Evaluation of Keratoconus Patients Refractive Status Before and after Corneal Collagen Cross-linking

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ABSTRACT

Background: Corneal Collagen Cross Linking (CXL) incorporated with riboflavin solution activated by UV (Ultraviolet) irradiation is a modern promising treatment protocol for keratoconus. Evaluation of the clinical effect of CXL treatment on keratoconus patients was the aim of this study.

Methods: This Quasi Experimental (before-and-after) study was comprised with 50 patients, having progressive keratoconus (progression was documented by Corneal Topography), reported to Cornea Clinic, CMH Dhaka, from February 2022 to January 2023. Before and after the CXL procedure; un-corrected and best-corrected visual acuity of study population was documented using Snellen visual acuity chart. Auto-refractometry readings were also noted.

Results: Among the 50 study subjects; 26 (52%) were men and 24 (48%) were female, age was 24.14 ± 5.07 (mean+SD) years and age range was 18-35 years. Mean preoperative spherical power was −1.84 ± 0.82 Diopter (D) and mean cylindrical power was −3.66 ± 0.97 D. Postoperatively, mean spherical power was found −1.15 ± 0.55 D and mean cylindrical power was −2.87 ± 0.99 D. After CXL treatment; significant vision improvement found in 15 (30%) patients (p<0.05).

Conclusion: Despite strengthening the corneal stromal collagen bond and halting the keratoconus progression, CXL treatment stabilize the refractive status of keratoconus patient and also in some extent, it improves vision.

Keywords: Progressive Keratoconus, Corneal Collagen Cross-Linking, Refractive Status

INTRODUCTION

Pellucid marginal degeneration, post-refractory or post-traumatic corneal alterations, and keratoconus Astigmatism, central steepening, and progressive central or paracentral corneal thinning are indicative of type ectasias. These conditions can seriously impair a person's vision and lower their quality of life. Prescription glasses and contact lenses (including hard contact lenses, such as scleral or hybrid contact lenses) are the mainstays of non-surgical treatment for corneal ectasias. Penetrating keratoplasty (PKP), deep anterior Lamellar Keratoplasty (DALK), and intra-corneal ring segments (ICRS) are among the surgical techniques. Currently, it has been observed that patients with progressive keratoconus can


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benefit from the use of Corneal Allogenic Intrastromal Ring Segment (CAIRS) implantation and Isolated Bowman Layer Transplantation (IBLT). 1-3 Although these methods are quite successful, they are expensive and require highly qualified surgeons for the best results. However, due to the damaged design of the cornea, individuals undergoing corneal transplantation may require long-term immunosuppressive medicine following the procedure, and they may also be at an elevated lifetime risk of developing globe rupture. 4

A treatment regimen called Corneal Collagen Cross-Linking (CXL) was initially presented in 1997 in Germany to patients with keratoconus by Eberhard Spoerl and colleagues at the Dresden University of Technology. 5 The Dresden Protocol is the name of this procedure, which entails injecting riboflavin solution into the eye and activating the CXL solution by exposing it to ultraviolet-A (UV-A) light for around half an hour. 6-7 In the cornea's stromal layer, riboflavin forms new linkages between neighboring collagen strands to help the cornea restore and maintain part of its mechanical strength. In order to improve the penetration of riboflavin solution into the corneal stroma, 7.5–8 mm of the central corneal epithelium are often removed. 8 Inducing a larger diameter of collagen fiber and boosting corneal anti-collagenase activity, CXL with riboflavin promotes resistance to the digestion of pepsin. 9 Research using confocal microscopy on the cornea has also revealed keratocyte apoptosis in the anterior and intermediate stroma, which is followed by a slow repopulation of keratocytes. 10

CXL treatment modality is creating a remarkable milestone in the field of keratoconus management. As it helps to strengthen inter-collagen & intra-collagen bond of the corneal stroma, which prevents further thinning progression of the cornea and helps to restore structural integrity and makes it possible for the patients to wear Rigid Gas Permeable Contact Lenses (RGPCLs) again. 11

Kohlhaas and colleagues demonstrated a considerable increase in porcine corneal stiffness in rabbit corneas following CXL in an animal research conducted in 2006. 8 Research patients with keratoconus have shown good results both in the short and long term, with significant topographic and refractive improvements after CXL. 12

CXL protocol for keratoconus patient introduced as a latest treatment modality in CMH Dhaka from October 2021. There is no study regarding its unknown effect to the patients receiving the treatment in Bangladesh Armed Forces Arena till date.

In this study, we attempted to evaluate the beneficial outcomes of CXL with riboflavin in keratoconus patients and these results will help Ophthalmologists for making early decision whether to providing CXL to keratoconus patients or not.

MATERIALS AND METHODS

In this Quasi experimental (before-and-after) study, 50 patients with progressive keratoconus reported to Cornea clinic, CMH Dhaka, from February 2022 to January 2023 were taken for the CXL procedure. Patients diagnosed as a case of progressive keratoconus, age between 18-35 years, both male & female, BCVA ranges 6/12 to 6/60 pre-operatively, thickness of cornea ≥400 µm at the thinnest location and willing to give consent for the procedure were included in the study. Single surgeon performed the CXL procedures in all patients.

Persons having pregnancy, recurrent corneal infections, severe dry eye disorder, history of
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After topical anesthesia instillation into the eye (tetracaine 0.5%) sterile draping applied, then 7.50 mm Trephine was set over the Cornea and 20% Alcohol instilled inside the Trephine hole onto the Epithelium of the Cornea for only 10 seconds (that helps to separate the Epithelium from underlying Bowman’s membrane), then inside Trephine hole Alcohol was soaked away by the help of dry swab stick and vigorous wash with Ringer’s Lactate solution done, after that separated central 7.50 mm corneal epithelium from basement membrane was easily removed with a Crescent Knife. Then Riboflavin 0.1% (PESCHKE D, Isotonic with Dextran for Epi-off procedure) solution was instilled in the eye on an interval of every three minutes for 30 minutes. After that, examination by operating microscope (Oculus) was performed to ensure the proper penetration of riboflavin into the corneal stroma. After this procedure, UV-A irradiation by PXL PLATINUM 330 Corneal Cross Linking system PESCHKE TRADE was applied to the cornea with a medium-sized UV beam aperture at a wavelength of 370 nm, the device was adjusted to operate safely at a distance of 5 cm from the corneal surface. In addition to the 30-minute radiation treatment, a 0.1% riboflavin solution was infused every three minutes while UV-A was being applied.
After CXL protocol, every patient received Bandage Contact Lens (BCL) for 7 days, topical Moxifloxacin 0.5% for 2 weeks, Flurometholone 0.1% for 4 weeks and Hypromellose 0.5% for 4 weeks.

On first and seventh post-operative day, each patient was examined to observe corneal epithelial healing and abstinence from postoperative infection. After 1, 3 and 6 months of operation, postoperative examinations were carried out with Slit lamp biomicroscope, visual acuity by SVAC and refraction done with the help of auto-refractometry.

The unpaired t-test was used for statistical analyses with SPSS26. Results were presented as mean ± SD or error where applicable. The statistical significance was set at p<0.05.

**RESULTS**

In this study, among the 50 study subjects; 26 (52%) were men and 24 (48%) were female, age was 24.14 ± 5.07 (mean+SD) years and age range was 18-35 years.

After 6 months of CXL treatment in respect of each case, the results of the main variables of our study are stated in Table-I and Table-II.

**DISCUSSION**

Wolf et al. (2008) conducted an uncontrolled, retrospective investigation that is the biggest reported series, with 241 eyes over a six-year study period. In their investigation, astigmatism, BSCVA, and maximum simulated keratometry values (Kmax) at 12 months of each case showed statistically significant
improvements following CXL. After CXL, 54% of eyes showed flattening of the central cornea, with a mean decrease in Kmax of -1.91 D (p<0.01). During the course of the follow-up, the effects of CXL were sustained, and only two patients' eyes showed evidence of disease development (which responded to retreatment next onwards). Numerous other research have reported comparable outcomes.13

In the present study, improvement in visual acuity was noticed and both spherical and cylindrical power improvement was documented. That indicates the CXL treatment is effective for keratoconus patients. Wollensak G et al in 2010 also found the positive effect of CXL in halting the progression of keratoconus.14

In 2010, Caporossi et al. discovered that following CXL treatment, the mean spherical equivalent (SE) decreased by 2.5 D. The results demonstrated a drop in mean keratometry, which was topographically significant.12

In this present study, the mean±SD preoperative Spherical power was –1.84 ± 0.82 D and the mean±SD postoperative Spherical power was –1.15 ± 0.55 D, the mean±SD preoperative Cylindrical power was –3.66 ± 0.97 D and the mean±SD postoperative Cylindrical power was –2.87 ± 0.99 D, both are significant in p value (p<0.05).

Wu D. et al in 2021 showed a statistically significant decrease in cylindrical power (p<0.05) and decline of spherical power (p<0.05) in their study. This also supports the study results.15

CXL has some advantages over other methods of keratoconus treatment.16-17 It can also be done non-invasively.18 CXL procedure is safer than PKP which was the main treatment module in the past (some grafts tend to last around 10-15 years), and than even RGPCLs.19 Risks associated with the PKP include infection, graft rejection, intractable astigmatism, secondary cataract, and secondary glaucoma. Penetrating corneal transplants performed for keratoconus do not differ in survival rate from those performed for all other reasons after 15 years of PKP.

Patients under 35 years old with keratoconus may require one or more corneal grafts throughout the course of their lifespan. Because CXL prevents the loss of the entire thickness of the corneal structural tissue (just the surface epithelial cells are removed, and these cells typically regrow in two days), issues associated to PKP cannot arise.20

CONCLUSION

This study showed a significant improvement and stability in refractive status of keratoconus patients after CXL. These results will encourage the keratoconus patients to take the CXL treatment without any hesitation. There are still few clinical trials on the efficacy and safety of CXL protocol in the population. Further studies on a large scale are necessary.

REFERENCES


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