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Research Article

Corneal Cross-Linking In Keratoconus

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Abstract

Purpose: To describe visual and refractive outcomes of conventional versus accelerated corneal cross linking in keratoconus. **Methods:** A prospective descriptive interventional case series. 20 eyes were evenly allocated into two groups. First group (20 eyes) was treated with conventional corneal collagen crosslinking (CXL) and the second group was treated using was treated with accelerated corneal collagen crosslinking (CXL). **Results:** Both groups showed statistically improvement in BSCVA, which was insignificantly different between both groups over the follow-up period.oth groups with conventional and accelerated corneal collagen crosslinking (CXL) showed statistically improvement in BSCVA, which was insignificantly different between both groups over the follow-up period.oth groups with conventional and accelerated corneal collagen crosslinking (CXL) showed statistically improvement in BSCVA, which was insignificantly different between both groups over the follow-up period.oth groups with conventional and accelerated corneal collagen crosslinking (CXL) showed statistically improvement in BSCVA, which was insignificantly different between both groups over the follow-up period. **Conclusion:** Both groups with conventional and accelerated corneal collagen crosslinking (CXL) showed statistically improvement in BSCVA, which was insignificantly different between both groups over the follow-up period.

Keywords: Keratoconus – corneal stroma– Corneal collagen crosslinking

Introduction

Keratoconus is a chronic noninflammatory progressive ectatic corneal condition occuring around puberty.[1] The incidence of keratoconus approximately one per two thousand in the general population. With the improvement of the diagnosis using recent technology of corneal topography, the incidence rate and prevalence rate increase is anticipated. Keratoconus affects both genders and all ethnicities. It is a multi-factorial disease with genetic and nongenetic or environmental predisposition. [2-4]

Clinical picture of keratoconus differs according to disease severity and it is associated with decrease of visual acuity. Clinical picture of keratoconus is classified to external signs as Munson's sign and Rizzuti's sign, retinoscopy signs as scissoring and Charleux oil drop and slit lamp biomicroscopic signs like focal thinning, Fleischer's ring, increased visibility of corneal nerves and hydrops cornea: which is intense stromal edema leading to acute drop of vision occurs due to fluid accumulation within the stroma caused by tear in the Descements' membrane ending with posterior scar after resolving of corneal oedema. [5-9]

Keratoconus is classified according to morphology into nipple type with round morphology where the cone has a diameter ≤ 5mm and is located in the central part of the cornea, oval type where the cone is paracentral with diameter > 5mm and keratoglobus where the cone is located within 75% of the cornea. Corneal irregularity in keratoconus appears as one pattern in topography of the following: pattern 1: Round, pattern 2: Oval, pattern 3:

Superior Steep (SS), pattern 4: Inferior Steep (IS), pattern 5: Irregular, pattern 6: Symmetric bowtie (SB), pattern 7: Symmetric bowtie (SB)/Skewed Steepest Radial Axis Index (SRAX), pattern 8: Asymmetric Bowtie (AB)/ IS, pattern 9: AB/SS. AB superiorly steep, pattern 10: AB/SRAX, pattern 11: Butterfly: the bowtie is horizontally aligned and the lobes inferiorly angulated, pattern 12: Claw pattern: it is also known as "kissing birds", pattern 13: Junctional: It is a circular shape and two lobes are laterally connected, pattern 14: Smiling face and pattern 15: Vortex pattern: named the "Nazi Logo". [10,11]

Treatment modalities: No drugs known to stop keratoconus. When spectacles or contacts are not effective, the surgical procedures to treat keratoconus are: Corneal collagen cross-linking (CXL) with ultraviolet A (UVA) irradiation and riboflavin is used for the stiffening of corneal stroma, corneal ring segments as they add thickness to the midperipheral corneal stroma produces flattening through arc shortening, and keratoplasty either deep anterior lamellar keratoplasty (DALK) or Penetrating keratoplasty (PK) and it is the treatment of choice in case of apical scarring formation. As a management for the patient current state intraocular lens implantation may be considered. [12-17]

Patients and methods

- The study was a prospective comparative interventional case series. It was conducted in Minia university hospitalVision from June 2019 to May 2021.
- 20 eyes of 16 patients were classified into two groups:

Diagnosis was based on slit-lamp observation and pentacam. Keratoconus after diagnosis were classified according to the Amsler–Krumeich system for grading.

Group (A): 10 eyes were treated by conventional corneal cross linking (epithelium off).
Group (B): 10 eyes were treated by accelerated corneal cross linking (epithelium off).

- An informed written consent to be involved in the study was obtained from each patient.
- Approval of the ethical committee of the faculty of medicine El- Minia university was obtained.

CXL (epi-off):

Topical anesthesia of benox eye drops was administered before surgery. Standard pre-operative preparation with betadine 5% (povidone iodine) was performed. The eyelids and eyelashes were covered with a sterile drape.

Mechanical removal of corneal epithelium over the central 9-10 mm (after application of diluted alcohol 25% for 25 seconds) was done using a blunt instrument. 0.1% Riboflavin in 20% hydroxymethyl propyl cellulose solution was instilled topically every 2 minutes for 30 minutes for conventional and for 10 minutes for accelerated. The cornea was exposed to UVA light of 366-374 nm at an irradiance of 3.6 mW/cm2 for 30 minutes for conventional and 7 mW/cm2 for 10 minutes for accalerated. Riboflavin was continued every 2 minutes. Then at the end of the surgery, antibiotic drops were administered and a therapeutic soft contact lens was placed on the cornea.

Results

Best Spectacle-Corrected Distance Visual Acuity (BSCVA):

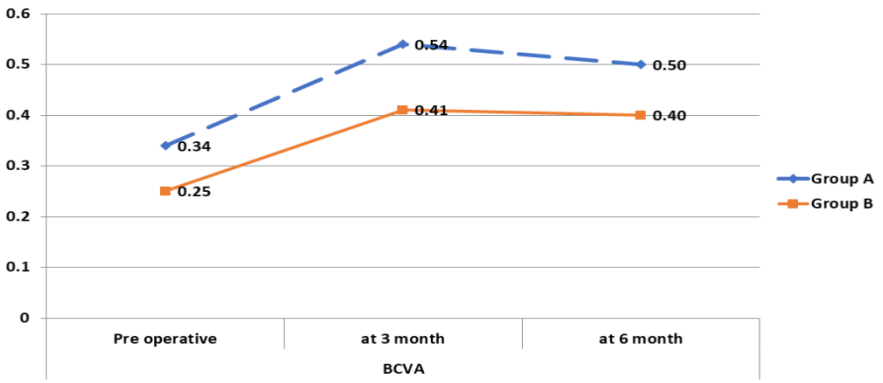
At group A, the mean preoperative best Spectacle-Corrected Distance Visual Acuity (BSCVA) was 0.33 ± 0.1, ranging from 0.2 to 0.6, While the mean postoperative BSCVA at 6 months was 0.53 ± 0.1 (range: 0.3 - 0.7), increasing by a mean of 0.2 ± 0.09 Snellen's line with p value 0.001*. At 12 months the mean BSCVA was 0.5 ± 0.1 (range: 0.2 - 0.7) and decreasing by a mean of 0.04 ± 0.5 in Snellen's Decimal values compared to BSCVA at 6 months with p value 0.03.*

On the other hand, group B, the mean preoperative BSCVA was 0.24 ± 0.1, (range: 0.1 - 0.6), While the mean postoperative BSCVA at 6 months was 0.40 ± 0.1 ranging from 0.1 to 0.7, increasing by a mean of 0.16 ± 0.08 Snellen's line with p value 0.001*. At 12 months the mean BSCVA was 0.4 ± 0.1 (range: 0.1 - 0.7) and decreasing with a mean of 0.01 ± 0.05 in Snellen's Decimal values compared to BSCVA at 6 months with p value 0.5.

Comparing the BSCVA changes preoperative and after 12 months between the 2 groups, it is noted that there is no statistically significant differences.

Table 1: comparison of BSCVA between group A and group B

Variables		Group A	Group B	P1
BCVA	**Pre**	0.33 ± 0.1	0.24 ± 0.1	0.1
	At 6 months	0.53 ± 0.1	0.40 ± 0.1	0.06
	At 12 months	0.5 ± 0.1	0.4 ± 0.1	0.1



Discussion

The study was a prospective comparative interventional case series which was conducted on 20 eyes of 14 patients.

The eyes were evenly classified into two groups: group A were treated with conventional corneal cross linking (epithelium off), and group B were treated with accelerated corneal cross linking (epithelium off)

Collagen cross-linking with ultraviolet-A (UVA) light irradiation exposure was reported by Klingman and Gebre in 1991 on the skin of hairless mice after chronic exposure to UVA light radiation. Collagen became highly resistant to pepsin digestion that means increased collagen cross-linking induced by UVA. Studies showed similar effects on corneal tissue on corneal collagen after exposure to UVA light and riboflavin. UVA Light is present in the solar spectrum includes UV rays, in between UVA radiation can cause corneal endothelial cell damage with a relatively high surface dose of 42.5 J/cm2. UVA dosage that used for CXL clinically is only 5.4 J/cm2. Riboflavin-UVA absorption within the satur-ated cornea with riboflavin increases to 95% compared to 32% without riboflavin, also enhances the collagen cross-linking effect in the corneal stroma and also reduces the exposure of the intraocular tissues and endothelium to UVA. [18-21]

Lipophilic nature of corneal epithelium prevents relatively the diffusion of riboflavin in the stroma and blocks UV rays, and so, removal of the corneal epithelium has been recommended.[22]

Mechanism of corneal stromal cross-linking:
Exposure of riboflavin in the stroma to UVA light causes the production of singlet oxygen, which produces more and more cross-linked bonds between stromal collagen. In the presence of light, riboflavin photosensitizing properties reacts with a range of electron donating substrates through mixed Type I – Type II photochemical mechanisms. Type II photochemical mechanisms predominate at the higher oxygen concentration found in the cornea during the first few seconds of irradiation, resulting in the formation of singlet molecular oxygen. Oxygen is depleted within first few seconds of UVA irradiation and then

Type I photochemical mechanisms rapidly starts. Type I reactions generate triplet riboflavin, which interacts with corneal proteins (as tyrosine and tryptophan) through radical reactions, causing corneal cross-linking. The corneal cross-

linking increases stiffening of human corneal stroma. The CXL is more effective in the anterior 300 microns of the corneal stroma which play a significant role in maintaining the corneal curvature. Collagen cross-linking then results in corneal flattening and reduction of sphero-cylinderical errors. Riboflavin generates active oxygen species singlet oxygen (1O2) and superoxide anion radicals (O2), which lead to enzyme inactivation. 23

It is mandatory to document progression of the condition before CXL which is confirmed if there is an increase in the K max of 1 D, increase of cylinder of 1 D or increase of spherical equivalent of 0.5 D over the period of one year. To reduce the risk of endothelial damage, the preoperative central corneal thickness should be greater than 400 μm, CXL is typically done under topical anaesthesia. 24

Conclusion:

Both groups with conventional and accelerated corneal collagen crosslinking (CXL) showed statistically improvement in BSCVA, which was insignificantly different between both groups over the follow-up period.

Conflict of interest:

None of the authors has any financial disclosure

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