Effect of corneal collagen crosslinking on femtosecond laser channel creation for intrastromal corneal ring segment implantation in keratoconus

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PURPOSE: To evaluate the effect of collagen crosslinking (CXL) on femtosecond laser channel creation for intrastromal corneal ring segments (ICRS) in keratoconic eyes.

SETTING: Magrabi Eye Hospital, Cairo, Egypt.

DESIGN: Comparative case series.

METHODS: Eyes with grade II or III keratoconus were treated by CXL. After 6 months, channel creation was performed using an IntraLase FS-60 femtosecond laser. The eyes were randomly divided into 3 groups. The default femtosecond machine power setting was 1.5 mJ in Group 1, 1.6 mJ in Group 2, and 1.7 mJ in Group 3. A control group included virgin noncrosslinked keratoconic eyes in which the default power setting was 1.5 mJ. The degree of difficulty of ICRS insertion was judged subjectively. The degree of postoperative corneal haze was recorded.

RESULTS: Fifteen eyes of 11 patients had CXL. Each group, including the control, comprised 5 eyes. After CXL, intracorneal channel creation using the 1.5 mJ default femtosecond power setting was incomplete and mechanical dissection was required to complete the channel. When the power setting was increased to 1.6 mJ or 1.7 mJ, channel creation could be completed; however, this increased the corneal reaction (haze) postoperatively. The corneal haze resolved in all eyes within 6 weeks, and there were no further complications.

CONCLUSIONS: Femtosecond laser channel creation can be performed after CXL; however, the laser power must be modified. Results show channel dissection and ICRS implantation should be performed before or concurrent with CXL.

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Keratoconus is a progressive noninflammatory ectatic disease of the cornea with onset at puberty in most cases.[1] A recently developed treatment for keratoconus is corneal collagen crosslinking (CXL). In CXL, stromal fibers are photopolymerized by the combined action of a photosensitizing substance (riboflavin or vitamin B2) and ultraviolet A.[2] Photopolymerization increases the rigidity of corneal collagen. The aim is to slow or arrest progression of the disease to delay or avoid keratoplasty.[3]

Intrastromal corneal ring segments (ICRS) have been proposed as an additive surgical procedure for keratoconus correction to delay, if not prevent, the need for corneal grafting.[4–6] The goal of ICRS implantation is to regularize the front surface of the cornea while maintaining the existing biomechanical status of the underlying stroma.[7]

Femtosecond laser technology was introduced to create intracorneal channels for ICRS implantation. There are several advantages over the mechanical method, including that femtosecond channel creation is minimally invasive, creates more uniform dissection, gives more consistent results, causes less patient discomfort, provides faster visual recovery, and allows more accurate ICRS placement.[8]

A combination of these modalities (CXL, ICRS, and femtosecond laser) should yield better results because the procedures complement one another. However,

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the ideal sequence of intervention is still unknown. The aim of this study was to evaluate the effect of previous CXL on femtosecond laser channel creation for ICRS implantation in keratoconic eyes.

PATIENTS AND METHODS

This prospective study included eyes with progressive grade II to III keratoconus (Amsler-Krumeich classification) that had CXL with subsequent insertion of poly(methyl methacrylate) ICRS (Kerarings, Mediphacos, Inc.) 6 months later at Magrabi Eye Hospital, Cairo, Egypt. All patients provided informed written consent, and an institutional review board approved the study.

Inclusion criteria included progressive keratoconus, CXL performed 6 months previously, contact lens intolerance, and a clear cornea (ie, no apical scarring). Other inclusion criteria were a maximum keratometric (K) reading after CXL of less than 60.0 diopters (D), a minimum corneal thickness of more than 400 μm, and the absence of other ocular or systemic disease.

The eyes were randomly divided into 3 groups using a random-number generator. The default femtosecond machine power setting was 1.5 mJ in Group 1, 1.6 mJ in Group 2, and 1.7 mJ in Group 3. A control group comprised virgin noncrosslinked eyes with grade II to III keratoconus; the default power setting in this group was 1.5 mJ.

Preoperative evaluation included uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA), refraction, and slitlamp and fundus examinations. Corneal topography (TMS-4, Tomey Corp.) and corneal thickness measurement using ultrasonic pachymetry (Nidek Co. Ltd.) were also performed.

Surgery was performed using topical anesthesia. The tunnel was created at 80% of corneal thickness with the aid of an IntraLase FS 60 kHz femtosecond laser (IntraLase Corp., Abbott Medical Optics, Inc.). The infrared neodymium-glass femtosecond laser has a wavelength of 1053 nm. The beam induces photodisruption to form a dissection plane. The tunnel was programmed for an inner diameter of 5.0 mm and an outer diameter of 5.8 mm using the laser software. A 1.4 mm incision was created on the steepest topographic axis with an entry cut thickness of 1 μm. The laser power used to create the tunnel and the incision varied by group (ie, 1.5 mJ, 1.6 mJ, or 1.7 mJ). After a lid speculum was placed, the center of the pupil was marked and the corneal thickness at the area of implantation (5.0 mm diameter) was measured using ultrasound pachymetry. The contact glass was lowered onto the cornea using the disposable cone of the femtosecond laser until the peripheral meniscus was eliminated and adequate pressure achieved. Final centration was achieved manually and confirmed using the laser's display. The laser was then engaged to create the channel.

After the corneal channel was completed, a spatula was used to locate the entrance of the channel. The ring segment was used to dissect the channel before the bubbles disappeared. The ICRS were implanted with a dedicated forceps and placed in final position with a Sinskey hook. The wound was not sutured. Insertion of the ICRS was graded subjectively as follows: 0 = easy, no resistance, fully dissected tunnel; 1+ = slight resistance, rings could dissect the weak fibers in the tunnel; 2+ = moderate resistance, some manual separation, mechanical dissection of noncleaved areas needed (Figure 1); 3+ = difficult, severe resistance, all manual dissection, mechanical dissection needed throughout the tunnel.

A bandage contact lens (Acuvue, Johnson & Johnson Vision Care, Inc.) was applied for 1 day. The postoperative treatment included tobramycin–dexamethasone (TobraDex) and artificial tears (Refresh Tears) 4 times daily, after which the dose was tapered over 1 month. In eyes with significant corneal stromal haze, combined tobramycin–dexamethasone was given hourly until improvement, after which the medication was tapered as in the regular regimen.

Postoperative evaluations were at 1 day (for contact lens removal), 1 week, and 1, 3, and 6 months. The UDVA, CDVA, and refraction were measured, and a slitlamp examination was performed. Corneal haze was quantified subjectively at the slitlamp as follows: 0 = no haze, totally transparent tunnel; 1+ = slight corneal haze, slight loss of transparency in the tunnel area; 2+ = moderate haze, iris details seen through the tunnel; 3+ = exaggerated haze, iris details barely seen through the tunnel and in the surrounding cornea (Figure 2).

Statistical analysis was performed using SPSS software (SPSS, Inc.). The independent-sample *t* test was used to compare the preoperative data between the 3 CXL groups.

RESULTS

Fifteen eyes of 11 patients (6 women and 5 men) had previous CXL. Each group, including the control, comprised 5 eyes. Table 1 shows the patients' demographic data by group.

The mean age of all CXL patients (Groups 1, 2, and 3) was 27.5 years ± 3.16 (SD) (range 23 to 32 years). The mean preoperative UDVA (decimal) was 0.13 ± 0.09 (range 0.01 to 0.20) and the mean CDVA, 0.45 ± 0.20 (range 0.10 to 0.80). The mean preoperative refractive values were spherical error, −4.06 ± 1.50 D (range −1.50 to −7.00 D); cylindrical error, 5.36 ± 0.86 D (range 3.75 to 6.50 D); steep K, 54.61 ± 1.77 D (range 52.0 to 57.0 D); and flat K, 48.63 ± 1.66 D (range 46.5 to 52.5 D). The mean preoperative pachymetric reading was 435.33 ± 23.1 μm (range 400 to 470 μm). There were no statistically significant differences between the 3 groups in any parameter except steep K ($P = .002$) and flat K ($P = .02$) between Group 1 and Group 2 (Table 2).

The mean age in the control group (no previous CXL) was 27.2 ± .92 years (range 24 to 29 years).

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Figure 1. Mechanical dissection of noncleaved areas of the tunnel (moderate resistance; 2+).

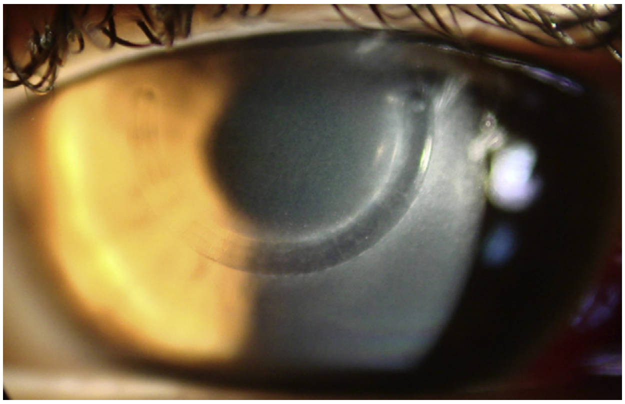

Figure 2. Exaggerated haze (3+) in the tunnel area and in the cornea around.

The mean preoperative UDVA was 0.11 ± 0.05 (range 0.05 to 0.20) and the mean CDVA, 0.46 ± 0.11 (range from 0.30 to 0.60). The mean preoperative refractive values were spherical error, −4.40 ± 1.39 D (range −3.00 to −6.00 D); cylindrical error, 5.40 ± 0.65 D (range 4.50 to 6.00 D); steep K, 54.10 ± 1.60 D (range 52.0 to 56.0 D); and flat K, 48.80 ± 1.15 D (range 47.5 to 50.5 D). The mean preoperative pachymetric reading was 438 ± 14.8 μm (range 420 to 460 μm).

Insertion Difficulty

The ring thickness ranged from 150 to 250 μm. Figure 3 shows the difficulty of ICRS insertion by group.

Table 1. Preoperative demographic data by group.

Group/Eye	Age (Y)	Sex	UDVA (Decimal)	CDVA (Decimal)	Sphere (D)	Cylinder (D)	Steep K (D)	Flat K (D)	Pachy (μm)
Group 1									
Eye 1	23	F	0.05	0.1	−2.50	4.50	54.5	48.5	440
Eye 2	23	F	0.10	0.4	−3.50	3.75	52.0	47.7	470
Eye 3	30	M	0.20	0.5	−7.00	5.25	52.0	46.5	430
Eye 4	30	M	0.20	0.1	−1.50	5.25	54.5	48.5	455
Eye 5	25	F	0.01	0.8	−5.00	6.00	53.0	46.7	410
Group 2									
Eye 1	32	F	0.20	0.7	−5.50	5.50	56.0	50.7	430
Eye 2	32	F	0.20	0.5	−3.50	5.75	55.5	49.0	450
Eye 3	27	M	0.20	0.6	−5.50	4.25	57.0	52.5	470
Eye 4	28	M	0.20	0.5	−2.00	6.50	55.5	48.0	400
Eye 5	28	M	0.01	0.1	−3.00	5.25	57.0	50.5	425
Group 3									
Eye 1	26	F	0.20	0.4	−3.50	6.50	56.25	49.0	460
Eye 2	23	M	0.01	0.6	−5.00	4.50	53.5	48.0	415
Eye 3	26	M	0.20	0.5	−4.25	6.00	54.5	47.5	450
Eye 4	29	F	0.01	0.5	−3.75	6.50	52.0	46.7	420
Eye 5	31	F	0.20	0.4	−5.50	5.00	56.0	49.5	405
Control									
Eye 1	24	F	0.10	0.5	−3.00	5.00	55.0	49.0	440
Eye 2	28	F	0.05	0.4	−5.50	6.00	53.0	48.0	430
Eye 3	27	M	0.10	0.6	−6.00	4.50	52.0	47.5	460
Eye 4	29	F	0.20	0.3	−4.50	6.00	54.5	49.0	420
Eye 5	28	F	0.10	0.5	−3.00	5.50	56.0	50.5	440

CDVA = corrected distance visual acuity; K = keratometry; Pachy = pachymetry; UDVA = uncorrected distance visual acuity

Table 2. Between-group comparison of preoperative data.

Group	Mean ± SD							
	Age (Y)	UDVA (Decimal)	CDVA (Decimal)	Sphere (D)	Cylinder (D)	Steep K (D)	Flat K (D)	Pachymetry (μm)
1	26.2 ± 3.56	0.11 ± 0.09	0.38 ± 0.3	−3.90 ± 2.2	4.95 ± 0.9	53.20 ± 1.3	47.60 ± 0.9	441 ± 23.0
2	29.4 ± 2.4	0.16 ± 0.08	0.48 ± 0.2	−3.90 ± 1.6	5.45 ± 0.8	56.20 ± 0.8	50.15 ± 1.7	435 ± 26.5
3	27.0 ± 3.08	0.12 ± 0.10	0.48 ± 0.1	−4.40 ± 0.8	5.70 ± 0.9	54.45 ± 1.8	48.15 ± 1.1	430 ± 23.7
P value								
Group 1 vs Group 2	.13	.38	.56	1.0	.37	.002	.02	.71
Group 2 vs Group 3	.21	.54	1.0	.55	.66	.077	.06	.76
Group 1 vs Group 3	.71	.85	.49	.64	.22	.23	.42	.48

CDVA = corrected distance visual acuity; K = keratometry; UDVA = uncorrected distance visual acuity

Insertion was most difficult in Group 1 and was least difficult in the control group followed by Group 3.

Postoperative Complications

Figure 4 shows the corneal haze intensity by group. The corneal haze was greatest in Group 3 and was the least in Group 1 and the control group. All cases of stromal haze resolved without sequelae.

One eye in Group 1 developed minimal intracorneal channel deposits. The deposits did not affect the patient's vision. There were no other intraoperative or postoperative complications, such as perforation, ICRS extrusion, or infection.

DISCUSSION

Collagen crosslinking has an additive effect on ICRS implantation in keratoconic eyes and can be considered an enhancement and stabilizing procedure. Collagen crosslinking after ICRS can improve UDVA and CDVA and yield a greater reduction in K readings.[9] Coskunseven et al.[7] found that ICRS implantation followed by CXL resulted in greater improvement in keratoconus than CXL followed by ICRS implantation. Another study[10] suggested that that CXL performed after another corneal surgery might result in severe haze that may end in scarring.

In this study, CXL was performed first and was followed by ICRS insertion 6 months later. The efficacy of femtosecond laser channel creation was lower in eyes that had previous CXL than in the control group, which did not have CXL before ICRS insertion. We could hypothesize that in addition to compacting the stromal lamellae in the superficial 300 μm, CXL affects the deeper stroma to some extent. In addition, a crosslinked cornea is less clear than a normal cornea, making femtosecond laser penetration less effective. Thus, we evaluated the results in 3 groups of eyes with previous CXL. The default femtosecond laser energy was increased from 1.5 mJ (manufacturer's recommendation) in the first group to 1.6 mJ and 1.7 mJ in the latter 2 groups, respectively, to achieve a proper dissection plane in the crosslinked corneas. Increasing the energy

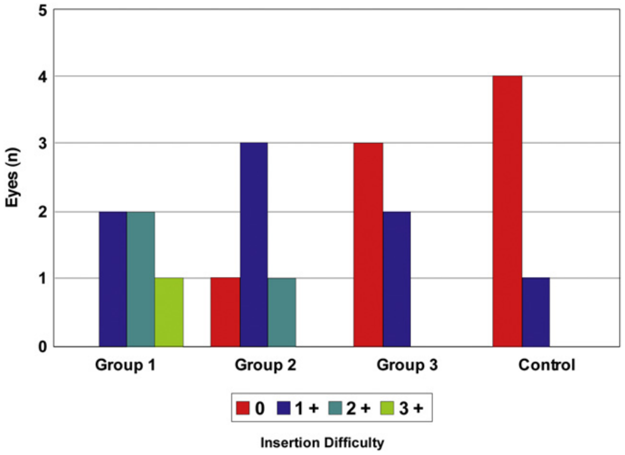

Figure 3. Difficulty of ICRS insertion.

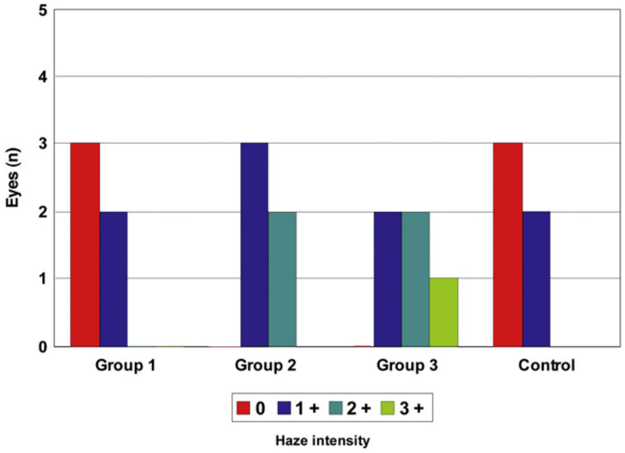

Figure 4. Postoperative haze intensity.

caused a more severe and persistent corneal reaction postoperatively; however, the reaction resolved without sequelae. In previous studies, the recommended laser energy for channel creation varies according to the femtosecond laser model used (eg, 5 mJ for the 15 kHz IntraLase[11] and 1.3 mJ for the 60 kHz IntraLase[7]).

A limitation of this study is the subjective nature of the parameters studied (ICRS insertion difficulty and haze grading). We used this method because no objective system is available at present. Another limitation is the small number of patients and the possibility of bias in patient assignment because there was a statistically significant difference in the preoperative steep and flat K readings between Group 1 and Group 2. Not evaluating these parameters, which might affect femtosecond laser outcomes (eg, corneal curvature), is another limitation. Although the femtosecond laser we used is not supposed to be affected by preoperative corneal curvature because of the corneal flattening induced by the applanation cone, further studies of whether there is a correlation between preoperative corneal curvature and outcomes would be beneficial.

To conclude, although femtosecond laser channel creation can be performed safely after CXL, it is better to perform channel dissection before or concurrent with CXL. This results in less energy use, better dissection, and less corneal haze.

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