

The Risks of CXL

Although rare, complications can cause stromal scarring and corneal edema, which have the potential to decrease postoperative visual acuity.

BY R. DOYLE STULTING, MD, PhD

Corneal collagen cross-linking (CXL) with riboflavin and ultraviolet light is generally accepted outside the United States as a safe and effective treatment for ectatic corneal disease and other indications.¹ Complications of the procedure are rare, with rates of visually significant complications reported to be approximately 3%.² Most of the reported complications relate to the removal of the epithelium. They include sterile infiltrates, infectious keratitis, nonhealing epithelial defects, corneal melting, and diffuse lamellar keratitis.³ Each of these complications has the potential to leave the patient with stromal scarring that can reduce postoperative vision, but a loss of BCVA after CXL is rare.^{2,3}

INFECTIOUS KERATITIS

Infectious keratitis probably occurs when microbes that are normal, transient inhabitants of the ocular surface replicate on the exposed stromal surface after CXL but before re-epithelialization. It is unlikely that infection occurs at the time of CXL because the procedure is toxic to microbes, just as it is toxic to corneal stromal cells. In fact, CXL has been used as a treatment for microbial keratitis that is recalcitrant to medical therapy.⁴ Microbial keratitis has been reported with various bacteria and acanthamoeba.^{4,5} Surgeons can probably minimize these potential complications with prophylactic topical antimicrobial therapy and frequent examinations until the epithelial defect closes.

CORNEAL HAZE

Appearing immediately after treatment and generally fading 6 to 12 months after treatment, corneal haze and a faint lamellar scar are normal findings after CXL. Typically appearing at a depth of 40% to 60% of corneal thickness, the lamellar scar—commonly called a *demarcation line*—is thought to represent the interface between the anterior stroma, where cross-linking

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takes place, and the deeper stroma, where it does not.⁶ Anterior stromal haze and the demarcation line are not visually significant.

ENDOTHELIAL CELL DAMAGE

Another possible complication of CXL is endothelial cell damage. Cytotoxic effects from the interaction of ultraviolet light and riboflavin have been estimated to extend to a depth of approximately 250 μm for keratocytes and 350 μm for endothelial cells when the surface irradiance is 3 mW/cm^2 .⁷ As a result, CXL is not recommended for corneas thinner than 400 μm .⁷ To comply with these guidelines, some surgeons have increased stromal thickness with hypotonic riboflavin solutions, by means of artificial tears, or simply by allowing the patient to sit with closed eyes. Despite this general knowledge and these precautions, both transient and permanent corneal edema have occurred after CXL.⁸

VISUAL LOSS

There is some evidence that complications resulting in visual loss are more common in patients over 35 years of age and eyes with a BSCVA of 20/25 or better.²

THE FUTURE

Much of the effort to improve the outcomes of CXL is directed toward reducing the incidence of vision-

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threatening complications. One method is to avoid epithelial removal, because most of the significant complications of CXL (infectious keratitis, noninfectious infiltrates, persistent epithelial defects, and resultant corneal scarring) are attributable to the transient absence of the epithelium. Improvements include the addition of enhancing substances such as benzalkonium chloride, ethylenediaminetetraacetic acid, and tris hydroxymethyl aminomethane to increase the epithelium’s permeability to riboflavin temporarily.⁹ Iontophoresis and specific permeability-enhancing molecules may facilitate the entry of riboflavin into the stroma in the future. Further improvements may include more rapid treatment protocols that use greater light energy for shorter periods of time, localized treatment of ectatic areas of the cornea, greater control of the depth of treatment, and better selection of appropriate patients for the procedure.

CONCLUSION

CXL is a procedure with the potential to treat corneal diseases that now have no effective treatment. Complications are rare, and when they occur, patients typically retain their vision. ■

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