Orginal Article

# Amniotic Membrane Transplantation In Ocular Surface Disorders

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We report our experience of amniotic membrane transplantation. Altogether eight cases were performed for different ocular surface disorders. Two cases of extensive symblepheron due to ocular cicatrical pemphigoid and acute epidermal toxic necrolysis. One each case of persistent epithelial defect due to Stevens-Johnson syndrome, Mooren's ulcer, shield ulcer in vernal keratoconjunctivitis, central corneal perforation following treated infective keratitis, conjunctival squamous cell carcinoma excision and Bowen's disease excision. All the cases were successful except one case of extensive symblepheron following epidermal toxic necrolysis, leading to detachment of amniotic membrane and perforation of cornea.

In 1910 Davis first reported use of fetal membranes for skin transplantation[1]. In Ophthalmology the first use of amniotic membrane transplantation (AMT) was by De Roth in 1940 for conjunctival epithelial defects after symblepharon[2]. Then after a long gap in 1995 AMT was reported by Kim and Tseng in severely damaged corneas in a rabbit model[3]. Since then AMT has been used in persistent corneal epithelial defects, neurotrophic corneal ulcers, leaking filtering blebs after glaucoma surgery, conjunctival surface reconstruction with or without limbal stem cell grafting and in patients with ocular cicatrical pemphigoid or Stevens Johnson syndrome.

The ocular surface is covered by corneal, limbal and conjunctival epithelial cells. Limbal stem cells give rise to corneal epithelium and in fornices lie the conjunctival stem cells, giving rise to conjunctival epithelium. Together with this ocular surface epithelium, stable tear film maintain the health of ocular surface and so allow good visual acuity. In certain ocular and systemic disorders there is damage to limbal stem cells or to corneal epithelium. This results in chronic epithelial defects in cornea which are resistant to conventional treatment. Conventionally these defects have been treated with topical lubrication, punctal occlusion, therapeutic contact lenses and temporary or permanent tarsorrhaphy. Human Amniotic Membrane Transplantation may be used as an alternative or adjunctive therapy in this situation.

Human Amniotic Membrane is derived from fetal membranes and consists of single epithelial layer, thick basement membrane and vascular stroma. Epithelial surface is shiny and non sticky, stromal surface is rough and sticky.

The exact mechanisms by which amniotic membrane delivers its beneficial effects on ocular surface are still being investigated. However it has been found that it modulates levels of cytokines and growth factors, which have unique properties that results in reduction of pain, including pain suppression of fibrosis and protection of wound. Its basement membrane acts as scaffold on which the

corneal epithelium can regrow. It has also very low antigenecity, so minimum chances of rejection.

To date, most clinical experience with AMT have been with tissue preserved using method described by Tseng and colleagues. However there have been some reports of use of fresh amniotic membrane.

## MATERIAL AND METHODS

We used amniotic membrane for 8 different cases of ocular surface disorders. In all cases stored membrane was used.

### Preparation of membrane

Human amniotic membrane was obtained from an elective C-Section without ruptured membranes in a seronegative (HIV, human hepatitis type B and C and Syphilis) woman. Under sterile conditions placental membrane was washed and cleaned from blood clots and any fetal remnants. This cleaned membrane was washed with sterile saline containing Penicillin (50 micro gm /ml), Streptomycin (50micro gm/ml), Gentamycin (l00micro gm/ml) and Amphoterecin B (2.5micro gm/ml). The amnion is separated from rest of chorion by blunt dissection through potential spaces between these tissues and chorion is discarded. The amniotic membrane is the stretched and flattened over sterile nitrocellulose filter paper with epithelial surface (shiny and non sticky) up and stromal matrix (rough and sticky) down in contact with paper and was stored in standard refrigeration at -20 degree centigrade and utilized with in a month.

### Case No. 1

A 65 year old male with ocular mucous membrane pemphigoid in both eyes left more than right had AMT in left (worst) eye (Fig. 1,2). All the fibrous tissue was excised, symblepharon released and conjunctiva recessed up to fornices. Amniotic membrane with epithelium up was placed on cornea and sclera up to both fornices. It was sutured with double armed 4-0 silk passing through the conjunctiva and the amniotic membrane at the intended depth of fornix and exiting at the eye lid skin and tied over silicone sponge (bolsters). The membrane was anchored to episclera with 10-0 nylon for amniotic membrane to cover cornea evenly without stretching and folding. Bandage contact lens was applied with conformer. Upper lid entropion with trichiasis was also corrected with anterior lamellar repositioning with anterior raw surface covered with amniotic membrane.

### Case No. 2

A 25 year old male having extensive symblepharon and ankyloblepharon as a result of acute toxic necrolysis, was treated with AMT in right eye (Fig. 3,4). Membranes were excised, lids separated, all fibrous tissue over cornea and conjunctiva was excised meticulously. Amniotic membrane was applied on all corneal and scleral surfaces with fornix forming sutures and episcleral sutures as was done in case no. 1.Bandage contact lens and conformer were applied.

### Case No. 3

A 22 year old lady having non healing corneal epithelial defect as a result of Stevens Johnson syndrome was treated with AMT in her left eye. Loose corneal epithelium was scraped leaving healthy edges. Amniotic membrane was transplanted with epithelial side up and sutured with 10-0 nylon on healthy cornea surrounding the defect. Bandage contact lens was applied.

### Case NO. 4

A 30 year old male having Mooren's Ulcer in left eye between 12 to $2^{0,}$ clock was treated with topical corticosteroids for one year with out any significant success. It was treated with conjunctival recession around the ulcer, limbal stem cell autograft from contralateral eye and amniotic membrane sutured all around the ulcerated area. Bandage contact lens was applied.

### Case No. 5

A 20 year old male with Vernal Keratoconjunctivitis (VKC) developed shield ulcer in left cornea. The cornea was thin and threatening to perforate. Patient's eye got worse after application of conjunctival hood flap. A multilayer AMT was performed with conjunctival recession. Amniotic membrane was sutured all around with both circumferential and interrupted sutures. Bandage contact lens was applied over it and treated with VKC treatment medically.

### Case No. 6

A 55 year old male had central corneal perforation following infective keratitis. A multilayer AMT was performed and bandage contact lens applied.

### Case No. 7

A 70 year old lady had biopsy proven squamous cell carcinoma of temporal bulbar conjunctiva in right eye. The neoplasm was removed leaving healthy edges with cryopexy applications around excised area in

circumferential fashion. The gap was filled with AMT.

**Case No. 8**

An 80 year old lady having a large Bowen's Disease in left eye covering conjunctiva, limbus and cornea was treated with excision of lesion along with perilimbal conjunctiva with circumferential cryopexy application. The gap was filled with AMT.

Fig. 1:

Fig. 2:

Fig. 3:

Fig. 4:

Fig. 5:

**RESULTS**

In case no.1 corneal and conjunctival epithelium reformed. Both fornices formed (Fig 2).Though excellent cosmetic results were achieved, patient developed dry eyes which needed life long treatment with lubrication. In case no.2, postoperatively for one week patient was improving nicely and his vision improved to counting fingure from perception of light

(Fig. 4). Then the membrane detached from upper half and following day cornea started melting (Fig. 5) .To protect the globe Tarsorrhaphy was performed. In case no.3 amniotic membrane was successfully taken up. Epithelial defect healed, leaving healthy corneal surface. Mooren's ulcer, which was case no.4, healed successfully without any recurrence with one year follow up but unfortunately ulcer occurred in other eye proving its strong autoimmune basis. He was advised 360 degree peritomy with AMT but he was lost to follow up. In case no.5 the ulcer healed, leaving quiet avascular corneal scar with good integrity. Perforation in case no.6 sealed nicely leaving small central scar with good integrity. In both cases no.7 and 8 the membrane epithelialized successfully leaving no defect in the excised area.

## DISCUSSION

Lately amniotic membrane has generated enormous interest among ophthalmologists, and the indication of its use are ever increasing. The ophthalmic uses of human amniotic membrane for transplantation are many and its rediscovery has greatly improved our ability to treat debilitating ocular surface diseases. While results from many studies are encouraging, others show less enthusiastic results. Meller De et al showed its successful use in mild to moderate acute chemical and thermal burns[4]. Honavar et al reported that AMT restores adequate bulbar surface and fornix depth and also prevents recurrence of symblepheron in severe cases of Stevens Johnson Syndrome[5]. Parbhasawat et all assessed the use of AMT in prevention of recurrence of pterygium and reported a relatively low recurrence rate for primary pterigia[6]. Tsubota et al reported its successful ocular surface reconstruction in advanced ocular cicatrical pemphigoid and in Stevens Johnson Syndrome[7]. Multilayer AMT has also been used for reconstruction of corneal epithelium and stroma in deep corneal ulcers[8]. Tseng and Lee have also reported that alternative method for persistent epithelial defects and sterile ulceration that are refractory to conventional treatment, can be treated with AMT before considering treatment with conjunctival flap and tarsorrhaphy[9].

In our study AMT was successful in treating persistent epithelial defects in Stevens Johnson Syndrome. AMT in ocular cicatrical pemphigoid resulted successfully in formation of fornix and epithelialization of corneal and conjunctival surface. Multilayer AMT for shield ulcer in Vernal keratoconjunctivitis was successful in prevention of perforation and eventually healing and maintaining corneal integrity. Mooren's ulcer was also successfully treated with AMT but it was combined with conjunctival recession and limbal cell auto graft. Central corneal perforation was also managed successfully with Filler technique. After excision of Squamous cell carcinoma and Bowen's disease conjunctival gap was filled with AMT and it was successfully taken up.

One of the disappointing case was cicatrizing ocular surface following Acute Epidermal Toxic Necrolysis. The membranes excised, Symblepharon released and AMT performed. Patient's vision improved to counting finger from perception of light. However after one week amniotic membrane was detached followed by melting of cornea. Then the eye was closed with tarsorrhaphy. It is likely that the limbal stem cell deficiency contributed to the lack of success.

Our overall experience showed that amniotic membrane transplantation is effective in ocular surface disorders when medical therapy fails. Future studies directly comparing AMT to other methods of treatment of persistent epithelial defects would help to better define the role of AMT in ocular surface disease and perhaps further explain mechanisms by which this therapy seems to work.


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