

Effectiveness and Safety of Overnight Orthokeratology with Roflufocon E High-Permeability Lens Material: A 36 Weeks Follow-Up Study

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Abbreviations: RGP: Rigid Gas Permeable; AL: Axial Length; FDA: Food and Drug Administration; IOL: Intraocular Lens; IOP: Intraocular Pressures; ITT: Intent-To-Treat; CCLRU: Cornea and Contact Lens Research Unit

ABSTRACT

Objective: To evaluate the safety and effectiveness of overnight orthokeratology lenses with Roflufocon E, a highly gas-permeable lens material, for the temporary and reversible correction of myopia.

Methods: Myopic individuals from 9 to 45 years of age were eligible for inclusion in the study. Participants ≤ 12 years of age were required to have myopia between $-1.00 \sim -4.00D$ and astigmatism $\leq -1.50D$, and for those 13-45 years of age myopia between $-1.00 \sim -6.00D$ and astigmatism $\leq -1.50D$. All participants were required to have normal, healthy eyes and not be receiving any ocular medications or systemic medications likely to affect the results of visual acuity.

Each participants wore the lenses for 8 to 9 hours while asleep, and they were evaluated on day 1 and weeks 1, 2, 4, 8, 12, 24, and 36. Success was defined as uncorrected visual acuity (UCVA) $\geq 0.8(0.1\text{LogMAR})$. Orthokeratology wear was discontinued after the week 36 visit. There then followed a further three follow-up visits on day 1 and weeks 1 and 4 after the final evaluation visit.

Results: A total of 85 participants (67.1% male) with a mean age of 15.9 ± 6.87 years were recruited. Baseline UCVA were $0.18 \pm 0.16(0.76 \pm 0.25\text{LogMAR})$ for the $\leq -4.00D$ group and $0.06 \pm 0.07(0.95 \pm 0.11\text{LogMAR})$ for the $> -4.00D$ group. A consistent increase in UCVA was noted from day 1 to week 36. The success rate increased with length of time. The success rates were 99.0% and 95.7% in the < -4.00 and > -4.00 groups respectively, from day 1 to week 36. No severe complications were noted.

Conclusion: The safety and efficacy study outlined here shows orthokeratology to be a safe and effective way to control myopia. Wearing orthokeratology long-term can profoundly reduce myopia, with excellent UCVA during the day, and is applicable to teenagers in controlling myopia.

Introduction

According to the statistics in 2006, myopia prevalence was 22.9% amongst the world's population. This increased to 28.3% in 2010, with an estimated increase to 34% in 2020 and to almost half of the world's population in 2050 [1]. The highest prevalence is

found in Asia [2]. Suggested reasons for this might include greater academic pressure than other countries, extended periods of near work and less outdoor activity [3]. The incidence of myopia does not just cause refractive error; it might also potentially be related to irreversible ocular disease such as retinal detachment,

glaucoma, choroidal neovascularization, optic disc abnormalities and posterior staphyloma [4]. These pose a serious threat to vision and have led to myopia being considered one of the most important public health issues globally. Ways to control myopia so far include corrective spectacles and contact lenses, atropine and orthokeratology [5,6].

Orthokeratology lenses are specially designed Rigid Gas Permeable (RGP) contact lenses mainly worn at night to reshape the front surface of the cornea [7]. This system flattens the cornea to reduce refractive error and obviate the need for wearing spectacles for refractive correction during the daytime. Also, due to the reshaping effect which makes the cornea thinner in the center and thicker in the periphery [8-10], this creates a peripheral defocus on the retina and it is suggested that this slows down the growth in Axial Length (AL) [11-13]. Many studies have shown that orthokeratology can slow myopia progression effectively [2,10,14-16]. Orthokeratology used to control the progression of myopia does not influence accommodation [17], corneal stroma [13] or endothelial cells [18,19]. Despite other research showing that orthokeratology can decrease contrast sensitivity and increase higher order aberration [9,20,21], thereby affecting vision quality, its usage is still growing [22].

Oxygen transmissibility (DK/t) is an important parameter when prescribing a contact lens. Since orthokeratology lenses are worn overnight, higher oxygen permeability rates are needed to avoid ocular hypoxia. For these lenses, oxygen permeability therefore becomes critical. Additionally, studies have shown that the effect of myopia control seems to increase with higher DK/t [23] with a concurrent decrease in the incidence of ocular complications. In a previous study, we proved that using BOSTON Equalens II material (Oprifocan A, Dk of 85) could slow myopia progression in adults and children in Taiwan effectively and safely. Therefore, this current study was to evaluate the long-term effectiveness and safety of wearing orthokeratology lenses in a material with a Dk of 125 in a group with different myopic refractive errors and a different age group. The influence on refraction after ceasing wearing should be further discuss.

Materials and Methods

Participants

The study complied with the tenets of the Declaration of Helsinki and was approved by Tri-Service General Hospital, Taiwan (Institutional Review Board NO.2-105-03-003) and Taipei Tzu Chi Hospital, Taiwan (Institutional Review Board NO.05-FS05-091). All participants or their legal guardians provided written informed consent.

Myopic individuals from 9 to 45 years of age were eligible for inclusion in the study. Participants ≤ 12 years of age were required to have myopia between $-1.00 \sim -4.00D$ and astigmatism $\leq -1.50D$, and for those 13-45 years of age myopia between $-1.00 \sim -6.00D$

and astigmatism $\leq -1.50D$. All participants were required to have normal, healthy eyes defined as no evidence of active infection involving the conjunctiva, lids, or adnexa (grade 2 or less tarsal conjunctival abnormalities were acceptable); no evidence of structural abnormalities of the lids, conjunctiva, or adnexal tissue; clear cornea with no edema, staining, or opacities as observed with slit-lamp examination; no iritis; no herpes keratitis or other disease that would contraindicate lens wear or decrease the attainability of visual acuity; no use of ocular medications.

Exclusion criteria were any disease that may affect the eye or be exacerbated by wearing contact lenses; an allergy to ingredients in the study lens care solutions; pregnant, lactating, or not using a reliable contraceptive; serious systemic disease; participants in another trial within 4 weeks of entering this study; prior intraocular or corneal surgery; Schirmer's test (without topical anesthesia) results >10 mm/5 min; endothelial cell count <2000 cells/mm²; use of systemic medications that may significantly affect vision or healing within the 2 weeks prior to entering the study; prior use of rigid contact lenses or use of soft contact lenses within the 4 weeks before entering the study.

Lens Design and Fitting

The orthokeratology lens design used in this study is one previously cleared by the US Food and Drug Administration (FDA). These were custom-designed lenses to reshape the corneal curvature according to each participant's corneal data. They were manufactured in Roflufocon E material (Dk 125) by Brighten Optix Company (Taipei, Taiwan). The lenses were manufactured in two colors to make it easier for participants to differentiate left and right. Lens diameters ranged from 9.8 to 11.2mm. Lens curvature was determined using a participant's K readings followed by topography. Participants were asked to wear their lenses for 8 to 9 hours every night, and to record the wearing and removal time.

Evaluation and Endpoint

Participants received a comprehensive ophthalmological examination at the screening visit (visit 1); lenses were then dispensed at the following, dispensing visit (visit 2). Participants were then seen on day 1 and weeks 1, 2, 4, 8, 12, and 24 (visits 3-9, respectively) for evaluation. They came in at week 36 (visit 10) for the final visit. Orthokeratology lens wear was discontinued, and the participants then had three more follow-up visits including the next day after the final visit, and then at weeks 1 and 4 (visits 11-13) to monitor VA and corneal recovery. The day 1 visit was performed in the morning, and all other visits in the afternoon. At each visit UCVA was measured with a standardized tumbling E acuity chart placed 6 m from the participant. Over-refraction was performed if UCVA was below 0.8(0.1LogMAR). Autorefractometry and autokeratometry were performed at each visit. Moreover, corneal topography was used with topography to measure the zone affected by the lens, while AL was measured with an Intraocular Lens (IOL)

master and Intraocular Pressures (IOP) with a tonometer. Slit-lamp biomicroscopy was performed at each visit, and the conjunctiva and cornea were evaluated for injection, edema, and neovascularization. Peripheral staining was assessed using fluorescein. The primary endpoint was the success rate of vision correction defined as UCVA \geq 0.8(0.1LogMAR) by using a Snellen chart, and over 85% of participants achieved this at their final evaluation visit. Secondary success outcomes were the lack of clinically significant ocular health issues as determined with biomicroscopy.

Statistical Analyses

Eyes which had never previously been treated with orthokeratology and met all entry criteria were considered as the Intent-To-Treat (ITT) dataset. Category variables were presented as number and percentage, while continuous variables were presented as mean and standard deviation. Data were analyzed for both eyes for each participant.

Results

Study Participants

A total of 85 participants (67.1% male) with a mean age of 15.9 \pm 6.87 years was recruited at the screening visit. Combining data for both right or left eyes, mean UCVA and steep corneal curvatures (Steep K) and flat corneal curvatures (Flat K) were 0.18 (0.76 LogMAR), 7.73mm, 7.95mm for the \leq -4.00D group, and for the $>$ -4.00D group these were 0.06 (0.95 LogMAR), 7.76mm, 8.00mm, respectively. The mean spheres of the \leq -4.00D and $>$ -4.00D groups were -2.67D and -4.76D, respectively. And the mean cylinders for the \leq -4.00D and $>$ -4.00D groups were -0.27D and -0.38D, respectively (Table 1). As a result, the ITT population consisted of 85 participants (169 eyes), one of them with only one eligible eye was still considered ITT. Five participants did not complete all 9 months of treatment due to withdrawing their consent and were excluded from PP (per protocol) population.

Table 1: *Participants characteristics (N=85).

Age		15.9 \pm 6.87
Sex	Male	28(32.9)
	Female	57(67.1)
VA (Decimal(LogMAR))	\leq -4.00D	0.18 \pm 0.16(0.76 \pm 0.25)
	$>$ -4.00D	0.06 \pm 0.07(0.95 \pm 0.11)
Steep K (mm)	\leq -4.00D	7.73 \pm 0.24
	$>$ -4.00D	7.76 \pm 0.32
Flat K (mm)	\leq -4.00D	7.95 \pm 0.24
	$>$ -4.00D	8.00 \pm 0.32
Sphere over-refraction	\leq -4.00D	-2.67 \pm 0.94
	$>$ -4.00D	-4.76 \pm 0.68
Cylinder over-refraction	\leq -4.00D	-0.27 \pm 0.42
	$>$ -4.00D	-0.38 \pm 0.43
Axial Length(mm)	\leq -4.00D	24.69 \pm 0.81
	$>$ -4.00D	25.74 \pm 0.87

IOP(mmHg)	\leq -4.00D	16.51 \pm 2.02
	$>$ -4.00D	15.53 \pm 2.34

Note: *Data presented as mean \pm standard deviation, except for sex which is presented as number (percentage).

Vision Correction Success Rate

The vision correction success rate UCVA \geq 0.8(0.1LogMAR) at each of the follow-up visits is shown in Figure 1. The success rate increased with length of time after beginning treatment (from 44.4% to 99.0% in the \leq -4.00D group, and from 12.9% to 95.7% in the $>$ -4.00D group, from day 1 to week 36). Specifically, the success rates were lower than 80% before week 2, and reached beyond 85% at week 8 for both groups. In addition, the different refraction power on baseline did not affect the correction results.

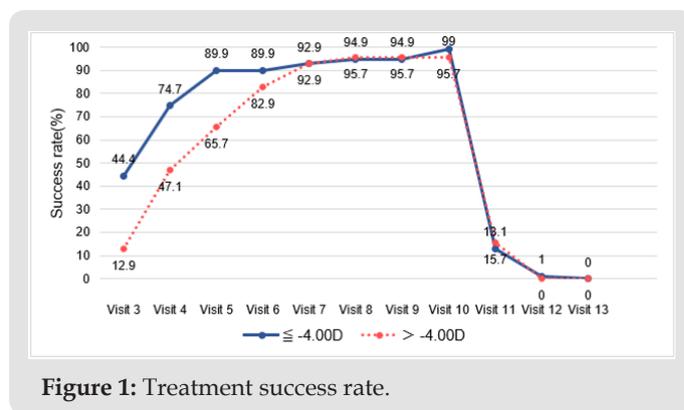


Figure 1: Treatment success rate.

Time Trends of LogMAR, Corneal Curvature, Sphere, Cylinder, Axial Length and IOP

The mean LogMAR at baseline was higher than at any of the follow-up visits. A significant decrease in LogMAR was noted from day 1 to week 36 (p-value for time trend $<$ 0.001 for both groups); there was a sharp decrease from day 1 to week 1, after which LogMAR remained stable (Figure 2.1). A slight flattening in both Steep K and Flat K were noted from screening to week 1 (Figures 2.2 & 2.3). Significant improvement of sphere was found in both groups (p-value for time trend $<$ 0.001 for both groups), and sphere reached a plateau at week 12 (Figure 2.4). All astigmatism, no matter in what refraction, were improved and back to the refraction similar to baseline after stop wearing lenses (Figure 2.5). The axial length did not change much and was meaningless clinically whether during the research or after stopping lens wear (Figure 2.6). In addition, IOP dropped between baseline and week 36. This might be due to thinning of the central cornea caused by orthokeratology (Table 2).

Table 2: Trends of IOP at Base line(V1) and Final visit(V10).

	\leq -4.00D	$>$ -4.00D
Baseline (Visit 1)		
N	99	70
Mean \pm standard	16.51 \pm 2.02	15.53 \pm 2.34
Final Visit (Visit 10)		

N	94	67
Mean ± standard	15.40 ± 2.19	14.72 ± 2.49

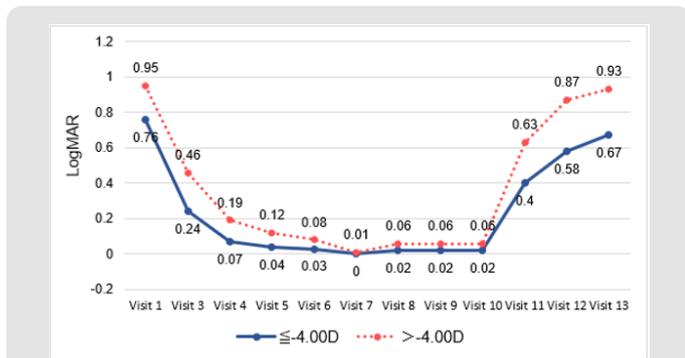


Figure 2(1): Time trends of LogMAR.

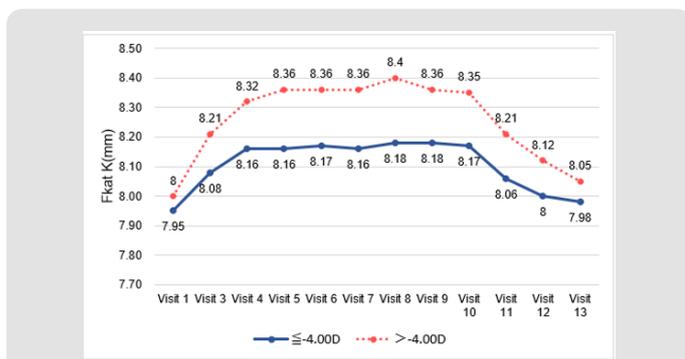


Figure 2(2): Time trends of corneal curvature (Flat K).

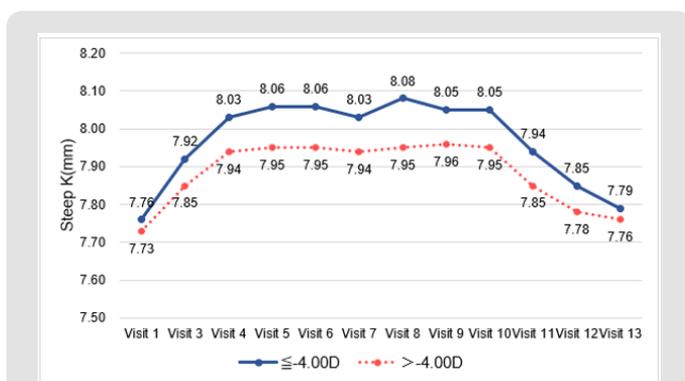


Figure 2(3): Time trends of corneal curvature (Steep K).

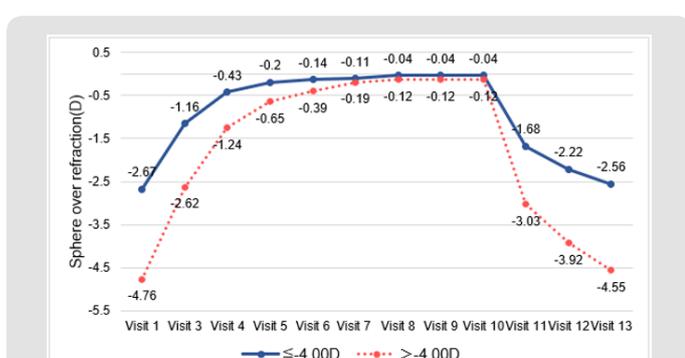


Figure 2(4): Time trends of sphere over refraction.

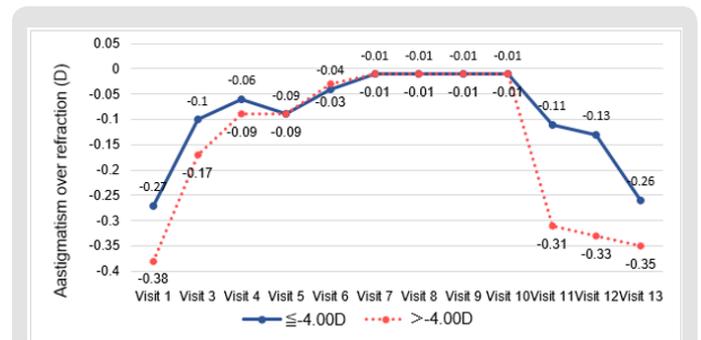


Figure 2(5): Time trends of astigmatism over refraction.

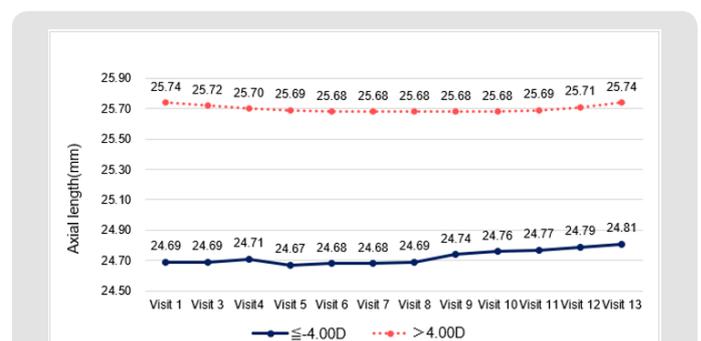


Figure 2(6): Time trends of Axial Length.

Safety Evaluation

Grading of injection, edema, neovascularization, staining, conjunctival hyperemia, palpebral conjunctival observations, other complications and dry eye classification with fluorescein was based on the Cornea and Contact Lens Research Unit (CCLRU) grading scale. No injection, edema or neovascularization was found during any visit. In 87 eyes corneal staining was noted (very slight, 80 eyes; slight, 7 eyes); in 36 eyes conjunctival hyperemia was noted (very slight, 31 eyes; slight, 5 eyes); in 24 eyes palpebral conjunctival observations were noted (very slight, 16 eyes; slight, 8 eyes); in 15 eyes other complication were noted (very slight) and dry eye was noted in 4 eyes (classification slight) (Figure 3).

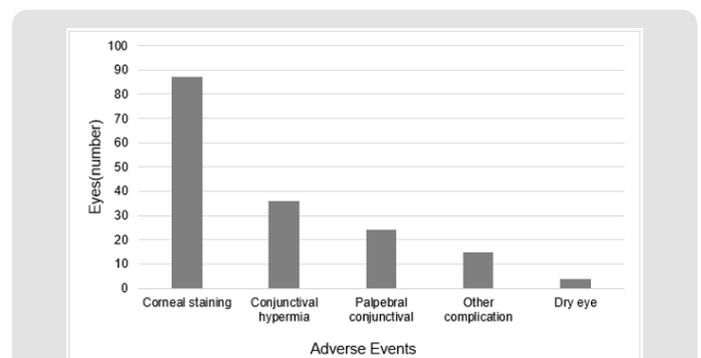


Figure 3: Safety evaluation.

Discussion

There have been several studies showing that orthokeratology can slow myopia progression effectively. In this study, corneal

curvature increased after 36 weeks, most notably in the 1st week, both in Flat K and Steep K. Other studies had similar outcomes whether in radius [24] or in diopter [25,26] value. Corneal toricity is a matter of concern when fitting orthokeratology. Chen et al. [26] found increased corneal toricity after discontinuing wear of long-term orthokeratology lenses. This could be one of the major check points when assessing participants who have been long term wearers of orthokeratology lenses. An incidence of 29.6% corneal staining and other mild complications was found in this study, which is consistent with other research [27,28]. Infection is of course a serious issue in contact lens wear. Recent studies have shown the incidence of infection in orthokeratology to be very low [27,29] which appears to be the same in this study. In addition, the effects of corneal flattening or steepening along with changes in corneal thickness were also observed. Several studies have shown that corneal thickness changes significantly after orthokeratology, especially mainly due to epithelial thinning while stromal changes had no influence or little contribution [13,30,31]. However, some studies have indicated no significant change in corneal thickness [18,32].

The exact mechanisms still require long term observation in the future. Oxygen permeability is an important parameter in contact lens material. Early studies showed that the lowest permeability rate to prevent corneal swelling when wearing lenses at night was a DK/t of 87 [33]. But studies in recent years have shown that this value in a closed eye situation has to be higher than 125 [34,35] to provide better corrective effect and lower cornea swelling [36]. This trial had some limits. Firstly, product safety is easily influenced by personal hygiene or storage conditions. Therefore, the cleanliness of the lens cannot be controlled. Secondly, corneal flexibility cannot be measured, which will cause the correction results to vary between participants. Thirdly, this study does not have a long-term follow-up. A longer follow-up would allow us to measure and analyze the change in all data recorded in this study. In summary, reviewing all of the research data presented in this study, this clearly shows that orthokeratology using Roflucon E high-permeability material is a safe and effective method to temporarily and reversibly correct myopia. In this way, one can have great UCVA during the day and effectively, and reversibly, correct myopia in teenagers.

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