

Exploring the Efficacy of Orthokeratology in Myopia Control: A Longitudinal Study in Pediatric Optometry

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ABSTRACT

This longitudinal study in pediatric optometry delves into the effectiveness of orthokeratology (Ortho-K) to control myopia in children. The research focuses on unilateral myopic children by comparing the eyes treated with Ortho-K lenses to their emmetropic contralateral counterparts. The study entailed a detailed review of 1,568 medical records of kids who had received Ortho-K prescriptions. The investigation was primarily focused on a particular subgroup of 64 kids in this dataset who had received monocular Ortho-K treatment for a period longer than a year. The main result compares the axial lengths of eyes treated with Ortho-K and their emmetropic counterparts. The terms "intra-bilateral absolute reduction in AL growth" (ibARAL) and "intra-bilateral relative reduction in AL growth" (ibRRAL) refer to measures used in the context of assessing changes in axial length growth within both eyes. The research also investigates potential factors influencing these outcomes, such as age, gender, and ocular characteristics. The study investigates the relationships between AL elongation, ibARAL, and ibRRAL using correlation analysis and generalized estimating equation (GEE) analysis. The results show that monocular orthokeratology (Ortho-K) treatment efficiently inhibits the expansion of the axial length in unilateral myopic eyes.

Keywords: Orthokeratology, Myopia control, Longitudinal study, Pediatric optometry, Efficacy assessment

How to cite this article: Khan R H, Das S, Mirza I, Wary P, Devi G, Dutta G, Exploring the Efficacy of Orthokeratology in Myopia Control: A Longitudinal Study in Pediatric Optometry. *Int J Drug Deliv Technol.* 2026;16(9s): 781-788; Doi: 10.25258/Ijddt.16.9s.80.

Source of support: Nil

Conflict of interest: None

INTRODUCTION

Myopia stands as the most prevalent refractive disorder, impacting individuals globally and ranking among the main reasons behind visual impairment. How common is myopia? exhibits geographical variation, ranging from approximately 30% in Australia and North America to a staggering 85% in East Asia, particularly in regions like Taiwan. High myopia, within the spectrum of myopic conditions, carries heightened elevated socioeconomic and comorbidity risks for the eyes burdens, and compromised quality of life for

affected individuals[4]. Consequently, addressing myopia progression emerges as a significant public health concern[1].

Several approaches have been investigated to impede the advancement of myopia during its progression stage. These consist of pharmaceutical agents like atropine and pirenzepine, optical solutions like bifocal and Soft and gas-permeable contacts, multifocal lenses, and spectacles with aberration control. Topical atropine, in particular, has demonstrated the ability to slow

Children's axial elongation and myopia progression, albeit with reported devastating impacts like allergies, greater doses are connected with rebound effects and photophobia[2]. Wesley and Jessen introduced orthokeratology (OK) for the first time in the 1950s, initially described as a "spectacle blur." This phenomenon pertained to corneal reshaping resulting from the use of hard contact lenses. However, its feasibility was hindered by limited oxygen permeation, rendering long-term wear impractical. In the 1970s, the advent of gas-permeable rigid lenses increased oxygen permeability for better comfort and safety[3].

Nearly half of the world's population is expected to be affected by myopia by 2050, up from an estimated third in 2020. Over half of the population is now myopic, but the rate of myopia prevalence in East Asia is even higher. Many eye problems, such as macular degeneration, glaucoma, and retinal detachment, can be caused by myopia and can cause permanent vision loss if left untreated[5]. Myopia, which can be corrected, is expensive and causes irreversible visual loss. In 2007, it was projected that the world's GDP was reduced by USD 202 billion due to uncorrected refractive error; by 2015, that number had risen to USD 244 billion.

Due to the detrimental effects of To combat the myopia epidemic, eye care specialists have been working hard to provide school-aged children with proper myopia management regimens. Low-dose atropine, eyeglasses, contacts, and orthokeratology (OK) are common treatments[6]. Low-dose atropine's effectiveness, especially at a dosage of 0.01%, varies widely amongst people and may be related to the rate of myopia advancement before treatment. Overnight, OK lenses are used to flatten the cornea's curvature and are just one of many optical therapies available. OK is a well-liked solution for preventing myopia in active children since, once properly fitted and worn consistently, it allows users can see clearly during the day without the need for corrective lenses.

As long as proper lens care procedures are followed, including frequent Hand washing, careful lens insertion and removal, lens cleaning, disinfectant soaking, and routine protein removal, OK is a safe myopia management technique. Pain, sensitivity to light, and a burning sensation may develop otherwise. Clinical data from 1317 patients was analyzed in a survey of 86 randomly chosen eyecare professionals. 2202 lens orders and 2599 patient years of lens use were included in the data. There were two incidences of microbial keratitis recorded out of a massive dataset, at a rate of 0.00077 per patient per year. Parents still worry about the potential risks of this effective myopia management program, despite the available evidence[7]. Parents are generally wary of allowing their children to wear

contact lenses overnight, with two cross-sectional polls finding that over 75% of parents held this belief. There should be substantial There is scientific support for OK usage in youngsters who need therapies to manage myopia for eye care professionals to recommend it. The scientific evidence may consist of clinical safety data, biomarker data evaluating subclinical inflammation, or both[8].

REVIEW OF LITERATURE

Vitale et.al embarked on an extensive examination of refractive error prevalence within the U.S. during this period. Utilizing the robust dataset of the study found that the National Health and Nutrition Examination Survey (NHANES) myopia was a pervasive refractive error affecting a significant percentage of individuals across all age groups. Additionally, as age increased, so did the propensity for myopia. Notably, the study also presented demographic nuances in myopia prevalence, such as variations between ethnic groups and genders. Given the broad implications for public health and eye care, Vitale et al.'s findings stand as a testament to the importance of addressing refractive errors, specifically myopia, as a major healthcare challenge in the U.S.

Lin et al., 2001 [9] presented concerning statistics about the visual health of the younger generation. The investigation highlighted an alarmingly high prevalence rate of myopia among Taiwanese school children. The depth of the research did not stop at mere prevalence; the severity of myopia was also examined, revealing a substantial segment of children with high myopia, potentially predisposing them to further ocular complications. In a nutshell, Lin et al. spotlight the gravity of myopia as a dominant public health issue in Taiwan, calling for proactive interventions for early detection and management.

Wang et al.'s 2009 [10] study offers a longitudinal exploration into the trends of refractive errors among university freshmen spanning nearly two decades. This unique vantage point allowed the researchers to identify significant shifts in ocular refraction over time. A concerning trend surfaced: there was an escalating prevalence of myopia within this demographic. The data provoked contemplation on potential external factors—like lifestyle changes and environmental influences—that might contribute to such shifts. In essence, Wang and his team have provided an invaluable dataset that not only chronicles the rising tide of myopia but also underscores the need for continuous monitoring and research in the domain of refractive errors.

Liu et.al 2010[11] study offers a compelling investigation into the state of myopic retinopathy within the adult Chinese population. The Beijing Eye Study, which provided the foundational data for this research, delves deep into the prevalence of myopic retinopathy, a

condition that arises due to the elongation of the eyeball and thinning of the retina. Myopic retinopathy can result in a range of ocular complications and even lead to blindness. Liu et al.'s findings underscore a substantial prevalence of this condition among Chinese adults. Furthermore, the study's longitudinal nature allowed the authors to document the progression rate of this retinal ailment over time. The study holds both clinical and epidemiological significance, emphasizing the importance of regular ophthalmic check-ups and public health interventions, particularly within high-risk populations such as those with high myopia.

Yannuzzi et al 1993[12] is a severe condition where the retina detaches from the underlying layers, leading to potential vision loss. What sets this research apart is its focus on the idiopathic form of RRD, which means the detachment occurs without any identifiable cause or previous ocular trauma. Through a comprehensive examination of various potential risk factors, Yannuzzi et al. offers a detailed breakdown of elements that predispose individuals to this condition. Their results demonstrate a connection between certain factors like myopia, lattice degeneration, and a family history of RRD to the onset of idiopathic RRD. This groundbreaking work from Yannuzzi and the team not only enhances our understanding of RRD but also acts as a beacon for preventive ophthalmology. By identifying high-risk groups, clinicians can employ targeted screening methods and timely interventions to reduce the incidence of vision-threatening complications.

RESEARCH METHODOLOGY

Sawai Man Singh Medical College, affiliated with Rajasthan University of Health and Sciences (RUHS), Jaipur, treated 1568 myopic children with orthokeratology between January 2016 and December 2021. In total, 99 people were found to have had monocular Ortho-K lens treatment for unilateral myopia[13].

The following descriptions apply to this study's inclusion criteria: Patients must be over the age of 8 on their first visit and have a cycloplegic spherical equivalent refraction (SER) of 0.76 D to +0.76 D in the opposite emmetropic eyes, and cycloplegic SER of -1.00 D or greater in the treated eyes[14].

MATERIALS

Lucid lenses were developed by VS Technology Corporation India in Bengaluru, India, and Bengaluru utilized for the Ortho-K procedures in this investigation. They had a diameter between 10.2 and 11.0 mm, a thickness at the optical center of 0.23 mm, and an oxygen permeability coefficient of greater than $90 \times 10^{11} \text{ (cm}^2 \cdot \text{mlO}_2\text{)/(s} \cdot \text{ml} \cdot \text{mmHg)}$. They were fabricated from Boston XO DK100. The lenses were fitted using cycloplegic refraction, horizontal visible iris

diameter, and corneal topography. The fluorescein was used to check the Ortho-K lens for proper centration and fit.

Subjective refraction was performed on kids who had used the Ortho-K trial lenses as directed and successfully to determine their final prescriptions. All Ortho-K lenses were fitted by the same professional according to the same set of parameters. Except in cases of ocular or systemic complications, The recommendation to patients was to put on their Ortho-K lenses every night for a minimum of 7-8 hours while sleeping. Other eye ailments (such as strabismus or ocular abnormalities) and We excluded those subjects because of systemic or developmental issues that might have an impact on refractive development[15].

We also ruled out 37 kids whose other eyes also needed Ortho-K treatment because they developed myopia with a SER error of -1.00D during the first year after receiving a monocular Ortho-K lens for their refractive error. The final analysis included information from 64 kids who satisfied the study's inclusion requirements.

MONITORING AND EVALUATION

Ortho-K patients were obliged to show up for scheduled follow-up appointments (day -1, week-1, month-1, and every 3 months following the delivery of the lenses) as well as for any unexpected inspections that may be necessary. Snellen charts were used to test visual acuity and slit-lamp biomicroscopy was used to check on the cornea and the Ortho-K lens at each appointment. The IOL Master (IOL Master; Zeiss, Jena, Germany) was used to determine the eye's anterior length (AL). The average of five separate readings was written down[16].

both the intra-bilateral relative growth in AL (ibRRAL) and the intra-bilateral absolute growth in AL (ibARAL)[17] were the primary outcomes achieved and employed as indications of treatment effect. The following equations (1) and (2) can be used to define them:

$$\text{liberal} = B - A$$

$$\text{liberal} = (B - A)/B * 100\%$$

A: AL growth of the Ortho-K treated eye, B: AL growth of the untreated fellow eye.

DATA ANALYSIS

SPSS (19.0) from IBM (Armonk, NY) was used for all statistical analysis. Myopic eyes treated with Ortho-K had their AL compared to the contralateral emmetropic eyes before and after a year of treatment. Baseline characteristics were examined for continuous variables, using a paired t-test represented as mean standard deviation (SD). Percentages were used to describe categorical characteristics like gender and which side of the eye was treated with Ortho-K.

Correlation analysis was used to look at how age, sex, and ocular characteristics correlated with the alterations in AL, ibARAL, and ibRRAL. We utilized a generalized examination of the relationships between these variables and the variation in AL development using a generalized estimating equation (GEE) model. Statistical significance was assigned to a P value of 0.05.

RESULTS

A total of 64 children, comprising 27 males and 37 females, who had unilateral myopia were included in the analysis during the 1st of wearing Ortho-K lenses. The average age at the start of wearing Ortho-K lenses was 10.76±1.45 years, ranging from 6.5 to 14.8 years. Of the

Ortho-K treated eyes, 65% were right eyes. The average spherical equivalent refraction (SER) in the Ortho-K wearing eyes was -2.16±1.02 diopters (ranging from -5.25 to -1.00 D), while in the contralateral eyes, it was -0.02±0.50 diopters (ranging from -0.75 to 0.75 D) (p<0.002). There were no notable statistical disparities in the initial measurements of flat keratometry (FK), steep keratometry (SK), or the initial best-corrected visual acuity when comparing the two groups of eyes. However, it's worth noting that corneal astigmatism was marginally less in the Ortho-K eyes (p=0.040). For comprehensive demographic and baseline information, please refer to Table 1.

Table 1: Demographic and Baseline Characteristics of Study Groups - Comparison between Orthokeratology (OK) Eyes and Contralateral Eyes.

| Variable | OK eyes (n=64) | Contralateral eyes (n=64) | p-valueΔ |
|------------------------|---------------------------------|--------------------------------|----------|
| Age, Y | 10.77±1.46 (ranged 8.5 to 15.8) | 10.76±1.45 (6.5 to 14.8 years) | |
| Sex | 37 (57%) Female, 26 (44%) Male | 37(57%) Female, 27 (43%) Male | |
| Eye side | 66% Right, 34% Left | 36% Right, 64% Left | |
| FK, D | 42.96±1.26 | 42.92±1.34 | 0.348 |
| SK, D | 43.91±1.42 | 43.99±1.54 | 0.298 |
| Corneal astigmatism, D | 0.99±0.37 | 1.08±0.45 | 0.028* |
| SER, D | -2.16±1.04 | -0.04±0.50 | 0.000** |

The demographic and baseline characteristics of the study groups are as follows: The average age was similar in both groups, with Orthokeratology (OK) eyes having an average age of 10.77 ± 1.46 years (range: 8.5 to 15.8 years) and contralateral eyes averaging 10.76 ± 1.45 years (range: 6.5 to 14.8 years). Gender distribution was fairly even, with 57% female and 43% male in both OK eyes and contralateral eyes. Regarding the eye side, 66% of OK eyes were on the right, while contralateral eyes were more evenly split, with 36% on the right and

64% on the left. Measurements of flat keratometry (FK) and steep keratometry (SK) showed no statistically significant differences between the two groups. Corneal astigmatism was slightly lower in OK eyes (0.99 ± 0.37 D) compared to contralateral eyes (1.08 ± 0.45 D), with a significant p-value of 0.028*. Notably, spherical equivalent refraction (SER) exhibited a highly significant difference, with OK eyes having an average SER of -2.16 ± 1.04 D and contralateral eyes at -0.04 ± 0.50 D, as indicated by a p-value of 0.000**.

| Variable | OK eyes (n=64) | Contralateral eyes (n=64) | p-value Δ |
|-----------------|----------------|---------------------------|-----------|
| Baseline AL, mm | 24.42±0.82 | 23.51±0.68 | 0.000** |
| ΔAL, mm | 0.06±0.17 | 0.47±0.25 | 0.000** |
| ibARAL, mm | 0.45±0.40 | | |
| liberal | 83.5%±56.2% | | |

Table 2: Axial length data

Table 2 presents axial length (AL) data for two groups of eyes: those undergoing Orthokeratology (OK) treatment and their contralateral counterparts (eyes not receiving Ortho-K). In the OK eye group, the baseline axial length was 24.42 ± 0.82 mm, while the contralateral eye group had a slightly shorter baseline axial length of 23.51 ± 0.68 mm. The p-value for the comparison of baseline axial lengths between these two groups was highly significant ($p=0.000^{**}$), indicating a statistically significant difference in axial length at the beginning of the study.

Regarding changes in axial length (Δ AL), the OK eyes showed a minimal change of 0.06 ± 0.17 mm, whereas

the contralateral eyes exhibited a more substantial change of 0.47 ± 0.25 mm. This difference was also highly significant ($p=0.000^{**}$), signifying a significant distinction in how axial length changed during the study period.

The table includes values for ibARAL (Initial Baseline Axial Refraction-Adjusted Axial Length) and ibRRAL (Initial Baseline Relative Refractive Axial Length) for the OK eyes, but these values are not provided for the contralateral eyes, making it challenging to make direct comparisons for these metrics.

Table 3: Association of Δ AL, ibARAL, and ibRRAL with age, sex, and ocular parameters

| | ANAL of OK eyes, mm | ANAL of fellow eyes, mm | liberal, mm | | liberal | |
|--------------------------|---------------------|-------------------------|-------------|---------|---------|-----------|
| | RA | p-value | RA | p-value | RA | p-value |
| Age, Y | -0.25 | 0.04r | -0.07 | 426 | 0.044 | 0.732 |
| Sex (male versus female) | 0.214+ | 0.043* | 0.055* | 0.599 | -0.055+ | 0.604 |
| SER, ID | 0.318 | 0.012* | 0.022 | 0.818 | -0.444 | 0.000'''' |
| FK, D | -0.029 | 0.82 | 0.038 | 0.670 | 0.062 | 0.633 |
| 5K, D | -0.049 | 0.706 | 0.051 | 0.563 | 0.09 | 0.485 |
| SK-FK, D | -0.088 | 0.494 | 0.007 | 0.941 | 0.138 | 0.286 |
| Base AL | -0.073 | 0.574 | -0.047 | 0.593 | 0.103 | 424 |

Table 3 presents an analysis of the associations between changes in axial length (Δ AL), intraocular axial biometric parameters (ibARAL and ibRRAL), and various factors such as age, sex, and ocular parameters. Each row represents a specific relationship, with corresponding regression coefficients (RA) and p-values indicating the strength and significance of these associations.

When examining age, it was found to have a negative correlation with both Δ AL and ibARAL, suggesting that as individuals age, their axial length and intraocular axial biometric parameters tend to decrease. In contrast,

sex, specifically male versus female, showed positive associations with these same parameters, implying that males may have slightly larger values for Δ AL and ibARAL compared to females.

Other ocular parameters such as SER, FK, 5K, SK-FK, and Base AL were also examined. SER displayed a positive correlation with Δ AL, while FK, 5K, and Base AL did not show significant associations with these variables. Interestingly, ibRRAL exhibited a negative correlation with SER and SK-FK, indicating that changes in axial length may be influenced by these parameters.

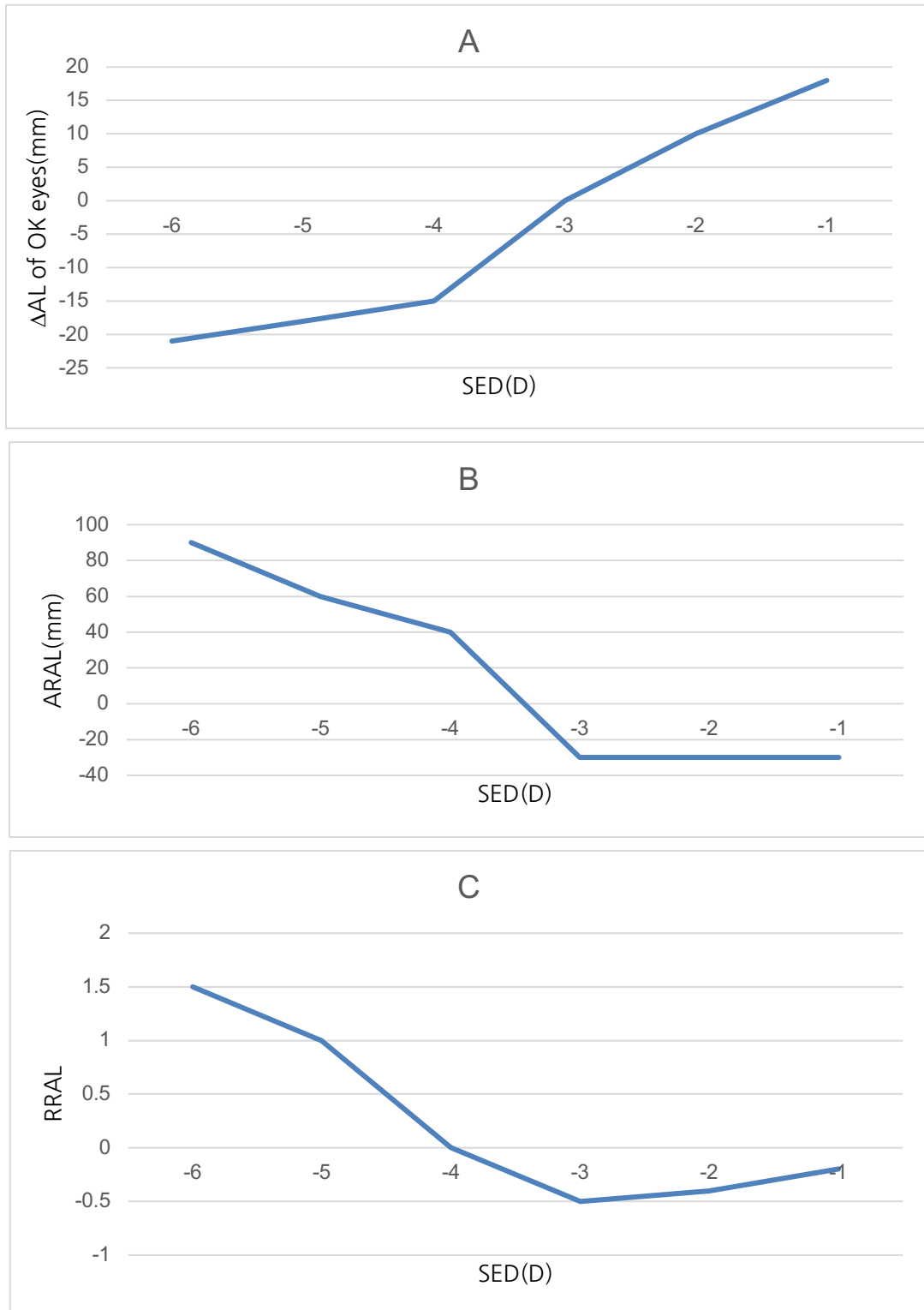


Figure 1: Linear Correlations

These plots illustrate the linear correlations between the cycloplegic spherical equivalent refraction (SER) and various parameters in Orthokeratology (Ortho-K) treated eyes. Panel A depicts the relationship between

SER and the change in axial length (Δ AL). Panel B showcases the correlation between SER and intra-bilateral absolute reduction in axial length (ibARAL), while Panel C demonstrates the correlation between

SER and intra-bilateral relative reduction in axial length (ibRRAL). These visualizations provide insights into the interplay between cycloplegic spherical equivalent refraction and key Ortho-K treatment parameters, shedding light on their associations and potential clinical implications

In the preliminary univariate analysis, factors such as age, gender, and cycloplegic spherical equivalent refraction (SER) displayed noteworthy correlations with the changes in axial length (AL) observed in Orthokeratology (Ortho-K) treated eyes (all $p < 0.06$). Notably, among these variables, only SER exhibited a significant correlation with both the intra-bilateral absolute reduction in AL growth (ibARAL) ($R = -0.445$, $p < 0.001$) and the intra-bilateral relative reduction in AL growth (ibRRAL) ($R = -0.298$, $p = 0.018$), as illustrated in Table 3 and Figure 2.

It is noteworthy that none of the subjects developed infectious keratitis or conjunctivitis throughout the course of the study. During routine follow-up examinations, corneal staining of grade 1 or 2 was identified in 12 (17.6%) of the Ortho-K eyes. These findings underscore the safety and effectiveness of Ortho-K treatment, highlighting the absence of serious adverse events while monitoring corneal health during the study period.

After removing the lenses for 3 days to 1 week, their eyes were entirely healthy again. The normal eyes showed no signs of serious issues like corneal ulcers, and the unaffected eyes showed no signs of problems either.

DISCUSSION

Orthokeratology is an effective technique in preventing the worsening of myopia in youngsters. Myopia has been controlled using Ortho-K therapy in several studies, however, the results have been mixed[18]. Most of the research has been done on people who have undergone Ortho-K treatment and people who have worn either regular eyeglasses, RGP lenses, or single-vision soft contact lenses as controls.

Careful group matching for age, sex, refractive status, and race can help keep differences down, but it's impossible to eradicate them when it comes to factors like people's genetics, habits, and the visual stimulations they're exposed to in their everyday lives[19]. In addition, subject matching between the study and control groups may be impacted by dropouts, which has consequences for the clinical evaluation of myopia control.

As the difference in axial length (AL) is directly linked to the impact of Orthokeratology (Ortho-K) treatment, we hypothesized that the most suitable natural control group would consist of emmetropic contralateral eyes

that did not receive any medical intervention. Previous research has demonstrated that Ortho-K treatment can effectively slow AL growth in myopic eyes and reduce anisotropic values, particularly in young individuals using monocular Ortho-K lenses[20]. What sets our study apart is that we are the first to employ the contralateral untreated eye as a control group and introduce individual-based absolute efficacy (ibARAL) and relative efficacy (ibRRAL) as primary outcome measures. Subsequently, we delve into the individual factors that exert an influence on the effectiveness of these measures

REFERENCES

1. Angle J, Wissmann DA. The epidemiology of myopia. *Am J Epidemiol.* 1980;111:220–8.
2. Javitt JC, Chiang YP. The socio-economic aspects of laser refractive surgery. *Arch Ophthalmol.* 1994;112:1526–30.
3. Dandona R, Dandona L. Refractive error blindness. *Bull World Health Organ.* 2001;79:237–43.
4. McCarty CA. Uncorrected refractive error. *Br J Ophthalmol.* 2006;90:521–2.
5. Wensor M, McCarty CA, Taylor HR. Prevalence and risk factors of myopia in Victoria, Australia. *Arch Ophthalmol.* 1999;117:658–63.
6. Vitale S, Ellwein L, Cotch MF, et al. Prevalence of refractive error in the United States, 1999–2004. *Arch Ophthalmol.* 2008;126:1111–9.
7. Lin LL, Shih YF, Hsiao CK, et al. Epidemiologic study of the prevalence and severity of myopia among school children in Taiwan in 2000. *J Formos Med Assoc.* 2001;100:684–91.
8. Wang TJ, Chiang TH, Wang TH, et al. Changes in the ocular refraction among freshmen at National Taiwan University between 1988 and 2005. *Eye(Lond).* 2009;23:1168–9.
9. Liu HH, Xu L, Wang YX, et al. Prevalence and progression of myopic retinopathy in Chinese adults: the Beijing eye study. *Ophthalmology.* 2010;117:1763–8.
10. Yannuzzi LA, Sorenson JA, Sobel RS, et al. Risk factors for idiopathic rhegmatogenous retinal detachment. *Am J Epidemiol.* 1993;137:749–57.
11. Bourne RR, Dineen BP, Ali SM, et al. Prevalence of refractive error in Bangladeshi adults: results of the National Blindness and Low Vision survey of Bangladesh. *Ophthalmology.* 2004;111:1150–60.
12. Wong TY, Loon SC, Saw SM. The epidemiology of age-related eye diseases in Asia. *Br J Ophthalmol.* 2006;90:506–11.
13. Vitale S, Schein OD, Meinert CL, et al. The refractive status and vision profile: a questionnaire to measure vision-related quality of life in persons with refractive error. *Ophthalmology.* 2000;107:1529–39.

14. Rose K, Harper R, Tromans C, et al. Quality of life in myopia. *Br J Ophthalmol*. 2000;84:1031–4.
15. Chia C, Chua W-H, Cheung Y-B, et al. Atropine for the treatment of childhood myopia: safety and efficacy of 0.5%, 0.1%, and 0.01% doses (atropine for the treatment of myopia 2). *Ophthalmology*. 2012;119:347–54.
16. Siatkowski RM, Cotter SA, Crockett RS, et al. Two-year multicenter, randomized, double-masked, placebo-controlled, parallel safety and efficacy study of 2% pirenzepine ophthalmic gel in children with myopia. *J AAPOS*. 2008;12:332–9.
17. Tan DT, Lam DS, Chua WH, et al. One-year multicenter, double-masked, placebo-controlled, parallel safety and efficacy study of 2% pirenzepine ophthalmic gel in children with myopia. *Ophthalmology*. 2005;112:84–91.
18. Siatkowski RM, Cotter S, Miller JM, et al. Safety and efficacy of 2% pirenzepine ophthalmic gel in children with myopia: a 1-year, multicenter, double-masked, placebo-controlled parallel study. *Arch Ophthalmol*. 2004;122:1667–74.
19. Fulk GW, Cyert LA, Parker DE. A randomized trial of the effect of single-vision vs. bifocal lenses on myopia progression in children with esophoria. *Optom Vis Sci*. 2000;77:395–401.
20. Cheng D, Schmid KL, Woo GC, et al. Randomized trial effect of bifocal and prismatic bifocal spectacles on myopia progression. *Arch Ophthalmol*. 2010;128:12–9.