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Original article

Accelerated corneal collagen cross-linking in pediatric keratoconus: One year study

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Abstract

Purpose: To evaluate the safety and effectiveness of accelerated corneal collagen crosslinking (CXL) in pediatric keratoconus.
Design: Prospective non-randomized observational study.
Methods: 33 eyes of 25 children with keratoconus were included. The corneal epithelium was mechanically removed. Next, riboflavin/hydroxypropyl methylcellulose solution) was applied for 10 min. Accelerated CXL (10 mW/cm^2 for 9 min), was accomplished. Visual acuity, slit lamp examination, refraction, keratometry readings, pachymetry, anterior and posterior elevations, average progression indices, and Q values were recorded. The follow-up visits were scheduled on one day, 3 days, 7 days, one month and then on 3, 6, 12 months after the procedure.
Results: It was statistically significant improvement of the mean UAVA, AVA, and the mean corneal astigmatism ($P < .0001$). The mean corneal thickness showed a significant reduction. The preoperative mean *K* max reading was reduced from 49.12 ± 3.7 D preoperatively to 47.9 ± 3.7 D at 12 months. The mean max anterior elevation, average progression index and Q value showed statistically significant improvement. No significant impact on posterior elevation was recorded. Serious complications were not encountered in this study.
Conclusion: Accelerated CXL shows a stabilization and beneficial clinical outcomes in pediatric keratoconus. It seems an effective and safe procedure in this age group. Effects of accelerated CXL on the posterior corneal surface will need further evaluation.

Keywords: Keratoconus, Accelerated, Cross-linking, Pediatric ophthalmology, Posterior corneal elevation

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Introduction

Visual impairment in children has a broad negative impact on their quality of life and of course will affect their social and educational development.[1]

Keratoconus is a degenerative disorder characterized by ectasia and thinning of the axial or para-axial region of the cornea resulting in irregular astigmatism, myopia and scarring with mild to marked impairment in the quality of vision.[2] Pediatric keratoconus displays a higher ratio of keratoconus eyes being about 88%. It is also diagnosed in more advanced stage (stage IV) comparing to adult patients (27.8% versus 7.8%).[3,4] Hence, keratoconus in children progresses aggressively with a higher rate of acute hydrops as compared to the adult group.[1,3,5]

Early treatment to stop the progression and to avoid future keratoplasty is of greater benefit in long run in those patients. For this reason, corneal cross-linking (CXL) has been widely utilized and evaluated in children after its success in adult keratoconus patients.[6–8]

The only treatment that is believed to be able to stop or decrease the keratoconus progression is collagen cross-linking.[9] The overall treatment time of CXL is still a drawback of this process, so a reduction in the operation time and shorter UVA exposure time (accelerated UVA exposure) to a few minutes are currently being investigated in the pediatric group for better cooperation and comfort.[10,11]

Since there are few published researches in this topic, this study is designed to evaluate this new modification of standard corneal collagen cross-linking (accelerated

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cross-linking) in treating the pediatric keratoconus and to estimate its clinical outcomes during one year follow-up.

Subjects and methods

Children with confirmed keratoconus were enrolled in this prospective study during the period from July 2013 to January 2015 at Mansoura Ophthalmic Center and Al-Mostakbel Ophthalmic Center, Mansoura, Egypt.

Inclusion criteria

Completely clear cornea with maximum keratometry (K max) reading less than 60 D, corneal thickness more than 400 microns at the thinnest location, and children (less than 18 years and older than 6 years) with the absence of any other ocular or systemic diseases.

Preoperative examination

Slit lamp examination, unaided visual acuity (UAVA), aided visual acuity (AVA) measurement, corneal tomography by Scheimpflug camera (Pentacam (Oculus, Wetzlar, Germany)), corneal thickness measurement by Scheimpflug camera and confirmed by a non-contact specular microscope (Tomy EM-3000). All patients underwent the above tests at baseline and at all follow-up visits. Dilated fundus examination was done also using indirect ophthalmoscope and/or non-contact lens (Volk 90). Topical steroid and anti-allergic eye drops were used in any eye with any signs of allergic-related surface inflammation till became preoperatively quiet.

Collagen cross-linking technique

The procedure was conducted under sterile conditions in the operating room of Al-Mostakbel ophthalmic center – Mansoura, Egypt. All the procedure steps were conducted with topical anesthesia (benoxinate hydrochloride 0.4% - Benox 0.4%; Eipico Inc., Cairo, Egypt), while additional sedation with monitored anesthesia care was needed for only 7 young and uncooperative children. After installation of the topical anesthetic eye drops every 5 min for 30 min, the epithelium was mechanically scraped within the central 8 mm diameter area using a Beaver blade. Next, riboflavin ophthalmic solution (0.1% riboflavin, Saline with hydroxypropyl methylcellulose (HPMC) solution) (VibeX Rapid™, Avedro, USA) was applied every 2 min for 10 min until the stroma was completely saturated. Ultraviolet A irradiation, was accomplished at an irradiance of 10 mW/cm^2 for 9 min and 5 cm distance from the cornea using a commercially available UVA system CBM Vega 10 mW X-Linker (UV Emitter Mod. VEGA C.S.O. srlViadegliStagnacci, 12/E 50018 Scandicci, Firenze, Italy). During irradiation, Vibex Rapid solution was applied every 2 min to secure saturation.

Vibex Rapid with its content of HPMC provides faster diffusion into the corneal stroma (twice the traditional riboflavin) and so decreasing the pre-irradiation saturation time under 10 min. In addition, Vega CBM X-Linker with an irradiation power of 10 mW (accelerated CXL) and an irradiation phase that lasts 9 min participate to shorten the total operative time. This will be convenient for children and young patients. The proper fixation of patients was in mind to avoid peripheral irradiation of limbal stem cells.

Postoperative care

Patients received Vigamox 0.5% eyedrops (moxifloxacin hydrochloride 0.5%) five times per day for one week. A soft contact lens was used till complete re-epithelialization. Then, combined topical steroid-antibiotic eyedrops (Dexamethasone and Tobramycin) were prescribed 4 times a day for another week and then tapered over the next three weeks. Carboxymethylcellulose - Sodium (CMC) (0.5%) eye lubricant also was given 6 times daily for one month.

Follow-up

Follow-up was first done one day postoperatively, 3 days for assurance of completion epithelization and contact lens removal, then after one week for prescription of steroid-antibiotic drops (Tobramycin and Dexamethasone) and one month for assessment of corneal haze. Unaided visual acuity, aided visual acuity, refractive changes, tomographic changes, and pachymetry were recorded at 3, 6, and 12 months. At least three measurements were performed to improve inter-session repeatability of pentacam.

This study was registered and reviewed by the Ethics Committee, Faculty of Medicine, Mansoura University. An approval from the Ethical Committee was taken and adhered to the Declaration of Helsinki (R/16.03.44). Written informed consent was obtained from all patients' parents after the nature of the procedure and its possible consequences were clearly explained.

Data analysis

The statistical analysis was carried out using the SPSS (Statistical Package for Social Science) program, version 16. Test for normal distribution of data was performed. Quantitative continuous data were summarized in mean and standard deviation. Preoperative and postoperative means were compared using the paired t-test. All values are declared as a mean ± standard deviation in tables. P value < 0.05 was deemed statistically valuable.

Results

Thirty-three eyes of 25 children (8 bilateral and 17 unilateral) with confirmed keratoconus were included in this prospective study. The mean age was 12 ± 2.02 years (range: 8–15 years). Eighty percent of the study population was boys, and 20% was girls. Of these, 29 eyes showed progression, as defined by an increase in anterior surface (K max) readings of at least 1.00 diopter (D) in serial corneal topographies over a maximum of one year.

Unaided visual acuity (UAVA): Visual acuity was measured using the Landolt C or Tumbling E metric charts and transformed into logarithm of the Minimum Angle of Resolution (Log MAR) for further statistical analysis as recommended by Holladay. [12]. Table 1 summarizes the UAVA and AVA data, expressed in Log MAR and covering 12-month follow-up period. There was a statistically significant improvement from the preoperative values ($P < 0.001$). The preoperative mean

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