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ROLE OF BIOLOGICAL GRADE CYANOACRYLATE GLUE IN CORNEAL ULCERS

***Dr. Deepak Mishra, Dr. Praveen Kumar Chaturvedi, Dr. Bibhuti P. Sinha and Dr. Nilesh Mohan**

[1]*Dr. Deepak Mishra, Assistant Professor, Department of Ophthalmology, Institute of Medical Sciences, Banaras Hindu University, Varanasi.

[2]Dr. Praveen Kumar Chaturvedi, Service Senior Resident, Department of Ophthalmology, Institute of Medical Sciences, Banaras Hindu University, Varanasi.

[3]Dr. Bibhuti P. Sinha, Professor and Head, Regional Institute of Ophthalmology, IGIMS, Patna, Bihar.

[4]Dr. Nilesh Mohan, Additional Professor, Regional Institute of Ophthalmology, IGIMS, Patna, Bihar.

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***Corresponding Author**
Dr. Deepak Mishra
Assistant Professor, Department of ophthalmology, Institute of Medical Sciences, Banaras Hindu University, Varanasi.

ABSTRACT

Purpose: To study the role of biological grade cyanoacrylate in perforated corneal ulcers. **Methods**: This is a Hospital based prospective study on 60 eyes with corneal perforation done at Department of Ophthalmology, IMS, BHU, Varanasi; a tertiary referral centre for ophthalmology. The study was conducted over 14 months of duration. **Results**: Cases range from 11 years of age to 66 years of age with a male to female ratio of 3:2 The cases reported to our centre as early as 3 days from onset of symptoms to maximum of 38 days from onset of symptoms with a median time interval of 22.5 days between onset of symptoms and the initial treatment. The causative organism or the secondary infection after corneal perforation showed fungal agent (31%) in majority cases. 56.7% of cases had central perforations whereas 43.3% cases had peripheral ulcerations with majority having grade 2 and grade 3 depth of ulceration. The median duration for which cyanoacrylate glue remained on cornea was 43.4 days. Favourable outcome in terms of improvement in visual acuity and healed corneal ulcer was reported in 33.3% cases. **Conclusions**: Cyanoacrylate glue application in cases of corneal perforations was used to be viewed as a temporary measure in the past, now it can be considered as a

definitive therapy in at least half of the patients but with a close monitoring for glue-related complications.

KEYWORDS: Corneal ulcer, Cyanoacrylate glue, Corneal perforation, Glue related complication, Visual outcome.

INTRODUCTION

Corneal perforation bearing grave visual outcomes is one of the ophthalmic emergencies that requires immediate intervention.[1] Among the available treatment options for corneal perforations like keratoplasty, graft patching, conjunctival flaps, tissues adhesives, bandage contact lenses[2,3]; tissue adhesives especially cyanoacrylate glue are increasingly used not only for corneal perforations but also for cataract surgery, and glaucoma bleb leak.[4-9] The Cyanoacrylate adhesives of ophthalmic use are of biological grade and all are commercially available off-label. These are esters of cyanoacrylic acid with moderate length alkyl side chains.[19]

Though cyanoacrylate glue is a temporary measure for sealing perforations, it provides a lag time awaiting favourable environment for definitive treatment.[11] Cyanoacrylate adhesives are used for the management of corneal perforations irrespective of cause of perforation like microbial keratitis, traumatic or post surgical wound leaks, chemical burns, neurotrophic keratitis, and rheumatologic or other non-infectious corneal melts.[10]

Ease of application, readily availability, long self life, low cost, low toxicity and less curvature changes make it preferred or first choice for sealing of corneal perforation. Cyanoacrylates not only inhibit keratolysis by arresting the migration of polymorphonuclear leukocytes;[12,13] and induction of stromal neovascularization, but also exhibits anti-microbial activities against Gram-positive pathogens such as Staphylococcus aureus , Streptococcus pyogenes , Streptococcus pneumoniae and few Gram negative pathogens like Escherichia coli.[14]

Reapplication of the glue, giant papillary conjunctivitis, and secondary Glaucoma due to formation of irido-corneal synechiae due to inadvertent instillation of glue into the anterior chamber, posterior synechiae, and polymerization on to the corneal endothelium are few common drawbacks.

Watchful vigilance needed for secondary microbial infiltrates, especially when contact lens and glue are used together for longer duration (greater than 6 weeks).

MATERIAL AND METHODS

This is a Hospital based prospective study on 60 eyes with corneal perforation done at Department of Ophthalmology, IMS, BHU, Varanasi; a tertiary referral centre for ophthalmology. The study was conducted over 14 months of duration. The ethical approval was obtained from the institution ethical committee and follows the tenets of the Declaration of Helsinki.

All the patients with frank perforation were taken as cases from the out patient department. Informed consent was taken from each case. They were divided randomly into two groups. Group 1 (G1) cases were treated with glue and bandage soft contact lens and Group 2 (G2) cases were treated with glue only. All patients were observed for at least 3 month for complications & outcome. Success of treatment was determined either by resolution of corneal perforation into scar, improvement in visual acuity or maintenance of anterior chamber.

Surgical procedure

After painting & draping the eye, all cases underwent application of the glue in the minor procedure room under sterile conditions using topical or peribulbar anaesthesia. The perforation site was identified using an operating microscope; necrotic tissue and epithelium was debrided and surface was dried with sterile cellulose sponge. Glue was then applied, allowed to dry and then checked whether perforation had sealed or not. In G1 cases SBCL (Plano-T lenses from Bausch & Lomb) was placed and in G2 cases, only glue was used to seal the defect. Some eyes required several episodes of gluing. Topical broad spectrum antibiotic was used 1 drop 2 hourly for 3 days followed by 4 times daily for 6 weeks. Topical antifungal, antiviral, artifical tear subsitutes, cycloplegic & antiglucoma drug were also used in different cases where required. All patients were followed up after day 15 and 1, 2 and 3 month for complications and outcomes.

RESULTS

In our study, age of the cases range from 11 years of age to 66 years of age with a male to female ratio of 3:2 The cases reported to our centre as early as 3 days from onset of

symptoms to maximum of 38 days from onset of symptoms with a median time interval of 22.5 days between onset of symptoms and the initial treatment.

Among the cases, 8 cases presented with no perception of light, 26 cases presented with only hand movements close to face, 16 cases presented with hand movement to 6/60 visual acuity on snellen's chart and 4 cases presented with visual acuity between 6/60 to 6/24 on snellen's chart. Out of all cases, 6 cases were lost to follow up during the study. Table 1.

Table 1: Visual acuity of cases at initial presentation.

Visual acuity	Cases (number, %)
No PL	8 (13.3%)
Up to HM	26 (43.3%)
HM to 6/60	16 (26.7%)
6/60 to 6/24	4 (6.7%)

PL- Perception of light, HM- Hand movement.

The etiological study of the causative organism or the secondary infection after corneal perforation showed fungal agent (31%) in majority cases followed by mixed flora in 30% cases. Bacterial agent was isolated in 20% cases whereas no growth was seen in 19% cases. Figure1.

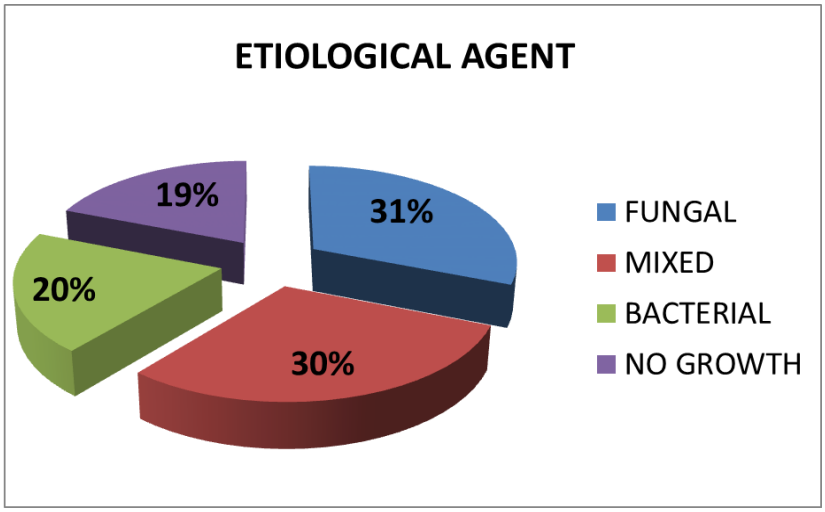

Figure. 1: Etiological agents isolated from cases.

Among the cases, 60% cases i.e. 36 eyes presented with frank perforation and 24 eyes i.e. 40% cases presented with uveal incarceration leading to sealing of the defect or secondary epithelisation. In 34 (56.7%) cases, there were central perforations whereas 26 (43.3%) cases had peripheral ulcerations. Corneal perforation of upto 2 milimeter of size was noted in 33%

cases i.e. 22 eyes, ulcer size of 2 to 4 milimeter of size was noted in 33% cases i.e. 22eyes and ulcer size of more than 4 milimeter was noted in 16 eyes i.e. 24% cases. Figure 2.

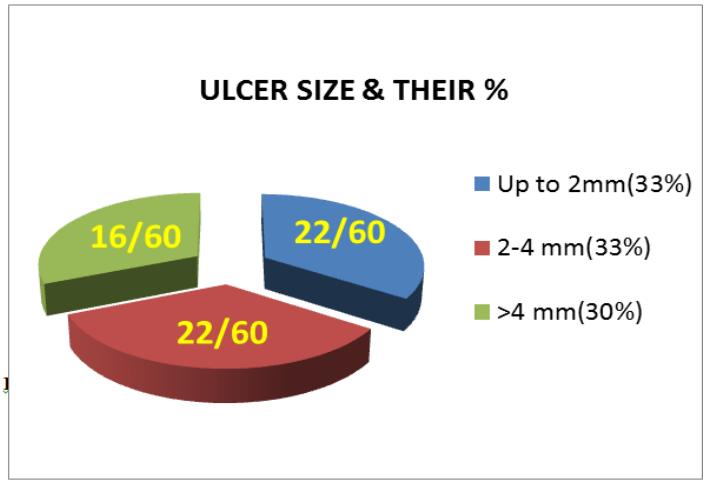

Figure. 2: Measured ulcer size and their percentage in cases.

As per modified Jones classification, all cases of ulcerations were of grade 2 and grade 3 depth with majority of the ulcerations (80%, 48 eyes) belonging to grade 3 involving middle to inner 3rd of the cornea. Table 2.

Table. 2: Grading of corneal ulcer and their percentage in cases.

Grades of ulcer depth	Cases (n, %)
Grade 1 (superficial 1/3rd)	0, 0%
Grade 2 (upto middle 1/3rd)	12, 20%
Grade 3 (upto inner 1/3rd)	48, 80%

The median duration for which cyanoacrylate glue remained on cornea was 43.4 days and 16 (26.6%) cases, 6 cases in group 1 and 10 cases in group 2, required second or multiple application of glue.

After application of glue, cases in both the groups were analysed during follow up for possible outcomes of healing of ulcer, development of conjunctival hooding, phthysis bulbi, unorganised anterior chamber, requirement of evisceration and follow up loss as shown in table 3.

Table. 3: Outcomes of cases during follow up.

Group, n	Healed ulcer (n, %)	Conjunctival hooding (n, %)	Unorganised anterior chamber (n, %)	Phthysis bulbi (n, %)	Evisceration required (n, %)	Follow up loss (n, %)
G1, 30	12, 40.00%	6, 20.00%	4, 13.33%	2, 6.67%	2, 6.67%	4, 13.33%
G2, 30	8, 26.67%	10, 33.33%	6, 20.00%	2, 6.67%	2, 6.67%	2, 6.67%

In our study, when visual outcomes at the end of the study was analysed, 20 (33.3%) cases showed improvement of at least one line on snellen's visual acuity chart. Table 4.

Table. 4: Visual outcome of cases at the end of follow up.

Visual acuity at presentation	Cases (n, %)	Visual improvement in cases (n)
No PL	8, 13.3%	No improvement
Upto HM	26, 43.3%	6
HM to 6/60	16, 26.7%	10
6/60 to 6/24	4, 6.7%	4

Regarding complications associated with application of cyanoacrylate glue, 6 cases showed persistent corneal infiltrates, 6 cases showed extension of disease, 2 cases developed raised intraocular pressure, 2 cases developed inflammation of uvea and 8 cases showed flaring of infection inspite of antimicrobial coverage. Table 5.

Table. 5: Complications noted in cyanoacrylate glue treated cases.

Complications	G1 group (n)	G2 group (n)
Corneal infiltrate	2	4
Extension of disease	2	4
Raised IOP	0	2
Inflammation of uvea	0	2
Flaring of infection	6	2

DISCUSSION

Our study revealed favourable outcome in terms of improvement in visual acuity and healed corneal ulcer in 20 (33.3%) cases when cyanoacrylate glue was used to seal corneal perforations which is comparable to the study of Moorthy et al.[15] and Setlik et al.[16] Moorthy et al.[15] reported a lesser success rate of 37% in 46 eyes treated for perforated herpetic stromal keratitis with n-butyl cyanoacrylate glue in addition to antiviral therapy whereas Setlik et al.[16] reported healing of 41% of their 22 eyes by a single application of isobutyl cyanoacrylate glue. Weiss et al.[17] also noted poorer success rate and higher complication rates with herpetic perforations treated with cyanoacrylate.

Contrary to our study, Garg et al.[18] reported healing by scarring in 64% of 66 eyes treated for perforated fungal keratitis with n-butyl cyanoacrylate combined with topical natamycin 5% and oral ketoconazole; and Kasetsuwan et al.[19] reported high success rate of 91% in 66 eyes treated for mixed aetiologies of cornea perforation using shorter alkyl side chain ethyl cyanoacrylate.

The median duration of cyanoacrylate adherent on cornea in our study was 43.4 days which is comparable to the study of Garg et al.[18] In their study, the average duration was 39 days for perforated herpetic keratitis, 12 to 52 days for perforated fungal keratitis.

The reported of complications from cyanoacrylate use is variable in studies. In our study, we noted 16 eyes with corneal vascularisation and conjunctival hooding and 14 eyes with ocular complications in the form of persistent corneal infiltrates and flaring of infection; which is more than expected when compared to the study of Kasetsuwan et al.[19] In their study, authors reported only one case of corneal inflammation out of 66 eyes.[19]

CONCLUSION

Though, the reported success rates of cyanoacrylate glue are variable. It has been observed from available studies and findings of our study that the success rate of cyanoacrylate glue as a sole agent in treating corneal perforations range between 30-60%. Therefore, glue application in cases of corneal perforations can be viewed not only as a temporary measure but as a definitive therapy in almost half of patients treated. However, results are not encouraging in cases with large ulcer size. Also, close monitoring is required for glue-related complications.

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