Keratometric Changes after Corneal Collagen Cross linking for Keratoconus

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ABSTRACT

Background: Keratoconus is an asymmetric, non-inflammatory, and progressive ectasia of the cornea that is characterized by the thinning, steepening, and central scarring of the cornea. Corneal collagen cross linking with riboflavin and ultraviolet light is an accepted procedure to stabilize keratoconus. This study is aimed at finding out keratometric changes after corneal collagen cross linking. Methods: A total of 30 patients were enrolled, 15 males and 15 females. They were subjected to corneal topography, refraction, slit lamp examination, preoperatively and postoperatively at 1 month 3rd month and 6th month after corneal collagen cross linking. Results: Flattening of Keratometry values were noticed in 12 eyes (40%). The mean pre-operative K was 50.32 D. The mean post-operative K was 49.61 D. In 5 eyes (16.66%) the corneal curvature was unchanged and stable. Conclusion: There is significant decrease in mean keratometric values and flattening of cornea after corneal collagen cross linking.

Key words: Corneal collagen cross linking, Keratoconus, Keratometry.

INTRODUCTION

The cornea is the front transparent window of the eye and forms the outermost one-sixth of the eyeball. It is lamellar in nature (like plywood) and is made up of 5 layers, each of which has a definite function. In order to be effective it must remain transparent. Due to absence of blood vessels in the cornea, much of its oxygen requirement comes from atmospheric oxygen dissolved in the tear film. When the eyelids are closed, oxygen enters the cornea from the superficial conjunctival vessels. Nutrients needed for the cornea pass into it by diffusion. Hence, carbon dioxide and waste products are also removed across the tear film. Hence, any deficiency of the tear film will directly or indirectly affect the cornea.[1]

Keratoconus is an asymmetric, non-inflammatory, and progressive ectasia of the cornea that is characterized by the thinning, steepening, and central scarring of the cornea. It is classified as degeneration rather than a disease. As the corneal distortion and irregular astigmatism intensify, affected patients experience a decrease in best-corrected spectacle acuity.[2] Clinical data and diagnostic examinations reveal several characteristic signs and symptoms that become more prevalent as the condition progresses [Figure 1,2].

These include worsening of best-corrected spectacle acuity, fluctuating visual acuity, increased regular and irregular corneal astigmatism, an inferiorly thinned and displaced ectasia of the cornea, deposition of hemosiderin in a ring or ring segment in the corneal epithelium surrounding the base of the cone(Fleischer’s ring or arc), and Vogt’s striae in the posterior corneal stroma. Corneal scarring occurs in more advanced cases and further reduces visual acuity. Scarring is usually at or surrounding the corneal apex. The collaborative Longitudinal Evaluation of Keratoconus (CLEK) Observational study was the largest multicentre, prospective, observational study designed to describe the course of keratoconus and the associations among its visual and physiological manifestations. The CLEK study characterized the course of keratoconus and identified factors related to vision, progression, and corneal scarring in keratoconus.[3-5]

Etiology of this condition is still not clear. It is possible that this condition could be secondary to increased breakdown of the stromal collagen lamellae by the lysosomal enzymes released by the basal epithelium in these eyes.[6]

Etiopathogenesis is still unclear. Essential pathological changes are thinning & ectasia which
occur as a result of defective synthesis of mucopolysaccharide & collagen tissue. Patients present with a defective vision due to progressive myopia & irregular astigmatism, which does not improve fully despite full correction with glasses.[7] Window reflex, Placido disc examination shows irregularity of the circles, Keratometry depicts extreme malalignment of mires. Photokeratoscopy reveal distortion of circles, Slit lamp examination may show thinning &ectasia of central stroma opacity at the apex & Fleischer’s ring at the base of cone, folds in Descemet’s & Bowman’s membrane very fine, vertical, deep stromal striae(Vogt lines) which disappear with external pressure on the are peculiar feature. On retinoscopy a yawning reflex (scissor reflex) & high oblique or irregular astigmatism is obtained. On distant direct ophthalmoscopy an annular dark shadow (due to total internal reflection of light) is seen which separates the central & peripheral areas of cornea(oil droplet reflex), Munson’s sign, i.e. localized bulging of lower lid when patient looks down is positive in late stage.[8,9]

**Figure 2**: Fleischer ring indicating base of cone

Morphologically Keratoconus could be classified depending upon the size & shape of cone. Nipple cone has a small size (<5mm) & steep curvature, Oval cone is larger(5-6mm) & ellipsoid in shape, Globus cone is very large (>6mm) & globe like.[10] KC may be complicated by development of acute hydrops due to rupture of Descemet’s membrane. The condition is characterized by sudden development of corneal oedema associated with marked defective vision, pain, photophobia & lacrimation.[11]

Spectacle correction may improve vision in very early cases. Contact lenses (RGP) usually improve vision in early cases. Intacs, the intracorneal ring segments, are reported to be useful in early cases. Corneal collagen cross linking with riboflavin(C3R) may slow the progression of disease. Keratoplasty may be required in later stages. Deep anterior lamellar keratoplasty (DALK) or penetrating keratoplasty (PK) may be perform.[12] The anterior surface of the cornea act as a convex mirror, so that the size of the image produced varies with its curvature. Greater the corneal curvature lesser is the image size. Corneal topography is also known as video-keratography. It is the process for mapping the surface curvature of cornea. Provides a detailed description of the shape & power of cornea. Gives quantitative measurement of the whole of cornea. CTS (corneal topography systems) consist of a Projection device, Video camera, Computer. Multiple light concentric rings are projected on the cornea and the reflected image is captured on CCD (charge-coupled devices) camera. Computer software analyses the thousands of data points captured and displays the results in the form of topography map. Interpretation of topography maps is based on warm colours Red, orange, yellow indicates steeper portions of cornea. Green colour indicates intermediate and Cool colors- light blue, dark blue indicates flatter portions of cornea. Analyses of the cornea are done by Scales and Maps [Figure 3]. Two scales are Absolute scale and Normalized scale. Maps are Axial Map, Curvature Map, Elevation Map and Wave front Map. Clinical application of topography are Detection of corneal pathologic conditions (keratoconus, PMD), Detecting & evaluating the severity of keratoconus, Screening tool before refractive surgery, Evaluation of irregular astigmatism especially after PK, Evaluation of the effects of corneal refractive surgery, Helps in planning of suture removal &post-operative fitting of contact lens.[13-15]

**Figure 3**: Keratometry map showing Keratocons

Corneal topographers allow both qualitative and quantitative descriptions of the corneal surfaces of keratoconic patients that are of clinical importance. The practitioner can locate the positions of the apex and conical area relative to the visual axis; identify the expanse of the conical area. The degree of tonicity and distortion can be seen. The dioptic difference between the steepness of the apical are and the flatter peripheral cornea is evident. The quickness of the curvature change from the apical area to the base of the cone in different radial directions (the eccentricity in various meridians)
can be estimated. Thus, corneal topography maps help explain the severity and types of visual symptoms encountered by the patient.[16] They are helpful during the prescribing of optical corrections and especially for the fitting of rigid contact lenses. In early and mild cases of keratoconus, the objective and subjective refractions are not significantly different from those performed on normal patients. Refraction of the moderate or advanced keratoconus patient is usually more difficult. Retinoscopy may give an adequate beginning estimate of the refractive error, although the retinoscopic image is distorted. Indeed, one of the early signs of keratoconus is scissors motion of the retinoscopic reflex.[8] The retinoscopic endpoint will not as accurately determine in the keratoconus eye, and the degree of certainty surrounding the endpoints will degrade with the progression of the condition. The refraction of a moderate or, especially, an advanced keratoconus patient has a similarity to that of a low-vision patient. This is because the best corrected visual acuity through a spectacle lens is low. Retinoscopy will reveal much about the optics of the cornea. One method of the more accurately and reliably ascertaining the refractive correction of the keratoconus patient is to perform the objective and subjective refractions over rigid contact lenses. Knowing the approximate refractive correction by having accomplished the refraction using lenses with regular optical powers and also knowing the K readings or corneal topography of the eyes, the practitioner should place rigid contact lenses of roughly the appropriate power and back surface geometry on the eye for diagnostic purposes.[17,19] Penetrating keratoplasty is performed for optical, tectonic, therapeutic and cosmetic indications. Keratoplasty for keratoconus is highly successful, but there is a long recovery period and a risk of substantial ocular complications.[20]

Photo-polymerization using UV-light was found to be the most promising technique to achieve cross-links in connective tissue. Photo-polymerization is activated by means of a non-toxic and soluble photo mediator and a wavelength which is absorbed strongly enough to protect deeper layers of the eye (riboflavin-UVA technique) [Figure 4,5]. UV-A radiation with concomitant administration of riboflavin solution leads to physical cross linking of the corneal collagen fibers. Thus progressive corneal thinning is slowed down or even stopped and the Bio-mechanical strength of corneal tissue is improved.[21,24]

The aim of the study is to compare the changes in the corneal curvature before and after C3R surgery in patients with progressive keratoconus.

**MATERIALS AND METHODS**

This prospective study was carried out in the dept. of Ophthalmology of MES Medical College in association with Al Salama group of Eye Hospitals in Kerala. All patients posted for C3R from November 2014 to April 2015, were included in the study. We included healthy male and female ranging between 15 and 35 years of age. A total of 30 patients were enrolled, 15 males and 15 females. Patients with CCT < 400, keratoconus with central scarring were excluded. All patients, undergone CXL treatment underwent a complete eye examination including assessment of Corneal Topography, pre operatively, and then post operatively at 1 month, 3rd month and 6th month. The OPTIKON KERATRON SCOUT topographer (OPTIKON 2000 S.p.A), is a unit that records corneal curvature, magnitude of cone location,
percentage of probability of keratoconus and higher order aberration of the anterior cornea. Subjective refraction was measured in the clinical by the universal accepted Snellen’s chart with standard chart and room illumination. All data was collected in an excel data base (MS Office 2007, Microsoft, Red mond, WA) and analyzed with SPSS for windows. Paired sample t test with 2 tail distribution was analyzed Keratometric parameter before & after C3R. P value of less than 0.001 is considered statistically significant.

**RESULTS**

The mean age of the study group was 29 yrs. Range 15 to 35 years. Out of the 30 patients 15 were males and 15 females. The uncorrected visual acuity were improved in 15 eyes (50%). The uncorrected visual acuity were stable in 6 eyes (20%). The best corrected visual acuity were improved in 12 eyes (40%). Best corrected visual acuity werestable in 9 eyes (30%). Flattening of Keratometry values were noticed in 12 eyes (40%). The mean pre-operative K was 50.32 D. The mean post-operative K was 49.61 D. In 5 eyes (16.66%) the corneal curvature was unchanged and stable. 40% flat and 43.33% of stable keratometric values during 3 months follow up post CXL in progressive keratoconus which was found statistically significant. P < 0.001. Even though there is slight increase in pre & post-operative best corrected visual acuity P value is greater than 0.001 is considered statistically not significant (0.95) [Table 1, Figure 6,7,8,9,10].

<table>
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<tr>
<th>S NO</th>
<th>Keratometric reading</th>
<th>Pre</th>
<th>Post</th>
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<tr>
<td>1</td>
<td>Mean</td>
<td>50.32</td>
<td>49.61</td>
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<tr>
<td>2</td>
<td>SD</td>
<td>7.65</td>
<td>6.8</td>
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<tr>
<td>3</td>
<td>Median</td>
<td>47.625</td>
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<tr>
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<td>68.875</td>
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<td>5</td>
<td>Mini</td>
<td>41.5</td>
<td>41.25</td>
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<tr>
<td>6</td>
<td>Range</td>
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<td>27.625</td>
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<tr>
<td>7</td>
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**DISCUSSION**

The study was conducted to compare the prospective analysis of corneal curvature who underwent C3R surgery. Mean of the pre-operative keratometric reading and post-operative keratometric reading was calculated and compared by using paired T test. The goal for the corneal collagen cross-linking treatment is to delay or halt the progression of keratoconus and to defer the need for a corneal transplant. The result of this study was encouraging as far as safety and effectiveness are concerned. No side effects were noted except for the subjective complaint of patients, namely, visual symptoms like fluctuating vision and double images.

In this study 30 eyes of 27 patients with progressive keratoconus were included in this prospective study. The maximum follow-up was 3 months. Ocular examinations including refraction, best corrected visual acuity (BCVA), corneal topography, were recorded at each visit. Maximum numbers of keratoconus patients were reported from cornea and refractive surgery 27. Six month study reveals that male: female ratio is seen significantly equal.
Six month study reveals that Right: Left ratio is seen significantly equal. The mean age of study was 27. Maximum numbers of keratoconus were reported from the age group of 25-29 yrs, followed by 20-24 yrs, 15-19 yrs and 30-35 yrs. The arithmetic mean values for patients before and after CXL treatment of keratometric reading 50.32, 49.61. Paired sample t test with 2 tail distribution was analyzed Keratometric parameter before & after C3R. P value of less than 0.05 is considered statistically significant (0.038). And based on pre & post-operative best corrected visual acuity P value is greater than 0.05 is considered statistically not significant (0.95). Because C3R doing for preventing the progression of keratoconus not the visual acuity.

Ocular examinations including refraction, best corrected visual acuity (BCVA), corneal topography, were recorded at each visit. The mean age was 16.9± 6.35 years (range 12-39 years) and the follow-up ranged from 12 to 16 months. Thirty seven eyes with a follow-up of at least 12 months were analyzed. The preoperative apex K value determined with the CLMI was 64.79 ± 7.22 D, the mean maximum keratometry was 53.26 ± 5.93 D (The apex values were determined using the Simulated K values method. Thus the apex is higher than maximum K), the mean astigmatism was 7.24 ± 4.67 D (this obtained from the topography derived K). BCVA was 0.34 ± 0.30 (vision was recorded by Snellen's and converted to decimal format for statistical calculations). Ultrasonic pachymetry (apex as determined by the topography and approximated to the eye) (Palmscan, Micromed Technologies, USA) was done in all eyes preoperatively to assess suitability and was 478 ± 45 µm. An evaluation of 37 eyes in which stable parameters were recorded and the preoperative values on the day of treatment were compared with postoperative values of the 12-month examination showed that BCVA improved at least one line in 54% (20/37) of eyes and remained stable in 28% (10/37) of eyes (P=0.006). Astigmatism decreased by a mean of 1.20 D in 47% (17/37) of eyes (P=0.005) and remained stable (within ± 0.50 D) in 42% (15/37) of eyes. The K value of the apex decreased by a mean of 2.73 D in 66% (24/37) of eyes (P=0.004) and remained stable (within ± 0.50 D) in 42% (15/37) of eyes. The maximum K value decreased by a mean of 2.47 D in 54% (20/37) of eyes (P=0.004) and remained stable (within ± 0.50 D) in 38% (14/37) of eyes. Corneal wave front surface aberrometry according to Keratron Scout software (Optikon, Italy) was also used. The result
show a stabilization and improvement in keratoconus after collagen cross-linking in Indian eyes. This suggests that it is an effective treatment for progressive keratoconus.

Result of this study was also consistent with the study by Raiskup[24], conducted a study on a long-term retrospective study of 480 eyes from 272 patients with progressive keratoconus (of which 241 eyes had a minimum follow-up of 6 months) showed corneal flattening by 2.68 D in the first year, 2.21 D in the second year and 4.84 D in the third year, with BCVA improvement by one or more lines in 53% of 142 eyes in the first year and 57% of 66 eyes in the second year. Two patients had continuous progression of keratoconus and underwent repeat CXL treatment. Two patients with keratoconus progressed despite CXL and were required a repeated applications of UVA/riboflavin. Another prospective, randomized controlled trial in Australia[5] on 66 eyes of 49 patients with documented progression of keratoconus showed flattening of the steepest simulated K value (K_max) by an average of 0.74 D at 3 months, 0.92 D at 6 months and 1.45 D at 1 year, while in the control eyes mean K_max steepened by 0.60 D in 3 months, 0.60 D in 6 months and by 1.28 D after 1 year. A trend towards improved best spectacle-corrected visual acuity was seen in the treated keratoconus eyes compared with that of the controls, which showed a progressive decrease. However, no statistically significant changes were found for spherical equivalents or endothelial cell density. Outcome of this study was also consistent with the other studies[25,26] on intra- and postoperative changes during and after collagen cross-linking therapy. For the protection of the endothelium a minimum of 400 μm corneal thickness is suggested prior to CXL treatment. In cases where corneal thickness is lower, a pretreatment of the cornea with hypotonic solution or trans epithelial CXL is suggested. Our study comprised 2 cases where patients were administered a pretreatment with hypotonic riboflavin solution for an hour, after which corneal thickness reached the safety zone. 41 eyes of 41 keratoconus patients (mean age 27.97±6.97 years, ranging from 18.0 to 44.06 years) were examined in our study. Prior to CXL treatment detailed above, Penta cam HR measurements were conducted and apical, central and the thinnest corneal thickness were recorded in all cases. When preoperative corneal thickness was below 400 μm we conducted a corneal soaking in a bulking hypotonic riboflavin solution for an hour (single use hypotonic eye drops; Medio Cross Medizin Produkte GmbH, Germany).[27] At 15 and 30 minutes of the treatment with isotonic riboflavin solution the cornea was rinsed and further corneal thickness measurements were conducted using the Penta cam HR device. Postoperative examinations were carried out 3 days, 1 week then 1, 3, 6 and 12 months after CXL treatment capturing further Penta cam HR images. Results Compared to preoperative data, corneal thickness decreased by 108.95±48.6 μm at 15 minutes and by 112.35±47.3 μm at 30 minutes intra operatively (p<0.001). The rate of the decrease showed no correlation with the values of the preoperative corneal thickness (r=0.16; p=0.7). 3 days after procedure, no further statistically significant deviations in corneal thickness were found compared to preoperative data (p=0.17). During the follow-up period corneal thickness remained stable and correlated well with the preoperative values.[28]

Through the study it’s found to bean improvement in visual outcome and the corneal stability, visual acuity & K-reading values are stabilized in most of the patients 3 months after CXL. Three-months follow up results after CXL showed that K-reading were statistically flattened or at least remained stable when compared to K-reading values before CXL. And post-operative best corrected visual acuity is statistically not significant, Because C3R doing for preventing the progression of keratoconus not the visual acuity.

CONCLUSION

There is decrease in mean keratometric values and flattening of cornea after corneal collagen cross linking. There is improvement in both uncorrected and best corrected visual acuity. There is reduction and stabilization of astigmatism after corneal collagen cross linking. Even though corneal collagen cross linking is aimed at stabilization and arrest of keratoconus, some amount of regression is demonstrated in our study.

REFERENCES


