Corneal Biomechanics and Corneal Reshaping Therapy
NCT02719535
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(a) Introduction
Myopia is highly prevalent in Asian populations, especially Chinese populations [1], and now affects Americans and Europeans as well.[2-3] Low to moderate myopia is not a major concern, but high myopia (more than 6D) is associated with retinopathy and glaucoma and is an economic burden on society.[4]

Various treatment options have been proposed to reduce the progression of myopia, including the use of pharmaceutical agents and different types of corrective lenses. [5-8] Corneal reshaping, also called orthokeratology, is an intervention with proven efficacy in retarding myopia progression.[10]

In orthokeratology, the corneal curvature is altered after a patient wears the lenses. The effective treatment range is usually not more than 5D of myopia and not more than 1.5D of astigmatism. In addition, orthokeratology can be slow or ineffective in some patients. This may be related to the pre-treatment corneal parameters such as the apical radius and eccentricity.[11] Corneal biomechanical properties may also be a factor, but accurate measurement of the influence is difficult.

Most interventions for myopia control begin in early childhood. After commencement of the treatment, several years of continual monitoring is required to confirm its efficacy. If the intervention is eventually ineffective, then the time would have been wasted. The goal of the proposed study is to investigate whether corneal biomechanics are predictive of successful orthokeratology. If pre-treatment corneal biomechanics combined with other conventional corneal parameters do not indicate successful orthokeratology, patients can be advised to try other more effective interventions earlier.

(b) Objectives
1. To monitor the changes of corneal biomechanics from long-term (6 months) successful orthokeratology
2. To determine if corneal biomechanics is predictive of the rate of orthokeratology

(c) Methods
Subjects
Young, healthy, myopic adults with no history of long-term contact lens wear and ocular disease were recruited. Subjects who occasionally wear soft lenses (such as for sports) were eligible. The inclusion criteria included myopia between -4.00D and -5.00D sphere, and with-the-rule astigmatism (axis 180 ± 30) of not more than 1.50D, where the spherical equivalent was between -4.00D to -5.75D. The difference in myopia between the two eyes was within 1D for both the sphere and cylinder components. The inclusion criterion in refractive error for this study is to eliminate the confounding factor for orthokeratology caused by a wide refractive range. The best-corrected visual acuity was at least 0.10 logMAR in each eye when measured using the Early Treatment Diabetic Retinopathy Study (ETDRS) charts (Prevision Vision, La Salle, IL) under a normal room lighting condition.

Procedures

The following baseline data were collected: non-cycloplegic manifest refraction, ocular biometry through partial coherence interferometry (Zeiss IOLMaster; Zeiss Humphrey, Dublin, CA), corneal topography (Medmont E300, Medmont Pty Ltd., Vermont, VIC, Australia), corneal thickness through swept-source optical coherence tomography (Casia SS-1000, Tomey, Nagoya, Japan), and corneal biomechanics using an Ocular Response Analyzer (ORA; Reichert Inc., USA).

Five valid axial length measurements were captured using the IOLMaster, and an average reading was generated for analysis. In corneal topography, three images (scores higher than 95) were automatically captured. The mean value of the simulated steepest and flattest keratometry readings was used for analysis. Corneal thickness was measured using a "3D Corneal Map" scan by the swept-source optical coherence tomography. Three automated measurements were obtained for each scan while the subject focused on a central target inside the instrument. In ORA, three acquisitions were obtained each with a waveform score of at least 6.0. Corneal hysteresis (CH), corneal resistance factor (CRF), and corneal-compensated intraocular pressure (IOPcc) were measured.

After all non-contact procedures, the cornea was anesthetized using one drop of 0.4% benoxinate. Intraocular pressure was measured using Goldmann applanation tonometry (GAT) followed by corneal biomechanics by using a corneal indentation device. Two GAT readings were taken and the mean result was used for analysis. The indenter first touched the central cornea. After the pre-load was stabilized (through an audible sound), the indenter moved forwards and backwards at 12mm/s to indent the cornea by 1mm. The indentation was completed in less than 0.25 seconds. The corneal stiffness was read from the device and the tangent modulus was calculated from the corneal radius of curvature and central thickness. Three corneal indentations were obtained, and the average was used for analysis.

Lenses used

After the suitability for wearing corneal reshaping lenses was confirmed through slit-lamp biomicroscopy, subjects were fitted with orthokeratology lenses. The lenses used were reverse geometry lenses (Menicon Z Night contact lens) made of super high gas permeable material (Menicon Z, DK 163 ISO). Lens fitting was based on the manufacturer's instructions (Easy Fit Software, Menicon Co Ltd., Nagoya, Japan) according to ocular information, including corneal topography, non-cycloplegic manifest refraction, and horizontal visible lens diameter. Lens fitting was assessed with fluorescein. An optimal fluorescein pattern consisted of 3 to 4mm of central touch, 1 to 1.5mm of mid-peripheral pooling and 1 to 1.5mm of peripheral alignment. A bull's eye fluorescein pattern was considered an optimum fit.

Wearing schedule

After a successful trial fit, a delivery visit was arranged. The subjects were returned to the clinic after an overnight lens wear. The same fluorescein pattern was maintained after overnight orthokeratology. The subjects wore the lenses every night and they were required to return regularly. Further follow-up visits were taken place after the first week, 1 month, 3 months and 6 months of lens wear. Each visit was within two hours after waking up in the morning and the lenses being removed.

In addition to corneal topography, corneal thickness, and corneal biomechanics measurements (using both ORA and corneal indentation device), subjective refraction and ocular biometry were included in all follow-up visits. Both the habitual and best-corrected visual acuities were measured.

Ethics clearance was obtained from the institutional review board of The Hong Kong Polytechnic University. Informed consent was obtained from all participants included in the study. This study was registered at ClinicalTrials.gov (NCT02719535, registered March 25, 2016) and in the University of Hong Kong HKU Clinical Trials Register (HKUCTR-1957, registered Feb 1, 2016).

Analysis of data

The corneal parameters and refractive error obtained in each aftercare visit were compared with the baseline data. Data of one eye of each subject who completed the 6-month orthokeratology were analyzed, with the eye with residual sphere closer to plano at the 6-month visit being selected. If the residual sphere was the same in both eyes, then the eye with less residual astigmatism was selected. For subjects with the same residual refractive errors in both eyes, the right eye was selected. Normality was checked using the Shapiro-Wilks test. Repeated-measure analysis of variance or the Friedman test were used to compare changes in ocular parameters throughout the study, that is, from baseline to the end of the 6-month orthokeratology. Baseline ocular parameters that could best predict myopia reduction were identified through linear regression (Pearson or Spearman). Reduction of sphere at the 6-month visit was used as the dependent outcome response, and the various baseline ocular parameters were treated as independent predictors. All data analysis and graphical presentation were completed using SigmaPlot 13 (Systat Software, Inc.).

(d) References

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