

Crosslinking a promising approach

Technique yields improved visual and topographic outcomes in keratoconus and ectasia

By Lynda Charters

Reviewed by Peter S. Hersh, MD

Teaneck, NJ—Corneal collagen crosslinking (CXL) is an effective treatment for improving uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA), and average and maximum K values. Patients with keratoconus seemed to fare better with more improved topography values compared with patients with ectasia.



Dr. Hersh

These are important findings considering the sequelae of keratoconus and ectasia,

which include irregular astigmatism, progressive myopia, or visual impairment secondary to stromal scarring.

Take-Home Message

Corneal collagen crosslinking is an effective treatment for improving the uncorrected distance visual acuity, the corrected distance visual acuity, and the average and the maximum K values. Patients with keratoconus fared better with more improved topography values compared with patients with ectasia.

In addition, optical aberrations can result from the progressive distortion of the cornea in both disorders, making rigid or complex-curvature contact lenses, rather than spectacles, necessary to provide patients with good vision. Despite this, patients can become contact lens-intolerant over time with progressive corneal distortion, according to Peter S. Hersh, MD, and co-authors Steven A. Greenstein and Kristen L. Fry, OD, MS. The investigators recently published the details of their study (*J Cataract Refract Surg.* 2011;37:149-160).

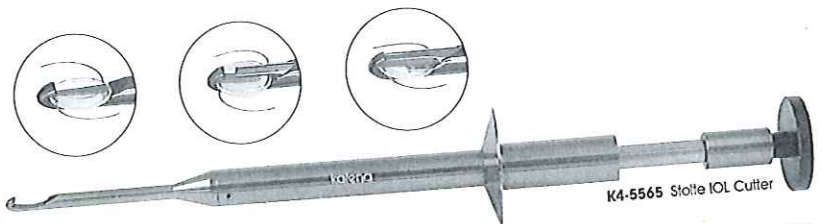
Treatment with CXL includes administration of riboflavin (vitamin B₂) with ultraviolet-A (UVA, 365 nm), the interaction of which results in formation of reactive oxygen species that cause the formation of covalent bonds within and between collagen molecules.

The ultimate result is consequent biomechanical stiffening of the cornea, said Dr. Hersh, director, Cornea and Laser Eye Institute, Hersh

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IOL Explantation *just got easier!*

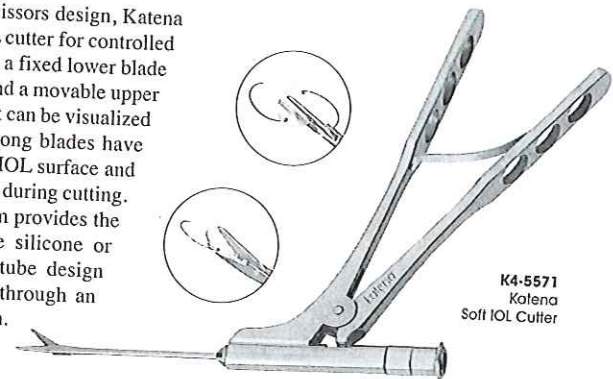
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Vision Group and the CLEI Center for Keratoconus, Teaneck, and clinical professor of ophthalmology, UMDNJ-New Jersey Medical School, Newark, NJ.

In their single-center analysis of a prospective, randomized, controlled clinical study, Dr. Hersh and colleagues analyzed the primary visual acuity and refractive and topographic outcomes in patients with keratoconus and post-LASIK ectasia during a 1-year period of follow-up. They also compared the results in the treatment groups with sham and fellow-eye control groups. The study was performed according to the guidelines of the FDA and approved and monitored by an investigational review board.

The patients in the treatment group (58 patients, 71 eyes) underwent standard UVA-riboflavin 0.1% CXL with removal of the corneal epithelium. Forty-nine eyes had keratoconus and 22 eyes developed ectasia after LASIK. The sham control group (41 eyes, 28 eyes with keratoconus and 13 eyes with ectasia) was treated with only riboflavin 0.1% ophthalmic solution and the epithelium was not removed. The study also included a fellow-eye control group (30 eyes, 21 with keratoconus and nine eyes with ectasia) that included patients who did not undergo bilateral crosslinking.

Study results

The authors reported that the UDVA in the groups treated with CXL improved significantly from 0.84 logMAR \pm 0.34 (standard deviation) (20/137) at baseline to 0.77 \pm 0.37 logMAR (20/117) ($p = 0.04$) at the 12-month examination. The UDVA improved by two or more Snellen lines in 18 eyes (25.4%), and six eyes (8.5%) lost two or more Snellen lines of UDVA.

The CDVA also improved significantly in the groups treated with CXL from 0.35 \pm 0.24 logMAR (20/45) at baseline to 0.23 \pm 0.21 logMAR (20/34) ($p < 0.001$) at the 12-month examination. Fifteen patients (21.1%) gained and one patient (1.4%) with ectasia lost two Snellen lines of CDVA. When the groups were analyzed separately and the time course of improvement analyzed, the mean CDVA in the keratoconus subgroup began to improve between 1 and 3 months after treatment (mean change, -0.07 ± 0.14 logMAR; $p = 0.001$) and then between 3 months and 6 months (mean change, -0.06 ± 0.12 logMAR; $p < 0.001$), and finally plateaued between 6 months and 12 months postoperatively (mean change -0.01 ± 0.11 logMAR; $p = 0.70$), the investigators

reported. The ectasia group, although showing a significant improvement in CDVA at 1 year over baseline, did not show significant interval changes between individual time points.

The maximum K value decreased significantly ($p < 0.001$) from baseline by 1.7 ± 3.9 D, 2.0 ± 4.4 D ($p = 0.002$), and 1.0 ± 2.5 D ($p = 0.08$), respectively, in the entire cohort, the keratoconus subgroup, and the ectasia subgroup, respectively. The maximum K values decreased by 2 D or more in 22 patients (31.0%) and increased by 2 D or more in three patients (4.2%). The other 46 patients remained stable over the time course of the study.

The average K value in the entire cohort decreased significantly (-1.10 ± 2.39 D; $p < 0.001$) from baseline to 12 months postoperatively. The keratoconus subgroup had a 1.50-D decrease in the mean average K value between preoperatively and 12 months postoperatively ($p < 0.001$). In the ectasia subgroup, the mean decrease of 0.3 D from baseline to 12 months postoperatively was not significant ($p = 0.22$).

In the sham treatment group, the UDVA significantly improved at 1 month (mean change, -0.09 ± 0.26 logMAR; $p = 0.03$) and 3 months after treatment (mean change, -0.08 ± 0.23 logMAR; $p = 0.03$) and the flat K value significantly improved between baseline and 3 months (mean change, 0.54 ± 1.65 D; $p = 0.04$). The cause of these improvements was unclear.

In the fellow-eye control group, there were no significant changes in the primary parameters evaluated. There was a significant increase in the manifest astigmatism (mean change, 0.34 ± 0.82 D; $p = 0.03$) at 12 months. The treatment group, as well as both the keratoconus and ectasia subgroups, showed a significant improvement compared with the fellow-eye control group in both CDVA and improvement in maximum K at the 1 year follow-up examination.

Study insights

According to the investigators, this study had some interesting factors.

“Unique to this investigation are the comparisons of the treatment group with a sham control group and a fellow-eye control group, an analysis of the postoperative time course of the CXL-mediated clinical changes, as well as an analysis of these patients as an entire cohort and individually within their respective keratoconus or ectasia subgroup,” they said.

Dr. Hersh and colleagues noted that only one eye lost 2 lines of CDVA, from 20/100 to 20/160. The loss “did not appear directly related to refractive error or change in corneal topography.”

Similarly, there was no clear factor related to the continued progression of the maximum K value in the three eyes in which the maximum K increased 2 D.

Dr. Hersh and co-authors are attempting to determine the preoperative predictors in patients in whom visual acuity either improved or decreased significantly following CXL as well as those in whom keratometry significantly either improved or worsened. The results of their multivariate analysis will be presented shortly.

The investigators also observed that the changes in the parameters evaluated in the study “seem to follow a reproducible time course after treatment. In general, the visual acuity and corneal steepness worsen somewhat at the 1-month time point. This is likely a result of both epithelial and stromal healing and remodeling. Resolution to baseline occurs by about 3 months, with improvement thereafter. This is similar to the clinical time course of CXL-associated corneal haze, which we reported elsewhere.”

In that study, the postoperative haze peaked at 1 month, plateaued at 3 months, and then decreased from 3 to 12 months. It appears, according to Dr. Hersh, that the stromal and epithelial healing after CXL continues over months along with the changes in the clinical outcomes.

“Clinical studies worldwide have shown that CXL offers a promising approach to stabilize the keratoconic and ectatic cornea,” he said. “Our hope is that crosslinking will decrease progression of the disease process and avoid the need for corneal transplantation in many patients in the future.

“Further studies should continue to elucidate the advantages and disadvantages of this procedure,” Dr. Hersh concluded. **OT**

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