

Amniotic Membrane Transplantation for Symptomatic Bullous Keratopathy

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ABSTRACT

Objectives: To evaluate the efficacy of amniotic membrane in the management of painful bullous Keratopathy. **Material and Method:** Amniotic membrane transplantation was performed at Ophthalmology Department Bahawal Victoria Hospital, Bahawalpur. The study included 15 eyes (15 patients) with symptomatic bullous keratopathy and poor visual potential. The underlying causes of bullous keratopathy included aphakia (4 eyes), pseudophakia (9 eyes), and others (2 eyes). **Results:** During the follow-up period of 6 weeks after amniotic membrane transplantation, 13 of the 15 eyes with intolerable pain preoperatively became pain free postoperatively. Among the 2 eyes with residual pain, 1 received repeated amniotic

membrane transplantation and 1 had reduced pain. Epithelial defects in 13 of the 15 eyes created and covered by amniotic membrane healed rapidly within 2 weeks. Only 2 eyes showed recurrent surface breakdown. Epithelial edema or bullae recurred in a smaller area in only 1 eye and that was effectively controlled with medical treatment. **Conclusion:** Amniotic membrane transplantation is a good treatment option for alleviating pain, promoting epithelial healing, and preserving cosmetic appearance in patients with symptomatic bullous keratopathy and poor visual potential

Key Words: Amnion, Bullae, Blister, Corneal Edema.

INTRODUCTION

The use of amniotic membrane (or amnion) for transplantation as graft in bullous keratopathy is reviewed. This technique has become widespread because of the availability of the amnion, convenience and ease of use, and high and reproducible success rates. The mechanisms of action of the transplantation are varied and include the prolongation and clonogenic maintenance of epithelial progenitor cells, promotion of goblet and nongoblet cell differentiation, exclusion of inflammatory cells with anti-protease activities, suppression of Transforming Growth Factor signaling and myoblast differentiation of normal fibroblasts. The observed clinical effects include facilitation of epithelialization, maintenance of normal phenotypes, and reduction of inflammation, vascularization and scarring. Amniotic membrane transplantation is being increasingly used as graft for various conjunctival and corneal diseases such as intractable Bullous Keratopathy.¹ Amniotic membrane is the innermost part of the placenta.

Since the study by Kim and Tseng on application of amniotic membrane to rehabilitate severely damaged cornea in 1995, its indications for use have been expanded rapidly.² Today, the use of amniotic membrane as a carrier for epithelial cells expansion is under investigation. The exact mechanisms for how amniotic membrane induces favorable responses in many diverse conditions are not fully understood, nor are the membrane's compositions. What is known about amniotic membrane so far is that it contains abundant extracellular matrix materials such as fibronectin, laminin, type IV collagen and integrin, as well as various protease and growth factors. So amniotic membrane acts as a mechanical barrier in many conditions in which ocular structural reinforcement is needed, and thereby, it lessens ocular pain in exposed cornea that has ocular surface pathology and offers substrate for epithelial migration. By affecting down regulation of TGF- β system, amniotic membrane can also help corneal cells to differentiate normally and retain

their cellular characteristics and thus prevent scar formation and maintains corneal clarity. The protease inhibitors may play some roles in restoring normal ocular architecture. The advantages of amniotic membrane over other materials are that it is easy to obtain, is relatively cheap, and is easy to manipulate. Also it does not induce rejection. When needed, the thickness of graft can be increased substantially by folding the membrane. Moreover, since it is semi-translucent, it renders cosmetically superb result and readily allows examination of the underlying structure, thus enabling early detection of any complications.³

STUDY DESIGN

Prospective experimental case series study.

MATERIAL AND METHODS

Amniotic membrane transplantation was performed at Ophthalmology Department Bahawal Victoria Hospital, Bahawalpur over a period of one year from Sep 2009 to Sep 2010. The study included 15 eyes (15 patients) with symptomatic bullous keratopathy and poor visual potential. The underlying causes of bullous keratopathy included aphakia (4 eyes), pseudophakia (9 eyes) and others (2 eyes). Amniotic membrane (AM) preparation was done as mentioned below: Detailed medical history and clinical condition of potential donor was judged to exclude risk of tissue transmissible infections. Consent of Donor for donation of placenta & subsequent use was taken. Donors were subsequently screened for HIV type 1 & 2, Hepatitis B & C virus, Syphilis. Amniotic membrane procured from elective caesarian section routinely done for their respective indications. In the operation theatre, the amniotic membrane dissected from placenta in two larger bits. As much of chorion as possible was peeled out before the bits were dropped into sterile container and washed with BSS containing antibiotics (50 g/ml gentamicin, 100 units/ml penicillin, 200 g/ml ciprofloxacin and 1mg/ml amphotericin B).

TECHNIQUE OF AMNIOTIC MEMBRANE TRANSPLANTATION

Amniotic membrane transplantation (AMT) was done after taking informed consent from the patient. The procedure was done under topical or peribulbar anaesthesia. Under all aseptic conditions,

the epithelium of the cornea was removed. The freshly prepared amniotic membrane was spread over the cornea with the basement membrane side facing up. The side of the basement membrane was distinguished from the stromal side by touching it with sponge; the latter being sticky, but not the former. The amniotic membrane was trimmed to cover the entire cornea extending beyond the limbus all around by 3mm (Fig 3). It was sutured to the bulbar conjunctiva using 10-0 nylon suture. A 360 degree conjunctival peritomy was followed by removal of the diseased corneal epithelium. Amniotic membrane was transplanted over the cornea as a patch and sutured to the free conjunctival edge.

Figure-1
Bullous Keratopathy



Figure-2
Removal of corneal epithelium



Figure-3
Placement of amniotic membrane



Figure -4
Suturing of amniotic membrane



Figure -5
Suturing of amniotic membrane



RESULTS

15 eyes of 15 patients with intractable bullous keratopathy were treated with amniotic membrane graft. During the follow-up period of 12 weeks after amniotic membrane transplantation, 13 Of the 15 eyes with intolerable pain preoperatively became pain free postoperatively within 24 hours. Associated symptoms including foreign body sensation, photophobia and tearing subsided significantly in all patients starting soon after the first postoperative day. Among the 2 eyes with

residual pain, 1 received repeated amniotic membrane transplantation and 1 had reduced pain after a few days. Epithelial defects in 13 of the 15 eyes created and covered by amniotic membrane healed rapidly within 2 weeks. Only 2 eyes showed recurrent surface breakdown. Epithelial edema or bullae recurred in a smaller area in only 1 eye and that was effectively controlled with medical treatment. The mean follow-up was 11 weeks (range 10 to 12 weeks). Pain relief was achieved in all seven (100%) eyes.

DISCUSSION

The transplantation of human amniotic membrane has been added to the therapeutic armamentarium. Amniotic membrane obtained from cesarean deliveries is prepared under sterile conditions and can be sutured onto the ocular surface. Amniotic membrane-covered surfaces have been shown to induce rapid re-epithelialization (in 2 to 4 weeks) to a smooth and wettable surface and reduce inflammation, vascularization and scarring, thus allowing successful surface reconstruction. The normal ocular surface is covered by corneal and conjunctival epithelium. The corneal epithelium is well known for its rapid self-renewal process, with ultimate tissue regeneration relying on the existence of stem cells located in the limbal epithelium (the junction zone between the corneal and conjunctival epithelia). Total loss or hypofunction of the stem cells can occur as a result of certain conditions that cause damage or alteration of the corneal surface (termed limbal deficiency). Normal healing of corneal epithelial defects is prevented and a unique pathological state ensues manifested by poor epithelialization (persistent defects or recurrent erosions), chronic stromal inflammation (keratitis mixed with scarring), corneal vascularization and conjunctival epithelial ingrowth. Since some of these features can be found in other corneal diseases, the sine qua non for making the diagnosis of limbal deficiency is the existence of conjunctival epithelial ingrowth onto the corneal surface. Clinically, this pathologic state can be confirmed by detecting conjunctival goblet cells on the corneal surface through the use of impression cytology. Persistent corneal epithelial defects refractory to conventional treatment remain a therapeutic challenge that often requires surgical intervention. Espana et al (2003)

evaluated the long-term outcomes of epithelial debridement and AMT for pain and discomfort relief in patients with symptomatic bullous keratopathy and poor visual potential. This retrospective study included 18 eyes (18 patients) with bullous keratopathy presenting with intractable pain or discomfort and poor visual potential. After epithelial debridement, all eyes had AMT with the basement membrane side up. During a mean follow-up of 25.1 months \pm 9.6 (SD) (range of 12 to 45 months), pain relief, epithelial healing, and visual changes were analyzed. Pain relief was obtained in 88 % of patients; 66 % of eyes had complete resolution of ocular discomfort starting soon after the first post-operative day. One eye had evisceration for persistent pain 10 months post-operatively. Corneal epithelial healing was complete in all except 1 eye. Remaining complaints included foreign-body sensation (5 %), tearing (11 %), and photophobia (5 %). The authors concluded that AMT was a safe, effective, and long-lasting treatment modality for intractable pain associated with chronic bullous keratopathy in eyes with poor visual potential. It can be an alternative to conjunctival flaps for the long-term management of patients with bullous keratopathy in whom corneal transplantation is not indicated.⁵ Chansanti and Horatanaruang (2005) assessed the outcomes of AMT for symptomatic relief in patients with bullous keratopathy. This retrospective study included 17 eyes (17 patients) with bullous keratopathy presenting with intractable pain or discomfort. Symptomatic relief epithelial healing, and visual changes were analyzed. During the follow-up period of 14.1 \pm 11.9 months (range of 1 to 36 months) after AMT, 14 eyes of 17 eyes (82.4 %) with intolerable pain pre-operatively had pain relief post-operatively. Corneal epithelial healing was complete in all except 2 eyes; 1 of which had evisceration because of severe corneal ulcer, and the other underwent penetrating keratoplasty soon after AMT. The authors concluded that AMT is a safe and effective treatment modality for pain relief associated with chronic bullous keratopathy. It can be an alternative to conjunctival flap, with better cosmetic appearance for the management of patients with bullous keratopathy.⁶ Srinivas et al (2007) examined the effectiveness of AMT in relieving pain and discomfort in patients with painful bullous

keratopathy and its role in improving vision in eyes with visual potential. A total of 7 eyes of 7 consecutive patients with painful corneal conditions were included in a retrospective interventional non-comparative case-series study. Pain relief, epithelial healing, and visual changes were evaluated. Pain relief and freedom from discomfort were considered for the success of the surgery. The mean follow-up was 26.57 weeks (range of 11 to 53 weeks). Pain relief was achieved in all 7 (100 %) eyes. Associated symptoms including foreign body sensation, photophobia, and tearing subsided significantly in all patients starting soon after the first post-operative day. Vision improved in 5 (71.42 %) patients. The authors concluded that AMT is an effective alternative for the management of patients with painful bullous keratopathy.⁷ In a prospective non-comparative interventional case-series study, Georgiadis et al (2008) reported the findings of cryopreserved human AMT for the management of symptomatic bullous keratopathy. Consecutive cases with symptomatic bullous keratopathy for more than 12 months not amenable to conservative treatment were managed with AMT. Patients were recruited over a 5-year period in one referral center. Only one eye of each patient (the worse affected eye in bilateral cases) was operated. A 360 degree conjunctivalperitomy was followed by removal of the diseased corneal epithelium. Amniotic membrane was transplanted over the cornea as a patch and sutured to the free conjunctival edges. Primary outcome measures were ocular pain and epithelial defects; secondary measures were visual acuity (VA) and ocular surface inflammation. Four out of 85 recruited cases did not complete the minimum observation of 12 months and were excluded from the study. The mean follow-up period for the remaining 81 cases was 21 \pm 4.2 months (range of 14 to 34 months). Seventy-one (87.6 %) eyes became asymptomatic with healed epithelium, 7 required repeated amniotic transplantation and 3 underwent penetrating keratoplasty. Visual acuity improved in 64 (79 %) patients and remained unchanged in 14. No complications were recorded. The authors concluded that AMT is a safe and effective treatment for symptomatic bullous keratopathy when penetrating keratoplasty is not available. It has been shown to alleviate pain, promote corneal epithelialization and

reduce conjunctival inflammation whereas in some cases it may also improve VA. The results of my study is very consistent with these international studies conducted world over. Considering that the incidence of bullous keratopathy is so high in our country this mode of treatment can play a pivotal role in the management of this condition.

CONCLUSION

In summary, amniotic membrane transplantation is an efficacious treatment for bullous keratopathy as it stabilizes ocular surface rapidly. Furthermore it is easily available and cheap and patients can easily afford the procedure.

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