

ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

Long-term effects of monocular myopic anisometropia correction on uncorrected ocular axial length in minors and its influencing factors

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Introduction/Objective The objective of the paper was to investigate the long-term effects of orthokeratology (ortho-k) correction for monocular myopia and the factors influencing axial length (AL) changes in the untreated eye of minors.

Methods A total of 81 patients with monocular myopia receiving ortho-k lenses for the first time were enrolled. Eyes corrected with ortho-k lenses were designated as the myopic group and contralateral non-myopic eyes formed the non-myopic group. Changes in AL from baseline to follow-up examinations were recorded. Univariate and multivariate linear regression analyses were performed sequentially to explore the correlation between baseline parameters and AL changes in the non-myopic eyes.

Results After wearing ortho-k lenses for six and 12 months, the AL of the corrected myopic group was 24.48 ± 0.35 and 24.56 ± 0.31 mm, respectively, whereas that of the uncorrected non-myopic group was 23.55 ± 0.24 and 23.7 ± 0.22 mm, respectively. After six and 12 months, the amount of change in the AL was higher in the uncorrected non-myopic group than in the corrected myopic group ($p < 0.001$). Moreover, the difference in AL between the two eyes gradually decreased ($t = 2.376$, $p = 0.018$); the change in AL difference (-0.10 ± 0.08 vs. -0.18 ± 0.13 , $p < 0.001$) was significant.

Conclusion Orthokeratology lens wear may accelerate myopia progression in contralateral, initially non-myopic eyes. Younger children with monocular myopia and a higher baseline spherical equivalent are likely to experience faster myopia progression in the other, unaffected eye following ortho-k lens correction.

Keywords: orthokeratology; unilateral myopic anisometropia; axial length

INTRODUCTION

Myopia is increasingly prevalent worldwide [1–4]. Epidemiological studies indicate a progressive increase in the prevalence of the condition, with the population prevalence as high as 60% in Asia and 40% in Europe [5, 6]. Children who develop myopia in adolescence are at greater risk of developing pathologic, high myopia in adulthood, with a risk of blindness. Therefore, the prevention and control of myopia, particularly during adolescence, are of great significance.

Anisometropia refers to a spherical equivalent (SE) refractive power difference greater than 1.00 diopters (D) [7, 8, 9]. Due to the disparity in the size of the retinal images of the two eyes of patients with anisometropia, visual fatigue and abnormalities in binocular vision may occur [10, 11]. Research indicates that when the disparity in diopter of the two eyes reaches 2.50 D, the differential in the size of the retinal images is 5% [12]. Patients with binocular visual impairment have a remarkable reduction in their visually guided motor ability. This primarily manifests as a slower pace, inferior accuracy and poor depth judgment [13, 14], which, in turn, impairs the precision of

visual–motor abilities [15] and affects learning, work and daily life. If minors exhibit anisometropia during the crucial period of visual development, the inferior eye is prone to retinal defocus, or the eye with the higher refractive diopter may develop monocular inhibition [16]. Moreover, relevant research suggests that the progression rate of myopia in both eyes of minors with anisometropia is faster than that in those without the condition [17]. As the degree of myopia and age increase, the degree of anisometropia will further amplify [9].

To date, the mechanism underlying the formation of myopia has not been fully elucidated. In addition to genetic and environmental factors, visual stimulation of the peripheral retina also plays a significant role in the formation of myopia [18]. Currently, methods proven to effectively control the progression of myopia primarily include the administration of atropine eye drops, orthokeratology (ortho-k) lenses and spectacle lenses, as well as contact lenses with a peripheral myopia defocus design.

Orthokeratology is an optical approach for controlling the progression of myopia in minors. It reduces peripheral astigmatism by reshaping the corneal curvature to better visualise external objects on the retina, effectively

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reducing axial elongation by 43–63% [19, 20]. Several recent studies have demonstrated that ortho-k effectively inhibits the axial elongation and reduces the degree of refractive interocular difference in adolescents with unilateral myopic anisometropia [21, 22]. However, few previous studies have investigated the changes in axial length of the contralateral eye without a lens and the factors affecting these changes.

METHODS

Study design

A total of 81 minors who were first fitted with ortho-k lenses for monocular myopia between January 2022 and June 2023 were selected using the convenience sampling method. The myopic eyes fitted with ortho-k lenses were then allocated to the corrected myopic eye group and the contralateral non-myopic eyes were allocated to the uncorrected non-myopic eye group. The inclusion criteria were as follows: (1) age 8–16 years; (2) unilateral myopic anisometropia with SE diopter of myopia of -6.00 to -0.75 D and corrected visual acuity ≥ 1.0 , and the contralateral eye with SE diopter of -0.50 to +1.50 D and visual acuity of > 1.0 ; (3) astigmatism with-the-rule in both eyes ≤ 2.00 D; (4) SE difference ≥ 1.00 D in both eyes; (5) first-time fitting of corneal contact lenses, with no contraindications to contact lens fitting; and (6) intraocular pressure (IOP) value = 10–21 mmHg. The exclusion criteria were as follows: patients (1) with presence of medications and history of treatment with myopia prevention tools that may affect refractive outcomes; (2) with presence of binocular vision problems such as dominant strabismus and amblyopia; (3) with past history of ocular trauma or surgery; (4) suffering from corneal diseases, glaucoma, uveitis, cataract or fundus diseases, which may affect vision, diopter or choroidal structure; (5) suffering from systemic diseases such as diabetes, hypertension or autoimmune diseases that may cause eye disease; and (6) unable to understand and cooperate with the examination. The study was approved by the hospital's ethics committee. This was a prospective study and all participants (or their guardians) signed an informed consent form before the start of the study.

Relevant inspection and methods

Visual acuity examination

Distance visual acuity is assessed at 5 m using an international standard chart under good illumination, with the 1.0 line at eye level. Each eye is tested separately: first uncorrected, then corrected, with the fellow eye fully occluded without pressure. Patients identify the gap direction in descending 'E' optotype order. If no optotype is discerned at 5 m, the patient moves closer until identifying the 0.1 line. Failure to see line 0.1 at 1 m prompts finger counting against light at the maximum discernible distance; inability to count fingers necessitates light perception testing. Near

acuity is measured at 30 cm with a standard chart; if line 1.0 is unclear, the chart is moved progressively closer.

Axial length examination

In this study, axial length (AL) measurements were obtained using an optical biometer (SW-9000, Suiwei, China). During examination, the chin rest height was adjusted to align the patient's outer canthus with the marking line. The operator then manoeuvred the instrument handle until the pupil was centred within the white dot-shaped aperture and the white dual light rays appeared clear; at this point, the button was pressed. Following this, the examination position was adjusted until a green aperture appeared. The handle was then adjusted to centre the pupil within the green aperture before pressing the button again, completing one measurement. Measurements were performed at least three times per eye, and the average value was used.

Diopter examination

The diopter examination began with an objective refraction test using a fully automatic computerized refractometer (Model: KR-800, Topcon Corporation, Japan). The examinee's chin rest and headrest were adjusted, and they were instructed to focus on the hot air balloon or small house inside the device. The tracking ball was adjusted to position the pupil centre between the inner and outer aligning rings, initiating automatic measurements. Three separate measurements were taken for each eye, with the average value, automatically calculated by the computerized refractometer, then recorded. The standard deviation of the three measurements had to be < 0.05 mm, otherwise the measurement had to be repeated. Next, subjective refraction was assessed using a fully automatic comprehensive optometry instrument (VT-10, Topcon Corporation). Briefly, the objective refractive values obtained from the computerised refractometer were inputted into the comprehensive optometry instrument, followed by the maximum plus to maximum visual acuity (MPMVA) procedure. During MPMVA, a fogging lens (typically +0.75 D) was employed to induce controlled myopia, relaxing accommodation for more accurate visual acuity determination. Under fogging conditions, the optometrist simultaneously evaluated binocular vision, ensuring binocular harmony by adjusting lenses. Binocular function was further assessed using the red-green test, based on accommodative balance. The fogging lens power was then gradually reduced until the patient achieved clear vision of the chart letters; the corresponding lens power was recorded as the endpoint. Cycloplegic refraction was performed after inducing cycloplegia. Participants aged 8–12 years received 1% cyclopentolate hydrochloride eye drops for mydriasis, whereas those aged ≥ 12 years received compound tropicamide eye drops. Here, 1% cyclopentolate was administered twice, with a five-minute interval between each administration, and compound tropicamide was administered three times, again with a 5-minute interval between each administration. Mydriatic refraction was conducted 30 minutes after

the last instillation, upon disappearance of the pupillary light reflex.

Intraocular pressure examination

Intraocular pressure was measured using a non-contact tonometer (CT-800, Topcon Corporation, Tokyo, Japan). The participant was instructed to place their chin on the chin rest and press their forehead against the headrest, aligning the eye with the examination nozzle at the appropriate height. The instrument's focal length was then aligned with the examined eye. The patient was asked to keep their eyes open and focus on the yellow-green fixation target inside the instrument. When the bright focal point within the pupil was clearly aligned with the instrument's focal point, the nozzle automatically emitted a puff of air. This measurement was repeated three times per eye, and the average value was recorded.

Corneal endothelial cell count examination

Corneal endothelial cell count is considered a reliable indicator of corneal hypoxia. It also serves as a key safety assessment parameter for ortho-k lenses during follow-up examinations. Here, the examination was performed using a non-contact specular microscope (SP-1P, Topcon Corporation). The chin rest was adjusted to position the patient's examined eye within the imaging aperture. The patient was instructed to keep their eyes open and focus on the fixation light within the instrument. The examiner adjusted the working distance to achieve a clear image and then captured it to complete the measurement.

Fitting method and recheck

All patients were fitted with either spherical or aspherical ortho-k lenses designed by Beijing Eyebright (made of fluorosilicone-acrylate material, oxygen permeability Dk value of $125 \times 10^{-11} [\text{cm}^2/\text{s}] \times [\text{mLO}_2/(\text{mL} \times \text{mmHg})]$), with a central optical thickness of 0.22 mm. All ortho-k lens users wore them continuously at night for 8–10 h and cleansed and soaked their lenses daily with a multifunctional solution (Menicon Co., Ltd, Nagoya, Japan). The lenses were worn continuously for 12 months, without the use of glasses during the day. Regular examinations were conducted at follow-ups after one, three, six, nine, and 12 months. All measurements, record keeping and patient follow-ups were conducted by an ophthalmologist at the time of the initial application of the ortho-k lenses and throughout subsequent follow-up visits.

Outcome measures

Baseline data were collected for analysis, including age at the initiation of ortho-k lens wear, sex, SE refraction at baseline (SE = spherical diopter + 1/2 astigmatism), IOP and cell density (CD). The changes in

AL during baseline examination and follow-up (six and 12 months) were recorded.

Statistical analysis

All data were statistically analyzed using IBM SPSS Statistics, Version 26.0 (IBM Corp., Armonk, NY, USA). Measurement data were expressed as mean $\pm$ standard deviation ($\bar{x} \pm s$), and a paired-sample t-test was used for comparing the parameters of both eyes. Enumeration data were expressed as the number of cases (n) and rate (%), and the chi-squared (χ^2) test was used for the intergroup comparison. A univariate analysis was performed on the fellow eyes of all patients to evaluate the correlation between baseline variables and changes in AL in these eyes. Factors showing a $p < 0.05$ in the univariate analysis were then entered into a multivariate regression model, with fellow eye AL change as the dependent variable. The correlation strength was expressed by beta (β) value, 95% confidence interval, corrected R^2 value and p value. The level of significance was set at $\alpha = 0.05$. There were no changes in personnel at baseline and subsequent follow-ups, and there were no participants with refractions < -0.5 D (as myopia is irreversible) and no adverse events.

Ethics: This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee. This was a prospective study and all participants (or their guardians) signed an informed consent form before the start of the study.

RESULTS

Baseline data

As shown in Table 1, 81 patients with unilateral myopic anisometropia were recruited, with an average age of 11.08 ± 2.57 years. The corrected myopic eye group had SE, IOP, AL and endothelial CD values of -2.35 ± 0.87 D, 18.13 ± 2.61 mmHg, 24.41 ± 0.29 mm and $3,361.21 \pm 35.15 \mu\text{m}^2$, respectively, whereas the values for those in the uncorrected non-myopic eye group were -0.04 ± 0.38 D, 18.02 ± 2.79 mmHg, 23.37 ± 0.31 mm and $3,352.53 \pm 37.18 \mu\text{m}^2$, respectively. Statistically significant differences in SE (-2.35 ± 0.87 vs. -0.04 ± 0.38 , $p < 0.001$) and AL (24.41 ± 0.29 vs. 23.37 ± 0.31 , $p < 0.001$) between the two groups.

Table 1. Comparison of baseline data of patients before wearing ortho-k lenses

Item	Corrected myopic eye (n = 81)	Uncorrected non-myopic eye (n = 81)	χ^2/t	p
SE/D	-2.35 ± 0.87	-0.04 ± 0.38	24.453	< 0.001
IOP/mmHg	18.13 ± 2.61	18.02 ± 2.79	0.289	0.773
AL/mm	24.41 ± 0.29	23.37 ± 0.31	24.622	< 0.001
Endothelial CD/(cells/mm ²)	3361.21 ± 35.15	3352.53 ± 37.18	1.705	0.090

SE – spherical equivalent; IOP – intraocular pressure; AL – axial length; CD – cell density

Axial length changes

The change in AL is defined as the difference between the AL at the follow-up time point and the baseline AL. As shown in Table 2, the changes in AL at six and 12 months for the corrected myopic eye group were 0.07 ± 0.04 and 0.15 ± 0.07 mm, respectively. In contrast, the changes in AL for the uncorrected non-myopic eye group at six and 12 months were 0.18 ± 0.07 and 0.33 ± 0.11 mm, respectively. The change in AL in the uncorrected non-myopic eye group was significantly greater than that in the corrected myopic eye group at both the six-month (0.07 ± 0.04 vs. 0.18 ± 0.07 , $p < 0.001$) and 12-month (0.15 ± 0.07 vs. 0.33 ± 0.11 , $p < 0.001$) follow-ups, with statistically significant differences.

Table 2. Changes of axial length after one year of wearing ortho-k lenses (mm)

Group	Wearing ortho-k lenses for six months	Wearing ortho-k lenses for 12 months
Corrected myopic eye (n = 81)	0.07 ± 0.04	0.15 ± 0.07
Uncorrected non-myopic eye (n = 81)	0.18 ± 0.07	0.33 ± 0.11
t	13.712	13.874
p	< 0.001	< 0.001

The interocular AL difference was defined as the difference in AL between a participant's eyes. The change in this difference over time was defined as a positive change if the difference increased and a negative change if it decreased. Before wearing corrective lenses, the average difference in AL between the eyes was 1.03 ± 0.33 mm (Table 3). After wearing lenses for six and 12 months, the AL of the corrected myopic eye group was 24.48 ± 0.35 and 24.56 ± 0.31 mm, respectively, and that of the uncorrected non-myopic eye group was 23.55 ± 0.24 and 23.7 ± 0.22 mm, respectively. The ocular AL differences in both eyes were 0.94 ± 0.28 and 0.86 ± 0.19 mm, with a

change of -0.10 ± 0.08 and -0.18 ± 0.13 mm, respectively. After wearing lenses for six and 12 months, the AL difference between eyes gradually decreased (0.94 ± 0.28 vs. 0.86 ± 0.19 , $t = 2.376$, $p = 0.018$), and the change in AL difference (-0.10 ± 0.08 vs. -0.18 ± 0.13 , $p < 0.001$) was statistically significant.

Univariate analysis results

Univariate analysis was conducted, with baseline non-myopic eye SE, non-myopic eye IOP, and non-myopic eye endothelial CD as independent variables, and non-myopic eye AL growth as the dependent variable. As shown in Table 4, a significant statistical correlation was found between baseline SE of non-myopic eyes ($p < 0.001$) and AL increment in those eyes.

Multivariate analysis results

A multiple regression analysis was performed with baseline age and fellow eye SE as independent variables and fellow eye AL change as the dependent variable. As shown in Table 5, baseline SE was positively correlated with non-myopic eye AL growth ($\beta = 0.073$, $p = 0.002$).

Table 5. Multivariate linear regression analysis between different variables and axial length growth of the uncorrected non-myopic eyes

Variable	β	p	95% CI
SE	0.073	0.002	0.027, 0.122
Final model	$R^2 = 0.296$	Corrected $R^2 = 0.284$	

SE – spherical equivalent

DISCUSSION

Recent years have witnessed a high and rising prevalence of myopia among minors in China, and a portion of the myopic population develops anisometropia [8]. As the age increases and the degree of myopia deepens,

both the prevalence and severity of myopic anisometropia increase [17]. Anisometropia-induced unequal visual input and blurred vision can impair visual function, potentially leading to monocular suppression, strabismus, impaired stereopsis and amblyopia [23]. Therefore, early correction of anisometropia to control its progression is crucial. Unilateral myopic anisometropia – defined as anisometropia where one eye is myopic and the fellow eye is almost emmetropic – represents a specific form of anisometropia. For managing anisometropia, particularly in eyes with relatively high myopia, ortho-k lenses have demonstrated superior efficacy to low-concentration atropine in controlling myopia

Table 3. Changes of axial length difference between eyes of patients after wearing ortho-k lenses

Item	Wearing ortho-k lenses for six months	Wearing ortho-k lenses for 12 months	t	p
Axial length of the corrected myopic eye group (mm)	24.48 ± 0.35	24.56 ± 0.31		
Axial length of the uncorrected non-myopic eye group (mm)	23.55 ± 0.24	23.70 ± 0.22		
Difference in axial length of both eyes (mm)	0.94 ± 0.28	0.86 ± 0.19	2.376	0.018
Change in axial length difference (mm)	-0.10 ± 0.08	-0.18 ± 0.13	5.267	< 0.001

Note: ‘-’ means that the difference has decreased.

Table 4. Univariate linear regression analysis between different variables and axial length growth of the uncorrected non-myopic eyes

Variable	Mean value	β	R^2	Corrected R^2	p	95% CI
SE/D	2.32 ± 0.84	0.074	0.18	0.16	< 0.001	0.027, 0.129
IOP/mmHg	18.74 ± 2.66	0.013	0.097	0.082	0.577	0.003, 0.023
Endothelial CD/ μm^2	3375.24 ± 35.86	-0.002	0.061	0.044	0.524	-0.005, 0.000

SE – spherical equivalent; IOP – intraocular pressure; AL – axial length; CD – cell density

progression [24]. Therefore, for minors with monocular myopia, ortho-k lenses are usually chosen as a means to correct and control myopia.

Orthokeratology lenses are rigid gas-permeable corneal contact lenses with a reverse-geometry design. When worn overnight, they induce changes in corneal morphology. This induces myopic defocus in the peripheral retina, thereby potentially slowing axial elongation and myopia progression. Additionally, ortho-k lenses can improve accommodative function and reduce accommodative lag [25]. The improvement of accommodation lag in myopic eyes following the use of the lenses also plays a role in delaying the growth of AL.

This study showed that the AL of the eyes increased after wearing lenses for six months and 12 months compared with baseline, and that the AL of non-myopic eyes increased more obviously than that of corrected myopic eyes (six months: 0.07 ± 0.04 vs. 0.18 ± 0.07 , $t = 13.712$, $p < 0.001$) and (12 months: 0.15 ± 0.07 vs. 0.33 ± 0.11 , $t = 13.874$, $p < 0.001$). However, the AL difference of both eyes gradually decreased (0.94 ± 0.28 vs. 0.86 ± 0.19 , $t = 2.376$, $p = 0.018$). While ortho-k lenses effectively controlled myopia progression in the treated eyes, the refractive error of the non-myopic eye progressed rapidly towards myopia. This suggests that the reduction in interocular refractive difference following ortho-k lens wear may result not only from slowed myopia progression in the treated eye but also from accelerated myopia development in the fellow eye. A controlled study discovered that the AL of minors with myopia wearing single-vision frame glasses increased by 0.63 ± 0.26 mm on average in two years, whereas that of minors with myopia wearing ortho-k lenses increased by an average of 0.36 ± 0.24 mm in the same period, with a statistically significant difference ($p < 0.01$) [26]. Compared with single-vision spectacles, ortho-k lenses slowed AL progression by 43% [27]. Given individual variations in genetics and visual behavior, researchers employed a self-controlled design in patients with unilateral myopia to evaluate the efficacy of ortho-k lenses in controlling axial elongation. Related research [28] found that the eyes treated with ortho-k experienced an average axial growth of 0.08 ± 0.15 mm over a year, whereas the contralateral eye showed a substantially faster average axial growth of 0.39 ± 0.32 mm ($p < 0.001$). It has been demonstrated that with one year of ortho-k treatment, the AL growth (0.05 ± 0.19 mm) of the myopic eye in minors with unilateral myopia was significantly less than that of the non-myopic eye (0.34 ± 0.12 mm) [28].

Univariate linear regression analyses were performed to assess the association between the change in AL of the fellow eye and the following independent variables: sex,

baseline age, baseline fellow eye SE, baseline fellow eye IOP and baseline fellow eye corneal endothelial CD. It was found that there was a significant statistical correlation between baseline age ($p = 0.033$), baseline non-myopic eye SE ($p < 0.001$) and non-myopic eye AL growth. Further multivariate linear regression analysis showed that the baseline age was negatively correlated with the growth of non-myopic eye AL ($\beta = -0.014$, $p = 0.031$), and that baseline non-myopic eye SE was positively correlated with the growth of non-myopic eye AL ($\beta = 0.073$, $p = 0.002$). Age is a predictive factor of axial elongation in minors with myopia wearing ortho-k lenses [29]. In a related study observing 31 minors wearing these lenses, it was concluded from single-variable and multivariable analyses that the greater the age, the lower the increase in AL [30]. In the present study, a larger baseline SE was significantly associated with less AL elongation. This association may be explained by the greater degree of peripheral retinal myopic defocus induced by ortho-k lenses in patients with high myopia, which more effectively impedes myopia progression [31].

This study has certain limitations. First, there was selection bias in the collection of the participants, limiting the applicability of the results. Second, a small sample was included, and larger samples and multicentre studies are still needed to provide a stronger basis. Finally, a limited number of independent variables were included in the process of exploring the factors influencing AL, and the impact of indices such as corneal curvature, astigmatism and central corneal thickness was not considered.

CONCLUSION

While ortho-k lenses function well in controlling the growth of AL of the myopic eye in minors with unilateral myopic anisometropia, they accelerate the progression of myopia in the contralateral non-myopic eye. Minors with monocular myopia who are of a younger age and have greater SE diopter at baseline will develop myopia faster in the contralateral eye following correction with ortho-k lenses.

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Authors' contributions: WTT conceived of the study, WLJ and GH participated in its design and data analysis and statistics, and XYX helped to draft the manuscript. All authors read and approved the final manuscript.

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Дугорочни ефекти корекције монокуларне миопичне анизометропије на некориговану аксијалну дужину ока код малолетника и фактори њеног утицаја

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САЖЕТАК

Увод/Циљ Циљ овог рада био је да испита дугорочне ефекте корекције монокуларне миопије ортокератолошким (орто-к) сочивима и факторе који утичу на промене аксијалне дужине (АД) у некоригованом оку код малолетника.

Методе У студију је укључен 81 пацијент са монокуларном миопијом који је први пут користио орто-к сочива. Очи које су кориговане орто-к сочивима сврстане су у миопичну групу, док су контралатералне некориговане очи сврстане у немиопичну групу.

Забележене су промене АД од почетног мерења до контролних прегледа, а униваријантне и мултиваријантне линеарне регресионе анализе вршене су секвенцијално да би се испитала корелација између почетних параметара и промена АД у некоригованим очима.

Резултати Након ношења орто-к сочива 6 и 12 месеци, АД у коригованој групи са миопијом износила је $24,48 \pm 0,35$ и $24,56 \pm 0,31$ mm, док је АД код некориговане немиопне групе била $23,55 \pm 0,24$ и $23,7 \pm 0,22$ mm. Након 6 и 12 месеци, промена АД била је већа у некоригованој немиопичној групи него у коригованој миопичној групи ($p < 0,001$), а разлика у АД између два ока се постепено смањивала ($t = 2,376$, $p = 0,018$). Промена разлике АД ($-0,10 \pm 0,08$ vs. $-0,18 \pm 0,13$, $p < 0,001$) била је статистички значајна.

Закључак Ортокератологија убрзава прогресију миопије код контралатералних немиопичних очију. Млађа деца са монокуларном миопијом и већом сферном еквивалентном диоптријом брже ће развити миопију у контралатералном оку након корекције орто-к сочивима.

Кључне речи: ортокератологија; једнострани миопична анизометропија; аксијална дужина очне јабучице