Research Article

Axial length in orthokeratology patients: large case series

Abstract

Purpose: To evaluate axial length measurements obtained over a three-year period in children undergoing Orthokeratology (Ortho-K).

Methods: Patient records were identified from a specialty contact lens practice. Data were obtained from myopic patients who were prescribed Ortho-K wear. Demographic data at baseline included age at commencement of Ortho-K and ethnicity. Clinical data recorded at baseline and at years 1, 2 and 3 included subjective refraction, corneal topography, corneal curvature, axial length, pupil size, and lens design, changes in lens parameters, lens wear habits, wearing time and unaided visual acuity. The primary outcome measure was change in axial length during the study period.

Results: 194 eyes of 97 subjects were included in data analysis. Mean age at start of Ortho-K was 10.4 years (SD=1.9). Mean axial length was 24.59 mm (SD=0.85) at baseline and 24.87 mm (SD=0.87) at the three year evaluation, for a mean change in axial length of 0.28 mm (SD=0.64). 65.5% of eyes (n=127) showed little or no change (<0.5 mm) in axial length during the study period. 20.1% of eyes (n=39) showed moderate increase in axial length of 0.5-1.0 mm and 14.4% of eyes (n=28) showed >1.0 mm increase in axial length during the 3-year study period. Linear mixed regression analysis showed a significant association between older age at initiation of Ortho-K and less increase in axial length (p=0.0077). Axial length changes were not associated with duration of wear (both hours/night and nights/week) or baseline corneal curvature.

Conclusion: Use of Ortho-K may help reduce axial length elongation in myopic eyes. Age of the initial treatment is a key factor. The baseline of cornea curvature and duration of the wear are not directly associated with treatment outcome. Of note, during the three-year study, 65.5% of treated eyes (n=127) showed a minimal or clinically insignificant increase of axial length (<0.5mm). Early treatment should be considered.

Keywords: axial length, myopia progression, orthokeratology, overnight corneal reshaping, biometry

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Introduction

The prevalence of myopia in the United States and throughout the world has increased dramatically over the last 30-40 years. The National Health and Nutrition Examination Survey of the US population, conducted from 1999 to 2004, reported the prevalence of myopia to be 42% of individuals in the 12 to 54-year-old age group, compared to 25% for the same age group 30 years previous.[1,2] In Singapore and Taiwan, prevalence has been estimated at 80% of young adults.[3] Within the next five years, it is estimated that myopia will affect nearly 2.5 billion people worldwide.[4] When myopia is initially seen in children 4-9 years old, it often progresses substantially during growth years that follow.[3] The increasing rate of myopia prevalence has been linked to both genetic and environmental factors. A child's risk of developing myopia increases threefold if both parents are myopic.[5,6] Two independent research groups, using genome-wide association studies, have identified 20 genetic loci that have been linked to myopia.[7] Environmental factors such as long periods of near work, type of optical correction, and limited outdoor time also affect myopia development.[8-11] One study reported that increasing time spent outdoors can delay the onset of myopia.[12] The complex nature of the genetic and environmental interactions that contribute to myopia progression is a topic of ongoing studies worldwide.

Identifying ways to prevent or reduce myopic progression are important to eye care providers as well as patients and parents of myopic children. Substantial increases in axial length and the resulting myopic progression requires repeated refractive corrections during childhood, and places those with higher myopia at risk of sight-threatening complications such as maculopathy, retinal detachment, cataracts and glaucoma.[13-17] Once myopia develops, various methods of slowing its progression have been attempted in conjunction with clinical testing of these methods.[11,18-20] These include pharmaceutical agents such as atropine, multifocal spectacle lenses, specially-designed soft contact lenses, rigid gas-permeable contact lenses, spectacle under-correction, and Orthokeratology (Ortho-K).[11] Ortho-K is the application of specially-designed, reverse-geometry; rigid-gas-permeable contact lenses worn only while sleeping to temporarily reshape the cornea, such that refractive error is corrected without the need to wear any correction during waking hours. To date, numerous clinical studies have reported a beneficial effect of Ortho-K on slowing or stopping myopic progression.[20-25] Ortho-K requires

adherence to prescribed wear time, and children in one retrospective study were shown to be very adherent to the prescribed Ortho-K wearing schedule.[26]

Although some clinical studies evaluating myopia progression have used change in cycloplegic refraction (objective and/or subjective) as the outcome measure to determine if refractive changes have occurred,[11] others used change in axial length as the outcome measure of growth-related refractive changes.[27,28] The advantage to using axial length is twofold: axial length is an objective measure and has been associated with complications of myopia.[14-17] In this observational study, we evaluated children who have worn Ortho-K lenses regularly for three years to analyze changes in axial length and refractive status after commencing use of Ortho-K. We performed this study to demonstrate results that could be expected with typical myopic patients presenting to practitioners in clinical practice. This large case series represents a sample of a common demographic seen by practitioners prescribing Ortho-K in the United States.

Methods

This study was approved by the University of Michigan Medical School Institutional Review Board (IRBMED). This was a retrospective study evaluating data from patients in the practice of the first author (MJL). Patients whose records were selected for analysis in the study included those who began regular wear of Ortho-K lenses between April 2007 and October 2011, were 7-14 years old, had myopia between -1.00D and -6.50D, had less than 2.00D of astigmatism, attended routine follow-up care at recommended intervals for at least 3 years after commencing Ortho-K wear, and did not wear spectacles at any time. Subjects excluded from analysis included those who had not worn Ortho-K lenses regularly (stopping for more than two weeks), had annual exams greater than 15 months from baseline or previous annual exam, or who were diabetic. Refractive data were based on subjective manifest refraction. Axial length was measured with a hand-held MMD PalmScanA2000 (Calabasas, CA) ultrasonic A-scan. This device has been validated as accurate in a previous study [29] that followed an identical protocol by the same operator (MJL) for all axial length measurements. Corneal curvature was monitored with manual keratometry and corneal topography with Carl Zeiss Meditec (Dublin, CA) - Humphrey Atlas 993 or Medmont (Nunawading, Victoria, Australia) - E300.

Baseline information obtained at the time of initial presentation for Ortho-K evaluation and fitting included the subject's age and the following for both eyes of each subject:

i.   Subjective refraction (sphere/cylinder/spherical equivalent).

ii.   Manual keratometry readings.

iii. SimK (Simulated Manual Keratometry) measurements from topography.

iv.   Corneal eccentricity/shape factor

v.   Pupil size (mesopic).

vi.   Best-corrected visual acuity –monocularly and binocularly.

vii. Horizontal visible iris diameter (HVID) / Corneal diameter.

viii. Lens design.

ix.   Axial length.

Follow-up data+ collected at exams 1, 2 and 3 years after initial fitting included:

I.   Axial length – as above

II.   Uncorrected visual acuity – monocular and binocular

III.   Average number of nights lenses worn per week

IV.   Average number of hours lenses worn per night

V.   Position of treatment zone (centered or direction of decentration)

VI.   Manifest refraction (sphere and cylinder)

VII.   Manual keratometry readings

VIII. SimK readings from topography

+ All follow-up data were obtained between 1 and 9 hours after lens removal.

Statistical methods

Descriptive statistics of the sample were summarized with means and standard deviations (SD) for continuous measures, and frequencies and percentages for categorical measures. Mixed linear regression[30] was used to estimate the effect of covariates on axial length change from baseline over time (yearly up to 3 years). This model accounted for the correlation between the two eyes of a subject and the correlation within a single eye over time. The following variables were investigated for a relationship with axial length change: age at start of Ortho-K, baseline measures of the eye (spherical component of myopia, cylinder, flat K reading (manual and simK), steep K (manual and simK), shape factor (eccentricity), pupil diameter, corneal diameter), time-varying measures of usage (hours/night and nights/week of contact wear), and location of treatment zone (from topography). Note: Flat K reading is the least curvature measurement in a particular meridian of the cornea taken from manual keratometry and from topography. SAS version 9.4 (Cary, NC) was used for all statistical analysis.

Results

141 patient records were screened for study participation. Of those, 44(31%) were not eligible. Reasons for exclusion included: lack of compliance with follow-up schedule (n=14), missing data (n=9), less than 3 years of follow-up (n=2), started Ortho-K elsewhere (n=5), no baseline axial length data (n=12) and discontinued Ortho-K (n=2). 97study participants (194 eyes) were included in the data analyses. Ethnicity of the subject population was Asian (n= 88, 90.7%) and Caucasian (n=9, 9.3%). Baseline descriptive data on eyes are detailed in (Table 1). Mean age at start of Ortho-K was 10.4 years (SD=1.9). Ortho-K lenses worn by the subjects were of four different designs: CRT lenses (Paragon Vision Science - Mesa, AZ) were used in 128 eyes (66%), CRT-Dual Axis Lenses (Paragon Vision Science - Mesa, AZ) were used in 20 eyes (10%), Emerald lenses (Euclid Systems- Herndon, VA) were used in 20 eyes (10%), and custom-designed Ortho-K lenses were used in 26 eyes (13%). The various lens designs were used to achieve optimally centered treatment (defined by post-treatment topography) and best unaided visual acuity during waking hours. Study subjects wore the same lens design in each eye except for one subject, who wore a CRT lens in one eye and a CRT-Dual Axis lens in the other eye.

Table 1 Baseline descriptive data on the study participants

Baseline Data (n=194 Eyes of 97 Subjects)		
Attribute	**Mean (SD)**	**Range**
Sphere (D)	-2.96(1.24)	-6.25 to -.75
Cylinder (D)	-.32(.38)	-2.50 to -0.25
Spherical Equivalent (D)	-3.12(1.25)	-6.50 to -.75
Manual Flat K (D)	42.42(1.14)	39.00 - 45.50
SimK Flat K (D)	42.81(1.23)	39.00 – 45.87
Shape Factor	.32(.10)	0.01 - 0.65
Pupil Size (mm)	6.0(.6)	4.0 – 8.0
Corneal Diameter (mm)	11.56(.36)	11.00 – 12.10
Axial Length (mm)	24.59(.85)	21.89 -28.03

The mean baseline axial length was 24.59mm (SD=0.85) and at the three year evaluation was 24.87mm (SD=0.87), for a mean increase in axial length of 0.28mm (SD=0.64), which was statistically significant (p<0.0001) (Table 2). 65.5% of eyes (n=127) showed little or no change in axial length during the study period (defined as

<0.50mm increase) for the 3-year study period.20.1% of eyes (n=39) showed moderate increase in axial length (defined as 0.50 to1.00mm increase). 14.4% of eyes (n=28) showed >1.00mm increase in axial length during the 3-year study period. Change in axial length stratified by starting age is shown in (Figure 1). Results show that for children starting Ortho-K at age 6-7 (n=26) at baseline, mean axial length change at 3 years was 0.57mm. For children ages 8-9 (n=60), 10-11 (n=58) and 12-14 (n=50), mean axial length change at 3 years since starting Ortho-K were 0.46mm,0.15mm and 0.06mm, respectively.

Linear mixed regression analysis was used to identify factors that predicted axial length change over time (Table 3). Age at Ortho-K initiation was associated with axial length change such that for every year older at Ortho-K initiation, axial length change decreased by 0.06mm (p-value = 0.0077). Descriptively, mean age at start of Ortho-K for eyes with little to no, moderate, and substantial change in axial length after 3 years was 10.8 years (SD=1.9), 9.6 years (SD=1.6), and 9.5 years (SD=1.8), respectively. On average, for every additional year of follow-up, change in axial length from baseline increased by 0.14mm (p-value < 0.0001). Pre-Ortho-K measures including the spherical component of myopia, cylinder, flat and steep K reading, shape factor, pupil diameter, corneal diameter, as well as Ortho-K usage, and location of treatment zone were not significantly associated with change in axial length.

Table 2 Descriptive statistics on axial length (mm), for the sample of 194 eyes

Axial Length Data				
Time	**Mean (SD)**	**Min, Max**	**Median**	**P-value***
Baseline	24.59 (0.85)	21.89, 28.03	24.57	
Year 1	24.58 (0.89)	22.09, 26.75	24.59	0.9826
Year 2	24.74 (0.57)	21.18, 27.16	24.74	0.0056
Year 3	24.87 (0.87)	22.68, 26.83	24.9	<0.0001
Baseline to Year 1 Change	-0.01 (0.53)	-2.08, 1.35	0.02	0.9826
Year 1 to Year 2 Change	0.16 (0.48)	-1.40, 1.18	0.18	0.0002
Year 2 to Year 3 Change	0.13 (0.37)	-0.69, 1.40	0.08	<0.0001
Baseline to Year 3 Change	0.28 (0.64)	-1.80, 2.44	0.23	<0.0001

*P-values from linear mixed regression for the comparison between baseline and follow-up measure, accounting for correlation between eyes of a subject
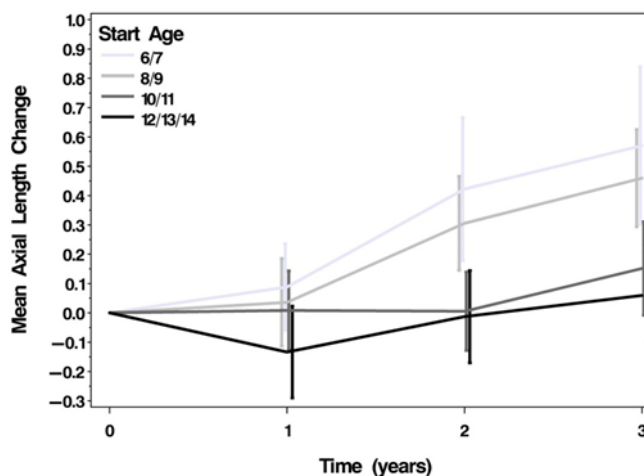
Figure 1 Plot of axial length change at each year of the study for different age groups. Sample size for each group: age 6-7, n=26: age 8-9, n=60: age 10-11, n=58: age 12-14, n=50. At three years, the axial length changes for each group are: age 6-7, 0.57 mm; age 8-9, 0.46 mm; age 10-11, 0.15 mm and age 12, 13 and 14, 0.06 mm.

Table 3 Linear mixed regression model results for the association of variables with axial length change from baseline over time. Note: each variable is entered into a separate model

Linear Mixed Regression Analysis of Baseline Attributes to Predict Axial Length Changes			
Variable	**Estimate**	**SE**	**P-value**
Time (years)	0.14	0.02	<0.0001
Spherical Equivalent	0.03	0.03	0.3196
Astigmatism	-0.04	0.11	0.6742
Age at start of OCR	-0.06	0.02	0.0077
Manual Flat K	-0.04	0.04	0.2897
Manual Steep K	-0.05	0.04	0.1872
SimK Flat	-0.07	0.03	0.0586
SimK Steep	-0.06	0.03	0.0721
Shape Factor	-0.23	0.43	0.5974
Pupil Diameter (mm)	-0.05	0.07	0.5104
Corneal Diameter (mm)	0.01	0.12	0.9505
Hours/Night	0.05	0.04	0.165
Nights/Week	-0.02	0.02	0.3167
Topography (Center vs Other)	0.04	0.05	0.377

SE: Standard Error

Discussion

This case series represents a large group of children treated with Ortho-K and followed for three years to monitor changes in axial length. Axial length changes were evaluated in the context of other factors, such as age at start of Ortho-K, initial refraction, pupil size, corneal topographical changes, lens design, and wearing time. These factors are listed in (Table 3).

Axial length changes with other modes of correction

Our results show that use of Ortho-K was associated with less axial length increase than historical increases in similar aged children wearing other forms of vision correction.[27,31,32] A study conducted in China, reported a mean of .36 mm increase in axial length in the first year following the onset of myopia.[31] In the second and third year following the onset of myopia, they reported 0.30mm and 0.21mm annual increases in axial length respectively. For the three years following the onset of myopia, this study showed a mean total increase in axial length of 0.87mm. While these data provide a reference point, they do not provide normative data on axial length increase during childhood. This is due to numerous variables that may contribute to refractive and axial length changes including age of myopia onset,[27,31] ethnicity,[31-36] hours of near work,[37] hours of time spent outdoors,[38] mode of refractive correction[20,24,39] and parental history of myopia.[40]

Ethnicity and axial length increases

It is notable that 91% of our study participants were Asian Americans. Asian children have been shown to develop myopia at younger age and progress at a higher rate than other ethnic/racial groups.[31,33,34] This may relate to differences in posterior scleral/retinal contour and the resulting difference in peripheral refraction.[41-43]

A recent 3-year study on myopic progression in Asian-Canadian children showed single vision spectacle wearers had a mean change in axial length of 0.82 (SD=0.05) mm over the 3-year study period (an increase of 0.39 mm after one year, an additional 0.23 mm after two years, and an additional 0.20 mm increase after three years).[44] The age and ethnicity of subjects in the study was very similar to that of our study subjects.

Age and axial length changes

As children get older, the rate of axial length change decreases for those who wear glasses or Ortho-K. But, children who start Ortho-K younger have the largest reduction in axial length change vs. children wearing glasses. In this study, children who started Ortho-K at age 6-7 showed a mean increase of 0.57mm in axial length over a 3 year period compared to spectacle-wearing children in a study by Hyman et al.,[33] who showed 1.10 mm of axial length increase in three years. In contrast, the 10-11 year-old Ortho-K wearers in our study showed 0.15 mm axial length increase versus 0.50 mm of axial length increase in the 11 year-old spectacle wearers. As a reference, (Table 4) summarizes axial length change for age groups for different modes of correction.

Axial length increases vs. refractive increases

As a point of reference in evaluating axial length changes relative to refractive changes, Hyman et al.,[33] reported that a 1 mm increase in axial length was associated with 2.04 D of myopia progression and alternatively, 1 D of myopia progression was associated with 0.50 mm of axial elongation. Those numbers, applied to our study, would suggest that our mean increase of 0.28 mm over the three-year study period would result in a 0.57D increase in myopic refraction.

Table 4 Axial length change (mm) for various studies by age, correction modality and total number of patients

Summary of Studies on 3 yr Increase in Axial Length (mm)					
Age at Start	**This Study**	**Cho et al.,[20]**	**Cho et al.,[20]**	**Hyman et al.,[33]**	**Cheng et al.,[43]**
Correction Modality	**Ortho-K**	**Ortho-K**	**Spectacles**	**Spectacles**	**Spectacles**
7-Jun	0.57			1.1	Age 8-13
9-Aug	0.46	0.49	0.81	0.82	
11-Oct	0.15	0.31	0.55	0.57	
12 +	0.06			None	
Mean 3 yr change	0.28	0.36 (2yr)	0.63 (2yr)	0.71	0.82

Studies of myopia control with ortho-k

Three meta-analysis evaluations of the effect of Ortho-K on reducing myopic progression and increasing axial length have been recently published. They report 41-45% less increase in axial length in wearers of Ortho-K compared to various control groups corrected with single vision spectacles or soft contact lenses.[45-47] Given the fact that we didn't have a control group, we summarized our findings in terms of the percentage of subjects who experienced little or no progression which is similar to what Cho et al.,[20] did in their study. Their study categorized myopic progression using "fast progressors" (refractive change of >1.00D /year or axial length changes of >0.36 mm/yr) vs. "slow progressors" (refractive change of ≤0.50D /year or axial length changes of ≤0.18 mm/yr) in wearers of Ortho-K lenses vs. a control group wearing single vision spectacles. That study found the percentage of fast progressors was 34% in the control group vs. 15% in the Ortho-K group and the percentage of slow progressors was 14% in the control group vs. 46% in the Ortho-K group. Using the criteria established in the Cho study, our results showed less myopic progression in Ortho-K wearers than reported in the Cho study.

How ortho-k slows myopic progression

Investigations into myopia control over the previous decade have generated theories to explain why Ortho-K slows axial length increases in myopic children.[48-50] Most have centered on the effect of the optical changes to the peripheral refractive profile created by Ortho-K. Similar to spectacles and contact lenses, Ortho-K creates sharp focus on the central area of the retina (macula and peri-macular area). But, peripheral to the macular area, while spectacle and contact lens correction creates relative peripheral hyperopia, Ortho-K creates relative peripheral myopia.[51-56] This relative peripheral myopic defocus inhibits the signaling for the eye to elongate.[50]

Axial length - other factors

While a previous study of Ortho-K wearers[48] documented corneal thickness changes, particularly of the epithelial layer, the changes reported in these studies were between 10 and 15 microns, which are not clinically substantial enough to affect our findings. Another study showed no significant changes in the length of the anterior segment, which indicates that axial length measurement, should be a valid method to monitor myopic progression in children undergoing Ortho-K.[49]

The future of myopia control with ortho-k

It is likely that there is more involved in myopia control with Ortho-K than reshaping the cornea for best central visual acuity. Individually designing Ortho-K lenses for optimal myopia control may involve creation of custom lens profiles generated from baseline measurements of posterior retinal shape and peripheral refraction.[52-56] The ideal amount and location of the relative peripheral myopia required for optimal myopia control is not known at this time.[57] Peripheral refraction was not performed on subjects in this study and the Ortho-K lenses used for this study's participants were not custom-designed based on this parameter. Future study of Ortho-K recipients that include collection of peripheral refractive data may reveal why some subjects showed no progression compared to those who still progressed.

Ortho-K vs. other modes of correction

Currently, myopic children and their parents who are concerned about myopic progression can consider Ortho-K as one option to slow myopic progression. Advantages for children choosing Ortho-K over spectacle correction include no vision correction required during daily activities and the slowing of myopic progression. The disadvantages of Ortho-K are the ongoing potential for eye irritation caused by debris under the lens while sleeping and potential for variable visual acuity dependent on a specific number of hours of nightly wear of the lenses. Ongoing risks of complications with Ortho-K relate to corneal abrasion and microbial keratitis. That said, recent studies have shown that Ortho-K poses less risk of microbial keratitis than that of overnight wear of soft lenses.[58]

Summary

Use of Ortho-K was associated with less axial length increase than historical increases in similar aged children wearing other forms of vision correction to correct their myopia. Age at start of Ortho-K was the only clinically significant factor associated with axial length changes during our three-year study. Because of the lack of concurrent controls in our study, and comparison of 3 year results with outcomes from populations that differ from ours, conclusions should be viewed with due caution. Our retrospective study showed the mean change in axial length in Ortho-K wearers over a three year period was an increase of 0.28 mm. Additional study of peripheral refractive profiles of children being treated with Ortho-K will add to our understanding of the ideal peripheral refractive profile that may stop or slow myopic progression even more effectively. For now, use of Ortho-K slows myopia progression for the majority of children.

Acknowledgments

Conflicts of interest

Authors declare that there is no conflict of interest.

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