Management of Early Post LASIK Ectasia by using Corneal Collagen Cross-Linking

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Abstract: Purpose: To study the results of corneal collagen cross-linking (CXL) in management of early ectasia after LASIK.**Patients and Methods:** Twenty-two eyes of 15 patients with postoperative ectasia after LASIK (22 eyes) were included with a mean age of 26±6 years at the time of treatment and a mean follow-up of 12 months (range, 9–15 months).All patients treated with CXL for progressive ectasia after LASIK. Best corrected visual acuity (BCVA), maximum keratometry readings (K_{max}), minimum radius of curvature (R_{min}), and corneal topography indices were assessed in this study. **Results:** Ninety five percent of BCVA postoperatively are equal to preoperatively BCVA or gained 1 or more lines.Mean BCVA before CXL was 0.6 units, which improved to a mean of 0.3 units (P<0.002). Best corrected visual acuity improved 1 line or more in 14 cases and remained unchanged in 7 patients. Mean K_{max} after CXL of 51.3±4.2 diopters (D) was significantly lower (P<0.003) than mean pre-CXL K_{max} of 51.9±5.1 D. The R_{min} after CXL was increased significantly (P = 0.005), whereas the index of surface variance (P = 0.04), the index of vertical asymmetry (P = 0.05), the keratoconus index (P = 0.04), and the central keratoconus index (P = 0.017) were reduced significantly. **Conclusions:** Corneal ectasia is a serious vision-threatening complication of laser in situ keratomileusis (LASIK). It is associated with progressive corneal steepening, an increase in myopia and astigmatism, and decrease in visual acuity. Ectasia after LASIK can be arrested by CXL with stabilization of BCVA Cross linking should be performed in patients with progressive post LASIK keratectasia as early as possible to prevent a further deterioration.
[Abdalla M. Elamin. **Management of Early Post LASIK Ectasia by using Corneal Collagen Cross-Linking.** *J Am Sci* 2014;10(8):78-82]. (ISSN: 1545-1003). http://www.jofamericanscience.org. 11

Keyword: Post LASIK ectasia. CXL

Introduction:

Iatrogenic ectasia after refractive laser surgery, a progressive stromal thinning and steepening of the cornea resulting in refractive aberrations and visual loss, increasingly has been reported since its first description by **Seiler et. al.,**[1] All excimer laser procedures remove corneal tissue, weakening corneal biomechanics. Iatrogenic keratectasia is a sight-threatening complication after LASIK, occurring in 0.1 % of cases, [2,3] and is less frequent after photorefractive keratectomy (PRK).[4] The major risk factors for ectasia after refractive laser surgery are deep ablation, residual stromal thickness of less than 250 µm,[5] retreatments, and pre-existing abnormal corneal topography such as forme fruste keratoconus and pellucid marginal degeneration.[6]

Recently, a new technique, corneal collagen cross linking, has been introduced by **Wollensak et al** to stabilize progressive keratoconus[7]. There are number of studies reported that CXL is safe and effective in halting the progression of keratoconus [8,9] and post-refractive surgery corneal ectasa[10].

The technique of corneal collagen cross-linking consists in photopolymerisation of stromal fibres by the combined action of a photosensitising substance (riboflavin or vitamin B2) and ultraviolet light from a solid state UVA source Photopolymerisation increases the rigidity of corneal collagen and its resistance to keratectasia. Corneal cross linking (CXL) minimally alter refractive error particularly when applied to cornea at an early stage [11].

Hafezi et al[10] investigated the effect of CXL on iatrogenic keratectasia and observed an improvement in best corrected visual acuity (BCVA) in 9 of 10 cases, improved keratometric readings in 5 of 10 cases, and reduction in cylinder in all patients. Salgado et al[12] similarly showed regression of corneal ectasia and improvement of spherical equivalent with a 6-month follow-up. Recently, **Hersh et al**[13] reported 1-year outcomes of a prospective, randomized clinical trial on CXL in both keratoconus and ectasia patients, showing significant improvement in CDVA and reduced maximum keratometric values; however, the CXL results were less notable in ectasia patients.

This study evaluates the effect of CXL in the treatment of early ectasia after LASIK with a mean follow-up period 12 months.

2. Patients and Methods

Twenty two eyes of fifteen patients with post lasik ectasia were included**.** Ectasia was defined as topographic steepening of 5 diopters (D) or more compared with immediate postoperative appearance, loss of 2 lines or more of Snellen acuity, and a change in manifest refraction of 2 D or more of either sphere or cylinder. Progression was defined by an increase of maximum keratometry readings (K_{max}) of the anterior corneal surface, at 3.0 mm from the apex, of at least

1.0 D in corneal topographies over a maximum of 12 months. Central corneal thickness (CCT) by optical and ultrasonic pachymetry was at least 300 ìm, with the exception of 1 patient with CCT of 297mm.

The main outcome measures were: BCVA, K_{max}, minimum radius of curvature, and 6 quantitative descriptors of corneal topography (Pentacam topography; Oculus Instruments, Wetzlar, Germany), including index of surface variance, index of vertical asymmetry, keratoconus index, central keratoconus index, center keratoconus index, index of height asymmetry, and index of height decentration.

Surgical technique

Thirty minutes before surgery, Proparacaine 2% eye drops were used to anesthetize the ocular surface. The patients face was prepped with povidone-iodine 10%. The eyelashes were isolated using sterile drape. A 9.0 mm trephine, centered on the pupil was used to mark corneal epithelium. 20% alcohol was applied using reservoir ring for 30 seconds then irrigation with balance salt solution (BSS) was done. Corneal epithelium was removed using blunt scraper with used of ultrasound pachymetry to locate the central and thinnest point. For CXL, riboflavin 0.1% drops were applied every 3 minutes for 30 minutes. we performed slit-lamp inspection, using blue light for riboflavin shielding, followed by irradiation with the UV-X Corneal Crosslinking System (Iroc Medical, Zurich, Switzerland; distributed by Peschke GmbH, Nuremberg, Germany). For the 30-minute treatment, the parameters were: 370 nm, 3mW/cm2, 5.4 j/cm2, balanced saline solution was applied, along with ofloxacin 0.3% and one drop of diclofenac ophthalmic eye drop and a bandage contact lens. Postoperative medications include oflaxacin0.3% four times/day, fluorometholone four times/day and lubricating eye drops every two hours.

Patients were reviewed on the first and seventh postoperative days, and subsequently at 3 weeks, 6 weeks, 3 months 6 months and one year. At each examination, best corrected visual acuity was determined, and the cornea was examined by the slit lamp. Autorefractometry as well as manifest subjective refraction were performed, and best corrected visual acuity (BCVA) was determined at the three weeks, six weeks and three months examinations. Post operative corneal topography was performed at the 3 months 6 month and one year.

Statistical analysis

A paired 2-tailed Student *t* test was performed to analyze the postoperative outcome changes compared with baseline values. A *P* value less than 0.05 was used to determine statistical significance.

Results

Twenty-two eyes of 15 patients with ectasia after LASIK. The mean ± standard deviation (SD) patient age at CXL treatment was 26±6 years (range, 23–46 years) 27% patients were male and 73 % of patients were female.Twenty-one of 22 eyes had a central CCT by optical and ultrasonic pachymetry of at least 300 µm; 1 eye had a CCT of 297 µm.

The mean BSCVA improved from 0.95 ± 0.14 preoperatively to.98 ± 0.11 and 1.0 ± 0.10 at 3 months and 12 months (P0.002) respectively. The improvement was statistically significant at 12 months table1.

Ninety five percent of BCVA are equal to pre-op BCVA or gained 1 or more lines 5% only Lost 1 or more lines.

Table (1) Show BSCVA preoperative and Postoperative.

Table (1)	BCVA
Preoperative	
Mean	.95
Minimum	0.84
Maximum	1.0
Postoperative	BCVA
Mean	.98
Minimum	0.4
Maximum	1.0

Keratometry

The mean average K-value decreased from45.04 ±3.29 D preoperatively to 43.14 ± 2.72 D and 43.01 ± 2.25 D at 3 months (P= 0.002) and 12 months (P=0.005) respectively (Table 2).

The changes in k-value were significant. The following table represent K.reading as regard the mean K, the maximum K and astigmatism by K in dioptre(D) Table(2).

The minimum radius of curvature was increased significantly after CXL. The index of surface variance, the index of vertical asymmetry, the keratoconus index, and the central keratoconus index were reduced significantly. There was no significant change in the index of height asymmetry or index of height decentration. The results and *P* values are summarized in how preoperative and postoperative topographies and their difference maps FIGURE (1).

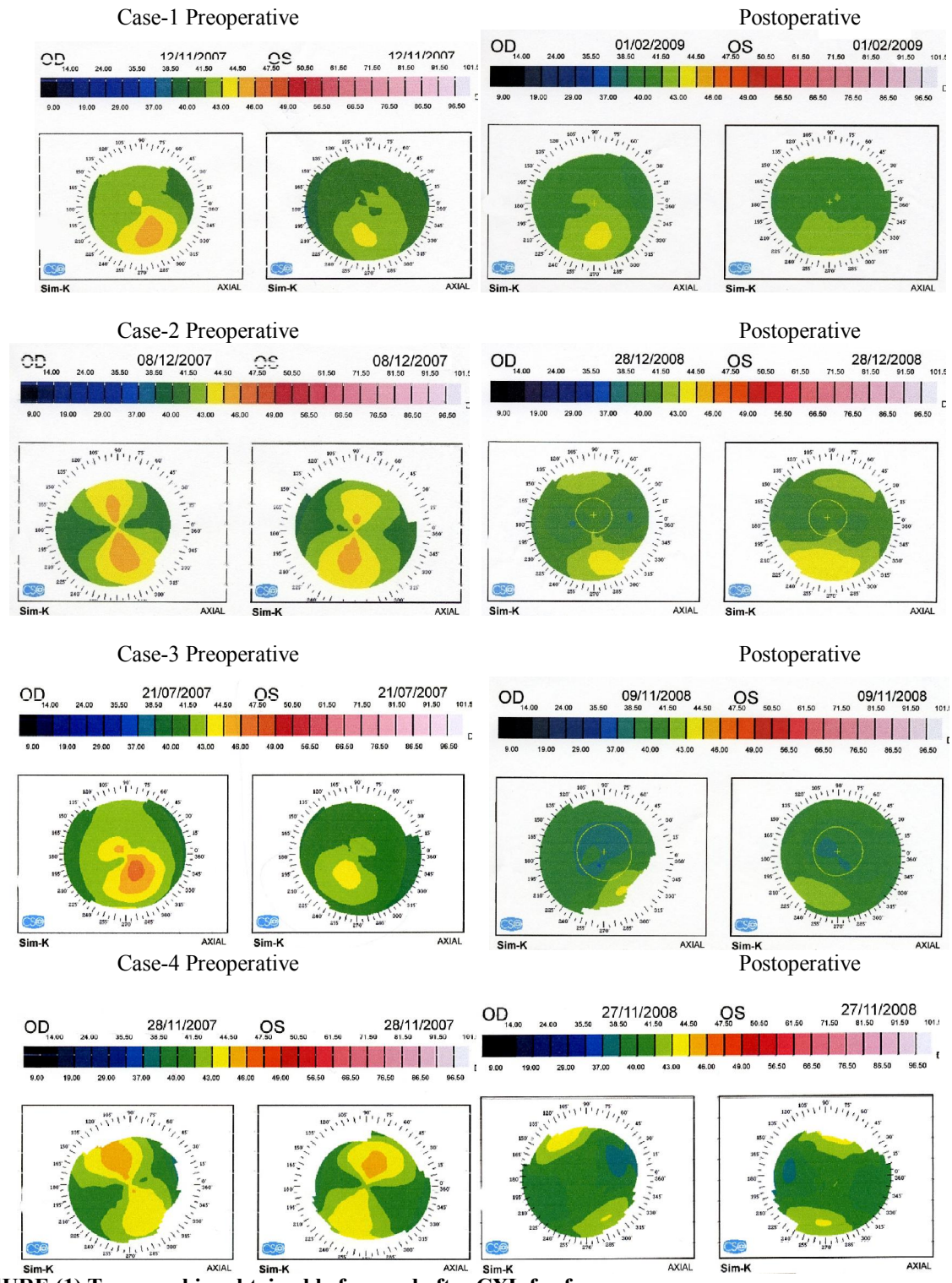

FIGURE (1) Topographies obtained before and after CXL for four cases.

Mean ± SD follow-up was 12±3 months (range, 12– months). Mean ± SD BCVA was 0.5±0.3 before CXL (range, 0.95–1.0) and improved to 0.3±0.14 (range, 0.98–1.1 l after treatment. Total mean ± SD CDVA improved to 0.2±0.16 (P<0.001). Best corrected distance visual acuity improved (gain of ≥1 line) in 19 eyes and remained stable in 3 patients. No patient showed deterioration (lost ≥1 line).

No serious complications were reported during the follow-up period.

Table(2). The changes in k-value.

Table (2)	K.READING		
Preoperative	Mean k (D)	Max.k (D)	Astigm.K (D)
Minimum	45.04	46.15	2.22
Median	45.26	42.97	0.82
Maximum	48.91	50.36	3.95
Postoperative	Mean k (D)	Max.k (D)	Astigm.K (D)
Minimum	43.14	45.31	2.09
Median	44.06	41.86	0.77
Maximum	47.21	48.44	3.01

4. Discussion

This study found an improvement in BCVA in 19 eyes of 22 eyes after CXL, with a mean improvement of 0.2. In a previous report, an improvement in BCVA was shown in 9 of 10 patients after CXL, but a recent report by **Hersh et al**[13] showed only a 0.07 increase inBCVA at 1 year after CXL. Corneal collagen cross-linking has been proven very effective in halting the progression of keratoconus and iatrogenic ectasia, but visual recovery, although statistically significant, usually is modest. It also seems that the visual outcome in patients with iatrogenic ectasia has been inferior compared with that of keratoconus patients after CXL.[13]

Mean K_{max} was significantly lower at 50.9 D (P<0.001) when compared with mean K_{max} before CXL of 52.8 D. In 19 eyes, K_{max} improved by more than 1 D, and in 7 eyes, it was stable. This is consistent with a previous report of 10 ectasia patients treated with CXL that showed a K_{max} reduction from 54.5 D to 52.6 D. However, another report of 22 eyes with ectasia that had undergone LASIK showed no significant difference in K_{max} before or after treatment (1.00 D decrease in K_{max}; P = 0.08). **Vinciguerra et al**[14] also reported no significant topographic changes (average keratometry, flat keratometry, or steep keratometry) in patients with iatrogenic keratectasia. Those results suggest that ectatic corneas may have a less robust response to CXL as opposed to keratoconic corneas. Although the cause for this potential difference in not clear, several explanations have been suggested. One is that CXL preferentially strengthens the anterior stroma, including the LASIK flap, which does not contribute to the mechanical stability of the cornea. The riboflavin diffusion may be reduced in corneas that have undergone LASIK, affecting the CXL result. Differences in the pathophysiologic features of keratoconus and ectasia occurring after refractive surgery also may account for a less pronounced CXL effect.[13]

Topographic evaluation showed marked improvement of irregularity (Figure 1), including significant reduction of corneal coma-like aberrations. As regard astigmatism about 59% of the eyes had Astigmatism by K-Reading within 1.0D and 68% of the eyes had Astigmatism by Refraction within 1.0D. Non of the eyes had > 2.0D. A reduction in topographic astigmatism was observed after 12 months' follow-up, with no significant improvement in visual outcomes.

The increase in the minimum radius of curvature in the present study is consistent with decreases in K_{max} after CXL in many studies.[15,16,17] Decreases in the index of surface variance indicate a decrease in the curvature variation compared with the mean curvature of the cornea, and decreases in the index of vertical asymmetry suggest a reduction of the difference between the superior and inferior corneal curvature. The decrease of this index may correspond to a decrease of the inferior-to-superior ratio.[18,19] The significant improvement in the keratoconus and central keratoconus indices reflect the reduction of the corneal steepening after CXL. Improvement in those parameters may explain the visual recovery and reverse of refractive aberrations in some ectasia patients.

In the early postoperative period, some eyes had corneal stromal opacity as other reports[20].As we known, corneal scarring is a deposit of amorphous collagen of keratocytes that has transformed into myofibroblasts, and so called haze is the product of disruption and death of keratocytes and as soon as the keratocytes repopulate that area, the cornea becomes homogeneously clear. Therefore we think this kind of corneal stromal opacity was termed haze because it was transient. However, this kind of haze was in the deep stromal, which was different with the PRK, the latter within a depth of 60μm under the corneal epithelium. Also, the postoperative best correct visual acuity data suggest that this haze did not seem to impair patient vision.

The evidence of this small series suggests that CXL appears to stabilise or partially reverse the progression of LASIK-induced keratectasia without apparent complication. We believe crosslinking should be performed in patients with progressive iatrogenic keratectasia as early as possible to prevent a

further deterioration. As an non-random, non-comparative, single-centre study, the present preliminary study is subject to limitation. However, the results are promising and suggest that it would be worthwhile to further investigate this procedure in iatrogenic ectasia after corneal refractive surgery. If CXL effect turns out to be stable over a longer period, the procedure could be combined with intracorneal ring or customized corneal surface refractive ablation to partially correct the refractive error of patients with keratoconus [21].

Previous studies from Koller et al[22] showed similar results. Koller et al found significant improvement in 4 of 7 Pentacam topography indices (central keratoconus index, keratoconus index, index of height asymmetry, and minimum radius of curvature) 1 year after CXL.

No serious complications were reported during the follow-up period, apart from an early corneal haze, which disappeared within 6 months after CXL**.**

Conclusion

Corneal ectasia is a serious vision-threatening complication of laser in situ keratomileusis (LASIK). It is associated with progressive corneal steepening, an increase in myopia and astigmatism, and decrease in visual acuity. Ectasia after LASIK can be arrested by CXL with stabilization of BCVA crosslinking should be performed in patients with progressive iatrogenic keratectasia as early as possible to prevent a further deterioration.

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