Is CXL an Alternative to Keratoplasty?

CXL may postpone or prevent corneal transplantation in patients with progressive keratoconus or pellucid marginal degeneration.

BY JOSEF REITER, MD

Corneal collagen crosslinking (CXL) is a promising new procedure with a low risk profile. After a few days of moderate discomfort and weeks of reduced visual acuity and glare, CXL offers the chance for stabilization of biomechanically and/or biochemically impaired corneas. In many cases, patients notice an improvement of UCVA, BCVA, and contact lens tolerance. But can it be an alternative to keratoplasty? It is my belief that the answer to this question is yes.

Between March 2007 and November 2008, we used CXL to treat 64 eyes with progressive keratoconus and 13 eyes with pellucid marginal degeneration (PMD). We used the CXL protocol developed by Seiler and Spoerl and confirmed by others, defining progressive keratoconus (Figure 1) or PMD as the worsening of refraction, visual acuity, and/or corneal topography within 6 months to 1 year.

Average patient age was 41.5 years (range, 14–82 years). We used general anesthesia in six patients, four of whom were less than 16 years of age and two of whom had Down syndrome; topical anesthesia was used in all other patients. Six- and 12-month follow-up are available for 41 and 19 eyes, respectively.

SURGICAL TREATMENT

In each case, we followed the same surgical protocol. Pretreatment began 2 days before surgery, with topical ofloxacin (Floxal; Bausch & Lomb, Rochester, New York) four times daily and 400 mg of systemic ibuprofen (Dolormin Extra; McNeil GmbH & Co, Düsseldorf, Germany) three times daily. We used ultrasound pachymetry to locate the central and thinnest point. We then removed 8 mm of the central epithelium using an Amoils brush. Ultrasound pachymetry was also performed on the residual bed (central and thinnest points) every 10 minutes.

For CXL, riboflavin 0.1% drops were applied every 2 minutes for 30 minutes. If the stromal depth was more than 400 µm, we used riboflavin 0.1% in 20% dextran 500; if it was less than 400 µm, we used riboflavin 0.1% in saline solution. Double-distilled water was also used to achieve corneal swelling if the stromal depth was less than 400 µm before irradiation. Afterward, 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: 365 nm, 3mW/cm², 5.4 j/cm², with limbal protection. Chilled balanced saline solution was applied, along with cyclopentolate, ofloxacin, and a bandage contact lens.

Patients were given cyclopentolate on the first postoperative day and prescribed tobramycin/dexamethasone/ofloxacin (Floxal; Mann Pharma, Berlin, Germany) four times daily until the bandage contact lens was removed. Patients were also asked to use Opti-Tears (Alcon Laboratories, Inc., Fort Worth, Texas) every 15 minutes until the contact lens was removed. If needed, proparacaine 0.5% could be used every 2 hours. Systemically, patients were given 100 mg sumatriptan in the operating room, 8 hours later, and then daily for 3 postoperative days. Patients were also asked to take ibuprofen 400 mg and methylprednisolon 8 g, both three times daily for 3 days.

After epithelial closure, fluorometholone eye drops were prescribed four times daily for 4 weeks. Patients were asked not to wear contact lenses for 4 weeks and were seen daily.
until contact lens removal and 1 week, 1 month, 3 months, 6 months, and 1 year thereafter.

Figure 2 shows four typical cases in which corneal dehydration occurred within the first 10 minutes, even after application of the hypotonic riboflavin 0.1% in saline solution. Rehydration was achieved with double-distilled water. This stresses the need to monitor corneal thickness at its thinnest point before irradiation to avoid the hazard of UV-A light on endothelial cells.

Pachymetry must be repeatedly performed during application of the isotonic riboflavin solution. Figure 3 shows a case of bullous keratopathy that reveals dehydration from 750 µm to 520 µm before UV-A light application.

**RESULTS**

There was no loss of endothelial cells (Figure 4) and no loss of UCVA or BCVA in patients whose follow-up extended to 12 months. Additionally, most eyes experienced substantial gains in UCVA and BCVA, with an average gain of two lines in 32 eyes with a documented follow-up of 6 or more months (Figure 5). Average gain of UCVA in this group was 0.11, and BCVA improved from 0.37 to 0.53.

Corresponding to the positive change of UCVA and BCVA, we found a 1.56 D reduction of myopia. Probably due to regularization of the cornea (Figure 6), subjectively accepted cylinder was higher after CXL in many cases. The underlying reason for the positive changes in visual acuity and refraction is the observed corneal flattening, as shown by the reduction of maximum and minimum keratometry values.

Complications were found in nine of 82 eyes. Two eyes lost one line of UCVA, and one eye lost one line of BCVA. Additionally, four eyes had prolonged central Descemet’s folds and stromal edema up to 12 weeks (Figure 7). Further follow-up of the eyes did not show reduction of endothelial cells. Kohlhass’ described a similar observation, discussing another mechanism responsible for this reaction, interface edema following CXL. In five eyes, peripheral corneal infil-

**TAKE-HOME MESSAGE**

- CXL may be an acceptable alternative to keratoplasty in some patients.
- Before irradiation, the surgeon must monitor corneal thickness at its thinnest point.
- Pachymetry should be performed repeatedly throughout riboflavin application.
Central plaque, recurrent herpetic keratitis (which resolved), and bullous keratopathy were each seen in one patient.

CXL may postpone or prevent corneal transplantation in some patients with keratoconus or PMD. Fewer donor corneas will be needed for unavoidable transplantation, and waiting lists will be reduced.

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