Results of a Three-Year Clinical Trial on Treatment of Myopia in Children and Adolescents Using High-Precision Orthokeratology Lenses (English translation)

CHANG Yong, XIE Pei-ying, WANG De-chen, CHI Hui, XHOU Jian-lan
Beijing Internet Eyecare Optometry & Ophthalmology Clinic

Abstract

Objective

To evaluate the effect and safety of long-term wearing high precision ORTHO-K contact lens for myopic children and adolescents. **Design** Retrospective case series. **Participants** 150 myopic children and adolescents. **Methods** We examined 150 patients (300 eyes) who wore ORTHO-K lens for 3 years in Beijing Internet Eyecare Optometry & Ophthalmology Clinic. Following examinations had been performed for baseline and all annual follow-up visits: slit lamp exam, uncorrected visual acuity (UCVA), and tear secretion, eye axial length, corneal thickness, corneal endothelial cell density, percentage of hexagon and corneal curvature values. We also selected 66 eyes switching to ORTHO-K from other brands for evaluation of comfort, clarity and cleanliness. **Main Outcome Measures** The UCVA corneal endothelial cell density, percentage of hexagon cells, axial length, tear secretion, corneal thickness, and corneal conjunctival health condition. **Results** No obvious adverse reaction was found on the cornea and conjunctival. The UCVA improved significantly (4.55 ± 0.34 before wearing vs. 4.88 ± 0.25 after three years, $P < 0.001$). The refractive error decreased during early wearing period. The spherical and cylindrical diopters were (-2.99 ± 2.44) D and (-1.17 ± 1.20) D at baseline; which decreased to (-1.95 ± 2.12) D and (-1.11± 1.06) D respectively after initial wearing stage (P = 0.01, P = 0.001). The axial length increased slightly but not significantly (0.28± 0.12) mm after three years. The corneal thickness decreased by (-7.71± 2.88) μm, (-2.56± 2.78) μm and (0.44± 2.95) μm at one, two and three year respectively, reaching to a significant thinning at 3 year compared to baseline (P = 0.001). The endothelial cell density was (3244± 309) pieces/mm^2, (3265 ± 304) cells/mm^2, (3264 ± 299) pieces/mm^2, (3270 ± 296) pieces/mm^2 at baseline, year 1, year 2 and year 3 respectively (all $P > 0.05$). There was no significant change on tear secretion. The scores of comfort, clarity, cleanliness of the original type of lenses were 8.69 ± 0.62, 9.26 ± 0.72, 9.37 ± 0.58, which improved significantly to 9.16 ± 0.36, 9.33 ± 0.65, and 9.62 ± 0.47 respectively (t = -2.181, -0.601, -0.830; all $P < 0.05$) after switching to high precision type. **Conclusion** The result of 3 years follow-up shows that the subjective comfort improved after switching to high precision lens. Wearing high precision ORTHO-K lens enhanced unaided vision acuity and showed myopia control effects. With regular and scientific fitting, ocular surface would remain unaffected. (*Ophthalmol CHN, 2018, 27: 353-357*)

Literature and Methods

1. Subjects

   150 children and adolescent cases (300 eyes) who were prescribed orthokeratology lenses from 2012 to 2013 at the Beijing Internet Eyecare Optometry & Ophthalmology Clinic and then wore them for three years. Upon initial examination the subjects were between 8 and 20 years old with a spherical power of -2.99 ± 2.44 (D) and cylindrical power of -1.17 ± 1.20 (D). None of the subjects had contraindications for orthokeratology lenses including those with ametropia or ocular diseases. The subjects and their guardians were informed of the precautions and possibility of complications before receiving treatment and gave informed consent by signing a release.

2. Lens types

   High-precision orthokeratology lenses fabricated on fully automated Japanese NC (precision: 1/10,000 mm), lens material: BOSTON EM, oxygen permeability (Dk): 104 x 10^{-11} (cm^2/s) (ml O_2/ml x mm Hg), refractive index: 1.422, contact angle: 35 degrees, with a five VST curve design, two alignment curves, and toric design.

3. Prescription method

   First, a series of general eye examinations were conducted, including an anterior eye examination, funduscopy examination, and intraocular pressure measurements. Next, a phenol red thread test was used to conduct a lacrimation function examination, tests were conducted with an autorefractor keratometer and phoropter, then a corneal endothelial cell density test was conducted. Corneal topography was then measured using TMS-4, then the eye axial length and corneal thickness were measured using Lenstar LS 900. Trial lenses were selected based on subject corneal topography and corneal curvature data to ensure the optimal orthokeratology lenses for the subject. After a 30 to 50-minute trial wear period, fluorescein was used to check the lens fit, appropriate adjustments were made to achieve an appropriate fit, and custom-made orthokeratology lenses were prescribed.

4. Lens pick-up, follow-up, and lens changes

   When picking up the lenses, subjects practiced lens care, insertion and removal, and received an explanation on overnight wear, then a follow-up examination was conducted after a full night of use. Follow-up examinations were then conducted one week later, two weeks later, and one month later, then every one to two months thereafter. The ORTHO-K lenses were worn every night, removed early each morning, and follow-up examinations were conducted 20 minutes to several hours after removal. Re-examination items: The anterior eye condition, uncorrected visual acuity, and TMS-4 corneal topography were tested. The lens fit was confirmed during use, then corrected visual acuity was measured with the lenses removed. Every three months, corneal endothelial cell density and conditions were examined, eye axial length and corneal thickness were measured with Lenstar LS 900, and tear conditions were measured via the phenol red thread test. Conventional orthokeratology lenses were replaced with high-precision ORTHO-K lenses for 66 eyes, then a subjective evaluation of these lenses after one month of use was compared to a subjective evaluation (out of 10 points) of the original lenses conducted based on each item of visual clarity stability, lens cleanliness, and comfort. (1) Comfort evaluation: A score of 5 points or less indicates

a clear feeling of a foreign body. A score of 5 to 7 points indicates a feeling of a foreign body, but within tolerable limits. A score of 8 to 10 points indicates a natural feeling, with generally no feeling of a foreign body. (2) Visual clarity evaluation: A score of 5 points or less is poor, 5 to 7 points is good, and 8 to 10 points indicates a highly ideal level of comfort. (3) Lens cleanliness: A score of 5 points or less indicates a significant amount of deposits on the lens surface and opaque across a wide area, being clearly visible to the unaided eye. A score of 5 to 7 points indicates opaque across a narrow area of the lens surface and a moderate level of deposits which can be confirmed by the uncorrected visual acuity. A score of 8 to 10 points indicates a small amount of deposits that can be confirmed with a slit lamp microscope or no deposits. Post-use examinations evaluated any complications with the cornea and conjunctiva based on correlation evaluation criteria with the cornea and conjunctiva. The correlation evaluation criteria for the cornea and conjunctiva are as follows. Inflammation of the eyelids, conjunctiva and corneal limbus: Scored from 0 to 4 points. Palpebral conjunctival papillae: Scored from 0 to 4 points. Superficial punctate keratopathy: Scored from 0 to 4 points. Corneal neovascularization: Scored from 0 to 4 points.

Lenses were replaced every one to one and a half years or as needed when any obvious scratches, damage, serious deposits, deformation, or other issues were present.

5. Statistical method

A one-way analysis of variance via SPSS 16.0 was employed to observe changes in visual acuity from before use and at one, two, and three years of use, changes in lacrimation conditions, corneal endothelial cell density, eye axial length and corneal thickness. A value of $P < 0.05$ was considered a statistically significant difference.

Results

1. Changes in visual acuity and refraction before and after use

Visual acuity was clearly improved after one year of use, showing a statistically significant difference ($P < 0.001$). Uncorrected visual acuity for all subjects was stable at an appropriate standard after three years of use (Table 1). Spherical power and cylindrical power before use were respectively -2.99 ± 2.44 (D) and 1.17 ± 1.20 (D). After one month of use, correction being stable, the spherical power and cylindrical power were respectively -1.95 ± 2.12 (D) and -1.11 ± 1.06 (D). Compared with before use, refraction due to corneal correction effects after one month of use clearly dropped, showing a statistically significant difference in spherical power ($P = 0.012$) and a statistically significant difference in cylindrical power as well ($P = 0.001$).

2. Changes to eye axial length after three years of use

Although extension of the eye axial length is slightly suppressed after three years of use, there were no statistically significant differences. ($P = 0.062$) (Table 1)

Table 1. Changes to uncorrected visual acuity, eye axial length, corneal endothelial cell density and shape, central corneal thickness, and lacrimation before use and three years after use

Item	Before use	After use			F value	P value
		1 year	2 years	3 years		
Uncorrected visual acuity	4.55 ± 0.34	4.86 ± 0.27	4.87 ± 0.26	4.88 ± 0.25	19.15	< 0.001
Eye axial length (mm)	25.47 ± 1.07	25.59 ± 1.06	25.73 ± 1.05	25.75 ± 2.25	2.447	0.062
Corneal endothelial cell density (cells/mm^2)	3244 ± 309	3265 ± 304	3264 ± 299	3270 ± 296	0.426	0.735
Corneal endothelial cell cv	35.20 ± 4.67	35.56 ± 5.87	35.97 ± 5.07	35.81 ± 4.49	1.313	0.269
Corneal endothelial cell 6A ratio (%)	61.81 ± 9.07	61.06 ± 8.94	60.19 ± 9.34	60.69 ± 8.57	1.739	0.157
Central corneal thickness (μm)	538.00 ± 35.59	531.29 ± 32.90	527.73 ± 35.06	528.17 ± 37.16	5.498	0.001
Lacrimation volume (mm)	20.99 ± 5.64	21.65 ± 5.97	21.65 ± 6.25	21.99 ± 6.50	1.151	0.327
BUT (s)	10.16 ± 7.50	9.97 ± 4.95	9.21 ± 4.13	9.62 ± 4.78	1.640	0.179

3. Changes to corneal endothelial cell density and shape before and after use
   There was no significant reduction in the corneal endothelial cell hexagonal ratio between before use and after three years of use, and there were also no clear increases in the coefficient of variation ($P > 0.05$) (Table 1).
4. Changes to central corneal thickness before and after use
   Compared with values before use, central corneal thickness became slightly thinner, thinning to -7.71 ± 2.88 (μm) within one year of use but stabilizing and no longer thinning after three years of use. Changes did not exceed 11 μm, with changes each year over three years respectively at: -7.71 ± 2.80 (μm), -2.56 ± 2.78 (μm), and 0.44 ± 2.95 (μm) (Table 1).
5. Evaluation of cornea and conjunctiva reaction in three years of use
   A total of 2,720 examinations were conducted for 300 eyes over three years of use, showing mild conjunctival hypermia and papillary follicles in rare cases among a few subjects. However, appropriate eye drops were prescribed and there were no adverse effects on lens wear. Superficial punctate keratopathy occurred in some rare cases. However, stopping lens use for a short period of time and prescribing the appropriate eye drops allowed the cornea to return to normal, after which lens wear was continued. Kayser-Fleischer rings appeared in extremely few cases during follow-up examinations. However, after an appropriate period where lens use was stopped, the fit was adjusted and the eye returned to normal (Table 2).

Table 2. Wear period and cornea/conjuctiva reaction

Item	Palpebral conjunctiva		Corneal epithelium		Corneal opacity ± to +	Kayser-Fleischer rings	Corneal neovas-cularization	Conjunctival inflammation	
	Papillary follicles (Class I)	Papillary follicles (Class II)	Superficial punctate keratitis (Class I)	Superficial punctate keratitis (Class II)				Class I	Class II
No. of abnormal symptom occurrences	327	0	67	4	10	8	0	716	0
Complication rate (%)	12.02	0	2.46	0.15	0.37	0.29	0	26.32	0
Continuation after recovery	Recovered or symptoms clearly improved		Yes	Yes	Yes	Yes		Yes	
Stopped use	No		No	Continued use after stopping for a short period	Continued use after stopping for a short period	Continued use after stopping for a short period		No	

6. Changes in tear volume and tear film break-up time after three years of use
   There was no abnormal reduction in tear volume after three years of use and stable tear film conditions were maintained. Tear film break-up times (BUT) were generally stable before use and over three years of use, and there were no statistically significant differences (Table 1).
7. Subjective evaluation upon switching to ORTHO-K lenses
   Of the subjects under observation, the 66 eyes of subjects who switched to ORTHO-K from non-high-precision lenses were subjectively evaluated by the subjects (out of 10 points), clearly showing improved lens comfort, cleanliness, and visual clarity stability after switching (Table 3).

Table 3. Subjective evaluation

Brand	Visual clarity stability	Lens cleanliness	Comfort
Original manufacturer	9.26 ± 0.72	9.37 ± 0.58	8.69 ± 0.62
ORTHO-K	9.33 ± 0.65	9.62 ± 0.47	9.16 ± 0.36
t value	-0.601	-0.83	-2.181
P value	0.039	0.046	0.018

Discussion

The main orthokeratology lenses used in the orthokeratology market in China feature a VST design that generally uses four zones. Even other brands base their design generally on four-zone four-curve, four-zone curve, or four zones five or more curves. Manufacturing precision differs between semi-automatic and fully automatic production equipment, and is divided into low, medium, and high-precision fabrication categories. The lens design used in this research features five curves, consisting of a base curve, reverse curve, alignment curve 1, alignment curve 2, and a peripheral curve. Alignment curves mainly serve as function of positioning, and the two alignment curves increase the size of the positioning zone, increase the contact area of the alignment curve zone and the cornea, and are advantageous for stabilizing lens positioning. At the same time, the alignment curve zone design of the applicable lenses can be customized with a toric design. The

curvature of the lens' horizontal and vertical direction alignment curves differ, enabling favorable positioning even for persons with obvious corneal astigmatism, achieving favorable correction effects in the end. Orthokeratology lenses utilize the interaction of elements such as fluid pressure and mechanical pressure to effectively flatten the central part of the cornea for a corrective effect, lowering the degree of myopia according to the period of use. During the period in which orthokeratology lenses are used, the epithelial cells in the center of the cornea move toward the periphery, flattening the center of the cornea, improving focusing problems in the retina. The shape of the cornea gradually stabilizes from one to six months after correction begins, maintaining stable corneal correction effects for the next seven years.

It was observed during the course of this research that the longer one wears orthokeratology lenses, the more marked improvements in uncorrected visual acuity become. A certain inhibitory effect against eye axial length elongation is achieved, which is consistent with previous reported results. Lacrimation and tear film conditions are both stable after three years of use, and both stability and comfort were favorable while using orthokeratology lenses. The myopia control effects of orthokeratology lenses were even more favorable than eyeglasses with a common frame structure. As wear time increased during the initial stages of using orthokeratology lenses, a certain level of slight thinning manifested in the flattened central section of the corrected cornea. The thinning remained 7 to 10 μm, with no obvious thinning of the cornea for the following three years, showing stable conditions. The results of the subjective evaluation of 66 eyes, selected by the researchers in this study, after switching from orthokeratology lenses of other brands to ORTHO-K lenses show marked improvements in visual clarity stability, comfort, and lens cleanliness with use of the high-precision orthokeratology lenses. No abnormal changes to corneal endothelial cell density or shape, no obvious cornea or conjunctiva complications, and no obvious symptoms from wearing the lenses were observed during the orthokeratology lens wear period in this study.

The ORTHO-K lenses used in this study were high-precision manufactured lenses with a high level of oxygen permeability material. They were manufactured in a fully automated, highly precise lathing process resulting in high lens surface smoothness, eliminating the need for excessive polishing which can change the lens design. These aspects make it possible to prevent adverse effects due to lens processing redundancy. Additionally, because the expected effect can be ensured with use, comfort during use is favorable and corneal complications is reduced, guaranteeing a close correlation between safety and corneal corrective effects. The clinical safety and effectiveness of ORTHO-K lenses has already been recognized. Additionally, elements such as the high surface smoothness and low 35-degree contact angle of high-precision lenses enhance the comfort of the wearer when using orthokeratology lenses, increasing the fitting success rate. The lenses used in this study were made of materials with high oxygen permeability to maintain oxygen supply to the cornea during use and prevent oxygen deficiency in the ocular tissue. There were no clear drops in corneal endothelial cell density, and no obvious abnormalities were seen in corneal endothelial cell shape. When used by younger subjects, orthokeratology lens wear methods must be selected according to the refractive conditions such as overnight use, day use, or flexible use during sleep. The type of orthokeratology lens is also key. Selection of high-precision

lenses can improve fitting success rates and improve safety and stability, enabling favorable correction and preventing corneal complications provided that fitting procedures are exemplary, rigorous follow-up examination is conducted, thorough, exemplary care is practiced, and the lenses are properly worn and removed. Additionally, communication in teaching the subject how to wear and manage the lenses is absolutely vital. Above all, management by the guardian is necessary for optimal use when worn by younger subjects, and strengthened communication with the prescribing eyecare professional is important. Carrying out the above actions and selecting superior lenses will result in remarkable effects in both safety and wearability. Exemplary use of orthokeratology lenses is extremely safe, and a favorable corrective therapeutic method for myopia control to a certain extent in younger subjects. Furthermore, high-precision lenses reduce adverse effects on the cornea and conjunctiva, clearly increasing safety.