Comparison of Tensile Strength of Fibrin Glue, 2-Octyl Cyanoacrylate, Liquid Ocular Bandage, and Conventional Nylon 10-0 Sutures in Corneal Laceration Repair in an Animal Model

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ABSTRACT

Objective: To compare the tensile strength of fibrin glue, 2-octyl cyanoacrylate, and liquid ocular bandage to conventional nylon 10-0 sutures in sealing central linear corneal lacerations.

Methods: An experimental in-vitro study was performed on 74 porcine eyes. A 27-gauge needle connected to an infusion system with balanced salt solution was inserted into the anterior chamber and the bottle height was adjusted accordingly. Full-thickness central corneal lacerations were created using a 3.2 mm keratome knife for the initial incision and enlarged by a 5.2 mm knife. The wounds were sealed with fibrin glue (Tisseel®), 2-octyl cyanoacrylate (Dermabond®), liquid ocular bandage (OcuSeal™), and nylon 10-0 with 3 sutures. Tensile strength of the wounds was measured by recording the bottle height above the level of the porcine eyes before leakage was detected and this was converted to IOP values. One-way ANOVA and post hoc t-test were used to analyze the data.

Results: Mean maximum IOP where leakage was resisted for the nylon 10-0 suture group was 52.37 ± 7.16 mm Hg. The mean maximum resisted IOP for the fibrin glue, 2-octyl cyanoacrylate, and liquid ocular bandage was 46.34 ± 12.64 mm Hg, 55.13 ± 10.46 mm Hg, and 56.99 ± 8.27 mm Hg respectively. There was no significant difference between the sutures and all of the adhesives groups (p=0.08, p=0.34, and p=0.08) and between 2-octyl cyanoacrylate and liquid ocular bandage (p=0.57). 2-Octyl cyanoacrylate and liquid ocular bandage demonstrated higher mean IOP as compared to the fibrin group (p = 0.024 and p = 0.007).

Conclusion: Fibrin glue, 2-octyl cyanoacrylate, and liquid ocular bandage were shown to be effective in sealing 5.2 mm linear corneal lacerations, with 2-octyl cyanoacrylate and liquid ocular bandage being superior to the fibrin glue.

Keywords: corneal laceration, tissue adhesives, tensile strength, 2-octyl cyanoacrylate, fibrin glue, liquid ocular bandage

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Penetrating corneal lacerations resulting from trauma is an ophthalmologic emergency that has debilitating complications on vision. In a study done at a tertiary government hospital, corneal laceration alone accounted for 26.4% of anterior segment trauma (Jaca, unpublished report, 2009). Generally, meticulous tissue apposition by sutures is the technique of choice for repair of corneal lacerations. The use of sutures, however, has several limitations and disadvantages. Corneal suturing itself can induce additional trauma to tissues especially if multiple passes are needed. Significant irregular astigmatism can also occur due to uneven tension exerted by the sutures. Depending on the suture material and postoperative integrity (i.e. loose sutures), sutures can incite infection, inflammation, and vascularization, subsequently leading to corneal scarring. Timely postoperative removal is also required increasing the number of follow-up visits. Finally, effective suture placement necessitates prolonged surgical time and acquired technical skill affecting the visual outcome.

Tissue adhesives have been advocated as an alternative to sutures for wound closure. Two types of adhesives, synthetic (cyanoacrylate) and biologic (fibrin glue) sealants, have been widely used in various ophthalmic surgeries. Cyanoacrylate derivatives, because of their binding strength and tissue barrier capability, are currently indicated for treatment of small corneal perforations and progressive corneal thinning. It has also been in strabismus surgery, scleral buckle attachment, blepharoplasty, temporary tarsorrhaphy, punctal occlusion and corneal cataract incisions. One of the newer cyanoacrylate derivatives, 2-octyl cyanoacrylate, available as Dermabond® and marketed as a topical skin adhesive differs from existing cyanoacrylates. This derivative is more flexible and tissue compatible with less inflammatory reaction. 2-Octyl cyanoacrylate have been investigated for different ophthalmic applications.

Fibrin-based glue, originally developed for cardiovascular surgery, have also been utilized off label for ocular surgeries. Their use in corneal perforations, sutureless lamellar keratoplasty, amniotic membrane transplantation, and conjunctival autograft closure in pterygium surgery have been well documented. Being biologic in nature, fibrin glue is more biodegradable and biocompatible as compared to cyanoacrylate.

Recently, a new class of tissue adhesives – liquid ocular bandage, made of polyethylene glycol (PEG) hydrogel polymers, have been introduced and developed. These hydrogel polymers, with their high water content, is a safe and tolerable sealant for ocular tissues. Currently, there are two ocular bandages commercially available, Ocuseal™ (Becton, Dickinson and Company, Waltham, MA, USA) and ReSure Adherent Ocular Bandage™ (Ocular Therapeutix, Inc, Bedford, MA, USA). Both of these products have been used for wound closure in cataract surgery, but they are also investigated for other ophthalmic surgeries, such as penetrating keratoplasty, sutureless sclerotomy, and pterygium surgery.

There have been studies showing the adhesive properties of these tissue sealants in sealing corneal cataract incisions. However, the authors have not found any literature comparing these tissue adhesives in sealing corneal lacerations. This study compared the tensile strength of fibrin glue, 2-octyl cyanoacrylate, and liquid ocular bandage to conventional nylon 10-0 sutures in sealing full thickness central corneal linear lacerations in porcine eyes.

**METHODOLOGY**

Three commercially available adhesives were used for comparison in this study: (1) Fibrin glue (Tisseel®; Baxter Healthcare Corp., Westlake Village, CA, USA), consists of a kit containing four separate vials for reconstitution; (2) 2-Octyl cyanoacrylate (Dermabond®; Ethicon, Sommerville, NJ, USA), a single use applicator consisting of a crushable glass ampule within a plastic vial with an attached applicator tip; and (3) Liquid ocular bandage (OcuSeal™), packaged in two separate components containing the diluent and polyethylene glycol powder with a special brush tip applicator (Figure 1).

![Figure 1. Tissue adhesives used in the study: A) 2-Octyl cyanoacrylate, B) fibrin glue, and C) liquid ocular bandage.](image-url)
Freshly enucleated porcine eyes were used. The globes were mounted on polystyrene foam and the excess conjunctivae secured in all quadrants with pins. A 27-gauge needle connected to a balanced salt solution bottle (BSS; EuroMed Laboratories, Philippines) via an infusion system was inserted into the anterior chamber 3 clock hours away relative to the surgeon’s view and in a parallel direction to the iris plane. Applanation tonometry (Tonopen XL; Medtronic, Jacksonville FL, USA) was used to measure the intraocular pressure (IOP). The bottle height was adjusted accordingly using a modified pulley system to maintain an IOP of 18 to 22 mm Hg.

IOP was subsequently increased in a stepwise fashion by raising the infusion bottle height by increments of 10 cm, starting at 30 cm above the level of the porcine eyes. IOP was measured a few minutes after the bottle height was adjusted to allow the pressure to stabilize. Pressures taken for each bottle height for all porcine eyes were used to establish reference values. By this procedure, the maximum bottle height and IOP in this experimental set up was determined.

To simulate a corneal laceration, a 3.2 mm angled keratome knife (Slit Knife, Alcon Surgical, USA) was used to make an initial incision perpendicular to the central cornea under microscopic visualization (Figure 2). The wound was extended using a 5.2 mm angled knife (ShortCut® Implant Knife, Alcon Surgical, USA) creating a full thickness central linear laceration. A caliper was used to confirm the measurement of each laceration. IOP was taken after the corneal laceration was performed. All wounds were observed to leak spontaneously with subsequent flattening of the anterior chamber. Seidel test was done using a 1.0 mg fluorescein strip applied directly to the external surface of the wound to confirm the leakage. The test was considered positive if there was a change in the color of the fluorescein dye (from orange to green) accompanied by a gush of fluid. Once leakage was confirmed, infusion was discontinued and the surface of the wounds dried with cellulose sponges. An air bubble was injected reforming the chamber and displacing the remaining fluid.

All adhesives were prepared according to the manufacturer’s instructions. Fibrin glue was prepared by reconstituting the two components – fibrin and thrombin. The Tisseel kit contained four separate vials: sealer protein concentrate, fibrinolysis inhibitor solution, thrombin, and calcium chloride solution. All four vials were pre-warmed using a fibrinotherm device provided by the distributor. Sealer protein concentrate and thrombin were reconstituted in fibrinolysis inhibitor solution and calcium chloride, respectively. They were transferred to a separate 2 mL dual syringe system with a common plunger (Duploject). These two components of the fibrin glue were then applied simultaneously in equal amounts (one to two droplets each) and spread evenly along the entire length of the wound. The glue was allowed to dry for at least 5 minutes during which time the wound edges were kept apposed by placing a sponge near the wound site. Full polymerization occurred when the glue transformed into a translucent whitish plug (Figure 3).

2-Octyl cyanoacrylate (Dermabond®) was prepared by applying pressure at the midpoint of the vial to crush the inner glass ampule. With the applicator tip facing downwards, the vial was gently squeezed to express the liquid adhesive and moisten the applicator tip. One to two droplets of 2-octyl cyanoacrylate was applied in a similar manner and was spread evenly using a cellulose sponge. Polymerization was considered complete when there was a grayish-white solid film along the wound (Figure 4).

Liquid ocular bandage (Ocuseal™) was prepared by mixing the diluent and the polyethylene glycol powder in a rubber container with a special brush tip applicator. The container was shaken for 5 seconds, then squeezed allowing the hydrogel to pool at the tip of the brush. One to two droplets of liquid hydrogel was applied immediately and was spread evenly using its applicator at the wound site within 20 seconds after its preparation. Formation of a soft, semi-

Figure 2. A 3.2 mm keratome knife was used to create an initial incision perpendicular to the central cornea.
transparent gel indicated complete polymerization (Figure 5).

**Measurement of Tensile Strength**

Once the adhesives were completely polymerized, fluid was infused into the chamber to displace the air bubble. Anterior chamber was allowed to stabilize before the infusion bottles were slowly elevated in stepwise increments as previously described. Tensile strength of the wounds was measured by recording the bottle height before leakage was detected and this was converted to IOP values using the reference values previously determined. Seidel test was performed to detect the leakage and was confirmed by a masked observer.

Linear lacerations in the control group were closed with 3 simple interrupted nylon 10-0 sutures (Ethilon; Ethicon, Sommerville, NJ, USA) at 90% depth and approximately of equal length. The control group was subjected to the same trials as the adhesive group. Tensile strength for this group was also recorded.

**Statistical Analysis**

Data were described using means and standard deviations, frequency counts, and percentages. One-way analysis of variance (ANOVA) test, post hoc t-test, and Fischer's exact test for comparison between the groups were performed. A 95% confidence level was considered significant (p = 0.05).

**RESULTS**

A total of 74 porcine eyes were used in the study: suture group 20 eyes, fibrin glue 18 eyes, 2-octyl cyanoacrylate 20 eyes, and liquid ocular bandage 16 eyes.

The mean baseline IOP in an intact globe (before the laceration was created) was 65.35 ± 9.17 mm Hg at a maximum bottle height of 140 cm above the level of the eye. This was the maximum bottle height achievable; hence, the maximum attainable IOP in this experimental set-up. The baseline IOP measurements were essentially similar among the four groups (Table 1).

The mean IOP, measured immediately after the corneal lacerations were performed, was 4 mm Hg among the groups, which was the lowest pressure...
detected by the Tonopen XL. Under these conditions, all wounds were noted to leak spontaneously.

In the nylon suture group, which was the control in the study, the mean maximum IOP where leakage was resisted was 52.37 ± 7.16 mm Hg. The fibrin group showed the lowest calculated mean maximum resisted IOP while liquid ocular bandage showed the highest mean maximum IOP (Table 2). 2-Octyl cyanoacrylate and liquid ocular bandage adhesives demonstrated higher mean IOP as compared to the fibrin group (p = 0.024 and p = 0.007). There was no significant difference between the suture group and all of the adhesive groups. No significant difference was detected between 2-octyl cyanoacrylate and liquid ocular bandage groups (Table 3).

In the fibrin group, there was one eye that did not show leakage even at the maximum IOP attainable at this study. There were also 6 and 4 eyes that withstood leakage at the highest attainable IOP for the 2-octyl cyanoacrylate and liquid bandage groups, respectively (Table 4).

### Table 1. Baseline Intraocular Pressure (IOP) at Maximum Bottle Height of 140 cm in an Intact Globe*

<table>
<thead>
<tr>
<th>Group 1 Suture</th>
<th>Group 2 Fibrin</th>
<th>Group 3 2-Octyl Cyanoacrylate</th>
<th>Group 4 Liquid Ocular Bandage</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=20 (mmHg)</td>
<td>n=18 (mmHg)</td>
<td>n=20 (mmHg)</td>
<td>n=16 (mmHg)</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>65.4</td>
<td>69.5</td>
<td>63.8</td>
<td>62.7</td>
</tr>
<tr>
<td>SD</td>
<td>±8.5</td>
<td>±10.6</td>
<td>±9.7</td>
<td>±6.4</td>
</tr>
<tr>
<td>Range</td>
<td>53-85</td>
<td>51-87</td>
<td>53-88</td>
<td>51-78</td>
</tr>
</tbody>
</table>

* Before the corneal laceration was created

### Table 2. Mean Maximum IOP Before Leakage was Detected

<table>
<thead>
<tr>
<th>Group 1 Suture</th>
<th>Group 2 Fibrin</th>
<th>Group 3 2-Octyl Cyanoacrylate</th>
<th>Group 4 Liquid Ocular Bandage</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=20 (mmHg)</td>
<td>n=18 (mmHg)</td>
<td>n=20 (mmHg)</td>
<td>n=16 (mmHg)</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>52.4</td>
<td>46.3</td>
<td>55.1</td>
<td>57.0</td>
</tr>
<tr>
<td>SD</td>
<td>±7.2</td>
<td>±12.6</td>
<td>±10.5</td>
<td>±8.3</td>
</tr>
<tr>
<td>Range</td>
<td>42.7-65.4</td>
<td>33.8-65.4</td>
<td>33.8-65.4</td>
<td>42.7-65.4</td>
</tr>
</tbody>
</table>

### Table 3. Post hoc t-test for Comparison Between Groups

<table>
<thead>
<tr>
<th>Pair</th>
<th>Mean Difference</th>
<th>t score</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suture vs fibrin</td>
<td>+5.99</td>
<td>1.82</td>
<td>0.08</td>
</tr>
<tr>
<td>Suture vs cyanoacrylate</td>
<td>-2.75</td>
<td>-0.97</td>
<td>0.34</td>
</tr>
<tr>
<td>Suture vs liquid ocular bandage</td>
<td>-4.62</td>
<td>-1.80</td>
<td>0.08</td>
</tr>
<tr>
<td>Fibrin vs cyanoacrylate</td>
<td>-8.76</td>
<td>-2.34</td>
<td>0.02*</td>
</tr>
<tr>
<td>Fibrin vs liquid ocular bandage</td>
<td>-10.62</td>
<td>-2.86</td>
<td>0.007*</td>
</tr>
<tr>
<td>Cyanoacrylate vs liquid ocular bandage</td>
<td>-1.06</td>
<td>-0.58</td>
<td>0.57</td>
</tr>
</tbody>
</table>

*p = 0.05

### Table 4. Number and Proportion of Eyes with Leakage

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>With Leak</th>
<th>Without Leak</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>20</td>
<td>20 (100%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Group 2</td>
<td>18</td>
<td>17 (94%)</td>
<td>1 (6%)</td>
<td>0.007*</td>
</tr>
<tr>
<td>Group 3</td>
<td>20</td>
<td>14 (70%)</td>
<td>6 (30%)</td>
<td></td>
</tr>
<tr>
<td>Group 4</td>
<td>16</td>
<td>12 (75%)</td>
<td>4 (25%)</td>
<td></td>
</tr>
</tbody>
</table>

*p = 0.05

**DISCUSSION**

The search for the most suitable adhesive for sutureless ocular surgery is not entirely a novel idea. There have been several studies that investigated the sealing properties of currently available tissue sealants in various ophthalmic fields, especially corneal cataract incisions. In corneal wound repair, the goal of a tissue adhesive is to achieve a watertight seal that can be mechanically resistant to IOP. This study compared the tensile strength of different tissue adhesives, such as fibrin glue, 2-octyl cyanoacrylate, and liquid ocular bandage in a corneal laceration repair by increasing the infusion bottle height, thereby increasing the IOP.

Despite the fact that the fibrin group had the lowest mean maximum resisted IOP, there was no difference when compared to the conventional nylon suture group. When compared to the 2-octyl cyanoacrylate and liquid ocular bandage, fibrin glue showed significantly lower mean resisted IOP. Chen reported that the maximum IOP that can be withstood by fibrin glue in sealing a 2.5 mm corneal incision in rabbits eyes were similar to that sealed by a single nylon 10-0 suture. They also reported that fibrin glue had lower mean IOPs when compared to N-butyl cyanoacrylate and methoxypropyl cyanoacrylate. Banitt showed that fibrin adhesive demonstrated higher IOP compared to closure with single nylon 10-0 suture in a 3 mm clear corneal incision. However, when incisions were enlarged to 4.5 and 6 mm, mean leakage pressures
were similar to the suture group. When compared to N-butyl 2-cyanoacrylate, mean leakage pressure decreased significantly as the incisions increased in size.\(^\text{19}\) There are no current literature comparing fibrin glue to 2-octyl cyanoacrylate and liquid ocular bandage. This study demonstrated that fibrin glue is comparable to sutures but had a lower tensile strength as compared to 2-octyl cyanoacrylate and liquid ocular bandage. Fibrin glue sealant simulates the final stage of the coagulation cascade, producing a matrix similar to plasma clot. Fibrin cross-links with collagen in tissues, which explains the sealing effect of fibrin glue to collagen-rich tissues such as the cornea.

Cyanoacrylates have been used since the 1960’s for sealing corneal perforations. They have recently been advocated for corneal cataract incisions as well. In this study, 2-octyl cyanoacrylate has no significant difference in the mean maximum resisted IOP compared to both sutures and liquid ocular bandage. In a preliminary in vitro study to seal corneal cataract incisions, mean leakage pressures of 2-octyl cyanoacrylate (113.80 ± 31.20 cm H₂O) were comparable with the suture group (100.20 ± 31.19 cm H₂O).\(^\text{7}\) Their results were comparable to our study. Meskin also demonstrated that 2-octyl cyanoacrylate can be used as an effective and safe adhesive for closure of 2.75 mm clear corneal incisions.\(^\text{9}\) There were no studies comparing 2-octyl cyanoacrylate and liquid ocular bandage. 2-Octyl cyanoacrylate was formulated to correct some of the deficiencies of the shorter-chain cyanoacrylate derivatives. The slower degradation of the octyl derivatives may result in lower concentrations of the cyanoacrylate polymer by-products in surrounding tissues, resulting in less inflammation. It is more flexible, biocompatible, and has a higher 3-dimensional breaking strength compared to its cyanoacrylate predecessors.

In our study, liquid ocular bandage did not show significant difference with the suture group. In preliminary studies, biodendrimers showed higher leaking pressures compared to the suture group in sealing linear corneal lacerations. However, the biodendrimer adhesive in that study required a handheld argon laser probe to polymerize.\(^\text{1}\) Hovanessian reported that liquid ocular bandage could create a watertight seal with no ingress or egress of fluid when incisions were closed.\(^\text{18}\) Maddula showed that the mean leaking pressure of liquid ocular bandage was 198.1 mm Hg and that eight of the corneal incisions did not leak at the highest attainable IOP of 246 mm Hg.\(^\text{20}\) Similarly, four eyes in the liquid ocular bandage group in our study withstood the maximum pressure. This means that the actual mean pressures at leakage with liquid bandage could be higher than reported in this study. Liquid ocular bandage are synthetic sealants made up of polyethylene glycol with approximately 85% water content after application. The material is similar to hydrogels used in bandage contact lens that imposes less inflammatory reactions compared to cyanoacrylate or fibrin glue.\(^\text{20}\)

Major limitations of this study were the experimental setting and the sample size. Using a modified pulley system to raise the infusion height, the maximum attainable IOP may not be enough to cause leakage in some of the eyes in the study group. A sample size of 64 eyes per group was initially computed for the study, which we did not attain because of logistics. Another limitation would be the learning curve for the application of liquid ocular bandage. This sealant polymerizes quickly within 20 seconds of preparation. Three sealants polymerized quickly before the investigator applied it in the porcine eyes resulting to a lower number of eyes for the group. Care should also be taken to avoid the adhesive materials from running sideways from the wound site and adhere to other surrounding tissues. This excess gel, however, could be peeled off and re-application of the sealant at the wound site could be done.

Since this is an in-vitro study, it did not include looking into the degradation time of each of the tissue adhesives before sufficient corneal wound healing occurs. Further study on this aspect is required.

In summary, fibrin glue, 2-octyl cyanoacrylate and liquid ocular bandage were shown to be effective in sealing 5.2 mm corneal lacerations, with 2-octyl cyanoacrylate and liquid ocular bandage being superior to the fibrin glue in this study. They could serve as alternatives to suturing in corneal laceration repair. Future studies with larger sample size may be done to further evaluate their efficacy.

REFERENCES