Corneal Collagen Crosslinking: Patient Selection

In selected cases, patients with keratoconus can benefit from this treatment.

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Experience indicates that corneal collagen cross-linking (CXL) is an effective method for stabilizing keratoconus and is particularly suitable for mild forms of progressive keratoconus. In many cases, mild keratoconus can be managed with glasses and contact lenses. However, glasses are not useful in patients with irregular astigmatism due to keratoconus, and not all patients can tolerate rigid gas permeable contact lenses; it is in these patients that CXL can be effective in arresting keratoconus progression.

Standalone CXL is not a refractive procedure. Patients with advanced keratoconus failing spectacle and hard contact lens rehabilitation are not suitable candidates for CXL because this treatment is not designed to achieve a refractive adjustment. The correct therapy in these cases is one that produces significant flattening of the cornea, such as intrastromal corneal ring segment (ICRS) implantation. The changes in corneal structure induced by such additive technologies can be roughly predicted by Barraquer’s law of thickness: When you add material to the periphery of the cornea or remove an equal amount of material from the central cornea, you achieve a resultant flattening effect. With CXL, we do not add any material to the periphery or remove central corneal tissue for flattening.

CXL is most useful in eyes with mild or early moderate progressive keratoconus with low myopia and astigmatism and with corneal thickness of at least 400 µm.

**Managing Early Keratoconus**

The onset of keratoconus typically occurs during adolescence and is progressive until patients are in their 30s or 40s. When the disease becomes advanced, spectacles are often not indicated due to the presence of irregular astigmatism. During a patient’s adolescence, the most active time of life, it is probable that he or she may not be tolerant of hard contact lenses. Additionally, contact lens wear can cause corneal warp-age, allergic reactions, dry eye, and infection. These are especially bothersome to young patients, who desire minimal-risk procedures that produce high-quality vision, rapid rehabilitation, and minimal discomfort and pain. Therefore, CXL is a helpful alternative technique in children or teenagers with early keratoconus who are intolerant to rigid gas permeable contact lenses and have clear central corneas.

The results of CXL are still under investigation, and there are not yet enough data regarding patient selection and predictability. Although clinical experience indicates that CXL is an alternative, minimally invasive, irreversible method for the treatment of mild or moderate keratoconus, it cannot replace the need for ICRS implantation and penetrating keratoplasty in patients with more advanced forms of the condition. Patients

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**Take-Home Message**

- Young patients with early progressive keratoconus, low myopia, and good visual acuity are suitable candidates for CXL.
- In severe keratoconic eyes with low visual acuity, high myopia, and irregular astigmatism, ICRS implantation will be more effective, as it provides refractive correction. In select cases, ICRS implantation can be combined with CXL.
should be informed that CXL is under investigation and may not satisfy the needs of individuals who have high expectations.

SEVERE KERATOCONUS

In eyes with severe progressive keratoconus, high myopia, and high irregular astigmatism, visual rehabilitation is a challenge, and treatment should always involve stabilization of the cone and correction of the refractive error by optical or surgical means. Stabilization of the cone is essential to obtain long-lasting refractive correction and provide the patient with functional vision.

One option for treatment in patients with keratoconus and high myopia is the combination of CXL and contact lenses or phakic IOLs. In the presence of significant irregular astigmatism, another option is performing ICRS implantation combined with CXL to regularize the anterior corneal surface, thereby decreasing irregular astigmatism and improving visual acuity. CXL can be performed simultaneously or sequentially with ICRS implantation. In patients who undergo ICRS implantation for more advanced forms of keratoconus, the addition of CXL may enhance the flattening effect of the implant. The optimal timing of CXL in relation to the insertion of the ICRS has not yet been determined; however, it seems logical to implant the ring segments first, wait several months to allow the effect of the segments to stabilize, and then perform CXL.

In severely keratoconic eyes, I prefer simultaneous combined treatment with CXL and ICRS, injecting riboflavin directly into the corneal stroma through the corneal channel. With this approach, removal of corneal epithelium may not be necessary to increase riboflavin penetration, which is important for CXL effectiveness. This can be beneficial for eyes with thin corneas.

In keratoconic patients with high myopia, the efficacy of ICRSs can be enhanced by combining CXL with ICRS implantation. In these cases, CXL adds rigidity and strength to the cornea and in some cases stops the progression of keratoconus after ICRS implantation.

CXL can also be performed to reverse the progression of LASIK-induced iatrogenic keratectasia, as CXL with riboflavin and ultraviolet-A has been shown to increase biomechanical stability of the cornea.

CONTRAINDICATIONS

ICRS implantation is contraindicated in patients with very thin corneas. Therefore, in these cases, only transepithelial CXL should be performed. The concern with leaving the epithelium intact is inadequate penetration of riboflavin. However, an important point to remember is that the thickness of the epithelial layer is not uniform over the entire keratoconic cornea; it is thinner over the cone area, with a thicker annulus around the cone. Additionally, these patients receive medicated drops every 2 to 3 minutes, which may result in damage to the epithelial junctions, allowing easier penetration of riboflavin and epithelial edema. This will cause corneal thickening in thin corneas (less than 400 µm).

Patients with keratoconus who have corneal scarring and are older than 35 years are not suitable candidates for CXL, as corneal elasticity decreases with age and disease progression is affected by age-related corneal biomechanical changes.

CONCLUSION

CXL stabilizes keratoconus and induces flattening of the cornea, but, when performed alone, it is not a refractive procedure. In my practice, severely keratoconic eyes with low visual acuity, high myopia, and high irregular astigmatism are not suitable for CXL as a standalone procedure. In severely keratoconic eyes, ICRS implantation is more effective, as it provides refractive correction, and this may be combined with CXL in select cases. Young patients with early progressive keratoconus, low myopia, and good visual acuity are good candidates for CXL treatment.