



A Study on Visual Outcome of Patients with Keratoconus after Corneal Collagen Crosslinking

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Abstract

Background and objectives: Cross-linking of the corneal collagen is regarded as a new treatment technique for a non-inflammatory thinning disease of the cornea-known as keratoconus, to strengthen the biomechanical elements of the cornea. Riboflavin (Vit.B2) and UV-A light have been shown to be effective at stopping progression of keratoconus.

Aim: to evaluate the effects of collagen cross-linking in patients with keratoconus.

Methods: A retrospective, non-controlled study was performed on forty-five patients (64 eyes) with keratoconus in whom collagen crosslinking was done between years (2017-2021). It was conducted in Bright Eye, Tooe Maleek, and the Eye Center private hospitals in sulaimaniya city. We measured the distance visual acuity with and without glasses (Snellen acuity chart and decimal notation), the, the spherical equivalent and cylindrical refractive error (autorefractometer), the central corneal thickness and the mean keratometric reading (corneal topography). These were taken before and after crosslinking in a period between 6-12 months, and then t-test was used to compare and analyze the results.

Results: After comparing the pre- and post-crosslinking findings, we found an improvement in the uncorrected VA (by 0.06 ± 0.04) and best corrected VA (by 0.10 ± 0.03). The central corneal thickness was decreased by a mean of ($13 \pm 12 \mu\text{m}$) and the mean keratometric reading decreased by a mean of (0.9D). However, each of the spherical equivalent and cylindrical refractive errors showed no significant difference before and after the procedure (stabilized).

Conclusion: The procedure (collagen crosslinking) was efficacious in stopping progression of the disease.

Key words: Cross-linking, Keratoconus, Pentacam topography

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Introduction

In simplest terms, keratoconus is a condition where the cornea gets thinner over time, that makes the surface curve or steepen more, which leads to myopic irregular astigmatism and decreased visual acuity.¹ The prevalence is estimated to be 37 cases per 100,000 people in the general population.² The course of the disease passes through different stages of severity, and the visual effects or disabilities it produces are different accordingly. In the early stages, patients will have slight blurring or distortion of the vision, mild refractive changes-myopic astigmatism with reduction of best spectacle corrected visual acuity, appearance of scissor and oil droplet reflexes on examination, along with mild topography changes. Moderate cases will experience more pronounced distortion of the vision with inability to achieve 6/6 vision with spectacles, but they may be able to do so with the use of contact lenses, more progression of the refractive changes, more apparent signs and topography findings with significant corneal thinning and severe cases are characterized by severely decreased vision (< 6/7.5 vision even with contact lens correction), marked irregular astigmatism, severe corneal steepening and thinning, appearance of corneal opacities, scarring and even development of corneal hydrops.³ When screening for keratoconus an enquiry should be made about symptoms along with careful slit lamp examination but currently the corneal topography remains the most reliable tool for detecting the condition.⁴ A two-dimensional image of the corneal surface can be obtained by corneal topography giving the surface curvature data, but corneal tomography is regarded as the most sensitive tool for diagnosing and staging, which gives anterior corneal surface curvature data, elevation data of both the anterior and posterior surfaces from a reference sphere, along with pachymetry or thickness distribution data.⁵ Corneal collagen

crosslinking (CXL) is a newly introduced surgical treatment option that has been successfully used for the management of corneal ectatic diseases, including keratoconus and post-refractive surgery corneal ectasia.⁶ Crosslinking of the corneal collagen is accomplished by using a natural photosensitizer (vitamin B2) or riboflavin and ultraviolet-A light to make crosslinks between the corneal collagen fibrils. This makes the biomechanical elements of the cornea stronger without changing the cornea's refractive index or clarity. It was said that the most important use was to stop the corneal stroma from protruding more and the corneal curvature from getting steeper, which would lead to patients having worse vision because of irregular myopic astigmatism. The procedure has been used primarily in the treatment of patients with keratoconus and ectasia following corneal refractive surgery.⁷ When used in treating keratoconus patients the main aim was to stop progression, and help corneal flattening but sometimes it was seen to be associated with improvement in the refractive status of the eye as well.⁸ Complications that can happen during or even after the procedure are creating corneal haze, which can make epithelial healing take longer, making the cornea less sensitive, causing infection, long-term swelling, and harming the endothelial cells. The crosslinking procedure is contraindicated if: (the cornea is less than 400µm thick; previous corneal herpes virus infection; significant corneal opacity or scarring; history of previous delayed or abnormal epithelial healing; diseases of autoimmune origin; and severe dry eyes).⁷ The aim of this study is to evaluate the effects of corneal collagen crosslinking in patients with keratoconus.

Patients and methods:

A retrospective, non-controlled study was performed on 45 patients (64 eyes) with keratoconus of ages between 15 and 33 years (mean age 21.34 years), (21 males and 24



females) for whom collagen crosslinking was done in the years 2017–2021. The data was collected in Bright Eye, Tooe Maleek, and The Eye Center private hospitals in sulaimaniya city. The parameters taken were uncorrected visual acuity, best corrected visual acuity (Snellen chart-decimal notation), spherical equivalent, and cylindric refractive error (measured by an autorefractometer). Then, topography findings (Pentacam eye scanner)-central corneal thickness and the mean keratometric reading were taken before and after the procedure in a period between 6-12 months and compared by t-test. The surgical technique involves administering riboflavin to the corneal tissue either on intact

epithelium or by the epithelium-off technique (after removal of the central 8–9 mm of the epithelium). The riboflavin solution (0.1%) should be given every 2–5 minutes for a total of 30 minutes until the appearance of a yellow flare in the anterior chamber to ensure complete saturation of the corneal stroma. Then 3 mw/cm² of surface irradiance of UV-A light is applied for 30 minutes with the use of a UV-A light meter for precise measurement of the above-stated level of energy. Following the procedure, a bandage contact lens is applied until the epithelium becomes healed, and postoperatively, topical corticosteroids and antibiotics are prescribed.⁶, Figure (1).

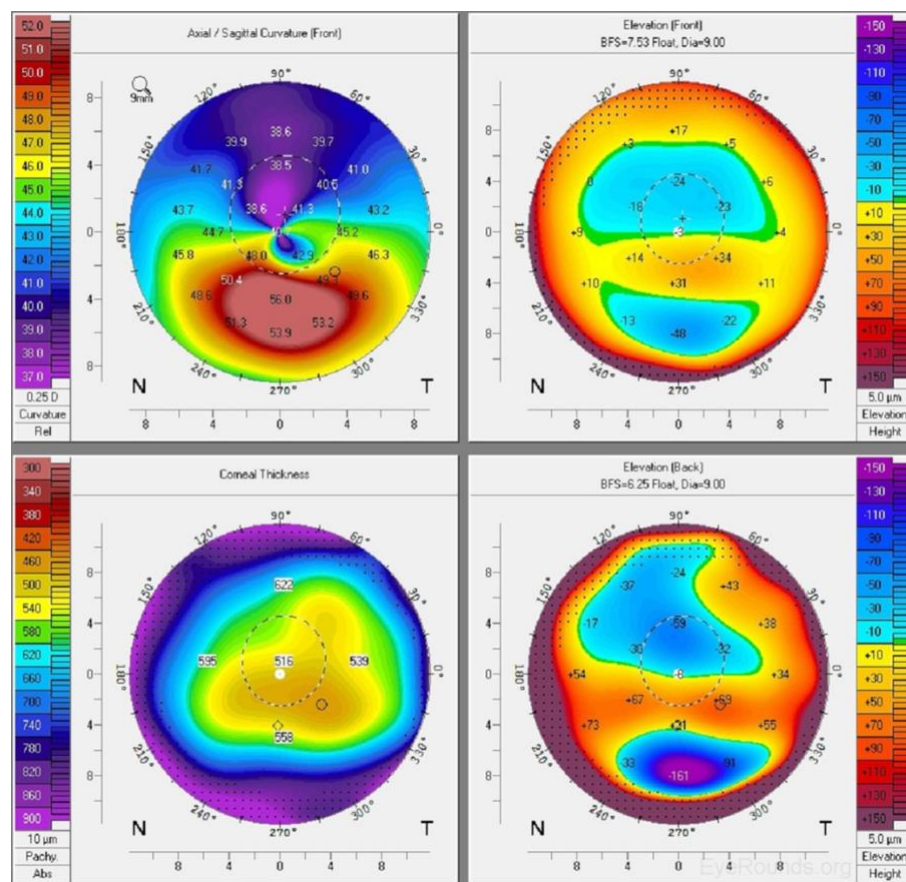


Figure (1): The Pentacam corneal topography printout showing the main four maps, the surgeon should study these maps for screening and diagnosing keratoconus. The maps are: sagittal curvature-upper left, showing inferior steepening, front elevation-upper right, back elevation map-lower right, and corneal thickness map-lower left.



Results

Among 45 patients (53%) were females and (47%) were males. Their age ranged from (15-33) years, with a mean age of 21.34 years, Figure (2) and (3).

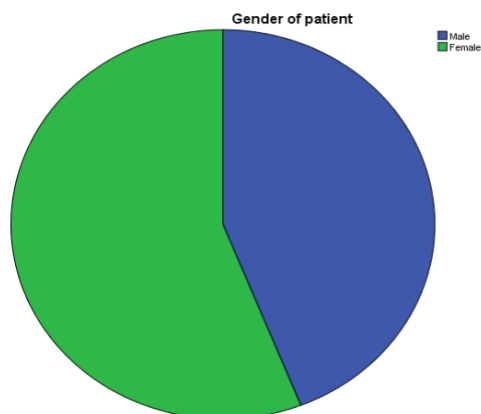


Figure (2): shows percentage of males to females.

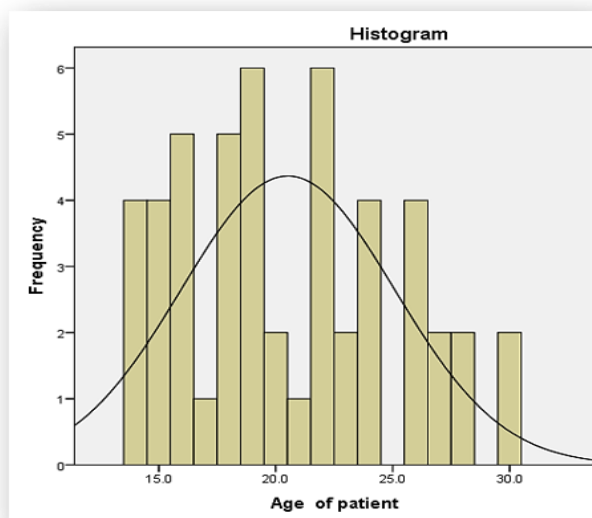


Figure (3): The range and mean age of patients.

After treatment with collagen crosslinking, patients showed an improvement in uncorrected visual acuity-UNCDVA of (0.06 ± 0.04), with an improvement in best corrected visual acuity-BSCVA of (0.10 ± 0.03), which were significant. However, we couldn't find a noticeable

difference between the pre- and post-crosslinking states in each of the spherical equivalent-SEQ and cylindrical refractive errors-CYL (stabilized). Regarding corneal topography findings, there was a mean decrease in central corneal thickness-CCT of $13 \pm 12 \mu\text{m}$, which was not significant statistically, and a decrease in the mean keratometric reading-K of 0.9 D, which was again statistically significant, Table(1).

Table (1): The significance of results between pre and post cross-linking states

	Studied time (mean $\pm$ S. D)		p values
	Preoperative	Postoperative	
UNCDVA	0.2744 $\pm$ 0.169	0.3378 $\pm$ 0.22	<0.01
BSCDVA	0.4436 $\pm$.21761	0.5386 $\pm$.25057	<0.01
SEQ	- 4.9750 $\pm$ 3.27921	- 4.8450 $\pm$ 3.73343	<0.50
CYL	- 3.8650 $\pm$ 1.94976	- 3.7900 $\pm$ 2.18550	<0.06
CCT	470.80 $\pm$ 23.656	457.86 $\pm$ 27.353	<0.06
Mean K	48.266 $\pm$ 3.6455	47.353 $\pm$ 3.7697	<0.01

Discussion

In comparing the results of our study with the previously done studies, we have found that the improvement seen with the visual acuity of our patients, both uncorrected (by a mean of 0.06 ± 0.04) and best corrected visual acuity (by a mean of 0.10 ± 0.03), is close to the results obtained by Uysal et al's retrospective study, which enrolled 111 patients with keratoconus.⁹ The patients were followed 12 months after crosslinking, in which the results confirmed a significant increase in uncorrected and best spectacle-corrected visual acuity when comparing pre and post cross-linking states, also In another retrospective study done by Bedawi et al, which included 136 patients, the period of follow-up was 12 months after the procedure, also showed significant improvement in best corrected visual acuity and the mean Kmax.¹⁰ The study done by Lamy et al, which enrolled (34 patients) also showed a significant improvement in visual acuity of the patients.¹¹ The stability achieved for



spherical equivalent and the cylindrical refractive error is comparable to a study done by Hashemi and his colleagues, which was performed on 32 patients with the disease and also showed stability in the aforementioned parameters.¹² also other studies confirmed stability and even reduction in spherical equivalent like the study done by Iqbal and colleagues which enrolled forty-nine eyes of 28 keratoconic patients in which the spherical equivalent was significantly reduced compared to preoperative refraction together with a parallel reduction in all keratometric readings.¹³ The stabilization in refraction and even reduction in spherical equivalent were also noted in the study done by drekhshan et al, which included 31 patients in a prospective study and the patients were followed 6 months after crosslinking. Postoperatively, the Spherical equivalent refraction was significantly decreased compared to preoperative state, together with a significant improvement in each of uncorrected and best corrected visual acuity and also the mean K values.¹⁴ Regarding corneal topography results, which showed a decrease in mean central corneal thickness of 13 μ m, is also close to the results of a study done by Sedaghat which included 97 eyes and, after the cross-linking procedure, showed a mean decrease in corneal thickness at the apex of 15 μ m.¹⁵ The keratometric-K reading (corneal curvature) is one of the most important parameters to compare in this study and decreased by mean of 0.9 D, is nearly similar to results obtained in the study done by Zarei, which enrolled ninety-two eyes of 53 subjects in a retrospective, nonrandomized, clinical study.¹⁶ Also the reduction in keratometric reading and corneal steepening found in our study can be compared with what is found by other researchers such as the Aixinjueluo et al's prospective study in which a significant decrease in average keratometry readings and an increased corrected visual acuity were

noticed.¹⁷ However different results were observed in grewal et al's prospective study which enrolled 102 patients with no significant change in the keratometric reading, corneal curvature and even visual acuity of patients when comparing the pre and post cross-linking results.¹⁸ Lastly, we recommend proper and careful examination of every patient with irregular myopic astigmatism to aid in early diagnosis and treatment of patients with keratoconus by less invasive treatment options and omitting the need to treat them with more invasive and less safe technique (Corneal transplantation), and the scope of future studies will be enlarged to know the longer term effects of the procedure in terms of safety and efficacy.

Conclusion

The crosslinking procedure was efficacious in preventing further progression in patients with keratoconus, as it was shown by stabilization of the spherical equivalent and cylindric refractive error in most cases and also by improvement in the un-corrected and best-corrected VA and a decrease in the mean keratometric reading.

Conflict of interest

The authors report no Conflicts of interest.

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