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著者別名	柿田 哲彦, 平岡 孝浩, 大鹿 哲郎
journal or publication title	Investigative ophthalmology & visual science
volume	52
number	5
page range	2170-2174
year	2011-04
権利	(C) 2011 by the Association for Research in Vision and Ophthalmology
URL	http://hdl.handle.net/2241/114760

doi: 10.1167/iovs.10-5485

<Clinical Article>

Influence of overnight orthokeratology on axial length elongation in childhood myopia

Tetsuhiko Kakita, MD,¹ Takahiro Hiraoka, MD,² Tetsuro Oshika, MD²

¹ Kakita Eye Clinic, Chiba, Japan

² Department of Ophthalmology, Institute of Clinical Medicine, University of Tsukuba, Ibaraki, Japan

Short title:

Influence of orthokeratology on axial length

Word counts:

3,338

Financial Disclosure:

The authors have no proprietary or commercial interest in any materials described in this article.

Correspondence:

Tetsuhiko Kakita, Kakita Eye Clinic, 4-1-15, Minaminagareyama, Nagareyama, Chiba, 270-0163, Japan.

Tel: +81-4-7159-8888; Fax: +81-4-7159-7372; E-mail: kec@kakitaeyeclinik.com

Abstract

Purpose: This prospective study was conducted to assess the influence of overnight orthokeratology (OK) on axial length elongation in children, with those wearing spectacles as controls.

Methods: One hundred five subjects (210 eyes) were enrolled in this study. The OK group comprised 45 patients (90 eyes, age 12.1 ± 2.5 years, mean \pm SD) (OK group) who matched the inclusion criteria for OK. The control group comprised 60 patients (120 eyes, 11.9 ± 2.0 years) who also matched the inclusion criteria for OK but preferred spectacles for myopia correction. Axial length was measured at baseline and after 2 years using the IOLMaster (Zeiss Humphrey System, CA, USA) and the changes were evaluated and compared between the groups.

Results: Ninety two subjects (42 and 50 in the OK and control groups, respectively) completed the 2-year follow-up examinations. At baseline, the spherical equivalent refractive error was -2.55 ± 1.82 D and -2.59 ± 1.66 D, and the axial length was 24.66 ± 1.11 mm and 24.79 ± 0.80 mm in the OK and control groups, respectively, with no significant differences between the groups. The increase in axial length during the 2-year study period was 0.39 ± 0.27 mm and 0.61 ± 0.24 mm, respectively, and the difference was significant ($P < 0.0001$, unpaired t test).

Conclusions: OK suppressed axial elongation in myopic children, suggesting that this treatment can slow the progression of myopia to a certain extent.

Myopia is one of the most common ocular abnormalities in humans. The prevalence of myopia is reported to be between 25 and 30% in the developed countries^{1,2} with the incidence being higher among certain Asian populations.³ It is generally considered that progression of youth-onset myopia is attributable to axial length elongation, which is not compensated for by reductions in the corneal and crystalline lens power.⁴⁻⁷

Myopia can be corrected by spectacles or contact lenses. However, these treatments do not solve the problem of ocular axial elongation. It is well known that myopia is often associated with sight-threatening complications, such as retinal detachment, macular degeneration, and glaucoma.⁸⁻¹¹ Furthermore, the risk of these complications increases with the severity of myopia and axial length.¹¹ Arresting the progression of this myopic condition and preventing accentuated myopia would therefore contribute to the prevention of these common ocular diseases, and thus would likely have a very significant effect in reducing medical expenditure.

So far, the scientific community has been trying to find an effective means to slow or even arrest the development of myopia in children.¹² A number of medical treatments have been tested, including topical application of tropicamide,¹³ atropine,¹⁴⁻¹⁶ pirenzepine¹⁷⁻¹⁹ and ocular hypotensive agents^{20,21}. However, there have been no ideal therapeutic modalities to effectively prevent myopic progression in light of efficacy, safety, economic feasibility, and ease of application.

One previous report has described the effectiveness of overnight orthokeratology (OK) for arresting the progression of myopia in the left eye of a 13-year-old boy, in whom it was found that axial elongation was less in the left eye than in the right after 2 years.²² This study showed the possibility that OK might be capable of suppressing ocular axial elongation in myopic children. Subsequently, Cho et al. conducted a 2-year pilot study to determine whether OK could ameliorate the progression of myopia in children.²³ The authors compared the growth of axial

length in 35 children undergoing OK with that of 35 children wearing single vision spectacles, and reported that the increases in axial length were significantly smaller in the OK group than the spectacles group. In that study, however, the data for the control group were obtained at other facilities, where axial length was measured using different devices.²⁴ Therefore, the study was not considered to have been adequately controlled. More recently, similar results have been confirmed by the study of Walline et al.²⁵ However, it was also a non-randomized study with an inappropriate control group, which had been recruited from a different study.²⁶ In addition, axial length measurements were performed using a conventional contact type a-scan ultrasound device. In recent years, it has been shown that a laser interferometer (IOLMaster, Zeiss Humphrey System, CA, USA) yields highly reproducible, precise, non-contact, and rapid axial length measurements with less burden on the patient.²⁷ Such features of the IOLMaster are considerably advantageous for repeated, longitudinal measurements of axial length in children.

We conducted the current prospective study using the IOLMaster to find out how the continued use of OK affects axial growth in children. Children wearing spectacles and attending the same clinic were recruited as controls.

Patients and Methods

The survey was conducted between November 2002 and June 2007. Forty five patients who matched the inclusion criteria (Table 1) were enrolled in the OK group. There were 22 boys and 23 girls, ranging in age from 8 to 16 (12.1 ± 2.5 [mean \pm SD]) years. One hundred twenty eyes of 60 individuals served as controls. They also matched the inclusion criteria for OK but preferred spectacles to OK for the correction of myopia. The control group included 28 boys and 32 girls, ranging in age from 8 to 16 (11.9 ± 2.0) years.

The study was conducted in accordance with the tenets of the Declaration of Helsinki and approved by the Ethics Committee of Kakita Eye Clinic. Informed consent was obtained in writing from all participants and their guardians following an explanation of the nature and possible consequences of the study.

The OK lenses used in this study were Emerald Lenses (Euclid Systems Corporations, Herndon, VA, USA), which are four-zone reverse geometry lenses manufactured from Boston® XO material (Polymer Technology Corp., Wilmington, MA, USA) with a nominal Dk of 100×10^{-11} ($\text{cm}^2/\text{sec})(\text{ml O}_2/\text{ml} \cdot \text{mmHg})$. The nominal central thickness of the lenses was 0.22 mm and the diameter was 10.6 mm. The patients were fitted with the lenses according to the manufacturer's specification. After the lenses had been dispensed, the patients were recommended to wear their OK lenses every night for at least 7 consecutive hours.

The patients in the control group wore single vision glasses, which were prescribed by a certified ophthalmic technician and modified according to any refractive changes during the follow-up period.

The OK group returned for examination every 3 months and underwent slitlamp examinations for any adverse events. The OK lens fit was evaluated at these visits. The control group returned

for examination every 6 months. OK lenses and spectacles were replaced if visual acuity was found to change by more than 0.30 logMAR units during the follow-up.

It has been reported that corneal thinning stabilizes by the end of the week following orthokeratology,²⁸ or that thinning continues for one²⁹ or two³⁰ months. In the current study, therefore, axial length was measured 3 months after the start of OK, which was used as the baseline data for axial length. As for refraction and visual acuity, data obtained before starting OK were used as the baseline values. In the control group, axial length, refraction, and visual acuity were measured when the subject started wearing spectacles. In both groups, OK or spectacles were continued for 2 years, and axial length, refraction, and visual acuity were measured at the end of the 2-year study period (i.e. 2 years and 3 months for the OK group).

The axial length was evaluated using a non-contact optic biometric device, IOLMaster, between 3 and 6 o'clock in the afternoon. On each occasion, 5 successive measurements were taken and their mean was used as a representative value. The measurements were performed by a single examiner who was blinded to the original refractive status and subjects' assignment to either group.

The changes in axial length were evaluated prospectively and compared. In each group, a paired t test was used to compare axial length at baseline and at 2 years after treatment. An unpaired t test was used to compare the changes in axial length between groups.

Results

Among the 45 patients who were enrolled initially in the OK group, 42 patients (male 21, female 21) successfully completed the 2-year follow-up examinations. Their ages ranged from 8 to 16 (12.0 ± 2.6) years. Thirteen patients (31%) were aged 8 to 10 years, 23 (55%) were aged 11 to 13 years, and 6 (14%) were aged 14 to 16 years. At baseline, their spherical equivalent

refractive error ranged from -0.50 to -10.00 (-2.55 ± 1.82) D; logMAR uncorrected visual acuity was between 0.30 and 1.40 (0.80 ± 0.32), and axial length ranged from 21.98 to 27.67 (24.66 ± 1.11) mm (Table 2). Three patients in the OK group dropped out of the study due to insufficient improvement in uncorrected visual acuity (2 patients) and loss to follow-up.

Among the 60 patients in the spectacle control group, 50 patients (male 22, female 28) successfully completed the 2-year follow-up examinations. Their ages ranged from 8 to 16 (11.9 ± 2.1) years. Seventeen patients (34%) were aged 8 to 10 years, 26 (52%) were aged 11 to 13 years, and 7 (14%) were aged 14 to 16 years. At baseline, their spherical equivalent refractive errors were between -0.50 and -9.00 (-2.59 ± 1.66) D; logMAR uncorrected visual acuity ranged from 0.10 to 1.40 (0.83 ± 0.31), and axial length ranged from 22.53 to 28.00 (24.79 ± 0.80) mm (Table 2). Ten patients in the control group missed follow-up examinations and dropped out of the study.

At baseline, the two groups were comparable in terms of spherical equivalent refractive error, uncorrected visual acuity, axial length, age (unpaired t test), and gender distribution (Mann-Whitney U test) (Table 2). There were also no significant differences in age distribution (8-10, 11-13, and 14-16 years) between the groups. In the OK group, spherical equivalent refractive error decreased significantly from -2.55 ± 1.82 D at baseline to -0.68 ± 1.02 D at 2 years after the treatment (paired t test, $p < 0.0001$). In the control group, refractive error increased significantly from -2.59 ± 1.66 D to -3.83 ± 1.76 D ($p < 0.0001$).

In 2 years, axial length increased from 24.66 ± 1.11 mm to 25.05 ± 1.06 mm in the OK group and from 24.79 ± 0.80 to 25.40 ± 0.84 mm in the spectacle control group. In both groups, significant elongation of axial length was recognized during 2 years ($p < 0.0001$). The increases in axial length were 0.39 ± 0.27 mm and 0.61 ± 0.24 mm in the OK and spectacle groups,

respectively, and the increase in the OK group was significantly smaller than that in the spectacle group (unpaired t test, $p < 0.0001$).

Increases in axial length were analyzed in relation to the spherical equivalent refractive error at baseline. A significant correlation was found between these parameters in the OK group (Pearson's correlation coefficient; $r = 0.290$, $p = 0.0076$), but not in the control group ($r = 0.038$, $p = 0.7090$) (Fig. 1, 2).

In the OK group, 2 patients developed mild corneal erosion, which improved after one week of treatment cessation, and subsequent OK treatment was resumed without any sequelae. No other complications, such as corneal ulcer, were noted. There were no adverse events in the spectacle group.

Discussion

In 2005, Cho et al. reported that axial length in children elongated over a 2-year-period by 0.29 ± 0.27 mm in an OK-treated group and by 0.54 ± 0.27 mm in a control group treated with spectacles.²³ In 2009, Walline et al. reported similar findings; the mean axial length elongation in 2 years was 0.25 mm in the OK group and 0.57 mm in the control group.²⁵ Although similar results were obtained in our study, our subjects showed slightly greater axial length elongation in 2 years, being 0.39 ± 0.27 mm in the OK group vs. 0.61 ± 0.24 mm in the control group.

There were several limitations to the study conducted by Cho et al.²³ First, they used a contact type ultrasonic A-mode device to measure the axial length. It is difficult to measure axial length precisely with proper fixation and no indentation in children between 7 and 12 years. Second, the data of the control spectacles-wearing group were taken from another study conducted by Edwards et al.,²⁴ in which a different ultrasonic device was used to measure axial length. Naturally, different examiners conducted the measurements in a non-masked way. Third, axial

length at the start of OK was used as the baseline data. It has been reported that the central corneal thinning caused by OK ranges from -12 to -19 μm over a span of 3 months.^{28,30,31} This thinning is considered to be the epithelium in origin, while stromal change is negligible.³¹ Furthermore, OK does not alter the posterior corneal curvature or the anterior chamber depth.³² Thus, corneal thinning due to OK is attributable to epithelial changes, which can confound the study results. The study by Walline et al.²⁵ also had similar weaknesses.

In the current study, the IOLMaster, a laser interferometer, was used to conduct non-contact measurements of axial length. This device is very suitable for axial length measurements in children thanks to its high reproducibility, precision, lack of direct contact, and rapidity.²⁷ Moreover, both the OK and spectacle groups in our study were examined at a single center, by a single examiner, using a single instrument. Because the axial length taken 3 months after the start of OK was used as the baseline data, any initial corneal flattening by OK was excluded from the analysis of changes in axial length. Our improved study design allowed us to demonstrate that OK significantly slowed the elongation of axial length in myopic children.

Little is known about how OK retards axial elongation in childhood myopia. It has been postulated that growth of the eye is modulated by a visual feedback response to the defocus produced by the eye's refractive state.^{33,34} Recently, some experimental studies of primates have yielded data to support the concept that peripheral retina is able to influence ocular growth and refractive development.³⁵⁻³⁸ Similarly in humans, it is known that peripheral retina can influence refractive development, e.g., retinal diseases that affect mainly the peripheral retina,^{39,40} and that peripheral laser photocoagulation for retinopathy of prematurity^{41,42} is often associated with significant refractive errors. Mutti et al.^{43,44} reported that myopic children had greater relative hyperopia in the periphery with respect to axial refraction, indicating a prolate ocular shape (an

axial length exceeding the equatorial diameter), as compared with relative peripheral myopia and an oblate shape (an equatorial diameter exceeding the axial length) for emmetropes and hyperopes, suggesting that hyperopic defocus in the periphery promotes axial myopia in humans. Treatment strategies and methods for correcting not only central refractive error but also peripheral defocus and image quality may be effective to control eye growth in myopic children.^{35,45} From this viewpoint, OK seems to be a promising method, inducing a reduction in central epithelial thickness and an increase in the more peripheral annular zone to yield a flatter central area.^{30,46}

Although these corneal changes eliminate myopic refractive error in the central area, there is probably an increase of myopia in intermediate peripheral areas caused by the annular ridge of epithelial and stromal thickening.⁴⁷ Therefore, light passing through the flattened central area of the cornea forms an image on the fovea, while light passing through the mid-peripheral cornea, which became steeper than the original shape after OK, focuses at a point closer to the retina at the periphery. In other words, this type of corneal morphology can eliminate or decrease relative peripheral hyperopia that is often associated with myopic eyes.⁴⁸ At this stage, however, this hypothesis remains speculative, and will need to be tested by detailed evaluation of ocular shape and peripheral refractive status before and after the start of OK, in addition to the parameters we examined in the present study. In addition, it may be useful to examine the relationship between peripheral aberrations and axial elongation, because substantial increases in higher-order aberrations after OK were observed also in the peripheral field of the eye.⁴⁸

There was a significant relationship between the increases in axial length and baseline refractive errors in the OK group, whereas this relationship was not significant in the control group. When compared between the two scatterplots (Fig. 1&2), the distributions of axial growth were similar in both groups for low baseline myopes, showing a wide variety of increases in axial

length. However, the distributions were different for high baseline myopes. The increases in axial length were much smaller in the OK group than in the spectacle group. This indicates that when the baseline myopia is more severe, the axial elongation after OK is less marked. Generally, the cornea becomes more oblate (with a flat central area and increasing power toward the periphery) when more severe myopia is corrected by OK lenses with a very flat base curve. This probably leads to a greater decrease of hyperopic defocus at the periphery, thus exerting a greater suppressive effect on axial growth.

Although almost all subjects were adequately treated by OK, the myopic refractive error of only one subject (12-year-old boy) was not sufficiently corrected over the 2-year study period. The original refractive error of this case was -10.0 and -8.75 D in the right and left eyes, respectively, and these myopic refractive errors were the largest in the OK group. The 2-year treatment of OK improved these refractive errors from -10.0 to -4.0 D and from -8.75 to -2.0 D in the right and left eyes, respectively. LogMAR uncorrected visual acuity was also improved from 1.398 to 0.523 in the right eye, and from 1.222 to 0.155 in the left eye. Despite the fact that his refractive error after the treatment was not emmetropia and his visual acuity did not reach 20/20 (0.00 logMAR) in both eyes, he was satisfied with his visual outcomes and able to perform his daily activities without additional spectacle corrections. In this case, the increase in axial length during the 2-year study period was 0.13 and 0.27 mm in the right and left eyes, respectively, showing much smaller axial elongation in comparison to that in the spectacle group. This fact may support the concept that improvement in peripheral refractive status itself exerts a suppressive effect on axial growth even if the central refraction is not fully corrected. However, the peripheral refractive status of this subject is unknown. Further studies are needed to investigate whether elimination or reduction in hyperopic defocus in the periphery without enough correction in the central retina can retard axial elongation in childhood myopia.

In conclusion, our study has demonstrated a significant elongation of axial length in two groups of children treated with OK and with spectacles over a 2-year period. However, the axial length elongation in the OK group was significantly smaller than that in the controls. The mean axial growth rate was 0.15 mm per year in the OK group and 0.30 mm per year in the spectacle control group: a very marked difference. Although OK cannot completely arrest axial elongation in myopic children, it can retard such elongation to a certain extent, suggesting the potential of this treatment for slowing the progression of myopia.

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Figure Legends

Figure 1. Scatterplots demonstrating increases in axial length and spherical equivalent refractive errors at the baseline in the OK group.

A significant correlation was found between the increases in axial length and spherical equivalent refractive errors at the baseline (Pearson's correlation coefficient; $r = 0.290$, $p = 0.0076$).

Figure 2. Scatterplots demonstrating increases in axial length and spherical equivalent refractive errors at the baseline in the spectacle group.

No significant correlation was observed between the increases in axial length and spherical equivalent refractive errors at the baseline (Pearson's correlation coefficient; $r = 0.038$, $p = 0.7090$).

Table 1. Inclusion criteria

1. Ages from 8 to 16 years at the baseline.
2. No history of orthokeratology or the use of contact lenses.
3. Non-cycloplegic autorefraction (spherical equivalent) from -10.00 to -0.50 D in both eyes.
4. Astigmatism (non-cycloplegic autorefraction) equal to or less than 1.50 D in both eyes.
5. Anisometropia (non-cycloplegic autorefraction) equal to or less than 1.50 D.
6. Best-corrected visual acuity being equal to or better than 0.00 logMAR units in both eyes
(Snellen equivalent to 20/20).
7. No strabismus by a cover-uncover test either with or without refractive correction.
8. Birth weight equal to or more than 1,250 g.
9. No known ocular, systemic or neurodevelopmental deviations that might affect refractive development.
10. No use of medications that might affect refractive development.

D = diopter, logMAR = logarithm of the minimum angle of resolution.

Table 2. Baseline data of patients who completed 2-year follow-up examinations in the OK and control groups

	Orthokeratology (mean \pm SD)	Control (mean \pm SD)	P value
Age (years)	12.0 \pm 2.6	11.9 \pm 2.1	p=0.6129
Gender	Male 21, Female 21	Male 22, Female 28	p*=0.4378
Spherical equivalent refractive error (D)	-2.55 \pm 1.82	-2.59 \pm 1.66	p=0.8771
Uncorrected visual acuity(logMAR)	0.80 \pm 0.32	0.83 \pm 0.31	p=0.5064
Axial length(mm)	24.66 \pm 1.11	24.79 \pm 0.80	p=0.3434

SD = standard deviation, D = diopter,

LogMAR = logarithm of the minimum angle of resolution.

p = probability values using unpaired t test.

p*= probability values using Mann-Whitney U test.

No significant inter-group differences or variations in distribution patterns at the baseline in spherical equivalent refractive error, uncorrected visual acuity, axial length, age or gender.

Figure 1.

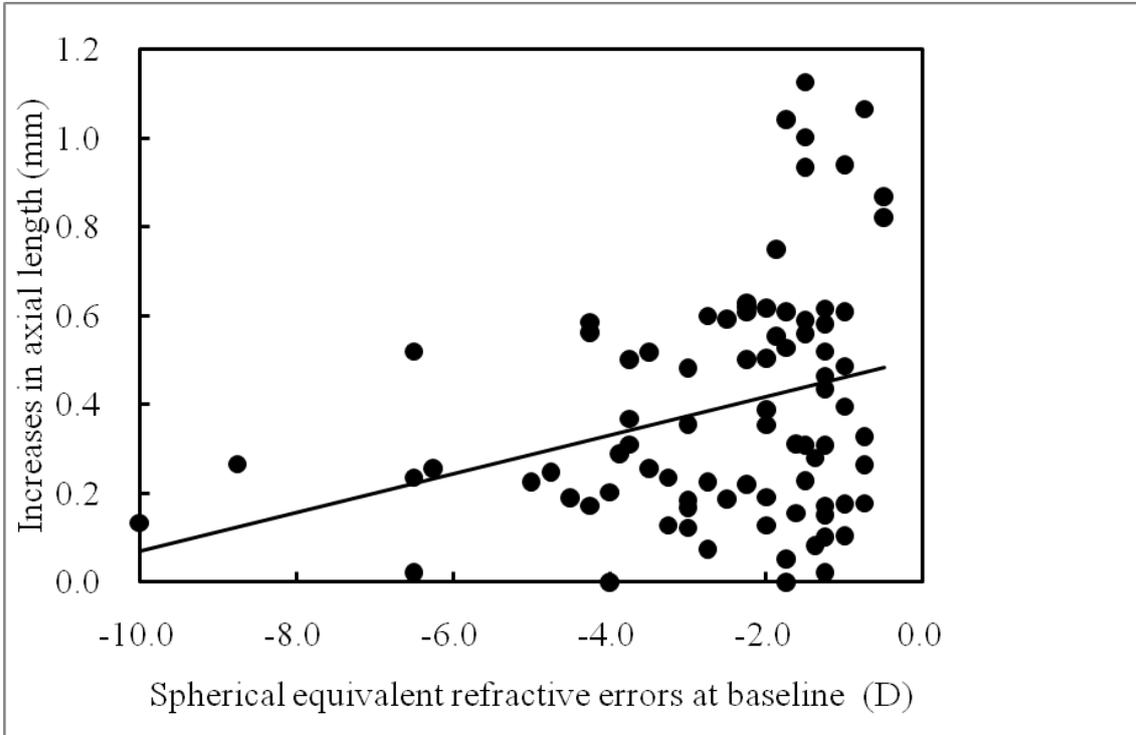


Figure 2.

