Polyethylene Glycol Hydrogel Polymer Sealant for Vitrectomy Surgery

An In Vitro Study of Sutureless Vitrectomy Incision Closure

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Objective: To test a novel hydrogel sealant to secure sutureless sclerotomies under variable intraocular pressure conditions.

Methods: In cadaver eyes, 23- and 20-gauge (G) sclerotomies were constructed. Sixteen 23-G beveled sclerotomies were constructed in 4 eyes: 8 of the incisions were treated with hydrogel sealant, while 8 were left bare. All sclerotomies were monitored for leaks while the intraocular pressure was elevated. The pressure on incision leakage was recorded as the leak pressure (maximum tested=140 mm Hg). Additionally, sixteen 20-G sclerotomies were constructed in 4 other eyes: 8 of the incisions were treated with hydrogel sealant, while 8 were sutured. These incisions were similarly pressure tested.

Results: Among the 23-G incisions, hydrogel sealant application to the incisions significantly increased the leak pressure relative to bare incisions: mean (SE), 131.8 (8.2) mm Hg, respectively (P<.001). Only 1 of the 8 sealant-treated 23-G incisions leaked below 140 mm Hg, compared with all of the 8 bare incisions. Among the 20-G incisions, there was no difference in leak pressure among sealant-treated and sutured incisions: mean (SE), 140.0 (0.0) mm Hg, respectively (P=.35). None of the 8 sealant-treated 20-G incisions leaked below 140 mm Hg, compared with 1 of the 8 sutured incisions.

Conclusions: Hydrogel sealant significantly increased the leak pressure among 23-G incisions relative to 23-G bare incisions and was equivalent to suturing among 20-G incisions.

Clinical Relevance: Hydrogel sealants effectively close vitrectomy incisions and may decrease the incidence of postoperative endophthalmitis and hypotony.

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METHODS

Eight fresh, intact, human whole globes were obtained from the Michigan Eye Bank. Each eye was analyzed for the absence of conjunctiva. The experimental setup consisted of a 16-G needle (BD 305197; BD, Franklin Lakes, New Jersey) under the operating microscope. The incisions were made in 2 of the quadrants, fashioned 4 mm posterior to the limbus. After removal of the vitreous cutter and cannula, the IOP was slowly elevated and the IOP at which the incisions leaked was recorded by observing for fluid leak with a Weck-Cel Sponge (Medtronic, Minneapolis, Minnesota) to seal ocular incisions. Tissue fibrin glue (TissueL; Baxter AG, Vienna, Austria) has been used as an alternative to sutures in a small surgical case series for closure of MIVS and 20-G vitrectomy incisions.8 Fibrin glue carries the theoretical risk of anaphylaxis and disease transmission.11

Synthetic polymers such as polyethylene glycol (PEG) hydrogel polymers are safe and biocompatible. These compounds can be engineered to form hydrogels of varying absorption, consistency, and flexibility depending on the indication of use. We designed a study to test the utility of a PEG polymerizable adherent synthetic hydrogel ocular bandage (Ocular Therapeutix, Inc, Bedford, Massachusetts) to seal sutureless 23-G vitrectomy incisions as well as to test its integrity for sealing 20-G vitrectomy incisions that have traditionally been closed with sutures.

RESULTS

GROUP A

Group A included sixteen 23-G MIVS incisions from 4 eyes. Sclerotomy sites sealed with hydrogel were compared with bare (ie, without hydrogel) sclerotomy sites. All 8 bare incisions leaked with increasing IOP. The mean (SE) IOP at which the bare incisions leaked was 39.5 (5.2) mm Hg (Table). One hydrogel-treated 23-G incision leaked at 74.2 mm Hg, while the remaining 7 incisions sustained pressures of up to 140 mm Hg without leakage for a mean (SE) leak pressure of 131.8 (8.2) mm Hg (P < .001).

GROUP B

Group B included sixteen 20-G sclerotomy incisions from 4 eyes. Sclerotomy sites closed with sutures were com-
The hydrogel sealant demonstrated a secure, watertight sealing effect for sutureless 23-G vitrectomy incisions as well as 20-G vitrectomy incisions. In the setting of this in vitro experiment, equivalency to sutured wound closures was observed. Our laboratory experiment showed that the hydrogel seal was sufficiently strong and maintained ocular integrity at IOPs beyond those experienced by the globe during eyelid blinking, eye rubbing, coughing, or eyelid squeezing.12

The hydrogel sealant is formed by a reaction of esterification of PEG and trilysine. Polyethylene glycol is one of the most widely used polymers in the pharmaceutical industry in both solid and liquid forms owing to its water solubility and inert nature, and it is frequently used as a component in topical drug formulations. Many ophthalmic products including lubricant eye drops, ophthalmic corticosteroids, ocular decongestants, and artificial tears also contain PEG. The hydrogel consists of about 95% water, with the solids consisting of PEG cross-linked with trilysine. The link between each PEG and trilysine molecule contains a hydrolyzable segment. Thus, in the months following implantation, the hydrogel gradually weakens and then liquefies, releasing the individual PEG and trilysine molecules. This gel degradation process is solely dependent on the presence of water and is not affected by enzymes. Trilysine is a synthesis product of L-lysine, which plays an important role in the formation of collagen and is a naturally occurring essential amino acid. The PEG and trilysine molecules are rapidly absorbed and cleared from the body via renal filtration.

Using a foam-tipped applicator, a small drop of precursor is applied to the incision, where the liquid polymerizes (solidifies) within 30 seconds without producing heat. This hydrogel also contains a blue colorant (FD&C blue 1) that acts as a visualization agent to assist the surgeon in determining hydrogel thickness and the location of the application. The blue colorant diffuses from the gel within hours of application, leaving an optically clear, transparent, smooth, adherent, lubricious bandage over the incision. Because the components are not derived from animal or human products, there is no potential for viral transmission. Similar PEG-based in situ-forming hydrogels are approved as medical devices for use as dura mater sealants, lung sealants, and abdominopelvic adhesion barriers.13 These compounds have been engineered to form adherent hydrogel coatings of varying absorption, consistency, and flexibility depending on the indication for use.

The hydrogel has been shown to be nontoxic, nonirritating to the ocular surface, and nonsensitizing and demonstrates no acute systemic toxic effects. Following application, the hydrogel bandage adheres to the incision and then sloughs off as the underlying tissue heals. A separate study in a different set of eyes has tested the ability of the hydrogel bandage to prevent the entry of ocular surface fluid into sutureless incisions. The eyes in this study underwent histological processing. On microscopic examination, the hydrogel bandage was seen as a hematoxylin-stained covering over the ocular surface.14

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<th>Table. Data From 23- and 20-Gauge Incisionsa</th>
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<td>Incision</td>
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<td>A, 23-Gauge Incision</td>
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<td>Mean (SE)</td>
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a If no leak was detected at 140 mm Hg, testing was stopped and that value was recorded as the leak pressure.
b Two-tailed t test, P<.001.
c Two-tailed t test, P=.35.
Sutureless vitrectomy incisions have been shown to allow ocular surface fluid ingress.\textsuperscript{13,16} The absence of immediate postoperative closure as well as the architecture of the wound may predispose to postoperative endophthalmitis as well as early postoperative hypotony.\textsuperscript{17} More recently, injection of subconjunctival antibiotics at all incision sites in sutureless vitrectomy procedures has been proposed as there may be vitreous prolapse at these locations.\textsuperscript{18} However, a potential concern is the entry of high antibiotic concentrations into the vitreous cavity, which could be toxic to the retina, especially in the air- or gas-filled eye. Furthermore, it has been observed that gas fill after certain retinal procedures may be less than expected after MIVS as gas may leak out of a poorly constructed MIVS port. A sealant applied over these ports would ensure a secure seal, thereby possibly decreasing rates of endophthalmitis or hypotony and rendering sutures unnecessary. In our experience, the hydrogel is found to be elastic and conforms to the contour of the globe where it is applied. This feature may enhance patient comfort.

This laboratory experiment suggests that the hydrogel bandage may allow a secure and strong closure of sutureless 23-G vitrectomy incisions. Furthermore, future research may show that the hydrogel functions as a novel substitute for sutures in standard 20-G vitrectomy incisions. This technology is a significant step toward making sutureless incisions safer as it may prevent incision leakage as well as the entry of microorganisms into the eye.

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Author Contributions: Dr Singh had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Financial Disclosure: Dr Hariprasad has been a consultant for Allcon, Allergan, Genentech, Baxter, OD-OS, Ocular Therapeutix, Optos, and Bayer and has participated in speaker’s bureaus for Allcon, Allergan, and Genentech.

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REFERENCES