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Brief communication (Original)

Efficacy and safety of ethyl-2-cyanoacrylate adhesives for corneal gluing

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Background: Ethyl-2-cyanoacrylate adhesive has been widely used for sealing small corneal perforations in Thailand. However, its efficacy has not been reported.
Objective: To study the efficacy and safety of ethyl-2-cyanoacrylate adhesive for corneal gluing in impending or perforated corneas.
Methods: This is a retrospective study of a case series of patients who had corneal gluing with ethyl-2-cyanoacrylate in a tertiary care center in Thailand from 1992–2010. Data includes demographic data, indications for treatment, visual acuity before and after gluing, number of gluing, definite treatment, success and complications after gluing.
Results: Sixty-six eyes were treated with ethyl-2-cyanoacrylate adhesive. There were 39 men (59%) and 27 women (41%). Age ranged from 11 to 87 years (mean age 49.74 years). The most common indications were perforated corneal ulcer (32%) and descemetocele (29%). Overall success rate of gluing was 91% (n = 60). Success rate on the first, second, third, and fifth attempt of gluing was 70% (n = 46), 14% (n = 9), 6% (n = 4), and 2% (n = 1), respectively. Definite treatments were performed on 17 patients after gluing. Six patients had penetrating keratoplasty, 6 had lamellar keratoplasty, 3 had amniotic membrane transplantation, 1 had corneal resuturing, and 1 immunocompromised patient with a severe corneal infection had an evisceration. One patient developed corneal irritation. No serious complications were found.
Conclusion: Ethyl-2-cyanoacrylate adhesive is safe and efficacious in gluing both noninfectious and infectious corneal perforations.

Keywords: Corneal perforation, descemetocele, gluing

Corneal perforation is a common, sight-threatening, ocular problem found worldwide that occurs when there are diseases affecting the eye, injuries to the eye or infection that can become serious if left untreated, resulting in blindness and poor quality of life for those afflicted. Treatment options for corneal perforation include corneal suturing, corneal transplantation, and gluing with medical grade adhesives. In a resource limited setting such as Thailand, where the number of cadaveric corneas is not sufficient, gluing with adhesives may be an alternative treatment.

For many years, cyanoacrylate adhesives have been used in ophthalmology for the treatment of corneal perforations because of corneal melting or thinning. Cyanoacrylate adhesives can be used as a temporary or adjunctive measure for the management of corneal perforations [1, 2]. Furthermore, this cyanoacrylate treatment has been shown to improve visual outcome with reduced enucleation.

Cyanoacrylates are esters of cyanoacrylic acid. These monomers are hardened by a process of polymerization or when the monomers come in to contact with water or a weak base. Many forms of cyanoacrylate adhesives have been developed [3]. Early derivatives of cyanoacrylates had short side chains (methyl, ethyl) which degraded rapidly into cyanoacetate and formaldehyde. These degraded products tend to accumulate in the tissues and cause significant histotoxicity, which results in acute and chronic inflammation of the eye [4]. The severity of histotoxicity varies with the tissue's vascularity.

According to avascular nature of the cornea, the histotoxicity of the cyanoacrylate in the cornea is less

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than in more vascularized tissue. Therefore, this compound is beneficial in managing corneal perforations.

Medical grade adhesives (long chained cyanoacrylates, butyl, and octyl cyanoacrylate) are not marketed in Thailand. Commercially available adhesives are early derivatives, short chained, ethyl cyanoacrylate, which has less biocompatibility, but is currently being used to seal small corneal perforations in Thailand.

This wide spread use of ethyl-2-cyanoacrylates may be facilitated by its affordability and availability, but to this date, there has been no report on its efficacy and safety in the treatment for corneal perforations. Because of this, we assessed the efficacy, safety and side effects of ethyl-2-cyanoacrylates in the management of corneal perforation by retrospectively reviewing cases from the last 19 years in a tertiary care center in Thailand. To our knowledge, we are the first to report that ethyl-2-cyanoacrylate adhesives are effective in the treatment of corneal perforation with minimal toxicity.

Materials and methods

This is a retrospective, case series study. The charts of all patients with frank or impending corneal perforations from either noninfectious or infectious etiology who had corneal gluing with ethyl-2-cyanoacrylate in the tertiary care center from 1992 to 2010 were reviewed. Patient selection criteria for gluing were corneal perforation of less than 3 mm diameter either from trauma, infection, corneal thinning, corneal melting, and descemetocele.

Technique

All of the procedures were performed using aseptic technique in operating theater. The surrounding area of corneal perforation was cleaned and kept dry. In the case of a flat anterior chamber, a paracentesis was performed and air/balanced salt solution/ viscoelastic substance was injected to reform the anterior chamber. Ethyl-2 cyanoacrylate glue was drawn into 1 ml syringe and injected slowly through 30-G needle at the site of perforation. The adhesive was left until it polymerized and hardened then searching for any remaining leakage was commenced. Finally, a soft contact lens bandage was placed over corneal surface. Patients in the infectious group were prescribed tobramycin (Tobrex) eye drops, while those with noninfectious cases were prescribed combined tobramycin and dexamethasone (TobraDex) eye drops 4 times a day.

Follow-up and outcome data were obtained from the patients' most recent outpatient records. Data collected consisted of demographic data (age, sex) and indications for corneal gluing, which were divided into either infectious or from noninfectious causes (traumatic perforated cornea, rupture descemetocele, corneal melting, and corneal thinning). Visual acuity (VA) after gluing was stratified into 3 groups: mild (VA better than 20/70), moderate (VA between 20/70 and 20/200) and severe (VA worse than 20/200). Other data such as the success rate and numbers of gluing, definite treatment after gluing, and side effects or complications after gluing (irritation of the eyes, infections, corneal decompensation, etc.) were also reviewed.

Results

Sixty-six eyes from 66 patients who were treated with tissue adhesive for either a grossly or impending perforation in an attempt to maintain the integrity of the eye were analyzed. There were 39 males (59%) and 27 females (41%) with an age range of 11 to 87 years and a mean age of 49.74 years. The most common underlying disease was neurotrophic keratitis (12.12%). Demographic data and underlying ocular status of the patients are shown in **Table 1**.

Forty-five eyes of 66 patients had noninfectious corneal perforation (**Table 2**). The most common cause of corneal perforation in this group was ruptured descemetocele (29%). By contrast, patients with infectious causes all had perforated corneal ulcers.

Success of gluing was defined as scarring of cornea, which maintained the integrity of the eye. The overall success rate of gluing was 91% (n = 60). Success rate on the first, second, third and fifth attempt of gluing was 70% (n = 46), 14% (n = 9), 6% (n = 4) and 2% (n = 1), respectively. Etiologies for the use of cyanoacrylate and results of the gluing are shown in **Table 2**.

Definite treatments were performed on 17 patients after gluing. Six patients had penetrating keratoplasty, 6 had lamellar keratoplasty, 3 had amniotic membrane transplantation, 1 had corneal resuturing and 1 immunocompromised patient with a severe corneal infection had an evisceration. Visual acuity before and after corneal gluing are shown in **Table 3**.

A side-effect was detected in one patient. This patient developed corneal irritation. Aside from this, there were no other serious complications. We did not detect any corneal decompensation, superimposed infection or adhesions of the intraocular tissue.

Table 1. Demographic data of the patients

	Number	Percent
Sex		
Male	39	59
Female	27	41
Age	11 to 87 (mean = 49.74)	
Underlying ocular disease		
None	35	53
Neurotrophic keratitis	8	12
Corneal scar	6	9
Steven Johnson syndrome	3	5
Chemical injury	3	5
Dry eye	3	5
Graft failure	2	3
Peripheral ulcerative keratitis	2	3
Limbal stem cell deficiency	1	2
Thermal burn	1	2
Trichiasis	1	2
Post trauma	1	2
Total	66	100

Table 2. Indication for corneal gluing and result

Etiology	Number (%)	Sealed	Not sealed
1. Infectious cause (perforated corneal ulcer)	21 (32)	19	2
2. Noninfectious cause	45 (68)		
Rupture descemetocele	19 (29)	19	0
Corneal melting	6 (9)	3	3
Corneal thinning	7 (11)	6	1
Others	13 (20)		
– post rust ring removal	5 (8)	5	0
– traumatic perforated cornea	3 (5)	3	0
– post band keratopathy removal	1 (2)	1	0
– sealed perforated cornea	1 (2)	1	0
– post pterygium excision	1 (2)	1	0
– post penetrating keratoplasty	1 (2)	1	0
– post primary repair corneal wound	1 (2)	1	0
Total	66 (100)	60	6

Table 3. Visual acuity before and after corneal gluing

Time of gluing	Visual acuity	Number	Percent
Before gluing	VA >20/70	3	5
	VA 20/70 to 20/200	5	8
	VA <20/200	58	88
1 week after gluing	VA >20/70	3	5
	VA 20/70 to 20/200	9	14
	VA <20/200	54	82
1 month after gluing	VA >20/70	4	6
	VA 20/70 to 20/200	6	9
	VA <20/200	42	64
After definite treatment	VA >20/70	8	12
	VA 20/70 to 20/200	4	6
	VA <20/200	13	20

Discussion

In patients with impending or gross corneal perforation, suture or surgical procedures such as penetrating keratoplasty [5-7], conjunctival patch [8], and lamellar patch graft [9-11] are usually performed to reestablish the integrity of the eye. Alternatively, medical grade tissue adhesives can also be used for the treatment of perforated corneas or descemetoceles [2, 7, 12-15].

To our knowledge, this is the first study to report the safety and efficacy of alternative tissue adhesive, ethyl-2-cyanoacrylates, for the treatment of corneal perforations in humans with various corneal diseases. This is in agreement with the finding that tissue adhesives can successfully treat perforations and descemetoceles and improve vision and reduce enucleation rate [16]. Data from all patients who attended a tertiary care center since 1992 to 2010 and had ethyl-2-cyanoacrylates adhesive were analyzed. The most common reasons for gluing were perforated corneal ulcer (31.82%) and ruptured descemetocele (28.79%). Most of the cases had successful sealing after the first attempt, especially in those with traumatic corneal perforations, in which 2 cases had VA of 20/20 postoperatively. Therefore, we believe that corneal gluing with ethyl-2-cyanoacrylates is a good alternative choice for the treatment of small, corneal traumas. As for patients with a perforated corneal ulcer, of a total of 21 eyes, only 19 cases were successful. Corneas from two cases failed to seal. In cases with corneal melting, 6 eyes were glued. Three out of 6 cases achieved good results. Failures to seal in 2 corneal ulcers and 3 melting cases probably result from severe inflammatory reaction because of the activity of phagocytosing neutrophils [17] and necrotic tissues. Therefore, it is recommended to remove all necrotic tissues as much as possible to achieve a successful seal.

This study was not able to identify microorganisms that were involved in the perforation of the corneal ulcer because most of the cases were referred to the hospital without any results for culture. Because of the frank perforation in the cornea, tissue scrapings were not performed. Nevertheless, none of the patients in this study developed any infections after gluing unlike a study of other cases reported [18]. In that study, three cases developed infectious keratitis after cyanoacrylate gluing even though they were taking prophylactic antibiotic therapy [18]. They reasoned that this may be because of the opaqueness of the glue, which prevented the detection of keratitis. This difference may be attributable to the fact that the antibiotics used in our study, Tobrex had a wider spectrum than antibiotics used by Cavanaugh et al., which were cefazolin and gentamycin.

Even though toxicity from cyanoacrylate has been reported, this study detected only one patient with a side effect of corneal irritation. Serious complications such as corneal decompensation, infection and adhesion of intraocular tissue were not detected in this study. This may be attributed to the dosage used and tissue being treated. Small amounts of ethyl-2-cyanoacrylate were used in this study and the avascular property of the corneal tissue may have minimized the inflammation and vascularization of the treated area. However, because of the small sample size, this data should be interpreted with caution.

Other limitations of the study include loss to follow-up (9/66), variable period of follow-up, intra- and interindividual variability of applying the glue, as well as incomplete data.

Conclusion

Ethyl-2-cyanoacrylate adhesive is an inexpensive and widely available alternative that is effective in the treatment of both infectious and noninfectious corneal perforations. There was no corneal toxicity or serious complication from using ethyl-2-cyanoacrylate adhesive. The results from this study provide an affordable, alternative tissue adhesive that is safe and efficacious for the treatment of corneal perforation of any etiology.

The authors have no conflicts of interest to report in this study.

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