Corneal Thickness Changes after Collagen Cross Linking in Keratoconus

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Abstract

**Aim of Study:** The aim of this study is to analyze changes in the central corneal thickness after collagen cross linking in eyes with progressive keratoconus.

**Methods:** Thirty eyes of 22 patients with mean age 24.56±3.79 years with progressive keratoconus were treated with UV-A-riboflavin CXL and central corneal thickness was assessed with Scheimpflug imaging (Pentacam) at baseline, 1 and 6 months after CXL. Associations with clinical outcomes (best corrected distance visual acuities and maximum keratometry) were analyzed.

**Results:** Mean preoperative central corneal pachymetry was 478.6±26.5um (range 405-531). Statistically significant corneal thinning was recorded after 1 months and 6 months with mean pachymetry (central cornea) of 452.8±23.8 and 469.46±27.93um respectively. There is statistically significant increase in mean central corneal thickness by 16.9±19.85um at 6 months compared to 1 month.

**Conclusion:** After collagen cross linking there is significant central corneal thinning at 1 month and increased at 6 months but still the thinning is significant compared to baseline thickness.

**Key Words:** Keratoconus – Collagen cross linking – Central corneal thickness – Pentacam.

Introduction

KERATOCONUS is a progressive, non-inflammatory dystrophy of the cornea of unknown pathogenesis, characterized by a number of histopathologic abnormalities, which lead to para axial stromal thinning and weakening that leads to corneal surface distortion. Visual loss occurs primarily from irregular astigmatism and myopia, and secondarily from corneal scarring. Protrusion usually but not exclusively affects the axial and inferonasal cornea [1].

In early stages of keratoconus corneal Collagen Cross Linking (CXL) is a safe and effective procedure used to increase the rigidity of the cornea by inducing additional cross links within or between collagen fibers using UVA light and a photomediator, riboflavin (vitamin B2), with the goal of slowing down, possibly stabilizing, and even perhaps reversing, the progression of corneal ectasia in patients with keratoconus [1,2].

Collagen cross linking in keratoconus can be performed in combination with surface ablation to correct residual refractive errors. A combination of topography-guided custom ablation and CXL was found to improve patients’ visual, refractive, and topography outcomes and halted the progression of keratectasia [3].

Material and Methods

All patients received a thorough explanation of the study design and aims. Study participants gave informed consent before initiation of any study-related procedures, and the study was conducted in compliance with informed consent regulations.

This is a prospective, interventional, nonrandomized and non-controlled study. It was carried out between 2011 to 2013 in Rowaad vision correcting center. The protocol was revised and approved by our Ophthalmology Department Ethical Committee.

**Inclusion criteria:**

Clear ocular media, corneal stromal thickness in the thinnest point at least 400 microns and their age more than 18 years either males or females, during the determined time period of the study.
Exclusion criteria: History of herpetic keratitis, any corneal infection, corneal stromal thickness less than 400 microns at any point, severe dry eye, diabetes and concomitant autoimmune diseases, any previous ocular surgery, pregnant or lactating females and patients with central or paracentral corneal opacities.

Preoperative evaluation:
- Full medical history (duration of diabetes, controlled or not), other systemic diseases.
- All eyes were subjected to examination of Best Corrected Visual Acuity (BCVA) using snellen’s chart.
- Slit lamp examination of anterior segment to exclude corneal abnormalities and significant cataract.
- Intraocular pressure measurement using Goldman applanation tonometry.
- Fundus examination was done using indirect ophthalmology.
- Pentacam tomographic evaluation using (Allegro oculoyzer, WaveLight AG, Erlangen, Germany).

Surgical technique:
- Riboflavin 0.1 % was prepared by diluting vitamin B2-riboflavin-5-phosphate 0.5% with dextran T500 to achieve a 0.1% riboflavin solution. The solution was protected from light and used within 12 hours.

Topical anesthesia was applied before the procedure using benoxinate eye drops. The corneal epithelium was mechanically removed over an area of 8mm in diameter using a blunt instrument (Hockey knife) and riboflavin 0.1 % solution was instilled repeatedly for approximately 30 minutes. Penetration of the cornea and presence of riboflavin in the anterior chamber (riboflavin shielding) was monitored with slit-lamp examination using blue filter. UVA irradiation was performed using an optical system (Kohler illumination) with a light source consisting of an array of 7 UV diodes (365nm; Nichia, Nurnberg, Germany) with a potentiometer in series to allow for regulation of voltage. Before treatment, intended irradiance of 3mW/cm² surface irradiance (5.4J/cm² surface dose) was calibrated using a UVA meter (LaserMate-Q; LASER 2000, Wessling, Germany) at a working distance of 1cm. Irradiance was performed for 30 minutes by using 3mW/cm², corresponding to a dose of 5.4J/cm². During treatment, riboflavin solution was applied every 3 minutes to saturate the cornea with riboflavin. After the treatment, a bandage contact lens was applied until complete regeneration of the corneal epithelium which was usually achieved completely after 3 days. Postoperatively patients were given topical antibiotic with artificial tear substitutes.

Post operative care:
- After removal of contact lens the patient is prescribed topical combination of steroid and antibiotic six times daily, with a gradual decrease over the following 6 weeks together with topical lubricant substitute.

Patients were examined every 2 days until complete epithelialization then at 1 and 6 months using slit lamp examination, best corrected visual acuity, and pentacam.

Results

Demographic data analysis:
- The study included 30 eyes of 22 patients, 14 of which were males (46.3%) and 16 were females (53.3%) as shown in Fig. (1), with mean age of 24.56±3.79 years, ranging from 19 to 35 years.

Pentacam findings:
- Central corneal thickness:
  - The corneal pachymetry was measured by the Oculus Pentacam. Statistical analysis revealed a mean preoperative central corneal pachymetry of 478.6±26.5um (range 405-531). Statistically significant corneal thinning was recorded after 1 months with mean pachymetry (central corneal) of 452.8±23.8. Mean central corneal pachymetry at 6 months was 469.46±27.93um. There is statistically significant increase in mean central corneal thickness by 16.9±19.85um at 6 months compared to 1 months (p-value=0.001) [(Table 1) & Fig. (2)].

- K-readings:
  - The topographic analysis done by the Pentacam revealed a mean preoperative Kmax of 47.8±2.2D ranging from 44.10D to 53.6D. The mean postoperative Kmax at 1 months was 47.9±2.6D ranging from 44.1D to 55.2D with an increase of 0.1±0.9D which was statistically in-significant (p-value= 0.551). The mean postoperative Kmax at 6 months was 47±2.2D ranging from 42.7D to 52.2D, thus showing a mean reduction of 0.85D±0.72D compared to preoperative Kmax which was statistically significant (p-value=0.001) as shown in [(Table 2) & Figs. (3,4)].
Best Corrected Visual Acuity (BCVA):

The mean preoperative BSCVA was 0.54±0.22, ranging from 0.2 to 1.00 while the mean postoperative BSCVA at one month was 0.48±0.22 ranging from 0.1 to 1.00, decreasing insignificantly by a mean of 0.07±0.17 Snellen's line with $p$-value 0.36. At 6 months the mean BSCVA was 0.62±0.19 ranging from 0.2 to 1.00 thus improving significantly by a mean of 0.0833±0.0874 Snellen's lines compared to preoperative BCVA with $p$-value 0.001 as shown in [Fig. (5) & (Table 3)].
Discussion

Riboflavin UV-A corneal collagen cross-linking represents the only method of interference in progressive keratoconus to delay its progression and to reduce the need for keratoplasty [4].

Our study has shown that collagen cross-linking appears to be effective in stopping the progression of keratoconus. Follow-up showed that, after a mild initial worsening of most of keratoconus indices (probably because of epithelial debridement), there was a slow but continuous improvement of the indices up to 6 months postoperatively. This was evident through several results.

The improvement in the BCVA was significant where the mean preoperative BSCVA was 0.54±0.22 while the mean postoperative BSCVA at 6 months was 0.62±0.19 improving by a mean of 0.16±0.02 Snellen lines.

Visual improvement generally started after the first month with treatment. The temporary visual reduction observed in many of treated patients in the first month is in line with the transient presence of corneal haze, clinically detectable by slit-lamp examination and steepening of keratometric readings evidenced by pentacam.

The above results were comparable with study conducted by Vinciguerra et al., in 2009 (28 eyes, mean follow-up 12 months) a mean baseline BSCVA 0.28±009 Log MAR. At 6 month post CXL, the mean BCVA was 0.17±0.08 Log MAR [5].

Similar results were found by Lamy et al., Mean preoperative BCVA was 0.28 Log MAR improved to 0.11 Log MAR at 6 months after CXL [6].

Topographic analysis done for our patients preoperatively revealed a mean Kmax of 47.8±2.2 D. The mean postoperative Kmax at 6 months was 47.0±2.2 thus showing a mean reduction of 0.85±0.72D. There was a significant statistical difference between the result of mean preoperative and mean postoperative Kmax at 6 months.

Vinciguerra et al., (28 eyes) showed decrease of the average keratometry from 48.08D preoperatively to 47.5D at 6 months thus a mean reduction of 0.58D. Also Ricardo et al., in 2013 (68 eyes) had a flattening of the mean central Kmax at 6 months by 0.7D. Both results are similar to our results [5].

On the other hand Hishemi et al., (40 eyes) had reduction in mean Kmax from 49.37±3.48 preoperatively to 49.36±3.26 at 6 months with mean flattening by 0.01 which was extremely worse than our results [7].

One of the important criteria to evaluate the effects of CXL in our study was to evaluate its effect on the corneal thickness, thus the patients’ pachymetry was recorded throughout the study using the Oculus Pentacam. The mean preoperative central corneal thickness was 478.6±26.5um. After 1 month the mean central corneal pachymetry was 452.8±23.8um and at 6 months the central corneal thickness was 469.46±27.93um.

Our results revealed that there was a statistically significant corneal thinning recorded in the first month postoperative then statistically significant increase in central corneal thickness was observed at 6 months after CXL compared to it at 1st month. At 6 months there is statistically significant thinning compared to preoperative value.

These initial thinning we think may be attributed to the corneal de-epithelialization that was performed during the operative procedure which increases the rate of evaporation from the corneal stroma.

Epithelial remodeling, anatomic and structural changes in corneal collagen fibrils, and keratocyte apoptosis, might be also implicated. A temporary increase in endothelial pump activity that may be caused by UVA exposure has been also suggested as a cause of the initial corneal thinning after CXL.

Our results are similar to that of the study conducted by Steven et al., who found similar statistically significant thinning in mean central corneal thickness at 1 month (mean central corneal thickness was 491.4±45.7 microns and 462.3±41.7 microns preoperative and at 1 months respectively).
At 6 months they found increase in central corneal thickness but still statistically significant thinner than preoperatively (477±44.9 microns) [8].

Heshemi et al., also recorded an initial significant decrease in the central corneal pachymetry (preoperative central corneal pachymetry was 483.87±29.07 microns and 454.92±32.81 microns at 1 month) then statistically insignificant difference in central corneal thickness was observed after 6 months of follow-up (central corneal thickness was 480.27±26.97um) compared to preoperative mean central corneal thickness [6].

References