

Changes in Endothelial Specular Microscopy findings before and after Corneal Cross-linking

Azza El- Sayed ; Ahmad Mostafa Abdallah; Hatem Gamal Ammar and; Khulood Muhammad Sayed.

Department of Ophthalmology, Faculty of Medicine, Sohag University

Abstract

Purpose: The purpose of our study is to assess safety of CXL with epithelium removal for the treatment of KC on the corneal endothelium by using endothelial specular microscopy comparing the following parameters (cct, cv, cd, hex) before and after CXL.

Patients and methods: This study was performed in Sohag ophthalmology department in Sohag university hospital in collaboration with Sohag Oyon Misr Centre. A total of 30 keratoconic eyes of 23 patients were evaluated for corneal thickness and endothelial cell changes before and 6 months after CXL (with specular microscopy).

Results: The mean age of the study group was 28.70 years \pm 3.5 years ranged from (22-33) years old. There was no significant difference between pre-and postoperative CCT or CD but CV increased and HEX decrease significantly.

Conclusion: Epi-off CXL method has been firmly established to be safe on corneal endothelium, effective and the global standard of care for the treatment of progressive keratoconus.

Introduction

Keratoconus is a bilateral non-inflammatory disease. One of its characteristics is reduction of biomechanical strength of cornea and stromal thinning, which gradually decreases corneal thickness and induces irregular astigmatism, myopia, corneal scarring, and reduction of visual acuity (1). For early stages of keratoconus, one would use spectacles and contact lenses though the progression of the disease can lead to irregular astigmatism or corneal scarring, leaving no other option but corneal transplantation in about 20% of patients (2). Corneal transplantation is an expensive procedure with many complications such as high astigmatism and graft rejection; hence, seeking for a way to halt this progressive disease seems to be of crucial importance (3).

For more than a decade, corneal cross-linking (CXL) has been considered as the only method for improving corneal

biomechanical power (4). Corneal collagen cross-linking (CXL) is a less-invasive treatment that aimed to strength biomechanical stability in eyes with keratectasia (5).

The "standard CXL protocol" described by Wollensak and his colleagues that aim to remove the corneal epithelium in a diameter of 9 mm, followed by corneal stromal saturated with using 0.1% isotonic riboflavin solution in 20% dextran (6). The procedure proved to be effective in increase corneal stiffness, stabilization of keratoconus and improve topographic and refractive features of cornea. Although, the epithelial removal can lead to various complications like infections (7), stromal haze (8), and corneal melting (9) with severe pain and decrease in vision which occur in the first days after the procedure. To avoid these complications, Boxer Wachler et al. explained a modification in epi-off

technique by keeping corneal epithelium intact (epi-on or trans-epithelial CXL) (10).

In this study, we sought to compare corneal parameters (cct,cv,cd,hex) before and after crosslinking by specular microscopy criteria to determine the impact of this procedure on corneal endothelium.

Patients and methods

This study was a prospective, non-randomized study was performed from September 2016 to March 2017, on patients with keratoconus in Sohag ophthalmology department in Sohag university hospital in collaboration with Sohag Oyon Misr Centre.

A total of 31 keratoconic eyes were evaluated for corneal thickness and endothelial cell changes before and 6 months after CXL (with specular microscopy).

Inclusion criteria:

-Age range from 18 to 35 years, Confirmed keratoconus, Central corneal thickness at least 400 μm , Clear cornea.

Exclusion criteria: Eyes with the following conditions were excluded from the study

- Corneal opacity, any previous surgery on eyes as rings, LASIK.
- Previous ophthalmic herpes infection, Past history of uveitis,
- Diabetes mellitus, Pregnancy.
- Collagen vascular diseases, Severe dry eye.

The procedure was first explained and the consent form was signed. Preoperatively, all patients were subjected to A) History taking including Name, age, gender, ocular medication, past history of ocular surgery or LASIK therapy. B) Complete ophthalmic examination including: (UCVA), manifest refraction, (BSCVA), slit lamp examination to exclude corneal opacity or inflammation, fundus examination for any posterior segment

abnormalities, measurement of IOP using applanation tonometry. C) Corneal assessment by Corneal tomography (Pentacam), specular microscopy by using (Topcon SP-1P version 1.10) with non- contact specular microscopy measuring the following parameters (cct, cv, cd, hex) before the CXL.

Epithelium-off collagen cross-linking procedure:

Topical anesthesia was given as benoxinate hydrochloride (one drop every 5 min half an hour before surgery). Skin disinfection was performed by providing iodine 10%. Removal of the epithelium with a blunt-tipped spatula. Sodium hyaluronate dropped on the limbus to keep riboflavin on the cornea. The room lights were turned off in order not to affect the composition and efficacy of riboflavin. The riboflavin was dropped every 3 min for 30 min. Cornea exposed to UVA irradiation performed for 30 min while installing the riboflavin every 3 min, irrigation of the eye by saline. A bandage soft contact lens put on the cornea. At the end of surgery, eye drops were applied including topical antibiotic, topical steroid, and cyclopentolate followed by eye patching. Postoperative treatment usually lasted for 2–4 weeks and included the following: Antibiotic eye drop, Steroid eye drops, Tears substitutes, Systemic vitamin C and vitamin A twice daily and systemic analgesic and anti-inflammatory. In the first week, the patient followed up daily until re-epithelization of the cornea occurs. Thereafter, the patient was followed up at 1, 3, 6, and 12 months postoperatively. The patient was advised to wear sunglasses for 2 weeks.

Statistical analysis

The demographic data for all subjects were analyzed using Microsoft Excel 2007. Statistical

analysis of the specular microscopy parameters (cct, cd, cv, hex) and other data (like age) was performed with a paired *t*-test using the SPSS software version 18. Data expressed as mean, standard deviation (SD), percentage and number. Mean and the standard deviation was used as descriptive value for quantitative data. Correlation analysis was performed by using Person's correlation test.

Results

This study included 30 eyes of 23 patients (15 females, 8 males), (13 in right eyes, 17 in left eyes), with progressive keratoconus; 8 patients with bilateral keratoconus.

The mean age of our patients was 28.70 years \pm 3.5 years ranged from (22-33) years old, 64% were females.

No intraoperative complications were recorded.

The mean preoperative and postoperative of corneal thickness CCT were 478.38 \pm 42.9 μ m and 493.2 \pm 16.70 μ m.

The mean preoperative and postoperative of endothelial cell densities CD were 3221.40 \pm 243.16 cells/mm and 3200.42 \pm 247 cells/mm. The mean preoperative and postoperative of CV were 38 \pm 3.70 and 41.71 \pm 2.74. The mean preoperative and postoperative of HEX were 41.73 \pm 5.08 and 38.13 \pm 5.24.

There was no significant difference between pre- and postoperative CCT or CD but CV increased and HEX decreased significantly.

Correlation between postoperative and preoperative parameters:

There was a strong correlation between postoperative CCT and preoperative CCT ($r=0.930$, $p=0.00$). There was a correlation between postoperative CD and preoperative CD ($r=0.792$, $p=0.00$). There was a correlation between postoperative HEX and postoperative

CV ($r=0.620$, $p=0.14$). No other correlation was found in our study.

When all parameters were entered in a regression model with the postoperative CCT is the dependent variable, preoperative CCT was the only predictor for the postoperative CCT ($r^2=0.930$), this predictability did not increase by adding any other factor.

Discussion

To assess the corneal endothelial cells with corneal specular microscopy is a photographic, noninvasive technique that permits visualization and analyzing of the corneal endothelium, with evaluation of shape, size, and population of endothelial cells (11).

CXL involves a photochemical reaction with (UV)-A illumination activates riboflavin which leads to strengthening the corneal bundles and stop the progression of keratoconus (12).

In study by Rossi et al on twenty eyes ten eyes treated with epi-off CXL, and other eyes treated with epi-on CXL. No significant differences in age keratometric and pachymetric parameters between the two groups were determined at baseline. No significant variations were recorded in spherical aberration and coma aberration, and CCT stilled constant at 12 months post-surgery. Several complications were reported especially after epi-off CXL, such as corneal haze, endothelial damage, melting, and sterile infiltrate infections (13).

In our study all patients treated with epi-off CXL, no significant variations were recorded in CCT before CXL and six months after procedure. No complications have been reported after epi-off CXL, such as corneal haze, melting, endothelial damage.

In the study by Galvis et al, it is a retrospective, non-randomized study

performed on 80 eyes, epi - off CXL is applied to 48 patients with progressive KC between April 2007 to March 2010, of which 19 patients were females and 29 patients were males. The mean age of the patients was 29.3 ± 8.2 years (range 17–44 years). Stabilization of KC was achieved in all eyes after CXL treatment (14).

In our study, we performed a prospective, non-randomized study of 30 eyes of 22 patients with progressive keratoconus treated with epi-off CXL technique, between September 2016 to March 2017. The age of our patients ranged between (22 -33) years old, with a mean (\pm SD) $28.70 \text{ years} \pm 3.5$ years. Stabilization of KC was achieved in all eyes after CXL treatment.

In study by Razmjoo et al divided patients into two groups first group of 22 eyes they removed ring (3 mm width) of corneal epithelium and outer left untouched the central 3 mm and second group of 22 eyes they performed total epithelium removal over 9 mm. After six months they found the partial de-epithelization group slightly better postoperative in DCVA.No significant difference between the groups related to the post-operative steeper keratometry (15).

In our study all 30 eyes treated with total epithelium removal over 9 mm, we did not found significant difference in corneal parameters six months after surgery This study was assessed the safety of CXL with epithelium removal for the treatment of progressive KC patients on the corneal endothelium by endothelial specular microscopy comparing corneal parameters (cct, cv, cd, hex) and we did not find statistically significant differences in (cct, cv, cd, hex) before and after CXL procedure.

So the epi-off CXL method has been firmly established to be safe on corneal endothelium, effective and the global

standard of care for the treatment of progressive keratoconus.

References

- 1- Rabinowitz YS. Keratoconus. *Surv Ophthalmol* 1998;42: 297-319.
- 2- Krachmer JH, Feder RS, Belin MW. Keratoconus and related non inflammatory corneal thinning disorders. *Surv Ophthalmol* 1984; 28:293- 322.
- 3- Kennedy RH, Bourne WM, Dyer JA. A 48-year clinical and epidemiologic study of keratoconus. *Am J Ophthalmol* 1986; 101:267-73 .
- 4- Keratoconus: Overview and update on treatment. *Middle East African J Ophthalmol* 2010; 17(1): 15-20.
- 5- Edwards M, McGhee CN,DeanS: The genetics of keratoconus . *Clin Exp Ophthalmol* 2001; 29:345-51.
- 6- Wachtmeister L, Ingemansson SO, Moller E. Atopy and HLA antigens in patients with keratoconus. *Acta Ophthalmol (Copenh)* 1982; 60:113-22.
- 7- Adachi W, Mitsuishi Y, Terai K, et al. The association of HLA with young-onset keratoconus in Japan. *Am J Ophthalmol* 2002; 133:557- 9 .
- 8- Wang Y, Rabinowitz YS, Rotter JJ, Yang H; Genetic epidemiological study of keratoconus: evidence for major gene determination. *Am J Med Genet* 2000;93:403-9.
- 9-Ihalainen A.Clinical and epidemiological features of keratoconus. Genetic and external factors in the pathogenesis of the disease. *Acta Ophthalmol (Copenh)* 1986; 64(Suppl.): 178.
- 10-Rahi A, Davies P, Ruben M, et al. Keratoconus and coexisting atopic disease. *Br J Ophthalmol* 1977;61:761-4.
- 11-Sharma A, Nottage JM, et al . Persistent corneal edema after collagen cross-linking for keratoconus. *Am J Ophthalmol.* 2012;154: 922-926.
- 12-Caporossi A, Mazzotta C, et al. Riboflavin-UVA-induced corneal collagen cross-linking in pediatric patients. *Cornea* 2012;31:227-231.

