Surgical Technique

Emulsion polymer isocyanate-gluing: Autologous epithelial transplant with cyanoacrylate glue application for small corneal perforations

Rahul K Bafna, Rinky Agarwal, Abhijeet Beniwal, Agam Bhandari, Namrata Sharma, Jeewan S Titiyal

Cyanoacrylate glue (CG) is a commonly employed modality for sealing small corneal perforations. Presently, we describe the technique of emulsion polymer isocyanate (EPI)-gluing, a modification of its application, and its results in nine eyes with noninfectious, nontraumatic sterile corneal perforation with size ≤3 mm. The method involves harvesting a small patch of autologous epithelium adjacent to the melt area with the help of 10% alcohol and transplanting to the site of melt with its basement membrane facing downwards. CG, loaded on the reverse side of Sinskey hook or Weck-Cel sponge, is instilled on this epithelium-melt site complex and withdrawn immediately following which a bandage contact lens is placed on the corneal surface. In our series of patients with nine eyes where EPI-gluing was undertaken, all eyes reported a healed corneal scar with spontaneously dislodged glue and no underlying vascularization at 3-months follow-up. EPI-gluing is an inexpensive and host-friendly technique for the treatment of small noninfectious corneal perforations particularly with iris tissue prolapse.

Key words: Corneal perforation, cyanoacrylate glue, internal limiting membrane

Video Available on:
www.ijo.in

Access this article online

Website:
www.ijo.in

DOI:
10.4103/ijo.IJO_69_20

Quick Response Code:

Cyanoacrylate glue (CG) is a synthetic glue composed of esters of cyanoacrylic acid that can be employed for the successful treatment of frank or impending corneal perforations ≤3 mm in size, located both centrally or peripherally, in 86% cases.[1] Additional anti-collagenolytic and bacteriostatic activity (against Gram-positive bacteria) of CG may also aid in preventing further corneal melting and infection.[1] Yet, its application may be limited by inadequate intraoperative polymerization (due to persistent aqueous leaks from perforation site) necessitating reapplication in 30–50% cases, and by postoperative deep corneal vascularization (45.5% cases), giant papillary conjunctivitis from its irritation (36.4% cases), and intraocular toxicity.[1,2] Presently available other alternatives have their own limitations such as amniotic membrane graft, tenon's patch graft, and conjunctival autograft lack adequate tensile strength, bio-engineered collagen-based fillers are costly, fragile, and scarcely available, Bowman's membrane transplant is associated with difficult donor dissection and unnecessary host manipulation and conventional corneal transplantation is restricted by scarcity of donor cornea and risk of transmission of infections, graft dislocation and graft rejection.[1,3-5]

We describe a relatively simple and safe method of CG application, emulsion polymer isocyanate (EPI)-gluing, to avoid the aforementioned shortcomings.

Methods

Nine consecutive patients affected by unilateral noninfectious nontraumatic corneal melts of size ≤3 mm with positive Siedel test, subjected to thorough slit-lamp examination by an experienced cornea specialist were selected for EPI-gluing after sending corneal scraping specimens for microbiological analysis. After explaining the need for repeat gluing or other tectonic procedures, written informed consent was obtained from all patients. All patients were prescribed topical antibiotic-steroid-lubricants and systemic control of the underlying disease was undertaken simultaneously.

Surgical Technique

The procedure is performed in an operation theater under supine posture and topical (Proparacaine hydrochloride 0.5%) anesthesia. Patients with melts >2 mm and/or iris tissue prolapse from the site of perforation are transfused intravenous mannitol (20% solution, 1 g/kg, over 30 min) preoperatively to reduce upward thrust from intraocular contents. After cleaning the surgical site with betadine 5% and gently placing an ophthalmic drape and self-retaining speculum, the margins of the corneal melt are debrided of the dead, unhealthy, and necrotic

Department of Ophthalmology, Dr Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi, India

Correspondence to: Dr. Namrata Sharma, Cornea, Lens and Refractive Surgery Services, Dr Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi, India. E-mail: namrata.sharma@gmail.com

Received: 11-Jan-2020 Revision: 25-Feb-2020
Accepted: 29-Feb-2020 Published: 24-Jul-2020

Cite this article as: Bafna RK, Agarwal R, Beniwal A, Bhandari A, Sharma N, Titiyal JS. Emulsion polymer isocyanate-gluing: Autologous epithelial transplant with cyanoacrylate glue application for small corneal perforations. Indian J Ophthalmol 2020;68:1636-9.

epithelium. The maximum diameter of the melt is measured with calipers and a suitable size (1–3 mm) dermatomal punch is used to mark the epithelium in the area adjacent to, but at least 2 mm away from the margins of the melt [Figs. 1 and 2]. The site of marked epithelium is superior in central melts and either temporal or nasal depending on the site of peripheral melt. The marked epithelium is loosened by filling 10% ethyl alcohol for 10 seconds in the same dermatomal punch and absorbing it with a Weck-Cel sponge (Merocel®, Beaver Visitec International, USA) before lifting the punch to prevent its intraocular entry. One of the epithelial margins is gently denuded with Sinskey hook and carefully grasped with a nontraumatic forceps and placed on the area of melt with the basement membrane side downwards (to maintain the natural anatomy of the corneal epithelium) after drying the site of the perforation. A thin layer of CG (Butyl cyanoacrylate, Endocryl, Samarth life science Ltd, India) is then instilled on the entire melt area-epithelial patch complex by harvesting it on the reverse side of the same Weck-Cel sponge or a sterile Sinskey hook. The applying agent is then instantly withdrawn to avoid dislodgement of the epithelium-glue complex (EGC). As soon as the adhesive solidifies, the area is examined for further leaks. In eyes with the collapsed anterior chamber, intracameral air is injected from a side-port and iris adhesions if any are released gently while forming it [Supplemental digital content, SDC-1 (Video)]. Finally, a bandage contact lens (BCL) is placed over the corneal surface. The patient is examined a few minutes later to ensure the intactness of epithelium-glue-BCL complex (EGBC)

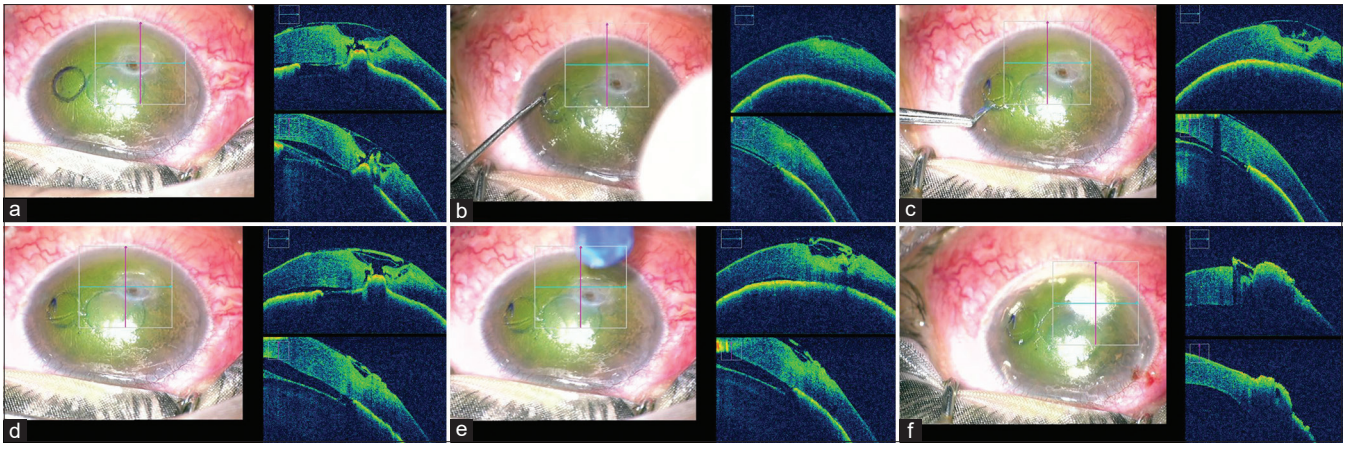

Figure 1: Steps of EPI-gluing; Iris prolapse in the melt area as seen on i-OCT (a); area of epithelial transplant marked (a), debrided (b and c); site of melt after epithelial transplant as seen on i-OCT (d); application of cyanoacrylate glue (e), melt-epithelium-glue complex as seen i-OCT (f)

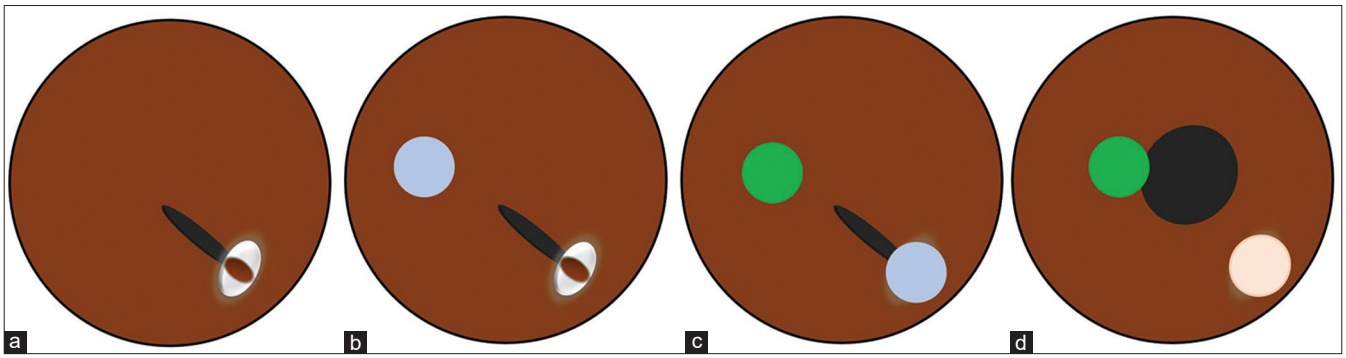

Figure 2: Animated steps of EPI-gluing; Melt area (a); area of epithelial transplant marked (b), debrided (c) and placed on the site of melt (c); cyanoacrylate glue application (d)

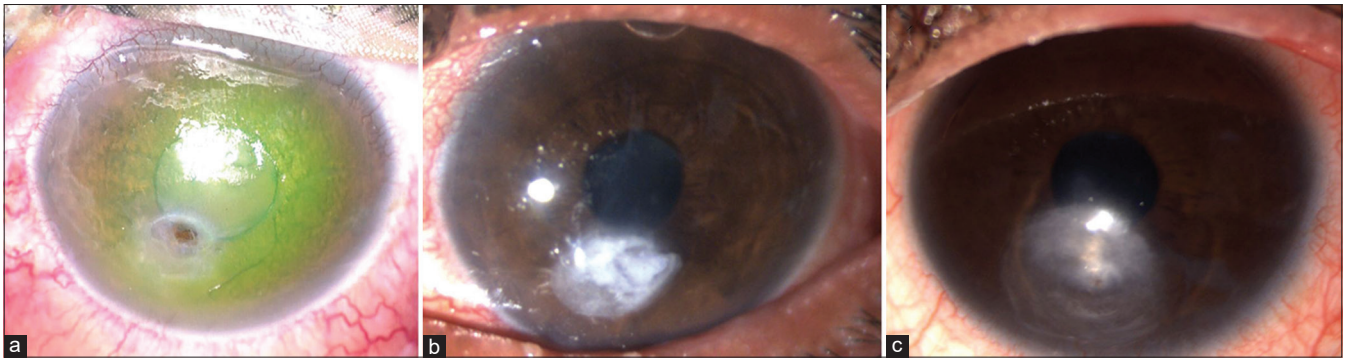

Figure 3: Intraoperative (a); 1st day (b) and 3 months (c) photographs after EPI-gluing

Table 1: Clinical details of the patients

Age/ gender	Diagnosis	Site of perforation	Size of perforation	Baseline VA	VA at 3 m F/u	Timing of shed glue
28 y/F	Steven Jhonson's Syndrome	Central	2.5 mm	HMCF	1/60	40 days
35 y/M	Peripheral ulcerative keratitis	Peripheral	2.7 mm	6/24	6/24	38 days
20 y/F	Steven Jhonson's Syndrome	Central	2.8 mm	HMCF	HMCF	48 days
56 y/M	Trachomatous keratopathy	Central	2.6 mm	1/60	3/60	42 days
58 y/F	Exposure keratopathy	Central	3 mm	1/60	5/60	51 days
49 y/F	Rheumatoid arthritis	Paracentral	1.5 mm	6/18	6/18	45 days
35 yr/M	Neurotrophic (viral keratitis)	Paracentral	2.5 mm	1/60	1/60	49 days
29 y/M	Neurotrophic (5th cranial nerve involvement)	Paracentral	2 mm	4/60	4/60	39 days
35 y/M	Peripheral ulcerative keratitis	Peripheral	2.7 mm	6/24	6/18	38 days

*HMCF: Hand movement close to face; VA: Visual acuity, F/u: Follow-up

and followed-up on day 1, day 7, and months 1 and 3 while continuing preoperative treatment regime with topical aqueous suppressants. The success of gluing was defined as scarring of the cornea, which maintains the integrity of the eye.

Results

The mean age of the patients was 38.33 ± 13.11 years (20–58 years) [Table 1]. The average size of the melt was 2.4 ± 0.45 mm (1.5–3 mm) and it was central, paracentral, and peripheral in four, three, and two patients, respectively. The procedure was successful in all eyes with all having an intact EGBC with no iris adhesions on the first postoperative day and none of them needing reapplication of glue. The mean time of spontaneous shedding of CG was 43.33 ± 5.04 days. At the end of three months, all patients had a healed corneal scar with no underlying superficial or deep vascularization or overlying residual glue [Fig. 3]. No other complications such as corneal irritation, anterior synechiae, corneal decompensation, superimposed infection or cataract were noted in any of our patients.

Discussion

While tectonic drape patch and double drape tectonic patch methods of CG application may prevent its direct contact with intraocular structures and lessen its ocular toxicity, these carry the risk of infection and foreign body reaction due to superadded non-biocompatible nature of plastic drape.[6,7] Our technique is a combination of sterile plastic drape or double drape technique of CG and free internal limiting membrane (ILM) flap technique for macular hole (MH) closure.[8] A small patch of autologous corneal epithelium utilized for sealing the corneal perforation prior to CG application in our technique serves as a more biogenic material thereby making it a safer alternative to plastic drape. At least a 2-mm distant epithelium is preferred as fragile, inflamed and necrotic epithelium in the peri-perforation area may release inflammatory mediators besides worsening the corneal integrity due to repeated manipulation during harvesting.

EPI-gluing is expected to enhance the postoperative anatomic and functional outcomes of CG application by acting as a scaffold for tissue proliferation and creating a microenvironment that enhances corneal stromal healing. The mechanism by which this technique accelerates restoration of corneal architecture remains elusive. We hypothesize that the multilayered healthy corneal epithelium and its basement membrane due to their ability to form an effective barricade to chemicals, water, microbes may prevent aqueous leak and secondary infections by forming a mechanical barrier at the site of perforation.[9,10] Clinically, this bridging membrane may allow comfortable application of CG on a dry surface, and a smooth release of iris adhesions in a closed globe without disturbing the overlying glue and make CG more biocompatible by preventing its direct contact with intraocular contents. This mechanical support along with its ability to prevent penetration of cytokines and regenerative and immunological potential may also provide a scaffold for stromal healing at the transplanted site and prevent further stromal melting by simultaneously counteracting the collagenolytic and proteolytic activities of CG. Despite the belief that the unhealthy epithelium at the site of melt may prevent adherence of CG, we believe that the microvilli on the surface of this freshly transplanted epithelium may lead to better adherence of CG to the corneal surface thereby limiting the amount of glue applied. Overall, these properties may be expected to decrease the incidence of foreign body reaction, intense inflammation, and resultant corneal vascularization induced by CG besides providing tectonic support to the cornea. However, it has to be remembered that the main supporting material is CG and epithelium is only supporting and not replacing its properties.

Application of glue on the reverse side of Sinskey hook or Weck-Cel sponge allows a uniplanar, thin, and uniform insertion of CG on the corneal surface besides minimizing risks associated with its direct application with a needle and of disruption and dislodgement of EBGC during its withdrawal. Additionally, the convex downwards shape of the instrument allows CG to conform to the shape of the corneal melt/defect thereby providing it better fittability and sealing ability. During EPI-gluing, high-quality images obtained on intraoperative optical coherence tomography helped us to ascertain the integrity of epithelium and CG individually and the success of iris adhesiolysis. However, it could not identify the EGC due to the shadowing effect of CG.

Repeat applications were neither recommended nor needed in our series of patients as the EGC if once dislodged was difficult to be re-harvested. The mean time of spontaneous shedding of CG 43.33 ± 5.04 days was

almost comparable to the study by Sharma *et al*.[1] Yet, our technique carries a theoretical risk of stromal melt at the site of epithelial delamination, reactivation of the virus in herpetic keratitis and a flare-up of infection in the freshly denuded area and requires constant vigilance and careful case selection and is presently not indicated for active microbial keratitis cases.

Conclusion

To conclude, EPI-gluing is an inexpensive and host-friendly technique for the treatment of small non-infectious corneal perforations, particularly with iris tissue prolapse. It is a relatively simple and reproducible technique and may be tried as a safe and an effective temporizing measure during the control of systemic and/or ocular inflammation or till definitive tectonic or visually rehabilitative procedures are undertaken. It may help in improving the survival of future corneal grafts by decreasing antecedent vascularization. However, the present evidence is insufficient to make such generalized and affirmative statements and larger long-term comparative studies are needed to validate our results.

Acknowledgment

We thank our institute for allowing us to continue with our research work.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Sharma A, Kaur R, Kumar S, Gupta P, Pandav S, Patnaik B, *et al*. Fibrin glue versus N-butyl-2-cyanoacrylate in corneal perforations. Ophthalmology 2003;110:291-8.
2. Vote BJ, Elder MJ. Cyanoacrylate glue for corneal perforations: A description of a surgical technique and a review of the literature. Clin Exp Ophthalmol 2000;28:437-42.
3. Sharma N, Singhal D, Maharana PK, Vajpayee RB. Tuck-in tenon patch graft in corneal perforation. Cornea 2019;38:951-4.
4. Samarawickrama C, Samanta A, Liszka A, Fagerholm P, Buznyk O, Griffith M, *et al*. Collagen-based fillers as alternatives to cyanoacrylate glue for the sealing of large corneal perforations. Cornea 2018;37:609-16.
5. Choudhary DS, Agrawal N. New surgical modality for management of corneal perforation using bowman membrane. Cornea 2018;37:919-22.
6. Khalifa YM, Bailony MR, Bloomer MM, Killingsworth D, Jeng BH. Management of nontraumatic corneal perforation with tectonic drape patch and cyanoacrylate glue. Cornea 2010;29:1173-5.
7. Gandhewar J, Savant V, Prydal J, Dua H. Double drape tectonic patch with cyanoacrylate glue in the management of corneal perforation with iris incarceration. Cornea 2013;32:137-8.
8. Velez-Montoya R, Ramirez-Estudillo JA, Sjoholm-Gomez de Liano C, Bejar-Cornejo F, Sanchez-Ramos J, Guerrero-Naranjo JL, *et al*. Inverted ILM flap, free ILM flap and conventional ILM peeling for large macular holes. Int J Retina Vitreous 2018;4:8.
9. Torricelli AAM, Singh V, Santhiago MR, Wilson SE. The corneal epithelial basement membrane: Structure, function, and disease. Invest Ophthalmol Vis Sci 2013;54:6390-400.
10. Mobaraki M, Abbasi R, Omidian Vandchali S, Ghaffari M, Moztarzadeh F, Mozafari M. Corneal repair and regeneration: Current concepts and future directions. Front Bioeng Biotechnol 2019;7:135.