Contact Lens and Anterior Eye xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Contact Lens and Anterior Eye

journal homepage: www.elsevier.com/locate/clae

# Choroidal thickness and axial length changes in myopic children treated with orthokeratology

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ARTICLE INFO

*Keywords:*
Orthokeratology
Choroidal thickness
Optical coherence tomography

ABSTRACT

*Purpose:* To analyze the change in subfoveal choroidal thickness (SFChT) and its relationship with changes in axial length (AL) in myopic children treated with Orthokeratology (Ortho-k).

*Methods:* Fifty myopic children participated in this study: 29 subjects were treated with Ortho-k lenses and 21 with single vision distance spectacles. The SFChT and ocular biometrics, including AL, were measured at baseline, one month, and six months after lens wear in both groups.

*Results:* AL significantly increased in both groups over time. In the Ortho-k group, SFChT also increased; however, there was no significant change in SFChT in the control group over time. At the six-month visit, the magnitude of eye growth was significantly reduced in the Ortho-k group compared to the control group ($0.06 \pm 0.10$ mm vs. $0.17 \pm 0.10$ mm, $P < 0.001$). SFChT was significantly thicker in the Ortho-k group compared to the control group at the one-month and six-month visits ($15.78 \pm 11.37$ μm vs. $-2.98 \pm 8.96$ μm, $P < 0.001$ (one-month visit); $21.03 \pm 12.74$ μm vs. $-2.50 \pm 14.43$ μm, $P < 0.001$ (six-month visit)), although there was no significant difference between the two follow-up visits ($P = 0.102$ for the Ortho-k group; $P = 0.898$ for the control group). Changes in the large choroidal vascular layer (LCVL) accounted for the majority of subfoveal choroidal thickening (approximately 77% and 80% at one-month and six-month visits, respectively).

*Conclusion:* Ortho-k treatment induced significant choroidal thickening and a slowing of eye growth. LCVL thickening accounted for the majority of SFChT thickening. However, its potential mechanism in myopia control requires further investigation.

## 1. Introduction

Experimental studies of both animals [1–6] and humans [7–11] shows that changes in choroidal thickness (ChT) are associated with eye growth. Imposed defocus can induce changes in ChT accompanied by the development of myopic or hyperopic refractive errors in animals, including chicks [1,2], macaque monkeys [3], and marmosets [4]. Negative spectacle lenses (hyperopic defocus) cause choroidal thinning, followed by an increase in eye growth [1–4]. Positive spectacle lenses (myopic defocus) cause choroidal thickening followed by a slowing of eye growth to minimize retinal defocus [1–4]. Despite being much smaller in magnitude, changes in ChT in response to defocus also occur in adult humans in the short term [12,13]. Moreover, pharmacologic treatments, such as dopaminergic agonists [5] and anti-muscarinic agents [6], have also been shown to induce transient choroidal thickening, followed by the inhibition of scleral growth in chicks. The choroid is thought to play a role in regulating scleral growth by delivering a signal to the sclera in response to visual stimuli [14]. For example, studies of both chicks [15,16] and mammals [17] have shown that changes in proteoglycan synthesis, collagen synthesis, and extracellular matrix constituents occur in response to visual stimuli, which could lead to the remodeling of the sclera.

Studies have consistently reported that Ortho-k treatment significantly inhibits myopia progression in children by slowing ocular growth [18–22]. It has been hypothesized that this effect may result from the induction of peripheral myopic defocus, due to the effects of the Ortho-k lens on the mid-peripheral cornea [23]. Several studies [24–26] have investigated the relationship between the change in ChT and the change in axial length (AL) in children treated with Ortho-k treatment with conflicting results. Both Chen et al. (using NIDEK spectral domain optical coherence tomography [SD-OCT]) [24] and Loertscher et al. [25] (using low-coherence reflectometry [Haag Streit Lenstar LS900]) found significant increases in ChT after short-term Ortho-k treatment. Chen et al. [24] examined primarily Asian children

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http://dx.doi.org/10.1016/j.clae.2017.09.010
Received 22 March 2017; Received in revised form 1 September 2017; Accepted 11 September 2017

over a short period (3 weeks) but did not perform a detailed analysis of the choroidal vascular layers, which might have enhanced the understanding of the potential mechanism of the effect of Ortho-k on ChT. Conversely, Gardner et al. [26] found no significant changes in subfoveal or parafoveal ChT in nine myopic children after short-term (1 month) and long-term (9 months) Ortho-k treatment using the Zeiss Cirrus HD-OCT. However, in this particular study [26], several methodological limitations may have limited the power to reliably detect a significant change in ChT including: the small sample size, the lack of a control group, non-registration of serial OCT images, a lack of control of the timing of follow up visits with respect to ChT diurnal changes, and possible effects of cycloplegia and ocular magnification upon OCT measurements.

Due to these inconsistent results regarding the potential effect of Ortho-k treatment on ChT [24–26], we conducted this prospective controlled study to determine the effect of Ortho-k treatment on ChT and AL in myopic children with a relatively long-term follow-up period. Unlike previous studies, an analysis of different choroidal vascular layers was also performed to investigate their relative contribution to changes in subfoveal ChT (SFChT), in order to enhance the understanding of the effect of Ortho-k treatment on SFChT. Changes in ocular biometrics, such as AL, central corneal thickness (CCT), anterior chamber depth (ACD), and lens thickness (LT), were measured to enhance our understanding of the relationship between the changes in SFChT and ocular biometrics.

## 2. Material and methods

### 2.1. Study design

This prospective, nonrandomized study was conducted at Zhongshan Ophthalmic Center, Sun Yat-Sen University (Guangzhou, China). The study was conducted in accordance with the tenets of the Declaration of Helsinki and was approved by the ethical committee of Zhongshan Ophthalmic Center, Sun Yat-sen University. All the subjects included in the Ortho-k treatment group were recruited from a clinical trial (Register No.: ChiCTR-IPR-14005505, starting from November, 2014 to March, 2017). Prior to the study, the nature of the study and the potential risks were explained to the participants and their parents or guardian, and consent was obtained before the start of the study.

Twenty-nine healthy children (13 males and 16 females; age: 12.31 ± 1.71 years) were enrolled for Ortho-k treatment, and another 21 subjects (9 males and 12 females; age: 11.52 ± 1.69 years) with single vision distance spectacles were enrolled as a control group. The inclusion criteria for both groups were an age between 8 and 15 years; corrected visual acuity of 20/20 or better, mean spherical equivalent refractive error (SER) between −1.00 and −4.00 D, and with-the-rule astigmatism no greater than −1.50D; and no use of any other myopia control modalities including rigid contact lenses, multifocal soft contact lenses, atropine, etc., except for single vision distance spectacles.

For the Ortho-k group, after lens dispensing, the participants were advised to wear their Ortho-k lenses every night for at least seven consecutive hours. They were then instructed to return for a follow-up visit after one day, one week, one month, three month and six months. At each visit the participants underwent a slit-lamp examination to check for contact lens related complications and any adverse events. The fitting of the Ortho-k lens, unaided visual acuity, cycloplegic manifest refraction (if unaided visual acuity was worse than 20/25), slit lamp biomicroscopy, and corneal topography (Medmont E-300, Australia) were evaluated at each visit. Ocular biometrics, SFChT, and large choroidal vessel layer (LCVL) thickness were measured at the baseline, one-month and six-month visits.

For the control group, participants were instructed to wear their spectacles throughout the day and return for follow-up visits at one month and six months after the first measurement session. Visual acuity with spectacle correction, cycloplegic manifest refraction (if visual acuity with spectacle correction was worse than 20/25), ocular biometrics, SFChT, and LCVL thickness were measured at each visit.

### 2.2. Lens fitting

For the Ortho-k group, eligible participants were fitted with a four-zone reverse-geometry lenses (Euclid Systems Ortho-k; Euclid System Corp., Herndon, USA), made from BOSTON EQUALENS II (oprifocona) with a nominal Dk of 127 × 10–11 ($cm^2$/s) (ml O2/ml_mmHg) (ISO/Fatt) according to the manufacturer's fitting guidelines. For the control group, cycloplegic manifest refractions were conducted and the single vision distance spectacle prescriptions were updated for all participants in our hospital before enrollment.

### 2.3. Measurements

To avoid the potentially confounding influence of diurnal ocular variations on the results [27], in particular axial length and ChT, all procedures were performed at approximately the same time of day, between 3 pm and 6 pm at each visit. In addition, to standardize the influence of the administration of the cycloplegic agent [28] on ChT and other ocular parameters, all measurements were performed approximately 30 min after the administration of the mydriatics (0.5% tropicamide plus 0.5% phenylephrine hydrochloride; three times at five minutes apart). All measurements were taken twice in the right eye only and the order of the measurements was maintained for all children (visual acuity, cycloplegic manifest refraction, ocular biometrics, followed by OCT imaging).

#### 2.3.1. Ocular biometrics measurements

Ocular biometrics, including AL, CCT, ACD, and LT, were measured using a non-contact biometer (Lenstar LS 900; Haag Streit AG, Koeniz, Switzerland). As suggested by Cho et al. [29], anterior segment length (ASL = CCT + ACD + LT) was calculated to investigate the effect of Ortho-k treatment on the anterior segment. Furthermore, AL, as defined by the instrument, refers to the distance between the anterior cornea and the retinal pigment epithelium (RPE). In addition to AL, we also calculated internal axial length (IAL: anterior cornea to anterior sclera) by adding the SFChT determined by OCT imaging to the AL measured with the Lenstar, which more precisely reflects the true nature of the change in ocular growth [25]. Five consecutive measurements were collected from each subject at each measurement session, and the values were later averaged.

#### 2.3.2. SD-OCT scanning and analysis

SD-OCT scanning was performed by one experienced investigator using the Heidelberg Spectralis instrument (Spectralis HRA + OCT, Heidelberg Engineering, Heidelberg, Germany) on all subjects at baseline one-month and six-month visits. The instrument uses a super luminescent diode with a central wavelength of 870 nm, and has an axial resolution of 3.9 μm, and a transverse resolution of 14 μm in retinal tissue. The enhanced depth imaging (EDI) mode was used to enhance the visibility of the choroid using 100 averaged scans to improve the signal to noise ratio. All B-scans included for analysis had a quality index of no less than 25 dB (mean 28.9 ± 2.8 dB). The confocal scanning laser ophthalmoscope (SLO) was adjusted manually to obtain a clear image of the fundus prior to imaging. According to the manufacturer's recommendation, to account for ocular magnification, each participant's keratometry values were entered into the instrument prior to each measurement to correct each OCT scan. Repeat scans were captured with the aid of automatic registration, and the follow-up mode Spectralis was utilized to ensure the same retinal location was imaged at each visit. The linear scan pattern (vertical and horizontal line) was used for every subject at each visit.

SFChT and LCVL thickness were measured by two independent observers experienced in analyzing OCT images using the Heidelberg