Collagen cross-linking as an adjunct for repair of corneal lacerations: A cadaveric study

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ABSTRACT ●

Objective: To determine the efficacy of collagen cross-linking (CXL) as an adjunct to suturing in the repair of corneal lacerations.

Methods: A cadaveric study was undertaken in which a linear 5 mm corneal laceration was created in the central cornea of 20 eyes. The eyes were then randomized to receive 1 (n = 8), 2 (n = 8), or 3 (n = 4) standard corneal sutures. The burst pressure of the wound was then measured. All eyes in the 1- and 2-suture group then underwent standard CXL, with burst pressure repeated afterward.

Results: The initial wound burst pressure in the 1-, 2-, and 3-suture groups was 54.9, 74.0, and 201.2 mm Hg, respectively. After CXL, wound burst pressure increased by a mean of 3.2 and 62.3 mm Hg in the 1- and 2-suture groups, respectively. This change was statistically significant in the 2-suture group ($p = 0.017$). After CXL, the 2-suture group still had a significantly lower burst pressure compared with the 3-suture group ($p = 0.011$).

Conclusions: The study highlights a potential novel application for CXL to strengthen corneal wounds. Provided that suture density is sufficient to appose the wound edges, CXL may result in short-term wound strengthening. This could potentially allow for decreased corneal suture density and a corresponding decrease in suture-related complications.

A penetrating globe injury is a potentially devastating condition characterized by loss of the structural integrity of the eye and often prolapse of and/or damage to intraocular structures. The gold standard treatment of penetrating injuries is prompt closure in an operating room setting to reposition prolapsed tissue and suture the wound closed.[1] Urgent primary repair is critical to reduce the risk of complications such as endophthalmitis, suprachoroidal hemorrhage, epithelial ingrowth, tissue necrosis, and loss of the eye.[2–4]

In the setting of corneal lacerations, meticulous repair is critical given the importance of a clear, regular surface for visual rehabilitation. Although sutures are effective, they themselves do not participate in healing and may induce damage to various layers of the corneal tissue.[5] In the long term, sutures can result in a number of undesirable complications, including vascularization, infection, and inflammation, all of which may result in corneal scarring.[6–9] Because of the high refractive power of the cornea, even small changes in surface contour from corneal scarring or suture tension may result in irregular astigmatism and decreased visual acuity.[3]

Considerable research has been undertaken to study alternatives to corneal sutures. For example, cyanoacrylate glue is frequently used to repair small lacerations or melts of the cornea.[10,11] Although fast and technically simple, these adhesives are not suitable for repairing larger lacerations because they require a dry surface, result in surface irregularity, and are opaque. More recently, studies have reported on the use of biodendrimer adhesives to close large simulated corneal lacerations.[6,7] These biodendrimers are large macromolecules that polymerize after exposure to a laser.[5] Although shown to be effective in various models and with potentially less toxic effects compared with cyanoacrylate, they have not been widely accepted into clinical practice.

Since 2003, collagen cross-linking (CXL) has been used as a treatment for corneal ectatic conditions to strengthen the cornea and reduce disease progression.[12–17] In brief, CXL involves the application of UVA light to activate riboflavin (vitamin B2) and induce covalent bonding between collagen fibrils through the creation of reactive oxygen species.[18,19] This results in an increase in rigidity and strength of the cornea, which is evident immediately after treatment.[20] Other corneal changes include apoptosis of keratocytes, resistance to enzymatic degradation, and an increase in collagen fibre thickness.[21–25] CXL has also been used for several off-label uses, including infectious keratitis, bullous keratopathy, corneal melting, and filtering bleb leakage.[26–29]

Although not suitable as a sole treatment for repair of corneal wounds, CXL has been proposed as an adjunct to corneal suturing to increase short- and long-term wound strength. In 2011, Rocha et al. reported results of a cadaver study in which human corneoscleral rims underwent penetrating keratoplasty with or without CXL.[30] In the eyes that underwent CXL, burst pressure was over 30 mm Hg greater compared with the group without CXL.

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Despite using a cadaver model, the effects of CXL were seen on electron microscopy as bridged areas across the wound, attachment plaques, cross-linked fibers, and plasmalemmal densities.[30]

To our knowledge, no study has evaluated CXL as an adjunct to corneal suturing in the setting of a traumatic corneal laceration. The objective of our study was to determine if adjunctive CXL results in increased wound strength in a cadaver model, with the goal of reducing the number of required sutures without compromising integrity of the wound.

Materials and Methods

We conducted a cadaveric bench study to compare wound strength with and without CXL with various suture spacing repairing a standardized corneal laceration. The study was conducted at a research laboratory at Queen's University in Kingston, Ontario. Ethics approval was obtained from Queen's University Ethics Review Board.

To simulate a traumatic corneal laceration, we created a full-thickness linear 5 mm wound in the central cornea using a keratome blade perpendicular to the surface. Based on initial trials, we found that 3 properly placed sutures in the wound resulted in a stable closure that usually burst open only when IOP rose high enough (above 200 mm Hg) to break the sutures. The placement of both 1 and 2 sutures in the wound resulted in a sealed wound that leaked without suture breakage when IOP was increased.

Twenty fresh cadaveric human eyes from the Canada Eye Bank were acquired for the study. Based on our initial trials described, eyes were then randomized to receive 1 suture (n = 8 eyes), 2 sutures (n = 8 eyes), or 3 sutures (n = 4 eyes). All study measurements were performed under an operating microscope with high-definition video recording throughout the study.

Cadaver eyes were first carefully inflated by injection of balanced salt solution (BSS) via a 30-gauge needle into the midvitreous. The eyes were then centred and secured on a mount without the use of vacuum and de-epithelialized using a Weck-cel sponge. We then inserted a short 25-gauge needle attached to flexible tubing through the limbus into the anterior chamber to use as an infusion port during the study (Fig. 1). The anterior chamber was gently filled with BSS.

To measure IOP, we used a cardiac transducer device (Carescape Monitor B850; GE Healthcare, Milwaukee, Wis.) inserted into the midvitreous via the equator of the eye. Our technique was similar to previous reports in the ophthalmologic literature.[6,30] The transducer provided real-time and accurate digital IOP and displayed a waveform that was continually recorded during the study (Fig. 2).

Both the infusion and IOP monitoring devices were carefully adjusted and secured so as to not induce torque

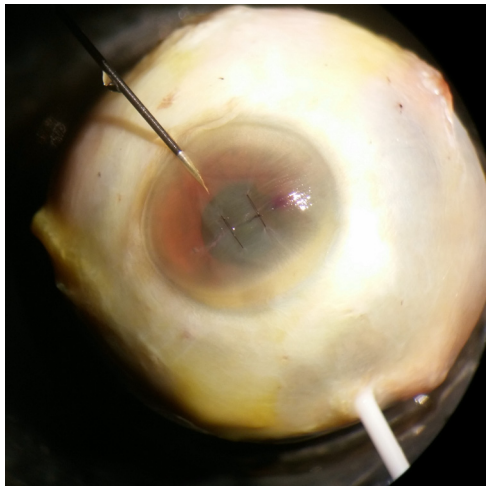

Fig. 1—Cadaveric eye with corneal perforation suture repair, intravitreal cardiac transducer, and anterior chamber infusion cannula.

or force on the eye. Throughout each trial, the intravitreal pressure transducer and limbal infusion catheters were examined to ensure a watertight seal. We then used calipers to measure a 5 mm line in the central cornea perpendicular to the infusion port entry. A fresh 2.75 mm keratome was then used to create a full-thickness central corneal laceration 5 mm long and perpendicular to the surface.

Repair of the wound was then completed according to group allocation using 1, 2, or 3 simple interrupted 10-O nylon sutures (slip knot, nonburied) by a single staff ophthalmologist trained in corneal surgery (D.J.). After sutures were completed, the anterior chamber was filled to a physiologic IOP of 20 mm Hg and the wound was tested to ensure that there was no leakage.

Under direct visualization through an operating microscope and blinded to the IOP waveform, BSS was slowly injected into the anterior chamber via a 3 mL syringe. This was continued until egress of fluid was seen from the

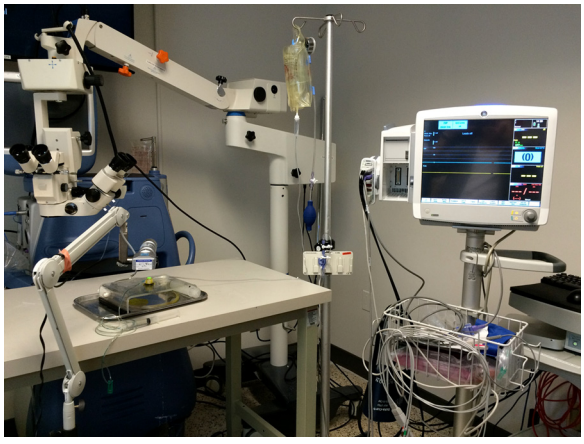

Fig. 2—Laboratory setup with operating microscope, ultraviolet emitter, cardiac pressure monitoring system, and eye mount.