Results of corneal collagen cross-linking with riboflavin and ultraviolet-A light for patients with keratoconus in Ramadi City

*Thakir Mohammed Mohsin, **Zeina Mohammed Hassan.
College of Medicine, University of Anbar, Anbar, Iraq

Abstract
To study the effectiveness of corneal collagen cross linking with riboflavin and ultraviolet-A light for keratoconus in Iraqi patients. Fifty four eyes of 27 patients with progressive keratoconus were studied in this prospective study. All eyes included in this study completed a follow up period of 6 months. Preoperative assessment of uncorrected visual acuity, best corrected visual acuity (BCVA), corneal topography using the pentacam, and Pachymetry were done and these tests were repeated at each postoperative visit. 9 male and 18 female patients were studied. The mean age was 24.9 ±5.35 (range 9-37 years) and the mean follow-up was 7.3 months. The preoperative values were compared with postoperative values. The BCVA improved at least one line in 55.5% (30 eyes) of eyes. 44.5% (24 eyes) showed stable BCVA (P< 0.001). The steepest corneal curvature was decreased by a mean of 1.74 Diopters ± 1.18 (D) in the total population studied. It was decreased by a mean of 2.04 Diopters ± 0.76 in 79.6% (43 eyes) (P<0.003) and remained stable (within ± 0.50 D) in 20.4% (11 eyes) of eyes. Corneal collagen cross linking with riboflavin and UVA light is effective treatment for progressive keratoconus in Iraqi patients
**Introduction**

Keratoconus is a common disorder (prevalence of about 50 per 100,000) in which the central or paracentral cornea undergoes progressive thinning and bulging, so the cornea takes on the shape of a cone. The hereditary pattern is not prominent or predictable, but positive family histories have been reported in 6%-8% of cases. Etiology is unknown and likely multifactorial because of the wide variety of associated syndromes. Histopathologically, keratoconus shows the following:

1. Fragmentation of Bowman's layer.
2. Thinning of the stroma and overlying epithelium.
3. Folds and breaks in Descemet's membrane.
4. Variable amount of diffuse scarring.

Nearly all cases are bilateral, but one eye may be much more severely involved. Keratoconus can be graded by keratometry according to severity as mild (<48 Diopters), moderate (48-54 Diopters) and severe (>54 Diopters).

The central and inferior regions of the cornea are likely to be affected preferentially (the main region of cone formation), since interlamellar cohesive strength is at a minimum in that area in normal corneas. Keratoectasia that occurs iatrogenically has similar characteristic to keratoconus and it occurs mostly after laser insitu keratomileousis (LASIK). Despite intensive biochemical and genetic research, nobody knows what causes keratoconus, although research in these disciplines will ultimately provide answers which could lead to a medical therapy. We do know that keratoconus typically commences at puberty, progressing until the patient's mid thirties, when it typically arrests. During this period, progression may stop and start at any time. It is not possible to predict when keratoconus will progress or stop without intervention. We also know that in keratoconus the cornea is biomechanically unstable. Some literature suggests this may be the result of a decrease in cross-links between and within collagen fibers in the anterior corneal stroma. If there were a way to increase these cross-links, it could provide a means to stiffen the cornea and confer biomechanical stability with the potential to slow the progression of the disorder.

**Patients & methods**

This prospective study included patients with signs of progressive keratoconus defined as an increase in maximum K (keratometric) readings in several consecutive measurements over a period of 3 to 6 months, changes in refraction, patient reports of deteriorating visual acuity and contact lens intolerance. All patients were asked to sign an informed consent. Patients less than 18 years of age were also included in our study as the occurrence of keratoconus is seen at a much earlier age and with rapid progression in Iraq. This study was performed in Ramadi city in the west of Iraq during the period from July 19, 2010 till March 24, 2011.

**Inclusion criteria**

- Progressive keratoconus
- Corneal thickness of at least 400 µm
- No slit-lamp evidence of corneal scarring

**Surgical technique**
The cross-linking was performed in A-Rahma Day Clinic, Ramadi, Iraq. After administration of topical anesthesia (propracaine hydrochloride 0.5% eye drops), the epithelium was removed using a blunt spatula in a 9.0 mm diameter area. This was to ensure that the riboflavin penetrated the stroma and that a high level of UVA absorption was achieved. As a photosensitizer, 0.1% riboflavin solution was applied to the cornea every 5 minutes for 30 minutes before the irradiation to allow sufficient saturation of the stroma. Next, an 8.0-mm diameter of central cornea was irradiated with UVA light with a wavelength of 370 nm and an irradiance of 3 mW/cm². The CBM Vega X-Link system (CSO, Italy), was used as the UVA radiation source. During the 30 min of irradiation, 2 drops of 0.1% riboflavin solution (Ricrolin) were applied to the cornea every 5 min to sustain the necessary concentration of the riboflavin. After the treatment, soft bandage contact lens was placed and removed after complete reepithelialization, usually within 4-5 days. The patients were instructed to use ciprofloxacin eye drops, 1% prednisolone acetate eye drops and tears naturale II for a period of two weeks. All drops were recommended for use at four times daily.

**Outcome measures and statistical analysis**

Follow-up examination was done at 5 days, 2 weeks, 3 months, and 6 months post-treatment. To study the effectiveness of the procedure the following tests were done 3 and 6 months after treatment; 1-The uncorrected and the best corrected visual acuity (Snellen visual acuity chart), 2-Keratometry and Corneal topography by the pentacam. 3-Pachymetry (Tomey, Japan).

These data were compared with the data collected preoperatively by the same tests. SPSS version 17 statistical software was used for statistical analysis.

**Results**

All patients in this study (9 male and 18 female patients) were followed for at least 6 months. Fifty-four eyes of 27 patients with a mean age of 24.9 ± 5.35 (range 9-37 years) were included. The highest preoperative K (keratometric) value determined by using the pentacam. The mean preoperative BCVA was 0.42 ± 0.21 (vision was recorded by Snellen's and converted to decimal format for statistical calculations). Ultrasonic pachymetry (Tomey, Japan) for the corneal center was done in all eyes preoperatively to assess suitability and was 432 ± 44 μm. The preoperative values on the day of treatment were compared with postoperative values of the 3 and 6-month examinations. The mean preoperative BCVA was 0.42 ± 0.21. While the mean BCVA 3 months postoperatively found to be 0.51 ± 0.22 (P value < 0.001) and the mean BCVA 6 months postoperatively found to be 0.56 ± 0.22 (P value < 0.001). The Snellen's VA test showed that the BCVA improved at least one line in 55.5% (30/54) of eyes and remained stable in 44.5% (24/54) of eyes [Table 1] and [Figure 1]. The maximum keratometric (K) readings obtained preoperatively were compared with those measured 3 and 6 months postoperatively [Table 2] and [Figure 2]. The steepest corneal curvature was decreased by a mean of 1.74 Diopters ± 1.18 (D) in the total population studied. It was decreased by a mean of 2.04 Diopters ± 0.76 in 79.6% (43 eyes) (P<0.003) and remained stable (within ± 0.50 D) in 20.4% (11 eyes) of eyes [Table 3].
Table (1):- The mean preoperative best corrected visual acuity (BCVA) compared with the mean BCVA 3 and 6 months postoperatively

<table>
<thead>
<tr>
<th>Total No.</th>
<th>Preoperative BCVA</th>
<th>BCVA 3 months postoperatively</th>
<th>BCVA 6 months postoperatively</th>
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<tbody>
<tr>
<td>54</td>
<td>Mean: 0.42 ± 0.21</td>
<td>Mean: 0.51 ± 0.22, P value &lt; 0.001</td>
<td>Mean: 0.56 ± 0.22, P value &lt; 0.001</td>
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Fig. (1):- the preoperative and the postoperative BCVA.

Table(2):- Comparison between the mean of the maximum keratometric readings obtained preoperatively and those obtained 3 and 6 months postoperatively.

<table>
<thead>
<tr>
<th>Total No.</th>
<th>Preoperative K readings</th>
<th>K readings 3 months postoperatively</th>
<th>K readings 6 months postoperatively</th>
</tr>
</thead>
<tbody>
<tr>
<td>54</td>
<td>50.81 Diopters ±4.52</td>
<td>50.18 Diopters ±4.53, P value &lt; 0.001</td>
<td>49.07 Diopters ±4.12, P value &lt; 0.001</td>
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Discussion
This prospective study was conducted in Ramadi city, Iraq. To our knowledge this is the first study of its kind. We found in this study that corneal collagen cross-linking with riboflavin is effective in stopping the progression of keratoconus by increasing the corneal rigidity. The same result was found by other studies. We found that this procedure is safe with no serious side effect. The safety of this procedure was studied by Eberhard Spoerl et al. and concluded that as long as the corneal stroma treated has a minimal thickness of 400 microns (as recommended), neither corneal endothelium nor deeper structures such as lens and retina will suffer any damages. Another study showed that the corneal innervations is restored normally after the procedure. Caporossi et al., showed in human eyes that refractive results showed a reduction of about 2.5 D in the mean spherical equivalent, topographically confirmed by the reduction in mean K. Raiskup-Wolf et al., who followed up the patients for six years and reported that the improvement in vision after cross-linking is caused by a decrease in astigmatism and corneal curvature as well as by topographical homogenization of the cornea as a result of the increased rigidity in the cross-linked cornea. This lead to an improvement in the BCVA, and even the UCVA, through K readings reduction( astigmatism improvement).
Another possible explanation of cross-linking success, especially concerning keratoconus stabilization, is the new more compact collagen lamellar structure after corneal cross-linking as demonstrated in recent studies by Wollensak and Mazzotta. On reviewing the epidemiological studies, it is found that 21% of patients with keratoconus have ended with keratoplasty for visual rehabilitation. The importance of cross-linking lies in the fact that it improves vision, helps regression of the disease and stabilize future progression, so it may eliminate or delay the need for keratoplasty. Because keratoconus is a common disease in our country and keratoplasty is not always available due to lack of eye bank and the delay in issuing the legal rules that organizes the organ transplant in general, we recommend doing this procedure for all patients with keratoconus as early as possible during the course of the disease unless there is a contraindication. Keratoconus is a disease of young people, so it leads to significant loss of productivity in the society and it has a very negative impact on the quality of life so that we should have screening program including all young people with astigmatism with special care to those with history of vernal keratoconjunctivitis as it is well known that they are more susceptible for keratoconus.

References


