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Amniotic membrane transplantation for painful bullous keratopathy

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PURPOSE. *To establish the effectiveness of amniotic membrane transplantation (AMT) in relieving pain and discomfort in patients with painful bullous keratopathy and also its role in improving vision in eyes with visual potential.*
METHODS. *Seven eyes of seven consecutive patients with painful corneal conditions were included in a retrospective interventional noncomparative case series performed at Maidstone General hospital, Maidstone, UK. Amniotic membrane transplantation was performed in seven eyes. Pain relief, epithelial healing, and visual changes were evaluated. Pain relief and freedom from discomfort were considered for the success of the surgery.*
RESULTS. *The mean follow-up was 26.57 weeks (range 11 to 53 weeks). Pain relief was achieved in all seven (100%) eyes. Associated symptoms including foreign body sensation, photophobia, and tearing subsided significantly in all patients starting soon after the first postoperative day. Vision improved in 5 (71.42%) patients.*
CONCLUSIONS. *AMT is an effective alternative for the management of patients with painful bullous keratopathy. Besides pain relief and reduction of ocular inflammation it remains unclear whether this procedure can also be used to improve vision in eyes with visual potential. (Eur J Ophthalmol 2007; 17: 7-10)*

KEY WORDS. *Amniotic membrane, Bullous keratopathy, Painful, Transplantation*

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INTRODUCTION

Ocular pain and discomfort are the characteristic complaints of most patients with keratopathy regardless of the underlying etiology. Pseudophakic bullous keratopathy, persistent epithelial defects following penetrating keratoplasty and corneal chemical injuries are some common causes. These conditions are associated with corneal stromal edema that irritates corneal nerve endings causing ocular pain and discomfort (1). Longstanding corneal edema predisposes to infection, ulceration and scarring further complicating the management and visual potential of these patients (2). A variety of management strategies are available for relieving the pain and restoring the corneal epithelial integrity, including bandage contact lenses in patients who are able to tolerate them (3), stromal micropuncture (4), conjunctival flaps (5), or phototherapeutic keratectomy (6).

Amniotic membrane transplantation (AMT) for painful bullous keratopathy was first reported by Pires et al (7). Significant relief from pain and reduction of ocular inflammation was subsequently reported by Mejia et al (8) and also by Espana et al (9). In the current study we report the safety and efficacy of AMT as an alternative to the above mentioned management

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strategies for pain relief and epithelial healing in patients with painful bullous keratopathy. Besides pain relief and reduction of inflammation, it remains unclear whether this procedure can also be used to improve vision in eyes with visual potential.

METHODS

Seven consecutive patients with painful corneal conditions and intractable pain, photophobia, tearing, and foreign body sensation were included in the study between August 2002 and May 2003. Clinical notes of all seven patients who underwent surgery were studied. Four patients had bullous keratopathy (due to pseudophakia and as a complication of corneal thinning in rheumatoid arthritis), two patients had failed penetrating keratoplasty with persistent epithelial defects, and one had corneal chemical injury. These patients with bullous keratopathy (BK) were not offered penetrating keratoplasty due to their poor visual potential.

Clinical data on age, sex, visual acuity changes, pain, epithelialization, and complications were recorded for analysis. Pain was recorded in the notes as four grades (grade 0, no pain; grade I, bearable pain; grade II, pain relieved by painkillers; grade III, severe pain not relieved by analgesics). Size of the corneal epithelial defect was also recorded preoperatively. Corneal epithelialization was monitored using fluorescein dye staining. Size of epithelial defect was recorded at each postoperative visit. The time taken for corneal re-epithelialization was noted.

After informed consent was obtained, AMT was performed by a single corneal surgeon (C.J.). All surgeries were performed under general anesthesia. Superficial corneal epithelial debridement was performed and whole unhealthy, loose epithelium was removed with cotton tip applicator.

Preserved (frozen) amniotic membrane was used in all cases. After the amniotic membrane was peeled off the nitrocellulose paper, it was placed over the created epithelial defect with the basement membrane side facing up. The membrane was sutured in apposition to the epithelial margin, and thus it was used as a contact lens. Conjunctival peritomy was not performed. First, four interrupted 10-0 nylon sutures were placed 90 degrees apart on the cornea to allow fixation of the amniotic membrane followed by strengthening sutures in between them to ensure that the amniotic membrane was flat. At the end of the procedure a subconjunctival injection of cefuroxime and betamethasone was given in all cases. No bandage contact lens or tarsorrhaphy was performed.

All patients were admitted overnight and were seen the following day. Postoperatively, all patients were treated with topical prednisolone acetate 1% and topical chloramphenicol four times per day for up to 4 weeks and progressively tapered. Ophthalmologic evaluation was performed in all cases postoperatively on day 1, weekly for the first month and then monthly for 5 months. The amniotic membrane was left to dissolve on its own and the sutures were removed 3 months postoperatively. Successful surgery was defined on the basis of pain relief (pain score), freedom from discomfort, and corneal epithelialization.

RESULTS

Seven patients (six women and one man) with mean age of 66.42 years (range 44 to 84) were included in the study (Tab. I). All patients had intractable pain (grade III) interfering with their daily activities and all reported associated symptoms including foreign body sensation, photophobia, and tearing.

After the treatment, visual acuity improved in 5 (71.42%) patients (from hand movement [HM] to counting fingers [CF] in three eyes, from 6/60 to 6/24 in one eye, and from HM to 6/24 in one eye) and remained unchanged (PL) in 2 (28.57%) eyes. Complete pain relief (grade 0 pain score) was achieved in all seven patients (100%) after a mean follow-up of 26.57 weeks (range from 11 to 53). The mean time for corneal surface epithelialization was 4.6 weeks (range from 3 to 8 weeks). Associated symptoms including foreign body sensation, photophobia, and tearing subsided significantly in all patients.

Inflammatory signs characterized by conjunctival and/or episcleral injection were a common finding before AMT but invariably subsided after the surgical procedure. No sign of inflammation was observed at the end of follow-up. Complications such as infection, pyogenic granuloma, symblepharon, or membrane traction were not seen. All patients were symptom free at the end of follow-up period.

TABLE I - DEMOGRAPHIC DATA, ETIOLOGY, AND FOLLOW-UP

Patient	Age, yr/sex	Eye	Etiology of painful cornea	Follow-up, in weeks	Preop pain score	Postop pain score	Preop visual acuity	Postop visual acuity	Symptoms at last follow-up
1	72/F	L	BK secondary to Fuchs heterochromic cyclitis with pseudophakia	15	Grade III	Grade 0	Hand movements	Counting fingers	None
2	84/F	L	BK secondary to AC-IOL to treat aphakia	20	Grade III	Grade 0	Perception of light	Perception of light	None
3	79/F	R	BK secondary to AC IOL for PC rupture during phaco	20	Grade III	Grade 0	Hand movements	Counting fingers	None
4	75/F	L	Failed corneal graft for BK	31	Grade III	Grade 0	Perception of light	Perception of light	None
5	46/F	R	Failed corneal graft for corneal ulcer related opacity	11	Grade III	Grade 0	Hand movements	Counting fingers	None
6	65/F	R	Failed corneal graft for rheumatoid arthritis related thinning resulting in bullous keratopathy	53	Grade III	Grade 0	6/60	6/24	None
7	44/M	R	Chemical corneal burn due to lime injury	36	Grade III	Grade 0	Hand movement	6/24	None

BK = Bullous keratopathy; AC-IOL = Anterior chamber intraocular lens; PC = Posterior capsule

DISCUSSION

AMT has been used since 1910 by Davis in surgery for skin transplantation. DeRotth performed AMT for the reconstruction of conjunctival defects in 1940 (10). In 1995, Kim and Tseng reported the use of preserved and dissected amniotic membrane for ocular surface reconstruction in animal models (11).

A variety of therapeutic modalities have been advocated for the treatment of painful bullous keratopathy. These treatments are not totally satisfactory for a variety of reasons: application of bandage contact lens may predispose to bacterial keratitis and corneal neovascularization and patients must be observed closely, conjunctival flaps may be cosmetically unsatisfactory and very painful postoperatively, and phototherapeutic keratectomy is an expensive procedure and carries the risk of epithelial breakdown, neurotrophic ulceration, and infection.

The anti-inflammatory and anti-angiogenic properties of amniotic membrane are well known, thus making it an ideal tissue substitute for reconstruction of ocular surfaces (12, 13).

In our study we have evaluated the efficacy and safety of AMT in painful bullous keratopathy and its role in improving vision. We found that AMT is an effective treatment modality for the relief of pain and restoration of epithelial integrity. All 7 patients (100%) were completely pain free after a mean of 26.57 weeks of follow-up while other ocular surface irritation symptoms such as foreign body sensation, photophobia, and tearing decreased significantly in all patients.

Unlike previous reports, transplantation of amniotic membrane was directed to eyes with no visual po-

tential, our study was carried out in eyes with some visual potential. The visual acuity improved after AMT in 5 eyes (71.42%). This is particularly significant in developing countries where facilities for performing penetrating keratoplasty are limited and corneal transplantation is in shortage.

In summary, it could be concluded that AMT proves to be an effective and safe surgical technique, accelerating the re-epithelialization of the ocular surface and relieving pain and other symptoms. Besides, it appears to have a role in improving the vision in eyes with some visual potential. However, it remains unclear whether it can be used as a routine procedure to improve the vision in eyes with visual potential.

The authors are aware that the study has a small number of patients and that a large prospective randomised case control study is needed to establish the effective role of AMT in painful bullous keratopathy. According to the literature and our observations, AMT is a simple, effective, and low cost technique that may be considered as the choice of treatment of patients with little or no potential of visual recovery who are not candidates for penetrating keratoplasty.

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