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Mechanical versus transepithelial phototherapeutic keratectomy epithelial removal followed by accelerated corneal crosslinking for pediatric keratoconus: Long-term results

Ozge Sarac, MD, Pinar Kosekahya, MD, Mehtap Caglayan, MD, Burak Tanriverdi, MD, Ayse Güzin Taslipinar Uzel, MD, Nurullah Cagil, MD

Purpose: To compare the 36-month outcomes of mechanical or transepithelial phototherapeutic keratectomy (PTK) epithelial removal before accelerated corneal crosslinking (CXL) for pediatric keratoconus.

Setting: Atatürk Training and Research Hospital, Ankara, Turkey.

Design: Retrospective case series.

Methods: Eyes that had accelerated CXL after mechanical (Group 1) or transepithelial PTK (Group 2) epithelial removal were evaluated preoperatively and 12, 24, and 36 months postoperatively. The uncorrected (UDVA) and corrected distance visual acuities, spherical equivalent (SE), manifest astigmatism, and corneal tomographic and aberrometric parameters were assessed.

Results: The study included 40 eyes of 35 consecutive keratoconus patients younger than 18 years with a 36-month follow-up. Group 1 comprised 15 patients, and Group 2 comprised 20 patients. Both groups had a significant improvement in UDVA ($P = .001$ and $P = .02$, respectively) and a significant decrease in maximum keratometry (K) and thinnest corneal thickness (all $P < .001$) 36 months postoperatively. The improvements in maximum K, topographic astigmatism, and spherical aberration were greater in Group 2 than in Group 1 at 12 months ($P = .03$, $P = .01$, and $P = .04$, respectively). After 12 months, the outcomes in the 2 groups were more similar.

Conclusions: The initial visual and topographic outcomes of transepithelial PTK ablation were better than those of mechanical epithelium removal before accelerated CXL in pediatric patients with keratoconus. Over the long-term, the results were similar between the 2 groups.

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Keratoconus is a degenerative and progressive corneal ectatic disease in which corneal stromal collagen matrix alterations lead to stromal thinning, corneal protrusion, and irregular astigmatism.[1] In the past, many treatment modalities have been used to overcome the refractive restrictions in keratoconus. In 2006, the new approach of corneal crosslinking (CXL) was introduced, bringing the promise of strengthening the cornea.[2,3]

The goal of CXL is to rebuild biomechanical strength in an ectatic cornea by creating covalent bonds within and between the collagen molecules using riboflavin and ultraviolet-A (UVA) radiation (370 nm).[4] Today, the accepted protocol for CXL includes deepithelialization of the cornea before the administration of riboflavin to increase its penetration through the corneal stroma to achieve a high level of UVA absorption.[4]

Over the past several years, the conventional CXL procedure included corneal epithelial removal performed mechanically using a rotating brush or a blade. Recently, a new transepithelial phototherapeutic keratectomy (PTK) protocol was introduced in which the epithelium is

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From the Departments of Ophthalmology, Yildirim Beyazit University, Ankara Atatürk Training and Research Hospital (Sarac, Tanriverdi, Cagil), Ulucanlar Eye Training and Research Hospital (Kosekahya), Ankara, Gazi Yasargil Training and Research Hospital (Caglayan), Diyarbakir, and Afyon Sandikli State Hospital (Uzel), Afyon, Turkey.

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Corresponding author: Ozge Sarac, MD, Department of Ophthalmology, Yildirim Beyazit University, Ankara Atatürk Training and Research Hospital, Bilkent, Ankara, Turkey. Email: drozgesarac@gmail.com.

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removed using an excimer laser before CXL.[5–7] Studies comparing the results of the 2 epithelium removal methods[5–7] found that transepithelial PTK before CXL resulted in equivalent or better visual outcomes than mechanical epithelium removal.

The aim of the present study was to evaluate and compare the 36-month visual, refractive, topographic, and aberrometric results of mechanical epithelial removal and transepithelial PTK epithelial removal followed by accelerated CXL in pediatric patients with keratoconus. To our knowledge, the effectiveness and safety of epithelial ablation via transepithelial PTK before CXL has not yet been determined in this population.

PATIENTS AND METHODS

This single-center retrospective study was performed in compliance with institutional and government review board regulations, informed consent regulations, and the tenets of the Declaration of Helsinki. The files of keratoconus patients younger than 18 years who had CXL and a follow-up of 36 months were retrospectively reviewed. Group 1 comprised eyes having mechanical epithelial removal and Group 2, eyes having transepithelial PTK epithelial removal. Accelerated CXL was performed after epithelial removal in both groups. To allow a valid comparison, the pachymetry and keratometry parameters in Group 1 were matched with those in Group 2, after which the patients were consecutively selected for each group.

Keratoconus was diagnosed clinically. In addition to the appearance of the topographic map, patients had at least 1 of the following clinical features: Munson sign, scissors reflex during retinoscopy, corneal thinning, Fleischer ring, Vogt striae, increased visibility of the corneal nerves, and Rizzutti sign. Exclusion criteria included age greater than 18 years, a corneal thickness less than 400 μm, the presence of central or paracentral corneal scar, a history of herpetic keratitis, active ophthalmic inflammation or infection, contact lens use, and pregnancy or lactation.

Ophthalmologic Examination

Patients had complete ophthalmologic examination including uncorrected distance visual acuity (UDVA) and corrected distance visual acuity (CDVA) measurements, slitlamp biomicroscopic examination, fundus evaluation, and tomographic analysis of the cornea using the Sirius 3D rotating Scheimpflug camera and tomography system (Costruzione Strumenti Oftalmici). The examination results were recorded preoperatively and 12, 24, and 36 months postoperatively.

The UDVA and CDVA were measured with a Snellen chart by a cornea specialist and converted to logarithm of the minimum angle of resolution notation for statistical analysis. The spherical refractive error, spherical equivalent (SE), and manifest astigmatism values were also recorded.

Postoperative corneal haze was graded as follows[8]: 0+ = clear cornea; 1+ = focal areas of corneal clouding or reticulation; 2+ = diffuse mild stromal clouding or reticulation; 3+ = diffuse stromal clouding or reticulation obscuring view of iris details; 4+ = focal or diffuse areas of dense stromal haze obscuring iris detail.

Scheimpflug Measurement Protocol

The tomographic measurements were performed with the Sirius 3D system, which has a Scheimpflug rotating camera combined with a Placido disk. The 22 Placido disk rings provide height, slope, and curvature data, while the 25 Scheimpflug images provide data in the anterior cornea, posterior cornea, anterior lens, and iris. An experienced technician performed all measurements under dim lighting with a natural pupil, and the pupil diameters were similar across all measurements. Patients were asked to blink 3 times before each measurement. The eye of the patient was aligned with the visual axis on the central fixation light of the device, and the scan was taken. Three measurements were taken for each eye, and the highest quality scans were evaluated.

The evaluated tomographic parameters included the flat keratometry (K), steep K, maximum K, thinnest corneal thickness, and topographic astigmatism. Total corneal higher-order aberrations (HOAs) on the central 6.0 mm, including anterior and posterior corneal surfaces, were recorded using Zernike coefficients based on 3rd-order to 8th-order aberrations. The following aberrations were analyzed: total root mean square (RMS), HOA RMS, vertical coma Z(3,−1), vertical trefoil Z(3,−3), horizontal coma Z(3,1), and spherical aberration Z(4,0).

Surgical Technique

All procedures were performed in an operating room under sterile conditions. Topical anesthesia of proxymetacaine hydrochloride 0.5% eyedrops (Alcaine) or general anesthesia was used. In Group 1, the corneal epithelium was removed mechanically using a crescent knife at an intended 8.5 mm zone after the corneal epithelium was loosened with a 20% alcohol solution in an 8.5 mm alcohol well was applied for 20 seconds over the cornea. In Group 2, the corneal epithelium was removed using transepithelial PTK performed with an Esiris scanning spot laser (Schwind eye-tech-solutions GmbH & Co. KG). A single-step transepithelial PTK ablation was performed on an 8.5 mm zone at a constant depth of 50 μm. Laser profiles were not based on the refractive parameters and were not topography or wavefront guided. Mitomycin-C was not used.

After epithelial removal, the residual corneal thickness was measured with an ultrasound pachymeter (Palmscan AP-2000-Ultima, Micromedical Devices, Inc.). Riboflavin drops were applied on the center of the cornea every 2 minutes for 30 minutes until the cornea had swollen to more than 400 μm and the aqueous stained yellow. Hypotonic riboflavin 0.1% in sodium chloride 0.009% (Meran) was used in all eyes. Ultraviolet-A irradiation was applied using a commercially available UVA system (Meran Tip, BNM, Inc.). Before treatment, the intended 9 mW/cm^2 surface irradiance (5.4 J/cm^2 surface dosage after 10 minutes) was calibrated using a UVA meter (UVA-365, Lutron Electronics Co., Inc.). During treatment, the riboflavin solution was applied every 2 minutes to ensure saturation and a balanced salt solution was applied every minute to moisten the cornea. Ultrasound pachymetry was taken once 5 minutes after the start of riboflavin drop administration. If patients were under topical anesthesia, the drops were instilled as needed throughout the procedure.

A silicone hydrogel bandage contact lens (Acuvue Oasys, Johnson & Johnson Vision Care, Inc.) was applied at the end of the surgery until full reepithelialization of the cornea. Postoperative treatment included ofloxacin eyedrops (Exocin) 4 times a day for 1 week, fluorometholone eyedrops (FML) 4 times a day on a tapering schedule for 1 month, and artificial tears 4 times a day for 6 months.

Statistical Analysis

Statistical analysis was performed using SPSS for Windows software (version 22.0, IBM Corp.). The normality of the data was analyzed with the Kolmogorov-Smirnov test. Descriptive statistics were recorded as the mean ± SD. Statistical analyses were performed with repeated-measures analysis of variance and the Bonferroni post hoc test. The assumption of sphericity was tested with Mauchly's test of sphericity. When the significance level was greater than the a priori α level ($P > .05$), sphericity was assumed and the value from the univariate test table was used. When the significance level was less than or equal to the a priori α level ($P \leq .05$), sphericity could not be assumed and Wilk's λ test value