ORIGINAL ARTICLE

A STUDY ON EFFICACY OF CORNEAL COLLAGEN CROSS LINKING IN PROGRESSIVE KERATOCONUS

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Background: Keratoconus is a progressive, noninflammatory, bilateral ectatic corneal disease, characterized by paraxial stromal thinning and weakening that leads to corneal surface distortion. The objective of this research was to determine the effectiveness and safety of collagen crosslinking in progressive keratoconus, with keratometry (K_{max}) value of 50 diopters or above. It was a retrospective study, conducted at Bodla Eye Care (BEC) and Multan Medical and Dental College, Multan (MMDC) from May 2018 to November 2019. **Methods:** In this research 52 eyes were studied. The best-corrected visual acuity, uncorrected visual acuity, maximum keratometry, mean keratometry value, and thinnest corneal thickness before surgery and 12 months after Cross-linking were observed. A Galeili G6 by Zeimer ophthalmic system was used to measure the clinical parameters. Dresden protocol was followed in this study. A written ethical approval was obtained and research was conducted under the light of declaration of Helsinki. **Results:** The average logarithm of the minimum angle of resolution (logMAR) of the uncorrected visual acuity decreased from 0.66±0.41 D to 0.49±0.40 D (p=0.012), while the mean thinnest point thickness of the cornea decreased from 435.31 37.91 μm to 419.41±70.12 μm (p=0.004) after 12 months. The decreases in the mean logMAR of the BCVA, K_{max} and K_{mean} values were not analytically important (p>0.05) at the 12-month follow-up 94.2% positive results were obtained. **Conclusion:** Collagen cross-linking treatment was safe and maintained both the visual acuity and tomographic parameters at the one-year follow-up in eyes.

Keywords: Keratoconus; Keratometry; Collagen cross-linking

Citation: Bodla AA, Moazzam A, Kazmi M, Aman MM, Bodla MA. A Study on Efficacy of corneal collagen cross linking in progressive keratoconus. J Ayub Med Coll Abbottabad 2021;33(2):175–8.

INTRODUCTION

Keratoconus is a noninflammatory and progressive disorder of corneal ectasia[1] with nearly equal incidence among males and females[2]. Keratoconus affects all races but its incidence and prevalence are comparatively higher in Asians.[3–6]. Moreover, clinical severity is inversely proportional to the age of onset of the disease.[7]

Classic cellular-pathologic features include deposition of iron in the epithelial basement membrane, thinning of stromal, breaks in Bowman's layer and collagen fragmentation.[8] These changes lead to mark corneal thinning eventually leading to corneal hydrops.

Keratoconus can be treated by correcting the disease based on histopathology. Collagen cross linking induces the cross-linking of collagen in corneal by riboflavin and ultraviolet light.[9] Mentioned treatment has a proven efficacy in improving biomechanical indices as well as keratometry readings, i.e., K values in some patients. This ultimately leads to a cease in disease progression as proposed in various published studies. This procedure is associated with some complications and limitations (patients with advanced keratoconus for instance) despite giving satisfactory results. A few cases require repeating the procedure. Thus, this study focused in assessing the effectiveness and protection of Collagen cross-linking in keratoconus effected candidates, having K_{max} value of >50D.

MATERIAL AND METHODS

It is a retrospective study of 52 eyes from 41 patients, who underwent corneal collagen cross-linking at BEC and MMDC, Multan from May 2018 till November 2019 and were followed up for a year. Procedure was explained and registered consent was obtained from the patients.

The research included candidates diagnosed with definitive keratoconus aged between 15 and 29 years. Diagnosis was made using Slit lamp examination showing any one of the following signs including stromal thinning, Vogt striae, Fleischer ring or any other were included. Patients with any systemic disease, previous ocular surgeries, neurological or retinal disease, pregnant or lactating ladies, and those with advanced keratoconus and corneal scarring were abandoned.

Pre-surgical data was collected including uncorrected and best corrected visual acuity, corneal findings on slit lamp examinations and corneal tomography using Galilei G6.

Dresden protocol was ensued. However, in patients with corneal thickness <400 µm despite epithelial removal, hypotonic riboflavin was used and applied topically every 3 min for 30 minutes. The patients were given 1% Alkane eye drops as topical anaesthetic, and the corneal epithelium from 8 mm central portion was debrided using a blunt spatula. Iso-osmolar riboflavin solution with 0.1% riboflavin in 20% dextran was used for most eyes.

The eyes were exposed at a wavelength of 370 nm with a surface radiation of 3.0 mW/cm^2 to UVA irradiation (CSO-Vega X-linker; Scandicci, Florence, Italy) for half an hour (surface dose limited at 5.4 J/cm^2). The riboflavin solution was applied every 3 min during the complete radio therapy, to ensure that the stromal surface was kept moist. A soft patched contact lens was used until re-epithelialization was complete. After surgery, the patients administered topical 0.5% Tobradex eye drops 4 times a day for 7 days. Systane by Alcon Inc eye drops were given to keep the ocular surface moist. Patients were re-examined on 7th day, 1, 3, 6, 9 and 12 months and imaging were done using Galilei G6 to complete the data. A written ethical approval was obtained and research was conducted under the light of declaration of Helsinki.

RESULTS

A total of 41 patients with 52 affected eyes were studied; among which 23 were women and 18 were men, the average age of the patients was 22±3 years (range of 15–29 years). The cross-linking was performed bilaterally in 15 patients and unilaterally in 22 patients. The left eye was studied in 51.9% of the cases (n = 27), and the right eye was studied in 42.3% of the cases (n = 22). Progression was ceased in 49 eyes (94.2%) while it failed in 3 eyes (5.8%). Variations in the values that were collected during the follow-up period are mentioned in the table-1 below.

Table-1: Mean and standard deviation of clinical and tomographic ophthalmologic measurements compared before and 6 and 12 months after surgery

Variable	Before surgery, (mean±SD)	6 months after surgery, (mean±SD)	*p**	12 months after surgery, (mean±SD)	*p**
UCVA (logMAR)	0.66±0.41	0.41±0.36	0.006	0.49±0.40	0.012
BCVA (logMAR)	0.58±0.39	0.49±0.23	0.061	0.43±0.31	0.079
K_{max} (D)	69.41±4.05	64.29±4.18	0.101	63.41±4.41	0.117
K_{mean} (D)	55.13±3.49	54.41±3.21	0.269	55.29±3.09	0.598
Thinness point thickness (µm)	435.31±37.91	422.19±44.05	0.045	419.41±70.12	0.004

UCVA (uncorrected visual acuity), BCVA (best corrected visual acuity), K_{max} (maximum keratometry), K_{mean} (mean keratometry)

DISCUSSION

In this study, the results of crosslinking on 41 patients with progressive keratoconus in corneas with a K_{max} ≥50 D were established. The 52 eyes that had been studied revealed a significant increase in uncorrected visual acuity and a decrease in total peripheral thickness although the improvement in best corrected visual acuity and the decreases in K_{max}, K_{mean}, and corneal astigmatism were not statistically significant at the 1-year follow-up. In the present study, the research team ophthalmologist (Bodla.A.A) confirmed the diagnosis of progressive keratoconus, and patients with Grades I–IV according to the Amsler–Krumeich classification underwent collagen crosslinking. The results confirmed the viability and safety of this procedure on different stages of keratoconus.

Keratoconus is a developed disease of cornea that cannot be rectified by using conventional methods.[10] Advent of collagen cross linking was a remarkable event in the treatment of keratoconus. However, despite performing this procedure, there remain a few areas that required to be examined further.[11] Several clinical investigations have been carried out across the world to determine the effectiveness of Collagen cross linking, first being published in 2003.[12] Respective studies have been performed regarding productiveness of cross-linking on halting the development of keratoconus. The preceding outcomes of this analysis depicted that the patients with uncorrected visual acuity and best corrected visual acuity can be improved by undergoing crosslinking. Moreover, in the previous studies authors specified that in order to reduce higher order aberrations in eyes, suffering from keratoconus and to improve the keratometric values, cross-linking is useful.[13] Moreover, the long-term consequences of preceding cross studies, assured that cross-linking is useful in inducing a durable stability for keratoconus.[14,15] K_{max} and K_{min} reduced prominently and BCVA showed a notable advancement, thus, showed that cross-linking can achieve the stabilization of keratoconus for a long term.[16] O'Bart concluded this too after follow-up of seven years.[17]

Apart from the efficacy, crosslinking is associated with complications including infections by microorganisms[18–20] and harm the cornea[21,22]. Complications depend on techniques used during the procedure including homogeneous irradiance of the light source (370 nm), the debridement of the epithelium to assist the diffusion of the riboflavin, applied 30 min before UV exposure, and corneal stroma thickness of 400 μm[23,24] along with patient selection. By previous studies, patients >35 and <12 are considered to be high risk for post interventional issues.

Of note with previous studies[25] the treatment has failed in patients with K_{max} >58 seen in cases of advanced keratoconus. While, patients with K_{max} <50 showed better outcomes, thus suggested as a safety margin. The outcomes of our study depicted that there was a notable improvement in the vision by decreasing uncorrected visual acuity up to 0.24D and best corrected visual acuity up to 0.13D. The unaffected astigmatism in our study showed method's efficacy in stabilizing the cone.

In review, there were no major complications and candidates with progressive keratoconus who underwent crosslinking were followed successfully for one year, and the outcome showed the relatively long-term effect of collagen crosslinking on the disease. However, there were a number of constraints to the study, including the limited sample size, lacking control group, and the non-randomized inclusion of patients into the subject.

CONCLUSION

In this study, 41 patients with 52 affected eyes having mean age of 22±3, underwent Cross-linking (Type-Collagen) using the combination of ultraviolet and riboflavin light and had a follow-up of 12 months, presented with the 94.2% success rate in terms of stability in keratoconus indices on corneal topography. Authors believe that further studies with larger sample sizes and prolonged follow up are required to evaluate the safety of mentioned procedure.

Acknowledgement: None to declare.
Disclaimer: None to declare.
Conflict of interest: None to declare.
Funding disclosure: None to declare.

AUTHORS' CONTRIBUTION

MAB: Formulated and study design. AAB, AM, MK, MMA: Data collection, statistical analysis and write-up. AAB: Review, final approval of manuscript and responsible for integrity of research.

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Submitted: March 23, 2020	*Revised: July 14, 2020*	*Accepted: August 12, 2020*

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