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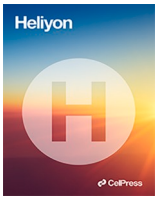

Research article

Effects of orthokeratology on corneal reshaping and the delaying of axial eye growth in children

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ABSTRACT

Purpose: To investigate the inhibition of myopia progression and axial elongation in children wearing orthokeratology (OK) lenses, as well as to evaluate the status of corneal reshaping, this study explores the relationship between changes in central corneal curvature (K-value) and e-value induced by OK lenses and axial elongation.

Methods: In this study, it is planned to select children aged 8–15 who wear orthokeratology lenses at the Pediatric Ophthalmology and Strabismus Clinic of the Second Affiliated Hospital of Dalian Medical University. All children will undergo slit lamp examination, visual acuity assessment, computerized refraction, intraocular pressure measurement, biometry, and corneal topography examination before lens wear and at 1 month, 3 months, and 6 months after lens wear in the pediatric ophthalmology clinic. Based on age (lower age group ($8 < \text{age} \leq 12$ years); higher age group ($12 < \text{age} \leq 15$ years)) and baseline equivalent spherical (SE) value (mild myopia group ($-1.00\ \text{D} < \text{SE} \leq -3.25\text{D}$); moderate myopia group ($-3.25\ \text{D} < \text{SE} \leq -6.00\ \text{D}$)), four groups will be formed by pairing these factors. Suitable data will be selected according to inclusion and exclusion criteria, and different groups will be included. Data will be organized, and statistical analysis will be performed using SPSS software to obtain the results. The expected results will be discussed and analyzed.

Results: After wearing OK lenses, all four groups achieved good visual acuity at follow-up. At 6 months, there were no significant differences in visual acuity among the four groups ($P = 0.149$, >0.05). There were no significant differences in refractive error among the four groups ($P = 0.066$, >0.05). Baseline axial length differed significantly among the four groups ($P = 0.000$, <0.001), with the LM group having longer axial length than the LL group ($P < 0.001$, paired samples *t*-test), and the HM group having longer axial length than the HL group ($P < 0.001$, paired samples *t*-test). However, there were no significant differences in axial length change compared to baseline among the groups at 1 month, 3 months, and 6 months ($P_1 = 0.053$; $P_3 = 0.557$; $P_6 = 0.329$, >0.05). Significant differences were observed in corneal flat K-value change compared to baseline among the four groups at 1 month, 3 months, and 6 months ($P_1 = 0.001$, $P_3 = 0.001$, $P_6 = 0.004$, <0.05). There were no significant differences in e-value change among the groups at 1 and 3 months ($P_1 = 0.205$, $P_3 = 0.252$, >0.05), but significant differences were found in e-value change compared to baseline at 6 months ($P_6 = 0.010$, <0.05). Multiple regression analysis with changes in central corneal flat K-value and e-value as independent variables and axial elongation as the dependent variable showed a correlation between e-value change at 6 months and axial elongation ($P = 0.004$, <0.05), indicating a negative correlation.

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Conclusion: Orthokeratology (OK) lenses effectively improve myopic children's vision by reshaping the cornea, leading to reduced central corneal curvature and flattening of its anterior surface. The effectiveness of OK lenses is not significantly affected by age or initial myopia severity. Children of varying ages and myopia levels experience similar levels of axial length control with OK lens wear. Changes in corneal shape due to OK lenses affect axial elongation, with greater changes in corneal morphology associated with smaller increases in axial length.

1. Introduction

Myopia is a common refractive error that primarily develops during childhood, with the prevalence increasing with age [1–3]. Worldwide, the prevalence of myopia is on the rise. Epidemiological data suggests that by 2050, approximately 50 % of the world's population, nearly 6 billion people, could be affected by myopia, with close to 1 billion having high myopia [4,5]. While the underlying risk factors for differential rates of myopia among different ethnicities remain uncertain, children in East Asia typically exhibit higher rates [6]. A recent study in the United States reported a myopia prevalence of about 42 % among Chinese students, with some regions reaching as high as 95.5 % [7]. Myopia has become a significant public health issue in China. National survey data indicates that in 2020, the overall myopia prevalence among Chinese children aged 6 to 18 was 52.7 %, with an estimated 100 million myopic individuals. Without effective intervention measures, it is estimated that by 2030, the myopia prevalence among Chinese children will reach 61.8 % [8–10]. Given its high prevalence and increasing trend, myopia has emerged as a global public health concern, requiring standardized scientific approaches for prevention and management. More and more researchers are focusing on the prevention and control of childhood myopia.

In epidemiological studies, myopia is most commonly defined as a spherical equivalent refraction (SE) of at least −0.50, −0.75, or −1.00 diopters (D) [11–13], although some studies define myopia as SE exceeding −0.25 D [14]. There's also no uniform definition for high myopia: different studies define it as SE of at least −5.00D, −6.00D, or −8.00D; or an axial length greater than 25.5 mm [15], 26 mm, or 26.5 mm[6,16–17]. Currently, the mechanisms underlying the onset and progression of myopia are poorly understood. Various hypotheses have been proposed regarding its occurrence and development. One adaptive theory suggests that during normal physiological emmetropization, the eye expands in all directions (axially and equatorially), while the lens undergoes mechanical stretching and thinning along the equatorial plane, leading to a decrease in lens power. Mismatch between this axial elongation and flattening of corneal and lenticular curvatures accelerates axial growth, leading to myopia by disrupting equatorial expansion to prevent thinning of the lens [18,19]. This axial myopia accounts for approximately 95 % of myopia cases. Less commonly, excessive corneal curvature, such as in keratoconus, can lead to rapid myopic progression [20]. Additionally, nuclear cataracts in individuals aged 50 or older can lead to nuclear myopia [21,22]. Any degree of myopia increases the risk of pathological ocular changes, with higher degrees of myopia corresponding to higher risks of complications [23]. Pathological retinal changes secondary to high myopia, such as retinal detachment, macular degeneration, posterior staphyloma, and choroidal neovascularization [24–26], can result in irreversible visual impairment or blindness.

Evidence from multiple studies suggests that for the majority of myopic patients, the key pathogenic factors are likely associated with prolonged education and near-work activities. Additionally, genetic factors play a decisive role in determining susceptibility to varying degrees of risk induced by these lifestyle risk factors [27]. Furthermore, other studies suggest insufficient near accommodative response [28], high AC/A ratio [29,30], hyperopia, and peripheral hyperopic defocus [31] are also risk factors for the onset and progression of myopia.

During critical developmental periods, the progression of myopia can be slowed down [19]. Among existing treatment methods, it has been demonstrated that pharmacological treatment with low-dose atropine and optical interventions can slow the progression of myopia. Specific methods include pharmacotherapy (such as atropine at concentrations of 1.0 %, 0.5 %, 0.1 %, and 0.01 %) and optical corrections (single vision lenses, bifocal lenses, progressive lenses, soft contact lenses with peripheral defocus, multifocal lenses, rigid gas-permeable lenses, bifocal RGP lenses, and orthokeratology) [5]. Among these, corneal reshaping lenses and soft contact lenses based on peripheral defocus are particularly effective and popular optical methods for myopia control.

Orthokeratology (Ortho-K or OK lenses) is a type of rigid contact lens with high oxygen permeability and a reverse geometry design [32]. These lenses help reshape the front surface of the cornea by flattening the central corneal zone and steepening the peripheral zone, correcting low to moderate refractive errors and providing improved daytime vision [33]. The effectiveness of orthokeratology in slowing axial elongation in children has been demonstrated. One study indicated that orthokeratology can effectively control myopia progression. Researchers found that OK lenses can reduce myopia progression by inhibiting axial lengthening, resulting in a decrease of 30–46 % in myopia progression [34].

The design of orthokeratology lenses consists of four or five zones, including: the central optical zone (Base Curve, BC), the reverse curve zone (Reverse Curve, RC), the alignment curve zone (Alignment Curve, AC), and the peripheral curve zone (Peripheral Curve, PC) [35]. Some brands, in order to improve the stability of the lenses, further divide the alignment curve zone into alignment curve 1 and alignment curve 2, resulting in five segments. Different segments collectively control the vertical height (sagittal height) of the lens to produce the effect of corneal reshaping. When worn by patients at night with closed eyes, the tears behind the lens generate positive and negative forces to alter the therapeutic effect. Positive forces can flatten the central cornea, while negative forces can attract the mid-peripheral cornea in the opposite direction, causing it to steepen. Under the influence of these positive and negative forces, corneal epithelial cells migrate from the central zone to the mid-peripheral area, resulting in a negative (concave) change in corneal curvature,

thereby correcting myopia.

The current theories regarding the control of myopia with orthokeratology include the Retinal Defocus Theory (Gardner, 2015 [35]; Smith, 2020 [36]), Chromatic Aberration Theory (Hiraoka, 2015 [37]; Zhang X., 2020 [38]; Lau, 2020 [39]), and Adaptation Theory (Batres, 2020 [5]; Song, 2021 [40]), among others. However, significant differences exist in the axial elongation rates among individuals after wearing orthokeratology lenses. Factors such as the patient's age, initial refractive error, corneal morphology, pupil size, and others may influence the effectiveness of corneal reshaping.

In this study, we conducted a retrospective analysis using regular follow-up data from 8 to 15-year-old children wearing orthokeratology lenses. The analysis included diverse indicators and detailed grouping, as outlined below. The groups were based on age and baseline refractive error during lens wear. The main focus was to explore improvements in visual acuity, reduction in daytime refractive error, inhibition of axial elongation, changes in central corneal flat curvature values (Flat K values), and changes in corneal morphology (e values) among different age and refractive error groups of children wearing orthokeratology lenses. Additionally, we investigated the relationship between corneal anterior surface remodeling post-OK lens wear, specifically changes in central corneal Flat K values and e values, and axial length changes. The conclusions drawn from this experiment aim to enhance ophthalmologists' understanding of orthokeratology lenses, aid in slowing myopia progression in children, and facilitate better clinical application and practice of orthokeratology lenses.

2. Materials and methods

2.1. Objects of the study

The clinically recorded data of orthokeratology (OK) contact lens wearers who were examined at the Strabismus Refractive Error Clinic of the Pediatric Ophthalmology Department of the Second Affiliated Hospital of Dalian Medical University from the initial assessment to the follow-up (May 2021–July 2022) were chosen for analysis. A total of 107 children aged 8–15 years with myopia (data were collected from the right eye) were selected for this study, and the inclusion and exclusion criteria are detailed below. Children who were eligible to wear OK lenses after the initial outpatient examination of visual acuity, optometry, intraocular pressure, axial length of the eye, and corneal topography were permitted to try on OK lenses at the outpatient clinic. Following the trial, assessments were conducted on the 2nd day, at 1 week, 1 month, 3 months, 6 months, 9 months, and 12 months. After the trial fitting, eligible children underwent additional tests on the 2nd day, 1 week, 3 months, 6 months, 9 months, and 12 months to evaluate visual acuity, optometry, intraocular pressure, axial length of the eye, corneal topography, and other examinations to determine the effectiveness of the trial fitting. Subsequently, customized keratoplasty lenses were tailored based on the trial fitting outcomes and the corneal conditions of the children. Parents were also provided with instructions to assist with the daily insertion, removal, and cleaning of the lenses. The lenses, including daily nursing care and de-proteinization nursing care following the Menicon Cleaning Protocol for one to two weeks, as well as the wearing procedures after distributing the OK lens. If there is any slippage, corneal epithelial damage, or conjunctivitis, we will assist the child and parents in administering medication and discontinue the use of OK lenses as necessary.

2.1.1. Inclusion and exclusion criteria

(i) Inclusion criteria

1. equivalent spherical prescription >100 diopters after pupil dilatation;
2. Myopia of <600°;
3. corneal *cis*-gauge astigmatism of <150° and retrograde astigmatism of <75°;
4. Astigmatism less than 1/2 the myopic value;
5. a refractive error of less than 150° in both eyes;
6. a flat K of <46 D in the central corneal area;
7. a central corneal e value between 0.3 and 0.6;
8. Informed consent signed by the patient's parent or guardian.

(ii) Exclusion criterion

1. Irregular shape of the cornea or significant lens astigmatism;
2. The cornea is very steep (central zone flat K $\geq$ 46 D) or very flat (central zone flat K $\leq$ 39 D)
3. Corneas that are spherical, i.e., e values that are too small (e $\leq$ 0.1)
4. corneal lesions, cataracts, glaucoma, fundus lesions, severe clouding of the refractive interstitium.
5. amblyopia, strabismus, nystagmus unable to fix the vision.
6. An intraocular pressure of more than 21 mmHg and a difference of more than 8 mmHg between the two eyes;
7. with systemic diseases.

2.1.2. Test groups

A total of 107 patients who met the inclusion and exclusion criteria were collected and grouped according to the initial refractive error and initial age of lens wearer. They were divided into four groups based on age: a low age group (8 $\leq$ age <12 years); a high age

group (12 ≤ age <15 years); and based on the initial degree of myopia: a low myopia group (−1.00 D ≤ SE < −3.25 D); and a moderate myopia group (−3.25 D ≤ SE < −6.00 D). 6.00 D) were divided into four groups: low age low myopia group (LL group); low age moderate myopia group (LM group); high age low myopia group (HL group); and high age moderate myopia group (HM group). As the age of myopia onset decreases and children are being diagnosed and treated at an earlier age, the data for each group showed a slightly higher prevalence in the younger age group compared to the older age group. All patients underwent slit lamp examination, visual acuity assessment, computerized optometry, intraocular pressure measurement, axial length measurement of the eye, and corneal topography at the pediatric ophthalmology strabismus and refractive error clinic before and at the first, third, and sixth months after lens wear treatment. This was done to evaluate changes in the indexes of the adolescents compared with the baseline level at the post-lens review and to organize and analyze the data for statistical analysis. In order to ensure the rigor of this study, data from children wearing CRT brand orthokeratology lenses (CRT lenses are rigid gas permeable contact lenses for overnight corneal reshaping) were used in this trial.

2.1.3. Instrument Inspection and methods

The visual quality improvement of orthokeratology (OK) lenses was assessed based on the enhancement of visual acuity and the degree of optometric improvement before and after wearing OK lenses. Parents were instructed to bring their children to the outpatient clinic for a follow-up examination promptly and to remove the OK lenses at 8:00 a.m. Observations were mainly based on objective examinations such as slit lamp examination, distance visual acuity (uncorrected and corrected), computerized optometry, intraocular pressure, intravitreal acuity, and intraocular pressure. Intraocular pressure, Axial length, and Corneal topography(Fig. 1). The objective examination was performed in the following order: distance visual acuity examination, optometry, intraocular pressure measurement, axial length measurement, and corneal topography assessment.

2.1.4. Statistical methods

SPSS 26.0 statistical software was used to organize and analyze each index, including the patients' age, visual acuity and its variation, equivalent spherical lens power and its variation, ocular axis length and its variation, corneal central zone flat K value and its variation, and corneal e value and its variation. The results were expressed as mean ± standard deviation. Between-group comparisons of the four groups were analyzed using one-way ANOVA with post hoc tests. Exploring the predictors of corneal central zone K-value, corneal e-value, and ocular axis was analyzed using multivariate regression analysis, and a significance level of $P < 0.05$ was considered statistically significant.

2.1.5. Ethicality

The study was approved by the Research Ethics Office of the Second Affiliated Hospital of Dalian Medical University (Ethics Approval No.: Lunxin 048, Lun Audit Hospital of the Second Affiliated Hospital of Dalian Medical University). It was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from guardians on behalf of the children. Factors considered included parental views on controlling the progression of myopia, concerns about the safety of lens wear, lens care, and financial costs. Physicians provided qualitative advice to parents, considering the suitability of lenses for each child's needs. All data analyzed were collected and retained from hospital records and did not need to be provided by the child or parents.

3. Results

3.1. Comparison of each evaluation indicator at baseline

This study collected data from a total of 107 pediatric patients who met the inclusion and exclusion criteria (to avoid the influence of correlations between the right and left eyes of the same patient, only the follow-up data of the right eyes were considered). Among

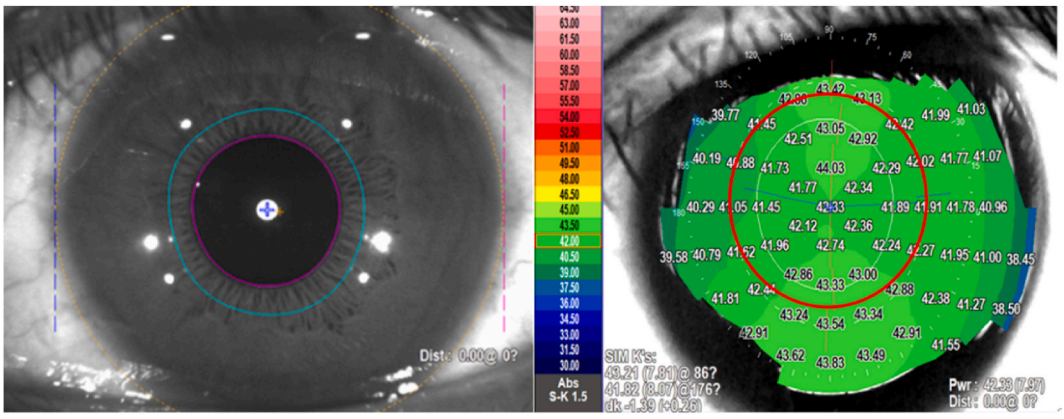

Fig. 1. Corneal topography (measured by OPD-Scan III).

them, there were 48 patients in the Low Age Low Myopia group (LL group), 25 patients in the Low Age Moderate Myopia group (LM group), 21 patients in the High Age Low Myopia group (HL group), and 13 patients in the High Age Moderate Myopia group (HM group). Comparisons of various evaluation indicators including uncorrected visual acuity, equivalent spherical power, axial length, and central corneal flat K values at baseline among the four groups showed statistically significant differences ($P < 0.05$), while the corneal morphology e value was measured from corneal topography data after the initial trial of OK lens wear, and there were no statistically significant differences among the four groups at baseline ($P = 0.820$, >0.05). Detailed data are presented in Table 1.

The organization and analysis results of the follow-up data of uncorrected visual acuity for the four groups of patients are shown in Table 2. The baseline visual acuity for the LL group was 0.37 ± 0.17, for the LM group was 0.24 ± 0.13, for the HL group was 0.43 ± 0.23, and for the HM group was 0.15 ± 0.07. There were significant differences in the baseline visual acuity among the four groups of right eyes (P = 0.000, <0.001). At 1 month, 3 months, and 6 months of wearing corneal reshaping lenses, the visual acuity for all four groups reached around 1.0. There were significant differences in visual acuity among the four groups at 1 month and 3 months ($P_1 = 0.018$, $P_3 = 0.018$, <0.05). However, at 6 months, the uncorrected visual acuity was 1.06 ± 0.17 for the LL group, 0.97 ± 0.22 for the LM group, 1.07 ± 0.13 for the HL group, and 0.91 ± 0.26 for the HM group, with no significant differences among the four groups ($P = 0.149$, >0.05). There were no significant differences in the changes in visual acuity from baseline among the four groups at 1 month, 3 months, and 6 months after wearing the lenses ($P_1 = 0.352$; $P_3 = 0.382$; $P_6 = 0.610$, >0.05).

The organization and analysis of the refraction values (equivalent spherical) follow-up data for the four groups of patients are presented in Table 2. The baseline refraction for the LL group was −2.12 ± 0.68D, for the LM group was −4.05 ± 0.62D, for the HL group was −1.87 ± 0.68D, and for the HM group was −4.73 ± 0.89D. There were significant differences in baseline refraction among the four groups of right eyes ($P = 0.000$, <0.001). At 1 month and 3 months of wearing corneal reshaping lenses, there were significant differences in refraction among the four groups ($P_1 = 0.000$, $P_3 = 0.001$, <0.05). However, at 6 months, the refraction was −0.45 ± 0.58D for the LL group, −1.10 ± 1.19D for the LM group, −0.28 ± 0.45D for the HL group, and −0.71 ± 0.85D for the HM group, with no significant differences among the four groups ($P = 0.066$, >0.05). There were significant differences in the changes in refraction from baseline among the four groups at 1 month, 3 months, and 6 months after wearing the lenses (P1 = 0.000; P3 = 0.000; P6 = 0.000, <0.05).

The organization and analysis of the follow-up data of axial length for the four groups of pediatric patients are presented in Table 3. Baseline axial lengths for the LL group were 24.11 ± 0.95 mm, for the LM group were 24.86 ± 0.57 mm, for the HL group were 24.51 ± 0.76 mm, and for the HM group were 25.63 ± 0.61 mm. There were significant differences in baseline axial length among the four groups of right eyes ($P = 0.000$, <0.001). Post-hoc tests showed that compared to LM group, LL group had shorter axial length ($P = 0.000$, <0.001, paired samples *t*-test), and HL group had shorter axial length compared to HM group ($P = 0.000$, <0.001, paired samples *t*-test). At 1 month, there were no significant differences in axial length among the four groups ($P = 0.085$, >0.05). However, at 3 months and 6 months of wearing corneal reshaping lenses, there were significant differences in axial length among the four groups ($P_3 = 0.000$, $P_6 = 0.001$, <0.05). There were no significant differences in the changes in axial length from baseline among the four groups at 1 month, 3 months, and 6 months after wearing the lenses ($P_1 = 0.053$; $P_3 = 0.557$; $P_6 = 0.329$, >0.05). Post-hoc LSD test results are shown in Table 4.

The reexamination data and analysis of corneal topography for the four groups of patients are shown in Table 5. The baseline corneal central zone mean K values for the LL, LM, HL, and HM groups were 42.68 ± 1.31D, 42.84 ± 1.38D, 41.99 ± 1.17D, and 41.99 ± 0.88D, respectively. There were significant differences in the baseline corneal central zone mean K values among the four groups' right eyes ($P = 0.043$, <0.05). At 1 month and 3 months of wearing orthokeratology lenses, significant differences in corneal central zone mean K values were observed among the four groups ($P_1 = 0.007$, $P_3 = 0.005$, <0.05), but at 6 months, the corneal central zone mean K values were 41.30 ± 1.29D for LL, 40.48 ± 1.54D for LM, 40.85 ± 1.21D for HL, and 41.99 ± 0.88D for HM, with no significant differences among the four groups ($P = 0.082$, >0.05). There were significant differences in the changes in corneal central zone mean K values from baseline at 1 month, 3 months, and 6 months after wearing lenses among the four groups ($P_1 = 0.001$; $P_3 = 0.001$; $P_6 = 0.004$, <0.05).

The baseline corneal e values for the LL, LM, HL, and HM groups were 0.42 ± 0.48, 0.50 ± 0.51, 0.55 ± 0.47, and 0.53 ± 0.58, respectively, with no significant differences among the four groups' right eyes (P = 0.820, >0.05). At 1 month, 3 months, and 6 months of wearing orthokeratology lenses, significant differences in corneal e values were observed among the four groups ($P_1 = 0.000$, $P_3 = 0.020$, $P_6 = 0.017$, <0.05). There were no significant differences in the changes in corneal e values from baseline at 1 month and 3 months after wearing lenses among the four groups ($P_1 = 0.205$; $P_3 = 0.252$; >0.05), but at 6 months, the corneal e values were −0.66

Table 1
Comparison of baseline demographic and data among the four groups of patients.

Variables	LL	LM	HL	HM	*P*
	n = 48	n = 25	n = 21	n = 13	
Visual acuity	0.37 ± 0.17	0.24 ± 0.13	0.43 ± 0.23	0.15 ± 0.07	0.000[a]
refraction (SE in diopters)	−2.12 ± 0.68	−4.05 ± 0.62	−1.87 ± 0.68	−4.73 ± 0.89	0.000[a]
axial length (in millimeters)	24.11 ± 0.95	24.86 ± 0.57	24.51 ± 0.76	25.63 ± 0.61	0.000[a]
central corneal flat K value	42.68 ± 1.31	42.84 ± 1.38	41.99 ± 1.17	41.99 ± 0.88	0.043[a]
corneal e value	0.42 ± 0.48	0.50 ± 0.51	0.55 ± 0.47	0.53 ± 0.58	0.820

[a] : P < 0.05; LL group: Low Age Low Myopia group; LM group: Low Age Moderate Myopia group; HL group: High Age Low Myopia group; HM group: High Age Moderate Myopia group.

Table 2
Comparison of visual acuity, refraction, and their changes before and after wearing orthokeratology lenses in four groups of patients.

Variables	LL	LM	HL	HM	F	*P*
	n = 48	n = 25	n = 21	n = 13		
Visual acuity						
Baseline	0.37 ± 0.17	0.24 ± 0.13	0.43 ± 0.23	0.15 ± 0.07	10.635	0.000[a]
1 month	1.04 ± 0.13	0.94 ± 0.21	1.10 ± 0.16	0.95 ± 0.33	3.515	0.018[a]
3 month	1.09 ± 0.19	0.93 ± 0.25	1.13 ± 0.13	1.00 ± 0.34	3.559	0.018[a]
6 month	1.06 ± 0.17	0.97 ± 0.22	1.07 ± 0.13	0.91 ± 0.26	1.842	0.149
change at 1 month	0.67 ± 0.20	0.70 ± 0.24	0.67 ± 0.28	0.80 ± 0.31	1.102	0.352
change at 3 month	0.73 ± 0.22	0.68 ± 0.28	0.74 ± 0.16	0.85 ± 0.31	1.033	0.382
change at 6 month	0.68 ± 0.20	0.72 ± 0.31	0.63 ± 0.28	0.77 ± 0.26	0.611	0.610
Refraction (D)						
Baseline	−2.12 ± 0.68	−4.05 ± 0.62	−1.87 ± 0.68	−4.73 ± 0.89	89.217	0.000[a]
1 month	−0.26 ± 0.55	−0.91 ± 1.11	−0.06 ± 0.38	−1.04 ± 1.13	9.408	0.000[a]
3 month	−0.25 ± 0.61	−0.83 ± 0.74	−0.02 ± 0.44	−0.70 ± 0.89	6.295	0.001[a]
6 month	−0.45 ± 0.58	−1.10 ± 1.19	−0.28 ± 0.45	−0.71 ± 0.85	2.524	0.066
change at 1 month	1.88 ± 0.74	3.14 ± 0.90	1.93 ± 0.60	3.71 ± 1.13	26.464	0.000[a]
change at 3 month	1.90 ± 0.79	3.20 ± 0.81	1.82 ± 0.81	3.93 ± 0.90	27.403	0.000[a]
change at 6 month	1.61 ± 0.81	3.12 ± 1.11	1.68 ± 0.83	3.71 ± 0.89	17.091	0.000[a]

[a] : P < 0.05; LL group: Low Age Low Myopia group; LM group: Low Age Moderate Myopia group; HL group: High Age Low Myopia group; HM group: High Age Moderate Myopia group.

Table 3
Comparison of axial length and its changes before and after wearing orthokeratology lenses in four groups of patients.

axial length(mm)	LL组	LM组	HL组	HM组	F	*P*
	n = 48	n = 25	n = 21	n = 13		
Baseline	24.11 ± 0.95	24.86 ± 0.57	24.51 ± 0.76	25.63 ± 0.61	12.356	0.000[a]
1 month	24.38 ± 0.83	24.88 ± 0.56	24.51 ± 0.77	25.35 ± 0.28	2.367	0.085
3 month	24.31 ± 0.89	24.85 ± 0.61	24.57 ± 0.70	25.80 ± 0.61	9.711	0.000[a]
6 month	24.47 ± 0.84	24.91 ± 0.62	24.41 ± 0.76	25.81 ± 0.62	6.731	0.001[a]
change at 1 month	0.02 ± 0.04	0.00 ± 0.05	0.03 ± 0.07	0.06 ± 0.09	2.786	0.053
change at 3 month	0.17 ± 0.46	0.07 ± 0.09	0.08 ± 0.12	0.04 ± 0.07	0.696	0.557
change at 6 month	0.31 ± 0.54	0.14 ± 0.16	0.14 ± 0.10	0.06 ± 0.15	1.171	0.329

[a] P < 0.05; LL group: Low Age Low Myopia group; LM group: Low Age Moderate Myopia group; HL group: High Age Low Myopia group; HM group: High Age Moderate Myopia group.

± 0.54 for LL, 0.80 ± 0.57 for LM, −0.61 ± 0.41 for HL, and −1.52 ± 0.29 for HM, with significant differences in the changes in corneal e values from baseline among the four groups ($P = 0.010$, <0.05). We can see in Table 6: post-hoc analysis showed that the change in e values at 6 months was lower in the LM group than in the HM group ($P = 0.010$, <0.05, paired sample *t*-test), and lower in the HL group than in the HM group ($P = 0.004$, <0.001, paired sample *t*-test).

The results of the multiple regression analysis are shown in Table 7: We used the changes in corneal central zone K values at 1 month, 3 months, and 6 months, as well as changes in e values at 1 month, 3 months, and 6 months, as independent variables, with changes in axial length as the dependent variable for multiple regression analysis. The results showed that the change in corneal morphology e value at 6 months was significantly correlated with axial elongation ($P = 0.004$, <0.05), indicating a negative correlation. That is, the greater the change in e value, the smaller the amount of axial elongation. This suggests that with 6 months of lens wear, the more pronounced the changes in corneal morphology from the central to peripheral zones in children, the better the inhibitory effect on axial elongation.

4. Discussion

The prevalence of myopia has been increasing every year, with a trend towards acceleration. In order to prevent and control childhood myopia, orthokeratology (OK) lenses have attracted increasing attention from ophthalmologists and myopic patients because of their good corrective effects and ability to control myopia progression. After more than 30 years of clinical application, the effectiveness of OK lenses in controlling myopia has been confirmed [41]. Studies have shown that compared to single-vision glasses and contact lenses, the inhibitory effect on axial elongation over 2 years ranges from 32 % to 63 % [42]. Because these lenses can be worn overnight and maintain good vision during the day, corneal reshaping lenses have been recognized by many patients and their families.

In our study, based on our statistical data and results, we found the following: in terms of visual acuity, there were significant differences in baseline visual acuity among the four groups, with the low myopia group having significantly better unaided visual acuity than the moderate myopia group. At 1 month of wearing orthokeratology (OK) lenses, unaided visual acuity of children in all

Table 4
Post-hoc analysis of variance comparison of axial length before and after wearing orthokeratology lenses in four groups of patients.

axial length(mm)			Mean difference (I-J)	standard error	significance *P*	95 % confidence interval	
						lower limit	upper limit
Baseline	LL	LM	−0.74354[a]	0.20147	0.000	−1.1434	−0.3437
		HL	−0.39354	0.21843	0.075	−0.8270	0.0399
		HM	−1.51081[a]	0.26939	0.000	−2.0454	−0.9762
	LM	LL	0.74354[a]	0.20147	0.000	0.3437	1.1434
		HL	0.35000	0.24747	0.160	−0.1411	0.8411
		HM	−0.76727[a]	0.29343	0.010	−1.3496	−0.1850
	HL	LL	0.39354	0.21843	0.075	−0.0399	0.8270
		LM	−0.35000	0.24747	0.160	−0.8411	0.1411
		HM	−1.11727[a]	0.30532	0.000	−1.7232	−0.5114
	HM	LL	1.51081[a]	0.26939	0.000	0.9762	2.0454
		LM	0.76727[a]	0.29343	0.010	0.1850	1.3496
		HL	1.11727[a]	0.30532	0.000	0.5114	1.7232
6 month	LL	LM	−0.44236	0.24210	0.073	−0.9273	0.0426
		HL	0.05964	0.27874	0.831	−0.4987	0.6180
		HM	−1.33893[a]	0.31974	0.000	−1.9794	−0.6984
	LM	LL	0.44236	0.24210	0.073	−0.0426	0.9273
		HL	0.50200	0.30890	0.110	−0.1168	1.1208
		HM	−0.89657[a]	0.34634	0.012	−1.5904	−0.2028
	HL	LL	−0.05964	0.27874	0.831	−0.6180	0.4987
		LM	−0.50200	0.30890	0.110	−1.1208	0.1168
		HM	−1.39857[a]	0.37288	0.000	−2.1455	−0.6516
	HM组	LL	1.33893[a]	0.31974	0.000	0.6984	1.9794
		LM	0.89657[a]	0.34634	0.012	0.2028	1.5904
		HL	1.39857[a]	0.37288	0.000	0.6516	2.1455

[a] : Significance level of mean difference $P < 0.05$; post-hoc analysis conducted using the LSD method, paired sample *t*-test.

Table 5
Comparison of corneal central zone K values, corneal morphology e values, and their changes before and after wearing OK lenses in the four groups of patients.

	LL	LM	HL	HM	F	*P*
	n = 48	n = 25	n = 21	n = 13		
central corneal flat K value						
Baseline	42.68 ± 1.31	42.84 ± 1.38	41.99 ± 1.17	41.99 ± 0.88	2.815	0.043[a]
1 month	41.46 ± 1.41	40.87 ± 1.45	40.50 ± 1.30	40.17 ± 1.08	4.289	0.007[a]
3 month	41.33 ± 1.43	40.71 ± 1.52	40.45 ± 1.11	39.59 ± 1.41	4.581	0.005[a]
6 month	41.30 ± 1.29	40.48 ± 1.54	40.85 ± 1.21	40.03 ± 1.27	2.348	0.082
change at 1 month	−1.20 ± 0.81	−2.01 ± 0.93	−1.40 ± 0.61	−1.83 ± 0.95	5.922	0.001[a]
change at 3 month	−1.40 ± 0.78	−2.21 ± 1.07	−1.30 ± 0.58	−2.29 ± 1.41	6.056	0.001[a]
change at 6 month	−1.37 ± 0.70	−2.34 ± 1.16	−1.34 ± 0.44	−2.07 ± 1.22	5.029	0.004[a]
corneal e value						
Baseline	0.42 ± 0.48	0.50 ± 0.51	0.55 ± 0.47	0.53 ± 0.58	0.307	0.820
1 month	−0.74 ± 0.25	−0.94 ± 0.50	−0.85 ± 0.21	−1.24 ± 0.28	7.825	0.000[a]
3 month	−0.69 ± 0.47	−0.84 ± 0.65	−0.86 ± 0.24	−1.27 ± 0.30	3.435	0.020[a]
6 month	−0.69 ± 0.39	−0.95 ± 0.49	−0.74 ± 0.28	−1.26 ± 0.13	3.689	0.017[a]
change at 1 month	−0.82 ± 0.56	−0.88 ± 0.73	−0.75 ± 0.44	−1.19 ± 0.62	1.558	0.205
change at 3 month	−0.74 ± 0.64	−0.79 ± 0.85	−0.76 ± 0.52	−1.27 ± 0.64	1.386	0.252
change at 6 month	−0.66 ± 0.54	−0.80 ± 0.57	−0.61 ± 0.41	−1.52 ± 0.29	4.158	0.010[a]

[a] : $P < 0.05$; LL group: Low Age Low Myopia group; LM group: Low Age Moderate Myopia group; HL group: High Age Low Myopia group; HM group: High Age Moderate Myopia group.

four groups could reach around 1.0, and when rechecked at 3 months and 6 months of wearing OK lenses, unaided visual acuity of children in all four groups could reach a more stable level. Regarding the change in visual acuity improvement, there were no statistically significant differences among the four groups of children at 1 month, 3 months, and 6 months. This result suggests that children with different initial ages and initial refractive states can achieve a stable level of visual acuity improvement by wearing appropriate orthokeratology lenses, reaching a final stable level of daytime unaided visual acuity. Similarly, in terms of baseline myopia degree (equivalent spherical value), significant differences were observed in the baseline levels of equivalent spherical value among the four groups. However, upon rechecking at 1 month, 3 months, and 6 months of lens wear, the equivalent spherical degree measured during refraction significantly decreased in all four groups, with the degrees being relatively stable at 3 months and 6 months, similar to those at 1 month recheck. However, in terms of refractive change, children in the two moderate myopia groups had larger changes, which also confirms that the greater the degree of myopia, the greater the "power" needed for corneal reshaping to

Table 6
Post-hoc analysis of variance comparison of corneal e values before and after wearing OK lenses in the four groups of patients.

Change of corneal e value			Mean difference (I-J)	standard error	significance *P*	95 % confidence interval	
						lower limit	upper limit
6 month	LL	LM	0.14582	0.16197	0.372	−0.1791	0.4707
		HL	−0.04793	0.21903	0.828	−0.4872	0.3914
		HM	0.86207[a]	0.25185	0.001	0.3569	1.3672
	LM	LL	−0.14582	0.16197	0.372	−0.4707	0.1791
		HL	−0.19375	0.23569	0.415	−0.6665	0.2790
		HM	0.71625[a]	0.26648	0.010	0.1818	1.2507
	HL	LL	0.04793	0.21903	0.828	−0.3914	0.4872
		LM	0.19375	0.23569	0.415	−0.2790	0.6665
		HM	0.91000[a]	0.30454	0.004	0.2992	1.5208
	HM	LL	−0.86207[a]	0.25185	0.001	−1.3672	−0.3569
		LM	−0.71625[a]	0.26648	0.010	−1.2507	−0.1818
		HL	−0.91000[a]	0.30454	0.004	−1.5208	−0.2992

[a] : Significance level of the mean difference $P < 0.05$; Post-hoc analysis was conducted using the LSD method and paired sample *t*-test.

Table 7
Comparison of multiple regression analysis with changes in axial length as the dependent variable.

Independent variable	*β*	*SE*	*P*	R^2
(constant)	0.037	0.021	0.085	0.031
corneal flat K, change in 1 month	0.010	0.010	0.316	
e, change in 1 month.	0.004	0.015	0.784	
(constant)	0.214	0.076	0.006	0.032
corneal flat K, change in 3 month	0.031	0.042	0.458	
e, change in 3 month.	0.059	0.059	0.317	
(constant)	0.444	0.110	0.000	0.170
corneal flat K, change in 6 month	0.001	0.057	0.992	
e, change in 6 month.	0.299	0.098	0.004[a]	

[a] :$P < 0.05$.

achieve stable daytime refractive power, hence resulting in larger changes.

In terms of axial length among the four groups, there were also significant differences in baseline axial length values of the children. It can be observed that as the degree of myopia increases, the axial length of the eye also increases relatively. Post hoc tests revealed that the axial length of children in the two moderate myopia groups was greater than that of children in the two low myopia groups. When the degree of myopia was similar, the axial length of the younger age group was shorter than that of the older age group. During our regular follow-up measurements of axial length in children, no significant differences were found among the four groups in terms of changes in axial length from baseline at 1 month, 3 months, and 6 months. Large-scale data analysis showed that the average annual increase in axial length for myopic children was approximately 0.55 mm/year. Compared to previous large-scale data on the rate of axial elongation in children, orthokeratology lenses slowed down the rate of axial elongation in myopic children. Furthermore, for children of different ages and initial degrees of myopia, the extent to which OK lenses delayed axial elongation was similar.

Additionally, we recognize that orthokeratology lenses work by reshaping the anterior surface of the cornea, making the corneal shape flatter. Therefore, we investigated the changes in central corneal curvature (K) in the four groups of children (data were taken from the right eye). There were statistically significant differences in baseline central corneal curvature values among the four groups ($P = 0.043$), with younger children having relatively steeper corneal curvature compared to older children. We speculate that this may be related to the growth and development of the eyeball. At 1 month and 3 months, there were also statistically significant differences in central corneal curvature values among the four groups. However, upon rechecking at 6 months, there were no significant statistical differences in central corneal curvature values among the four groups. We believe that by 6 months, the reshaping of the corneal anterior surface tends to stabilize. There were also significant statistical differences among the four groups in terms of changes in central corneal curvature values. According to post hoc tests, at 6 months, we found that the changes in the two moderate myopia groups were higher than those in the two low myopia groups, which confirms that the mechanism of action of OK lenses indeed alters the central corneal curvature, making the central cornea flatter. The higher the initial degree of myopia, the greater the degree of corneal flattening, and thus the greater the change in central corneal curvature. However, the change in K values was not significantly related to age.

In terms of corneal morphology, represented by the e value, there were no significant differences in the initial corneal morphology among the four groups of children, indicating that children of different ages and initial degrees of myopia had similar corneal eccentricity. At 1 month, 3 months, and 6 months, there were statistically significant differences in e values among the four groups, all showing negative values. This indicates that the corneal morphology changed from being steeper centrally and flatter peripherally to being flatter centrally and steeper peripherally after orthokeratology reshaping. Regarding the change in e values, at 1 month and 3 months, there were no statistically significant differences in the change in e values among the four groups. This again confirms the

consistent reshaping effect of orthokeratology lenses. However, at 6 months, there were statistically significant differences in the change in e values among the four groups. According to post hoc tests, we found that the change in e values in the older age low myopia group was less than that in the older age moderate myopia group, indicating that the greater the initial degree of myopia, the greater the difference in curvature change between the central and peripheral cornea.

In this study, we conducted a multiple regression analysis to explore the effect of corneal reshaping induced by orthokeratology lenses, specifically the impact of changes in central corneal curvature (K) and corneal eccentricity (e) on axial elongation. Therefore, we used the changes in central K and e values at 1 month, 3 months, and 6 months as independent variables and axial elongation as the dependent variable for regression analysis. The results showed that the change in axial length was significantly influenced by the change in corneal e value at 6 months, showing a negative correlation. That is, the greater the change in corneal e value, the smaller the increase in axial length. Other variables such as change in K value were not significantly correlated with axial length increase and were not statistically significant in the analysis. Previous studies have also indicated similar findings. For instance, Hiraoka et al. evaluated the maximum corneal power difference induced by orthokeratology lenses within the central 4 mm pupil area and found a negative correlation with axial elongation in simple correlation analysis [43]. Similarly, Lee et al. developed a parameter called the vertex-peripheral power difference (the maximum power difference between the peripheral cornea and the vertex) and found a negative correlation with the rate of axial elongation. However, this correlation became statistically insignificant in multivariate regression analysis [44]. Furthermore, we observed that the results at 1 month were similar to those at 3 months and 6 months. From this, we can infer that the reshaping effect of orthokeratology lenses can be initially reflected at 1 month and become more stable at 3 months and 6 months. Therefore, by examining various parameters of children wearing orthokeratology lenses at 1 month, we can roughly assess whether the lenses are suitable and provide predictive indications for adjustments if needed. A detailed analysis of the benefits of wearing orthokeratology lenses for children of different ages and initial myopia degrees suggests that immediate intervention usually yields significant benefits for rapidly progressing myopic children.

Of course, orthokeratology lenses are not without their drawbacks. Since they are worn directly on the cornea at night for at least 8 h, they can alter the state of the ocular surface and potentially lead to characteristic spatial disruption of tear film stability [45]. Tear film plays a crucial role in achieving good ocular optical quality as it is the foremost refractive surface of the eye. The irregularity of pathological tear film can significantly disrupt light rays. In patients undergoing corneal refractive treatment, the reshaped corneal surface can redistribute tear film, leading to tear film breakup. There is debate among researchers regarding changes in the ocular surface after overnight orthokeratology lens wear. Na et al. suggested that overnight wear of orthokeratology lenses may induce changes in meibomian glands and tear film stability [46]. Wang et al. reported that overnight orthokeratology lens wear could reduce tear film stability but would not affect meibomian gland function [47]. However, Li and Xie noted that after orthokeratology lens treatment, basal tear secretion and ocular inflammation were unaffected, with only a short-term decrease in tear film breakup time [48]. They suggested that the increase in tear film evaporation might be related to the distribution of tear film, which is caused by transient changes in tear film morphology. It is speculated that in pediatric patients undergoing corneal refractive treatment, the spatial distribution of tear film breakup can provide an easier, more rational, and more concentrated way to monitor pediatric tear film instability, thus better preventing any potential subsequent epithelial erosion, microbial colonization, or microbial keratitis development.

Furthermore, improper lens fitting may result in decentration of orthokeratology lenses, severe corneal staining, meibomian gland loss, and even serious conditions such as keratitis, ghosting or glare, pain, or foreign body sensation, leading to the failure of orthokeratology lens wear [47–50]. Additionally, a study indicated that orthokeratology lenses did not cause significant tear deficiency or conjunctival injection but might lead to corneal iron deposition after wear [48]. The eccentricity of the cornea is provided by most corneal topography systems, represented as the e value in our aforementioned study. In comparison to the e value, the E value indicates greater flattening of the peripheral cornea [49]. This characteristic of the cornea significantly influences the fitting parameters of the lenses. Traditionally, the initial trial lens alignment curve radius is selected based on the central flat K value reading and eccentricity value (e value) obtained from the corneal topography, and the final lens parameters are determined after several lens trials. In recent years, there have been clearer requirements for the fitting and trial process of orthokeratology lenses, and related fitting guidelines have provided better guidance for the clinical application of orthokeratology lenses. As long as the standards are met, strict attention to the ocular conditions of pediatric patients before lens wear, designing lenses based on individualized parameters of the patient's eyes, proper disinfection and care of the lenses during wear, regular clinic follow-ups, promoting doctor-patient communication, close monitoring, timely management of complications, will all contribute to the clinical application of orthokeratology lenses benefiting more myopic children.

5. Conclusion

Orthokeratology lenses are increasingly being used to control the progression of childhood myopia. Although the mechanism by which orthokeratology lenses delay axial elongation is not fully understood, it has been proposed that flattening of the central corneal curvature and steepening of the peripheral corneal curvature lead to reshaping of the anterior corneal surface, thus delaying axial elongation. In our study, we found that orthokeratology lenses effectively improve uncorrected visual acuity in myopic children. Additionally, orthokeratology lenses can reduce the flat K values in the central corneal zone, flattening the cornea to achieve corneal reshaping. The corneal shaping effect of orthokeratology lenses was not significantly correlated with the age of the children or the initial degree of myopia, indicating that children of different ages and initial degrees of myopia wearing appropriate orthokeratology lenses achieve similar degrees of slowing in axial elongation. Changes in the central corneal K values and corneal morphology e values may affect the shaping effect of orthokeratology lenses, thereby influencing axial elongation. In our regression analysis, we found a

negative causal relationship between changes in e values and changes in axial length, indicating that changes in corneal morphology affect the rate of axial elongation. Since e represents corneal morphology, specifically the curvature change from the central to peripheral zones, larger changes in e values imply greater changes in corneal morphology due to orthokeratology lenses, resulting in slower rates of axial elongation as the corneal curvature change from the central to peripheral zones increases.

Declarations

Ethical approval

The study was ethically reviewed by the Ethics Committee of the Second Affiliated Hospital of Dalian Medical University, which agreed to publish the study.

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Availability of data and materials

Data associated with the study has not been deposited into a publicly available repository. Data are available from the corresponding author on reasonable request.

CRediT authorship contribution statement

Siqi Zhang: Writing – original draft, Methodology. **Huailin Zhu:** Supervision, Data curation. **Lan Zhang:** Investigation. **Mingjun Gao:** Validation, Data curation. **Changyang Liu:** Validation, Data curation. **Qi Zhao:** Writing – review & editing, Methodology.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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