**Original Article**

# Amniotic Membrane Transplantation in Ocular Surface Disorders

Muhammad Salman Hamza, M. Rizwan Ullah, Anwaar ul Haq Hashmi, Imran Akram Sahaf

*Pak J Ophthalmol 2011, Vol. 27 No. 3*

See end of article for authors affiliations

Correspondence to:
Muhammad Salman Hamza
Institute of Ophthalmology
KEMU/Mayo Hospital
Lahore

Submission of paper
April' 2011

Acceptance for publication
August' 2011

**Purpose:** To evaluate the usefulness of amniotic membrane in the patients with ocular surface diseases.

**Material and Methods:** This case series study of one year duration was conducted in Institute of Ophthalmology, Mayo Hospital Lahore. 30 patients having ocular surface disorders were treated with amniotic membrane transplant (AMT) and improvement in the signs and symptoms of ocular irritation like pain, photophobia was evaluated.

**Results:** Out of 30 patients 18 (60%) were male and 12 (40 %) female. Ocular surface disorders include 8 (26.7%) cases of bullous keratopathy, 5 (16.7%) Mooren's ulcer, 5 (16.7%) Shabbir syndrome, 4(13.3%) impending perforations, 3 (10.0%) Chemical injury, 3 (10%) Steven Johnson syndrome and 2 (6.7%) cases of neurotrophic ulcer. More than 90% of the cases after AMT showed remarkable improvement in the symptoms of ocular irritation.

**Conclusion:** Amniotic membrane is a useful material for the treatment of ocular surface disorders.

The normal ocular surface is covered by epithelial cells which can be[1] damaged by certain systemic inflammatory diseases,[1] primary ocular diseases, and trauma resulting in the breakdown of ocular surface.[2] If the normal epithelialization process fails ocular defect becomes chronic. Chronic inflammation leads to neovascularization, corneal scarring, opacification, corneal thinning, and possible corneal perforation.

Traditional treatments for ocular surface disorders include correcting underlying pathology, suppressing inflammation and promoting healing process. Currently, artificial tears, lubricants, fibronectins,[3,4] growth factors,[5] and substance P[6] are used. However, if defect persists and stromal thinning develops, more invasive surgical options like tissue adhesive[7,] bandage contact lens,[8] conjunctival flap[9], and tarsorrhaphy can be performed[10]. But these treatments have their own complications. In this background amniotic membrane can be considered as an option for treating the ocular surface defects[3,4].

In 1910, Davis reported the use of fetal membrane in skin transplantation for the first time[11]. Amniotic membrane transplantation in ophthalmology was reported by De Roth in 1914 who achieved partial success in treatment of conjunctival epithelial defects[12]. There was very little information available in ophthalmic literature until the study by Kim and Tseng in 1995 who used amniotic membrane transplantation for ocular surface reconstruction of severely damaged cornea in rabbit model. Since that experimental study, amniotic membrane transplanttation has been used for persistent corneal epithelial defects, neurotrophic corneal ulcers, conjunctival surface reconstruction, bullous keratopathy, chemical or thermal burns and in patients of Steven-Johnson syndrome[13-15].

Ocular surface disorders are a common problem and current management is not satisfactory. Amniotic membrane transplantation has shown better results in treating these disorders. In Pakistan, a very little work has been done so far in this regard. So, I scientifically studied this new technique in local setup.

## MATERIAL AND METHODS

This Case series was conducted at Institute of Ophthalmology, Mayo Hospital Lahore for one year starting from 13 January 2008 with non-probability purposive sampling. Thirty cases with ocular surface diseases were included. Age of patients was 18 - 70 years. Patients with any active ocular infection or with perforated globes were excluded from surgery.

### Preparation of Amniotic membrane:

Amniotic membrane was obtained from prospective donors undergoing Caesarean section, who were negative for communicable diseases including HIV, hepatitis and syphilis. Different protocols exist for the processing and storage. We used protocol described by Kim et al[16]. According to which placenta is cleaned and stored with balanced salt solution containing a cocktail of antibiotics (Table 1) under sterile conditions.

### Surgical Techniques

I. Inlay or graft technique: When Amniotic membrane is tailored to the size of the defect, is meant to act as a scaffold for the epithelial cells and which then merges with the host tissue, it is referred to as a graft.[17] Amniotic membrane was secured with its basement membrane or epithelial side up to allow migration of the surrounding epithelial cells on the membrane (Fig. 1).

II. Overlay or patch technique: When the Amniotic membrane is used akin to a biological contact lens in order to protect the healing surface defect beneath; it is referred to as a patch[18]. A patch also reduces inflammation by its barrier effect against the chemical mediators from the tear film. When used as patch the membrane is secured with its epithelial side up and it either falls off or is removed.

III. Filling-in or layered technique: In this technique the entire depth of an ulcer crater is filled with small pieces of AM trimmed to the size of the defect. A larger graft is sutured to the edges of the defect in an inlay fashion and an additional patch may help in preserving the deeper layers for a longer duration[19].

Preoperative evaluation was applied to all patients with special attention given to patient's symptoms with respect to pain and photophobia, best corrected visual acuity. Follow up was done at first post operative day, 1st week, 2nd week and 1 month for best corrected visual acuity, ocular symptoms (pain and photophobia) and complications. The data was analyzed by SPSS version 10.00, the variables of outcome measures (pain, photophobia, best corrected visual acuity, graft uptake) was presented as proportions and ratios. The variables of outcome were compared with some of variables of demography. Since this study was a quasi experimental, no test of significance was necessary.

## RESULTS

Of the 30 patients of different ocular surface disorders 18 were males (60%) and 12 were females (40 %). Ocular surface disorders of various types were included in this study, most was the bullous keratopathy 8 (26.7%) followed by Mooren's ulcer 5 (16.7%), Shabbir syndrome 5 (16.7%), impending perforations 4(13.3%), Chemical injury 3 (10.0%), Steven Johnson syndrome 3 (10%) and 2 (6.7%) cases of neurotrophic ulcer.

The ocular surface defects was present in both eyes of 9 (30.0%) cases. 13 (43.3%) cases had these defects in right eye, while 8 (26.7%) cases left eye was involved out of total 30 cases.

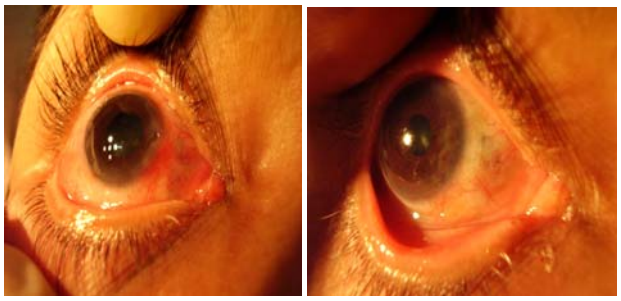
Ocular pain was one of the most important variable of study. It was recorded on the pain scale from grade 0 – 4 as described by the patient. Three (10.0%) patients did not complain any pain (Grade 0). Six (20.0%) cases had mild pain (grade 1).Seven (23.3%) cases were having moderate pain (Grade 2). Thirteen (43.3%) patients described severe pain. One (3.3%) case was having maximum pain imaginable (Fig.2). After one month of amniotic membrane transplantation, most of the patients 25 (83.3%) were having no pain (Grade 0). Only 2 (6.7%) and 3 (10.0%) patients described mild (Grade 1) and moderate (Grade 2) pain. No patient described grade 3 and 4 level of pain (Fig. 3).

Twenty seven (90%) of the patients were photophobic, only 3 (10.0%) out of 30 did not complain of photophobia. A remarkable improvement was noted in this regard. At one month after surgery, 26 (86.7%) patients did not complain of photophobia and only 4 (13.3%) cases were still complaining of it.

There was a little improvement of best corrected visual acuity noted, after 1month of surgery 4 (13.3%) had best corrected visual acuity 6/12, while 1 (3.3%) case had 6/18 and 2 (6.7%) patients were having 6/24. Majority of the cases 23 (67%) were still having best corrected visual acuity 6/60 or less.

**Table 1**: Contents and concentrations of antibiotics solution

| Antimicrobial Agent | Dose |
|---|---|
| Penicillin | 50 mg/ml |
| Streptomycin | 50 µg/ml |
| Neomycin | 100 mg/ml |
| Amphotericin B | 2.5 mg/ml |



A B

**Fig.1:** Inlay technique used on Mooren's ulcer A. Pre operative B. Post operative

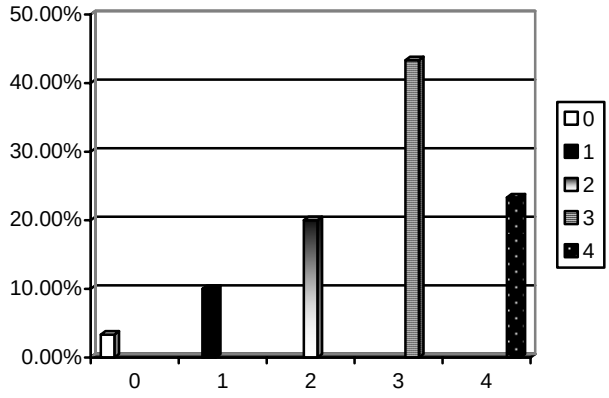



**Fig. 2:** Pre Operative Pain Grade

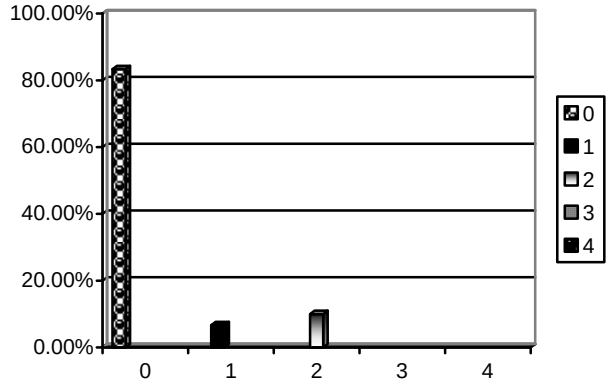



**Fig. 3:** Post Operative pain grade

## DISCUSSION

Ocular surface disorders are a common problem that presents not only with decrease of vision but also pain and photophobia. Unfortunately, its currently medical or surgical treatment has not shown satisfactory results so far. Amniotic membrane that had been used for other purposes like biological dressing to cover the open wounds and skin transplantation, have also shown good results in ocular surface defects healing and thus relieving the symptoms of ocular irritation.

Human amniotic membrane is derived from the fetal membranes and is loosely attached to the chorion. [20] It is composed of three layers: a single epithelial layer, thick basement membrane, and a vascular stroma. Human amniotic membrane has been shown to contain collagen types III and V. It also contains collagen types IV and VII similar to corneal epithelial basement membrane as well as fibronectin and laminin[21]. Additionally, it contains fibroblast and other growth factors. Amnion prevents inflammatory cell infiltration and reduces apoptosis in keratocytes after transplantation onto the corneal surface[22]. Due to all these properties amniotic membrane transplantation is found to be an important tool for reconstruction of ocular surface disorders.

Reduction in symptoms of ocular irritation that includes pain and photophobia was 90 % in our study which is comparable to the other studies[23]. Increased comfort level, improved the quality of life of the patients. There was no remarkable improvement in best corrected visual acuity observed in our study. The final visual acuity less than 6/60 was recorded in 67 % of cases in our study which was quite similar to study by Prabhasawat P, Tesavibul N who also observed the similar ratio in their study[23]. However increased comfort level improved the quality of life of these patients and visual acuity was not the issue in these patients.

Failure was noted in 3 (10%) cases in our study. This was due to graft necrosis, active infection and intractable corneal perforation. This failure points out the limitations of AMT in treating ocular surface disorders. The possible causes of failure could be, continuous tissue destruction compounded with active infection underneath the graft had retarded healing and secondly there might have been inadequate limbal stem cells and intact sensory innervations which is mandatory for repairing and maintaining ocular surface integrity[24]. Thirdly normal

keratocytes from adjacent area might be important in restoring stromal integrity after AMT.

The results of study showed that amniotic membrane transplantation is effective in ocular surface disorders when all other existing methods of management fail.

## CONCLUSION

Amniotic membrane transplantation appears to be a useful method to alleviate symptoms of ocular surface irritation like pain, photophobia and lacrimation caused by the ocular surface disorders. It does not only heal the corneal surface defect but also helps in preserving the globe. The future studies are required for further elaboration of usefulness of this tissue.


### Author's affiliation

Dr. Muhammad Salman Hamza
Institute of Ophthalmology
KEMU/Mayo Hospital
Lahore

Dr. M. Rizwan Ullah
Institute of Ophthalmology
Lahore General Hospital (LGH)
Lahore

Dr. Anwaar Hashmi
Institute of Ophthalmology
KEMU/Mayo Hospital
Lahore

Dr. Imran Akram Sahaf
Institute of Ophthalmology
Lahore General Hospital (LGH)
Lahore


## REFERENCE


1. **Mejia LF, Acosta C, Santamaria P.** Use of nonpreserved human amniotic membrane for the reconstruction of ocular surface. Cornea. 2000; 19: 288-91
2. **Sangwan VS, Tseng SCG**. New Perspectives in ocular surface disorders. An integrated approach for diagnosis and management. Indian J Ophthalmol. 2001; 49:153-68.
3. **Spigelman AV, Deutsch TA, Sugar J.** Application of homologous fibronectin to persistent human corneal epithelial defects. Cornea. 1987; 104: 494-501.
4. **Nishida T, Nakagawa S, Manabe R.** Clinical evaluation of ibronection eye drops on epithelial disorders after herpetic keratitis. Ophthalmology. 1985; 92: 213-16.
5. **Feldman ST.** The effect of epidermal growth factor on corneal wound healing: practical consideration of therapeutic use. Refract Corneal Surg. 1991; 7: 232-9.
6. **Brown SM, Lamberts DW, Reid TW, et al.** Neurotrophic and anhidrotic keratopathy treated with substance P and insulinlike growth factor I. Arch Ophthalmol. 1997; 115: 926-7.
7. **Globovic S, Paronovic A.** Cyanoacrylate glue in the treatment of corneal ulcerations. Fortschr Ophthalmol. 1990; 87: 378-81.
8. **Pfiser RR.** Clinical measures to promote corneal epithelial healing. Acta Ophthalmol. 1992; 70: 78-83.
9. **Lugo M, Arentsen JJ.** Treatment of neurotrophic ulcers with conjunctival flaps. Am J Ophthalmol. 1987; 103: 711-2.
10. **Welch C, Baum J.** Tarsorrhaphy for corneal disease in patients with rheumatoid arthritis. Ophthalmol Surg. 1988;19:31-32
11. Davis JW. Skin transplantation with a review of 550 cases at the Johns Hopkins Hospital. Johns Hopkins Med J. 1910; 15: 307-96.
12. **De Rotth A.** Plastic repair of conjunctival defects with fetal membranes. Arch Ophthalmol. 1940; 23: 522-5.
13. **Shimazaki J, Yang HY, Tsubota K.** Amniotic membrane transplantation for ocular surface reconstruction in patients with chemical and thermal burns. Ophthalmology. 1997; 104: 2068-76.
14. **Meller D, Pires RT, Mack RJS.** Amniotic membrane transplantation for acute chemical and thermal burns. Ophthalmology. 2000; 107: 980-90.
15. **Ucakhan OO, Koklu G, Firat E.** Nonpreserved human amniotic membrane transplantation in acute and chronic chemical eye injuries. Cornea. 2002; 21: 169-72.
16. **Kim JC, Tseng SC.** Transplantation of preserved human amniotic membrane for surface reconstruction in severely damaged rabbit corneas. Cornea. 1995; 14: 473-84.
17. Sippel KC, Ma JJ, Foster CS. Amniotic membrane surgery. Curr Opin Ophthalmol. 2001; 12: 269-81
18. **Azuara-Blanco A, Pillai CT, Dua HS.** Amniotic membrane transplantation for ocular surface reconstruction. Br J Ophthalmol. 1999; 83: 300-402.
19. **Hanada K, Shimazaki J, Shimmura S, et al.** Multilayered amniotic membrane transplantation for severe ulceration of the cornea and sclera. Am J Ophthalmol. 2001;131:324-31
20. **Trelford JD, Trelford-Sauder M.** The amnion in surgery, past and present. Am J Obstet and Gynecol. 1979; 134: 833-45.
21. **Fukada K, Chikama T, Nakamura M, et al.** Differential distribution of subchains of the basement membrane components type IV collagen and laminin among the amniotic membrane, cornea, and conjunctiva. Cornea. 1999; 18: 73-9.
22. **Wang M, Gray T, Prabhasawat P, et al.** Corneal haze is reduced by amniotic membrane matrix in excimer laser photoablation in rabbits. Invest Ophthalmol Vis Sci. 1997; 38: 405.
23. **Prabhasawat P, Tesavibul N, Omolsuradej W.** Single and multilayer amniotic membrane transplantation for persistent corneal epithelial defect with and without stromal thinning and perforation. Br J Ophthalmol. 2001; 85: 1455-63.
24. **Van Herendael BJ, Oberti C, Brosens I.** Microanatomy of the human amniotic membranes. Am J Obstet Gynecol. 1978; 131: 872-8.