into the observed treatment effect, cross-tab analyses were used to compare the proportions of fast progressors in the ortho-k and control groups, although each subgroup sample size in these analyses was small.

Results

In all, 173 subjects passed the phone screening and 102 subjects were eligible at the baseline visit; 50% were randomly assigned to the ortho-k group and 50% to control group (Fig. 1). No significant differences in age, sex, refractive errors, and corneal shape were found between the two groups of subjects ($P > 0.05$) (Table 2). Ten control subjects and 14 ortho-k subjects were excluded at different stages of the study (Fig. 1). Nine control subjects were lost to follow-up (eight and one

Table 2. Demographic Data (Mean ± SD or Median [Range]) of the 102 Subjects in the Ortho-k and the Control Subjects

	All		Completed Cases		Dropout	
	Ortho-k, *n* = 51	**Control, *n* = 51**	**Ortho-k, *n* = 37**	**Control, *n* = 41**	**Ortho-k, *n* = 14**	**Control, *n* = 10**
Age, y	9 [6, 10]	9 [7, 10]	9 [7, 10]	9 [7, 10]	8 [6, 10]	9 [7, 10]
Sex	25F; 26M	25F; 26M	18F; 19M	19F; 22M	7F; 7M	6F; 4M
Myopia, D	2.12 ± 0.87	2.29 ± 0.87	2.05 ± 0.72	2.23 ± 0.84	2.32 ± 1.19	2.53 ± 1.00
Astigmatism, D	0 [0, 1.25]	0.25 [0, 1.25]	0 [0, 1.00]	0 [0, 1.25]	0.38 [0, 1.25]	0.25 [0, 0.75]
Flat keratometry reading, D	42.93 ± 1.21	43.12 ± 1.37	42.85 ± 1.18	43.21 ± 1.46	43.16 ± 1.32	42.74 ± 0.86
Eccentricity	0.65 ± 0.09	0.62 ± 0.09	0.66 ± 0.08	0.62 ± 0.09	0.63 ± 0.10	0.64 ± 0.09
Axial length, mm	24.46 ± 0.75	24.46 ± 0.79	24.48 ± 0.71	24.40 ± 0.84	24.42 ± 0.88	24.70 ± 0.53
Habitual logMAR VA	0.25 ± 0.22	0.21 ± 0.22	0.24 ± 0.22	0.22 ± 0.22	0.27 ± 0.24	0.18 ± 0.25
Best-corrected logMAR VA	0.00 [–0.10, 0.10]	–0.04 [–0.20, 0.08]	–0.04 [–0.10, 0.06]	–0.04 [–0.20, 0.08]	0.00* [–0.06, 0.10]	–0.01 [–0.10, 0.04]

* Significantly different from the completed subjects in the corresponding group ($P = 0.014$).

before 6- and 12-month visits, respectively) and one was excluded before the 6-month visit due to recurrent eye inflammation. Nine ortho-k subjects could not achieve the desired myopic correction despite lens modifications and another five were contraindicated to continue ortho-k treatment due to general conditions (Fig. 1; see subheading Adverse Events in the following text) affecting the ocular health (four and one before the 18- and 24-month visits, respectively). There were no significant differences in the baseline characteristics in the completed and dropout cases for both groups ($P > 0.20$), except that in the ortho-k group, the best-corrected VA of the completed subjects was significantly better than that of the dropouts ($P = 0.014$); however, the difference was clinically insignificant (Table 2).

A total of 37 (18 females, 19 males) ortho-k subjects and 41 (19 females, 22 males) control subjects completed the 2-year study. There were no significant differences in the baseline data between the two groups of subjects ($P > 0.05$). The mean ± SD age was 9.23 ± 1.06 years in the ortho-k group and 9.39 ± 1.00 years in the control groups. The mean ± SD of initial myopia was 2.05 ± 0.72D in the ortho-k group and 2.23 ± 0.84D in the control group. At the 24-month visit, the habitual logMAR VA was 0.02 ± 0.10 in the ortho-k subjects and 0.07 ± 0.11 in the control subjects and the best-corrected logMAR VA was –0.06 ± 0.04 in the ortho-k subjects and –0.04 ± 0.05 in the control subjects. The habitual logMAR VA was slightly better (by 2–3 letters) in the ortho-k group than that in the control group ($P = 0.03$), but there was no significant difference in the best-corrected VA between the two groups of subjects ($P = 0.11$) (Table 3).

Efficacy of Myopic Control

Figure 2 shows that axial length increased with time in both groups of subjects. The increase with time was statistically significant (repeated-measures ANOVA, $P < 0.01$) and significantly faster in the control groups (repeated-measures ANOVA, $P < 0.01$). The rate of axial elongation was significantly slower in the ortho-k group compared with that in the control group at all follow-up visits (unpaired *t*-tests, $P < 0.001$) (Table 3). The mean increase in axial length in ortho-k subjects was 0.27 mm less than that in control subjects after 2 years.

The 6-monthly axial elongation was significantly slower in the ortho-k group than that in the control group at all visits (unpaired *t*-tests, $P < 0.05$) (Fig. 2). In the ortho-k group, the 6-monthly change in axial length was rather consistent during the study period and was only significantly higher between the second and fourth 6-month periods (mean difference ± SD: 0.05 ± 0.09 mm, 95% confidence interval [CI]: 0.02 to 0.08, paired *t*-test, $P = 0.003$) (Fig. 2). In the control group, a gradual slowing of axial elongation with age was observed. Axial elongation was significantly faster in the first 6-month period compared with the third and fourth 6-month periods (mean difference ± SD [first–third 6-month period]: 0.06 ± 0.12 mm, 95% CI: 0.03 to 0.10 mm, paired *t*-tests, $P = 0.002$; mean difference ± SD [first–fourth 6-month period]: 0.07 ± 0.11 mm, 95% CI: 0.04 to 0.11 mm, paired *t*-tests, $P < 0.001$) (Fig. 2). As a result, the efficacy of myopic control varied at different stages of the study period: 55%, 32%, 29%, and 54% in the first, second, third, and fourth 6-month periods. On average, at the end of the study period, axial elongation was slower by 43% in the ortho-k subjects compared with the control subjects.

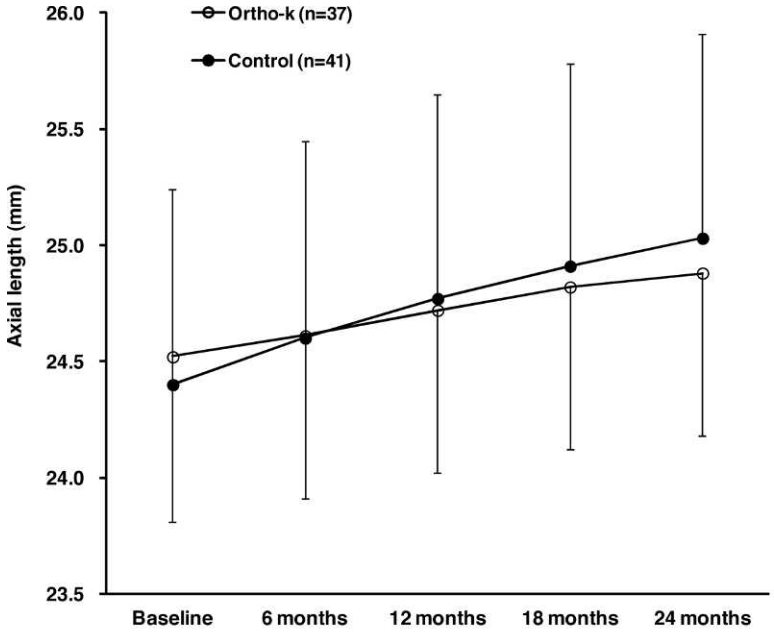
Stepwise multiple linear regression analysis showed that among all the predicting factors, axial elongation was significantly correlated with the treatment (standardized beta = –0.45, $P < 0.001$) and initial age (standardized beta = –0.39, $P < 0.001$) of the subjects but not with sex, initial myopia, or the initial corneal shape of the subjects (partial *r*: –0.21 to

Table 3. Changes (Mean ± SD) in Axial Length in Subjects Who Completed the 2-Year Study and Differences (Mean ± SE) in Axial Elongation between the Two Groups at Each Visit

	Orthokeratology, $n = 37$	Control, $n = 41$	Difference	95% CI
6 months	0.09 ± 0.10	0.20 ± 0.11	0.10 ± 0.02	0.07 to 0.15
12 months	0.20 ± 0.15	0.37 ± 0.16	0.16 ± 0.04	0.09 to 0.24
18 months	0.30 ± 0.20	0.50 ± 0.21	0.20 ± 0.05	0.11 to 0.30
24 months	0.36 ± 0.24	0.63 ± 0.26	0.27 ± 0.06	0.16 to 0.38

0.09, $P > 0.08$). The regression of the model using treatment and initial age to predict axial elongation was fair (adjusted $R^2 = 0.37$) but significant ($F_{2,75} = 23.49$, $P < 0.001$). Since axial elongation was significantly affected by treatment, linear regression of axial elongation and initial age was performed for each group. Figure 3 shows significant negative correlations between axial elongation and the initial ages in both group of subjects (ortho-k group: Pearson $r = 0.33$, $F_{1,35} = 4.28$, $P = 0.046$; control group: Pearson $r = 0.54$, $F_{1,39} = 15.90$, $P < 0.001$). Figure 4 shows the lack of association between changes in the axial length and the initial myopia in either group of subjects ($P > 0.05$).

The ortho-k group had fewer fast progressors compared with the control group (χ^2, $P = 0.006$). The percentage of fast progressors reduced from 34% in the control group to 15% in the ortho-k group, whereas the percentage of slow progressors increased from 14% in the control group to 46% in the ortho-k group. Because the myopic control effect was affected by age, subjects were further divided into younger and older subjects to study the effect of age on the percentage of fast progressors. The median age of 9 years was arbitrarily selected as the cutoff value. Subjects younger than 9 years of age (i.e., range, 7–8 years) were considered as younger subjects, whereas subjects ranging in age from 9 to 10 years were considered as older subjects. As shown in Figure 5, the percentages of older subjects with fast myopic progression were 9% and 13% in the ortho-k and control groups, respectively. However, the percentages of younger subjects with fast myopic progression were 65% in the control group compared with 20% in the ortho-k group. The proportion of younger subjects with faster myopic progression was significantly higher when compared with older subjects in the control group (χ^2, $P = 0.002$) but not in the ortho-k group (χ^2, $P = 0.61$).



6-monthly increase	Ortho-k	Control	p-value #
First	0.09±0.10	0.20±0.11	<0.001
Second	0.11±0.09	0.16±0.09	0.004
Third	0.10±0.08	0.14±0.09 *	0.043
Fourth	0.06±0.08 ^	0.13±0.08 *	0.001

statistical significance of the between group difference (unpaired t tests)
^ significantly different from the second 6-monthly increase in the ortho-k group, paired t test, p=0.003
* significantly different from the first 6-monthly increase in the control group, paired t tests, p<0.002

Figure 2. Means and SD of axial length in the ortho-k and control groups over 2 years.

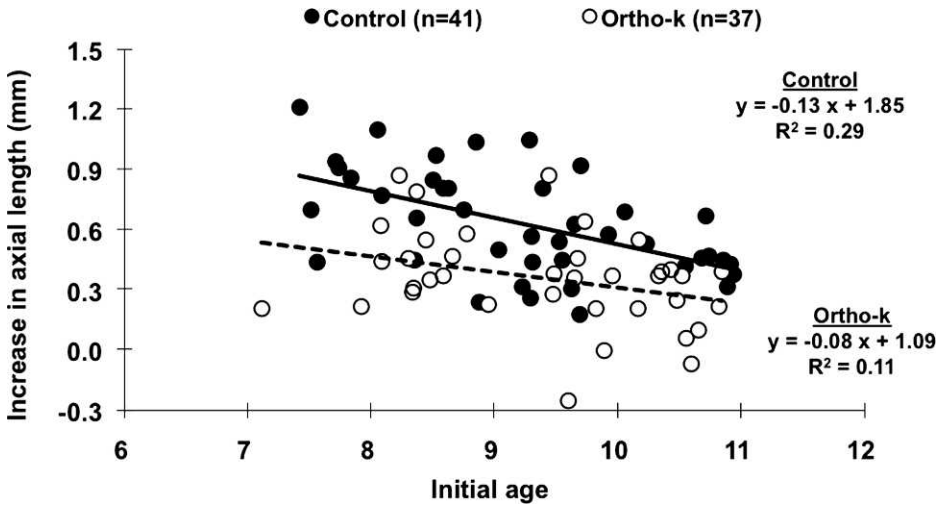


FIGURE 3. Changes in axial length after 2 years of monitoring versus the initial age in the two groups of subjects.

Adverse Events

One recurrent corneal inflammation was reported in the control group and the subject was excluded from the study. The five dropouts due to ocular health issue in the ortho-k group were excluded because they were not deemed suitable to continue contact lens wear; three had mild rhinitis, resulting in persistent and significant inferior-nasal corneal staining, one had increased conjunctival hyperemia after failing to comply with care procedures despite reeducation, and the remaining subject developed chalazion in the right eye after 21 months of lens wear. Ocular conditions and vision of these ortho-k subjects were not affected after cessation of ortho-k treatment.

DISCUSSION

The current study is the first long-term randomized clinical trial to confirm that ortho-k can effectively slow myopic progression by 43% in children with low-to-moderate myopia compared with those wearing single-vision glasses. Table 4 compares the study designs and the 2-year results obtained from published reports[12–16] on myopic control using ortho-k and the current study. Study design varies in the ethnicity and the initial age of the targeted subjects, the method of assignment of intervention, and the treatment for control subjects. All studies showed a positive myopic control effect of 32% to 55% slower axial elongation with ortho-k.

In a review paper on treatment for myopia, Gwiazda[25] commented that the myopic control effect using pharmaceutical agents and bifocal/progressive glasses reduced after the initial treatment period. The study by Hiaroka et al.[15] also showed an apparent reduced efficacy on myopic control using ortho-k. Their study was an extension of the 2-year study by the same group[14] on selected subjects fulfilling their inclusion criteria (Table 4). They reported no additional beneficial effect for myopic control using ortho-k after 3 years of lens wear.

However, although their data showed an apparent reduction in efficacy of ortho-k with time, the reduction was not due to reduced efficacy of ortho-k but due to the gradual slowing of myopic progression in the control group with age, which may be expected. Literature has reported that myopic progression in children slowed with age.[17,26–30] Meta-analysis performed by Donovan et al.[26] showed that myopic progression was faster in younger children and in subjects of Asian than that in subjects of European descent. Myopia in Caucasian children was reported to increase in age from 6 to 14 years,[27] but the rate of myopic progression decreased with age[28] and stopped after

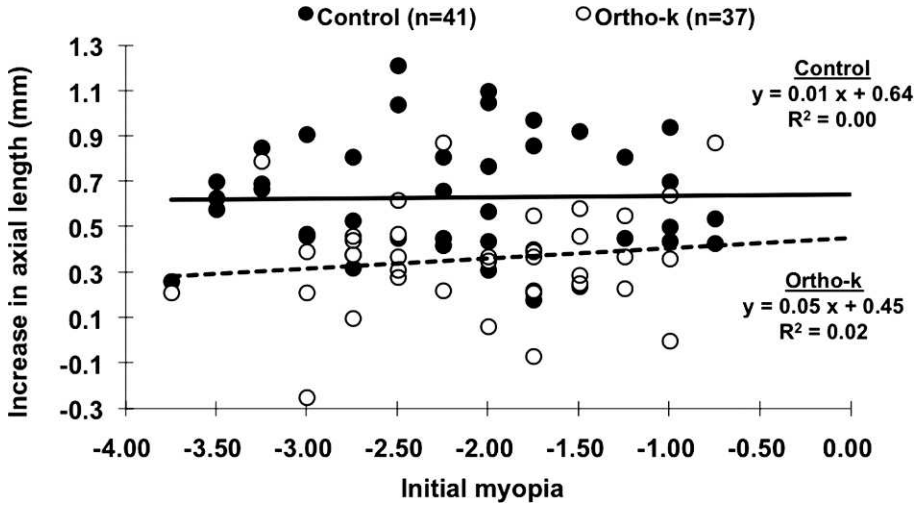


FIGURE 4. Changes in axial length after 2 years of monitoring versus the initial myopia.

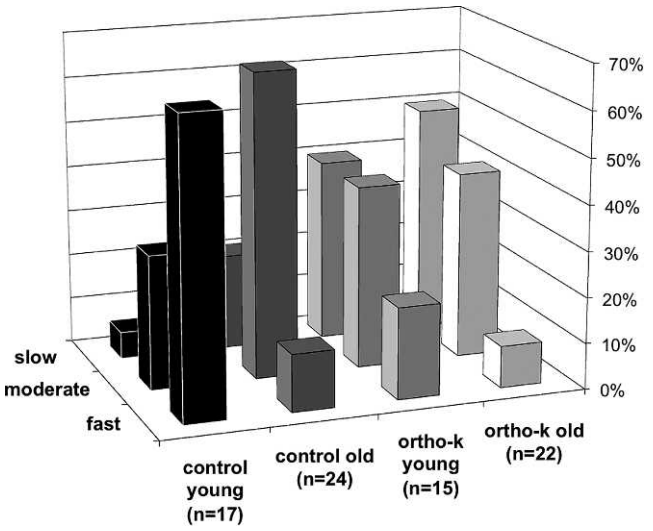


FIGURE 5. Percentages of subjects demonstrating slow (0.18 mm/y), moderate (>0.18 and ≤0.36 mm/y), and fast (>0.36 mm/y) myopic progression in younger (6–8 years old) and older (9–10 years old) children in the ortho-k and control groups.

the age of 15 years in males and 14 years in females.[29] The greatest change in myopia in Chinese children was reported in those ranging in age from 9 to 11 years.[17]

The subjects in the study reported by Hiraoka et al.[15] started with a mean age of 10 years and would be 14 to 15 years old after 4 to 5 years (study period), which may explain the slower myopic progression in the control group. In their study, except for the second year, the annual axial elongation in their ortho-k subjects was rather consistent (0.16–0.19 mm) during the 5-year monitoring period. On the contrary, the annual axial elongation in their control subjects reduced from an average of 0.33 and 0.38 mm in the first 2 years to 0.17 and 0.24 mm in year 4 and year 5, respectively, and the latter was comparable to the average increase in their ortho-k subjects in that year.

The annual axial elongation in the current study was 0.36 and 0.27 mm in the first and second years, respectively, in the control subjects, and was 0.20 and 0.16 mm, respectively, in the ortho-k subjects. Our results were similar to the annual growth in the first 2 years as reported by Hiraoka et al.[15] Our results showed relatively better myopic control in the first 6-months of the study period (55%) compared with the other 6-month periods (Fig. 2). The reduced myopic control effect may be due to the slowing of myopic progression in the control group and this was also observed and reported by Hiraoka et al.[15] The apparent decline in axial elongation in control subjects may have offset the myopic control effect with ortho-k and narrowed the differences between the two groups, thus leading to an impression of reduced efficacy of myopic control treatment with time. Another possible explanation may be the adaptation of subjects to the signal that slows myopic progression in the ortho-k group. Our results also showed accrual of effect with continuation of ortho-k after 1 year.

Our results suggested that ortho-k has the potential to reduce the development of high myopia by reducing the proportion of fast progressors. Among all the currently available methods, 1% atropine is the most effective treatment reported for myopic control in myopic children in Asia.[20–22] Shin et al.[20] showed that the proportions of fast progression were 33%, 17%, and 4% in children on 0.1%, 0.25%, and 0.5% atropine, respectively. However, they did not have control subjects in their study. Chua et al.[21] showed that the

TABLE 4. Studies on Controlled Clinical Treatment on Myopic Control Using Ortho-k

	Cho et al.[12] (2005)	Walline et al.[13] (2009)	Kakita et al.[14] (2011)	Hiraoka et. al.[15] (2012)	Santodomingo-Rubido et al.[16] (2012)	Current Study (2012)
Age, y	7 to 12 (mean 9.6)	8 to 11 (mean 10.5)	8 to 16 (mean 12)	8 to 12 (mean 10)	6 to 12 (mean 10)	7 to 10 (median 9)
Race	Chinese	Caucasian	Japanese	Japanese	White European	Chinese
Duration of study, y	2	2	2	5	2	2
With control group	Yes	Yes	Yes	Yes	Yes	Yes
Method of assignment	Historic data	Historic data	Self-selection	Self-selection	Self-selection	Randomized
Control treatment	Glasses	Soft lenses	Glasses	Glasses	Glasses	Glasses
Initial SER (Ortho-k, D)	−2.27 ± 1.09	—	−2.55 ± 1.82	−1.89 ± 0.82	Myopia: −2.20 ± 1.09	−2.16 ± 0.77
Initial SER (Control, D)	−2.55 ± 0.98	—	−2.59 ± 1.66	−1.83 ± 1.06	Myopia: −2.35 ± 1.17	−2.36 ± 0.86
Increase in axial length in 2 y (Ortho-k, mm)	0.29 ± 0.27	0.25 ± 0.27	0.39 ± 0.27	0.45 ± 0.21	0.47	0.36 ± 0.24
Increase in axial length in 2 y (Control, mm)	0.54 ± 0.27	0.57 ± 0.27	0.61 ± 0.24	0.71 ± 0.40	0.69	0.63 ± 0.26
Myopic control effect	46%	55%	36%	37%	32%	43%
Dropout rate (Ortho-k)	19% (8/43)	30% (12/40)	7% (3/45)	24% (7/29)*	6% (2/31)	27% (14/51)
Dropout rate (Control)	—	—	17% (10/60)	30% (9/30)*	20% (6/30)	20% (10/51)

* Between 3rd and 5th years.

proportion of fast progressors reduced from 64% in the placebo-treated eyes to 14% in 1% atropine–treated eyes, whereas the proportion of slow progressors increased from 16% in the placebo-treated eyes to 66% in the 1% atropine–treated eyes. Our results showed that 15% of subjects (age range: 7–10 years) demonstrated fast myopic progression, which is comparable to the effect of the use of atropine.[21] Our results also showed that younger subjects (age range: 7–8 years) tended to show faster axial elongation (Fig. 3) and ortho-k would be more beneficial to this age group, given that the percentage of younger subjects with fast myopic progression reduced from 65% in the control group to 20% in the ortho-k group (Fig. 5). Therefore, early initiation of ortho-k treatment may be necessary to reduce the prevalence of high myopia.

The LORIC (longitudinal orthokeratology research in children [in Hong Kong]) study reported slower axial elongation in higher myopic (2.00–4.00D) subjects undergoing ortho-k when compared with higher myopic subjects wearing single-vision glasses and no between-group difference in axial elongation when initial myopia was <2.00D.[12] Walline et al.[13] and Santodomingo-Rubido et al.[16] did not investigate the relationship between eyeball elongation and initial refractive errors. Kakita et al.[14] reported an association between eyeball elongation and initial refractive error only in the higher myopic ortho-k subjects, but they did not define high myopia in their study. Using ANCOVA to control the covariances, Hiraoka et al.[15] showed that axial elongation was associated with age but not with initial refractive errors and the findings in the current study supported their results. Again, the results suggest that myopic control treatment would be more beneficial to younger than that to older myopic children.

A good myopic control treatment, apart from being effective, should be well received by the targeted population without causing significant adverse effect or inconveniences to daily activities. Not everybody can wear contact lenses and not every child is suitable for ortho-k treatment. A treatment with high dropout rate would not be useful even if it is effective and high dropout rates could affect the results. The dropout rate reported in previous studies with ortho-k varies from 6%[16] to 30%.[13] The dropout rate of the current study was 27% and 20% in the ortho-k and control groups, respectively. Fourteen ortho-k subjects were withdrawn from the study. Nine were withdrawn from the study because of unsatisfactory myopic reduction, five due to poor lens centration, and the other four due to undercorrection. The five subjects with poor lens centration were refitted with toric ortho-k lenses and four were successfully fitted. The four undercorrected subjects were prescribed with spectacles to correct their residual refractive errors for daily activities. All eight subjects continued ortho-k lens wear outside the study. Thus, if other lens designs were included (see the following text), the dropout rate would have been lower. Five ortho-k subjects were withdrawn from the study due to contraindication to continued ortho-k treatment. Termination of ortho-k treatment was essential to ensure good ocular integrity. For safe ortho-k treatment, there is a need for good compliance from the practitioners, the wearers, and parents (if children are involved). Careful patient selection and monitoring during the course of the treatment are essential to minimize risk and development of serious complications (e.g., microbial keratitis) in ortho-k treatment. With proper and regular eye examination, ortho-k can slow myopic progression in children and provide clear unaided vision for well-adapted wearers without affecting ocular health.

Only one lens design (spherical 4-zone lens) was used in the current study and the current result applies only to children with low-to-moderate myopia and low astigmatism and who could achieve satisfactory ortho-k response. As mentioned earlier, eight of the nine subjects who could not achieve the desired ortho-k response using the designated lens design and were excluded from the current study due to deviation from protocol, continued ortho-k treatment after they were successfully refitted with other lens design or with the use of low prescription eye glasses to aid daytime vision. There are a number of different lens designs currently available in the market aiming at improving the performance of ortho-k lenses, for example, toric ortho-k designs.[31] A number of research studies are currently under way to investigate the potential of these lenses for refractive correction as well as myopic control. Results of these studies would be helpful toward the application of ortho-k for myopic control to a wider population with different degrees of myopia and astigmatism, thereby allowing more children to benefit from the myopic control treatment using ortho-k.

In conclusion, this randomized clinical trial confirmed that ortho-k slowed axial elongation (by 43%) and reduced the percentage of fast progressors in younger subjects (from 65% to 20% in subjects ranging in age from 7–8 years). Our results suggested that it would be beneficial to commence ortho-k treatment in younger myopic children.

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