

Tissue Adhesives in Ophthalmology

Manoj P. Shettigar

Pandit Bhagwat Dayal Sharma Post Graduate Institute of Medical Sciences, Rohtak, Haryana, India

Abstract

Tissue glue is increasingly becoming a material of choice as an adjuvant to surgical wound closure in ophthalmology. Various types of glues have been unique in terms of their advantages and limitations and so are used in different indications. However, acceptance of these adhesives by clinicians promises this to be a standard procedure for surgical wound closure.

Keywords: Cyanoacrylate, Fibrin glue, Newer tissue adhesives, Tissue glue.

INTRODUCTION

Tissue adhesives are a group of synthetic or naturally occurring compounds which helps in wound reconstruction, either natural or intra and postoperative. This reduces overall surgical time and inflammation, improving postoperative comfort without compromising wound strength and is more economical.

Cyanoacrylate Glue

It is a type of synthetic glue that polymerizes rapidly when coming in contact with a wet surface. Its application leads to a mild eosinophilic reaction, which occurs within 24 hours and is minimal by the 7th day. After 1–2 weeks, the glue cast extrudes. It has significant bacteriostatic properties (Figure 1). Practical and early application of cyanoacrylate glue as a corneal patch adds in the management of small corneal perforations, melts, and wound leaks, though it is also extended to sealing clear corneal incisions in cataract surgery.

Using corneal pathologies gives improved visual outcomes, with reduced need for tectonic keratoplasty in many situations.¹⁻³

The mode of application of cyanoacrylate varies according to the surgeon's preference. Some surgeons use an insulin syringe, draw glue on it, and apply a small amount of glue over the area of perforation after completely drying the surface. There is a quick polymerization of the glue, leaving a brittle, opaque piece of glue. It's rough on the surface and needs a bandage contact lens to avoid friction and discomfort. Another way of application is to use a special applicator.

In both cases, the tissue heals beneath the glue, which is then extruded. In India, it is available as Amcrylate (Concord drug limited, AP.)

Excess glue leads to intolerance or extrusion before healing and too little will leave areas of leaking. Its potential toxicity to the surrounding tissue also is a limiting factor. The toxicity of the glue is mainly by direct contact of the glue with corneal endothelium and lens. Secondary infection can happen when the glue has been in place for more than six weeks.^{4,5}

Corneal patching with cyanoacrylate glue helps in temporarily saving the eye anatomically, thus buying time for healing of the underlying pathology and control of associated inflammation. All this, in turn, calls for visual rehabilitation in a quiet eye as an elective procedure to improve the final visual outcome.

Fibrin Glue

It includes a fibrinogen component and a thrombin content, both of which are prepared by processing plasma. In India, it is available as tisseal fibrin sealant (Baxter AG Vienna, Austria) and Reliseal (from Reliance life-sciences) (Figure 2).

Address for correspondence: Manoj P. Shettigar,

Pandit Bhagwat Dayal Sharma Post Graduate Institute of Medical Sciences,
Rohtak, Haryana, India

E-mail: drmhitchatra@gmail.com

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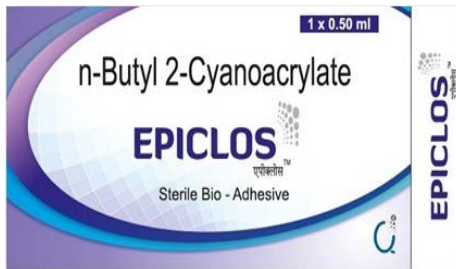


Figure 1: Cyanoacrylate glue.



Figure 2: Fibrin glue

The kit contains the following in separate vials.

- Large Blue Bottle:** Sealer protein concentrate (human), freeze dried, vapour treated, containing:
 - Clottable protein 75–115 mg
 - Fibrinogen 70–110 mg
 - Plasma fibronectin 2–9 mg
 - Factor XIII 10–50 IU
 - Plasminogen 40–120 µg
 - Small blue bottle:** Aprotinin solution, bovine 3000 KIU/ mL
 - White bottle:** Thrombin 4 (bovine), freeze-dried reconstituted contains 4 IU/mL
 - Large black bottle:** Thrombin 500 (bovine), freeze-dried reconstituted contains 500 IU/mL
 - Small black bottle:** Calcium chloride solution, 40 mmol/L
- Before use, the syringes containing two components of fibrin glue, namely, thrombin (black) and fibrinogen (blue) are taken out from the deep freeze and thawed to room temperature. Mix

1 + 2 (fibrin component)

3 + 5 (thrombin component)-Used for slow release

4 + 5 (thrombin component)-Used for rapid release

To slow the process of fibrin formation, only 0.1 mL of the thrombin-calcium chloride solution is withdrawn into a disposable syringe to which 0.9 mL of balanced salt solution (Acorn Inc., Decatur, IL, USA) is added to achieve a 1:10 dilution. This syringe is placed into the duplojet injector along with a parallel disposable syringe containing the fibrin sealer protein and fibrinolysis inhibitor. The two components of fibrin glue can either be applied simultaneously or sequentially, depending on the surgeon's preference.

In all cases, before the application of the glue, the surgical field must be dried meticulously. After application, the tissue is pressed gently over the glue for 3 minutes for firm adhesion. At the end of the procedure, a pad, and bandage are applied after the instillation of antibiotic drops.^{6,7}

Fibrin glue reduces the total surgical time when compared to suturing. It is better tolerated, non-toxic, and has antimicrobial activity when compared to cyanoacrylate glue.

It also lowers the risk of postoperative wound infection and is hypoallergenic. The smooth seal along the entire length of the wound edge results in higher tensile strength, with the bond being resistant to more significant shearing stress. Rarely, anaphylactic reactions following its application have been reported due to the presence of aprotinin in fibrin glue.⁸ The major drawback to its use is the risk of transmitted disease, mainly viral, from pooled blood donors.

Clinical Applications of Fibrin Glue

Conjunctival Surgery

Fibrin glue has shown promising results in traumatic conjunctival tear repairs, for conjunctival or amniotic membrane transplant (AMT); primary and recurrent pterygium surgery, mucous or AMT after symblepharon release, for conjunctivochalasis repair, for primary and secondary surgeries in chemical injuries, and Steven Johnson syndrome. It can also be used as a substrate transplant after the excision of large conjunctival tumors, including ocular surface squamous neoplasia.

Pterygium surgery is carried out with conjunctival autotransplant or a primary amniotic membrane. The graft needs to adhere to the recipient's conjunctival margins in both cases.⁹

Fibrin glue reduces operating time, reducing postoperative inflammation and discomfort with the ultimate reduction in the recurrence rate in primary surgery.¹⁰ When used in recurrent pterygium, its anti-inflammatory effect controls postoperative fibrosis.

In Strabismus Surgery

In strabismus surgery, conjunctival closure with fibrin glue is an excellent alternative to suturing for conjunctival closure. It also results in a more comfortable postoperative course.

In Corneal Surgery

• Corneal Perforation and Melt

Fibrin glue is commonly used for perforated corneal ulcers and those with impending perforations, descemetocoele, and extremely thinned-out corneas. Fibrin glue and cyanoacrylate glue are both effective in the closure of corneal perforations up to 3 mm in diameter. Glue is also used to fix the amniotic membrane in refractory and perforated corneal ulcers and is a viable option. Fibrin glue has the advantage of faster healing and significantly less corneal inflammation and neovascularization. In irregular corneal tears, fibrin glue act

as an adjuvant to seal leaks left due to poor approximation of the wound. The very advantage of replacing fibrin with cyanoacrylate lies in controlled postoperative inflammation, which increases the patient's comfort and reduces corneal neovascularization with no need to remove the glue.¹¹

- **Amniotic Membrane Transplantation**

Fibrin glue is the most effective and safe method for fixing the amniotic membrane graft (AMG) amniotic membrane to the ocular surface in almost all surgeries like partial and total limbal stem cell deficiency (LSCD), as a substrate for cultivation of limbal stem cells, to fix a polymethylene methacrylate ring to AMG on the ocular surface. AMG, when used as a substitute transplant also works better with fibrin glue rather than with sutures. All surgeries that need substitute transplants on the cornea, conjunctiva, or limbus are associated with the use of fibrin glue for better comfort, controlled inflammation, and better cosmetics and scarless tissue repair.^{12,13}

- **Corneal Grafts**

Isolated use of fibrin glue is not a choice for obvious reasons of poor wound strength. The combined use of fibrin glue with 8-16 sutures proved to be a good choice. Using sutures in corneal surgeries, especially lamellar ones, increases the risk of interface infiltrating through the suture track. Fibrin glue assisted carried out deep lamellar keratoplasty using supported overlay sutures. They found it to be a time-efficient and effective technique.¹⁴

- **Limbal Cell Transplantation**

Fibrin glue has also been used effectively and safely to fix the donor limbal lenticular on the recipient's bed in cases of LSCD. Fibrin sealant is used in carrier-free sheets that were more differentiated than AM sheets while retaining similar levels of colony-forming progenitor cells.¹⁵

Refractive Surgery

- **Lasik**

Fibrin glue can be used to manage a buttonhole in a flap with epithelial ingrowth. It can be used to repair flap tears/traumatic flap dislocation.¹⁶⁻¹⁸

- **Photorefractive Keratectomy**

Fibrin glue is being used on PRK operated corneas to reduce corneal haze. In surface ablations like PRK, covering the entire treated area with fibrin glue not only makes the surface smoother and regularly reduces postoperative discomfort, but the glue at the same time also acts as a temporary membrane for corneal epithelium. This reduces the reepithelization time.¹⁸

- **Glaucoma**

Autologous fibrin tissue glue (AFTG) is used to achieve conjunctival wound closure after all drainage procedures. Its

successful use has also been reported in the management of post-trabeculectomy hypotony due to leaking bleb.^{19,20}

Cataract Surgery

Its use in cataract surgery is to seal the wound in small incision cataract surgery. Glued IOL can be done both as a primary and secondary procedure in cases where the lens capsule is deficient or absent. As a primary procedure, it can be done in all cases of intraoperative posterior capsule rupture. It can also be done in all cases of subluxation or dislocation of lens e.g. Marfans syndrome, traumatic dislocation of the lens, etc. As a secondary procedure, it can be done in all the aphakic cases or can also be done as a part of IOL exchange following an anterior chamber IOL, subluxated or dislocated IOL.^{21,22}

Vitreoretinal Surgery

It can be used for conjunctival wound closure following retinal detachment surgery. However, that fibrin glue offers significantly better results than suturing or closure of conjunctival wounds.

Tissue glue can be used to stimulate adhesion of the elevated cuff of the neurosensory retina surrounding a full-thickness macular hole, in sutureless scleral buckling to fixate a silicone band to the sclera, posterior retinal breaks associated with retinal detachments.^{23,24}

Lid Surgery

The glue was used in eyelid surgery to fix the free autologous skin transplants for covering skin defects. The procedure is advantageous as early fibrovascular ingrowth into the transplant is stimulated. It is also helpful in the lid split procedure combined with free skin graft for severe upper eyelid entropion.

In lower eyelid trichiasis, the glue has been used for fixation of free autologous conjunctival transplants from the upper fornix after separation of the lashes from the posterior lamella with a lid split technique.^{25,26}

Lacrimal Surgery

It has been used for reconstructing lacerated canaliculi, canaliculo cystotomy, for the micro anastomosis between canaliculi and lacrimal sac, and for attaching lacrimal and nasal mucosal flaps.^{27,28}

Combined Procedures

Glue with AMG

Cyanoacrylate prevents epithelization into the zone of damaged stroma and prevents the development of collagenase production that can lead to stromal melting. The combination of glue with the biological bandage in the form of an AMG is highly indicated in cases where the lesion is large or some amount of tissue melt is seen. The membrane protects the glue and prevents further melt, reducing the inflammatory reaction induced by glue.^{2,3}

Glue with Glue

The combination of both cyanoacrylate and fibrin glue is used in cases of infectious keratitis where a large area infiltrate is associated with a small actual or threatening perforation, a combined approach is used wherein debulking of infiltrate is combined with the application of cyanoacrylate glue over the area of perforation is followed by covering the entire pathological area with AMG adhered with fibrin glue. It serves the purpose firstly: sealing the perforation and biological bandage serves as a drug delivery system and controls the inflammation, thereby preventing tissue melt.

Newer Generations of Tissue Glue

ReSure sealant (polyethylene glycol and triglycine solution) can be used for sealing clear corneal incisions. The photo-activated dendritic polymers have ocular applications like repairing central corneal lacerations, clear corneal cataract incisions, LASIK flaps, scleral incisions, and penetrating keratoplasties. Chemical crosslinking (two-component) dendritic polymers have significantly improved bonding strength over commercially available fibrin glue, It is easy to handle and causes minimal to nil effect on the surrounding tissue. This group includes adhesives like chondroitin sulfate-aldehyde adhesive, gelatin resorcinol, and albumin-glutaraldehyde adhesive.²⁹

Photocrosslinkable Adhesives

The bovine serum albumin-based bioadhesives is a photoactivated tissue adhesive and has been tried in squint surgery for a muscle to muscle adhesions, for sclera to sclera, and muscle-to-sclera adhesions because of its very high bioadhesive properties. Another photocrosslinkable adhesive is a riboflavin based bioadhesive. Hyaluronic acid-based photocatalytic glue can be applied on a lacerated corneal wound and then activated with argon laser beam to polymerize it and seals the wound.

CONCLUSION

Tissue glue is increasingly becoming a choice of material as an alternative or adjuvant to surgical wound closure in ophthalmology. Each type of glue is unique in terms of its advantages and limitations and so is used in different indications. Although the presently available tissue adhesives are good enough for the procedures mentioned, there is still a demand for newer adhesives with better biocompatibility, rapid sealing properties and increased binding forces. These novel developing adhesives promise to overcome the drawbacks and risks of existing ones. The clinicians' increasing acceptance of these adhesives promises this to be a standard procedure for surgical wound closure.

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