
Study of amniotic membrane transplantation in the treatment of ocular injuries

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Abstract

Amniotic membrane is the innermost layer of the placental membrane and consists of a thick basement membrane and an avascular stroma. It can be used as a substrate to replace the damaged mucosal surface, and has recently been used successfully for reconstructing corneal and conjunctival surface damaged by various ocular surface disorders including chemical and thermal burns. The present study was undertaken in department of ophthalmology at Ashwini Rural Medical College and Research Center, Kumbhari, Solapur between 1st Jan 2013 to 31 Dec 2014 that is over a period of 2 years to know amniotic membrane transplantation as a treatment modality in the treatment of ocular injuries. After taking written informed consent from the patients and following standard operating procedures, a total of 40 patients were included in the study, non consenting patients were not included in the study.

Amniotic membrane transplantation is an effective way of treating ocular and thermal injuries in the acute stage. Such an acute intervention can break the vicious cycle leading to the progressive melting or scarring sequelae in the chronic stage. Amniotic membrane transplantation is more effective in preserving the anatomical as well as the functional structure of the conjunctival and corneal surface in terms of decreased corneal vascularisation, preventing conjunctivalization of the cornea, improved tear film status and preventing fibrosis in mild grade II to moderate (grade III) burns but cannot do so in severe (grade IV) burns with total limbal deficiency.

Keywords: Ocular Injuries, amniotic membrane transplantation, symblepharon formation, corneal perforation

1. Introduction

Chemical and thermal injuries to the eye may produce extensive damage to the ocular surface epithelium, cornea and anterior segment resulting in permanent visual impairment. The principles of managing the ocular burns in the acute stage are to promote epithelization, reduce inflammation, and prevent progressive tissue melting. The objective is to prevent a vicious cycle of complications that may lead to scarring sequelae and severe visual loss.[1]

As the conventional medical methods in the management of ocular burns have met with only a limited success, it remains one of the challenging entities facing the clinician today.[2] One of the recent approaches to treating these patients is amniotic membrane transplantation. It was utilized in the eye for the first time, way back in 1940 by De Roth [3], but it disappeared from the literature, until in 1995, when Kim and Tseng [4], showed that the amniotic membrane facilitated the corneal surface

reconstruction in rabbits after epithelial removal and limbal keratectomy.

Amniotic membrane is the innermost layer of the placental membrane and consists of a thick basement membrane and an avascular stroma. It can be used as a substrate to replace the damaged mucosal surface, and has recently been used successfully for reconstructing corneal and conjunctival surface damaged by various ocular surface disorders including chemical and thermal burns. Collectively these studies have shown that amniotic membrane transplantation facilitates epithelization and reduces inflammation, vascularisation and scarring.[5][6] Based on these clinical studies, we reviewed the potential efficiency of amniotic membrane transplantation (AMT) in treating ocular chemical and thermal injuries in the acute stage.

2. Materials and Methods

In the present study conducted, 40 patients who had grade II or severe ocular burns, according to Roper Hall classification were counseled for the benefits Vs risks especially of the transmission of the diseases from AMT. Informed consent was obtained from all the patients. During emergency treatment, patient's eye was examined for, visual acuity, lid injury, conjunctival hyperemia, necrosis, limbal ischemia, corneal haze, pupil size and reaction, iris pattern; IOP was checked digitally after ruling out perforation. The patient's were classified according to Roper Hall classification.

After anesthesia (Topical 4% Lignocaine) fornices evaluated for deeply embedded lime particles or foreign body. In case of children, examination under anesthesia was performed. Irrigating solutions used were either normal saline or ringer lactate. The eyes were irrigated for 15-30 min or till the pH of the tears in the conjunctival fornices returned to normal (range 7.3-7.7). Patients were started on systemic antibiotics and analgesics (tab amoxicillin 50 mg/kg/day in three divided doses and Ibuprofen 15 mg/kg/day in three divided doses) and Tab. Acetazolamide 15 mg/kg/day in three divided doses, tab. Vitamin C 500 mg four times a day. Topically antibiotic (tobramycin 0.3%) six times a day, for 7-10 days, 10% ascorbic acid in preservative free lubricating eye drops every hourly, atropine eye ointment 1% was prescribed once a day.

In consultation with the Gynecology department, the amniotic membrane graft was obtained under sterile conditions after elective caesarean section. Donors at risk of having HIV, HBV, HCV and VDRL were all excluded. Consent for donation, subsequent use and for screening for infection was obtained.

The placenta was first washed free of blood clots with balanced salt solution containing 1mg/ml amikacin. The inner amniotic membrane was separated from the rest of the chorion. The membrane was then flattered on a sterile gauze piece, with the epithelial surface up, and placed in a sterile container. The fresh membrane was used as early as possible preferably within 24 hours.

2.1 Surgical Technique of AMT

A written informed consent is obtained. Depending on the age of the patient, they were taken up for operation under general anesthesia (patients < 18 yrs of age) or local peribulbar anesthesia with 2% Lignocaine with adrenaline (7ml) and bupivacaine (3ml) mixed with hylase. All surgeries were performed under operating microscope. Perilimbal conjunctival peritomy was performed.

Amniotic membrane was removed from the sterile container and again washed with balanced salt solution containing 1mg/ml amikacin. The membrane was palced on the recipient eye, with the epithelial surface up. If the conjunctiva is not necrosed and is not ischemic, the amniotic membrane grafting was performed so as to cover the entire cornea and limbus. However, if conjunctiva was ischemic or necrosed and conjunctival debridement had been performed, then amniotic membrane was spread and anchored by sutures to the entire ocular surface from the upper eyelid margin to the lower eyelid margin. This membrane was secured to the ocular surface with episcleral bites (interrupted or continuous) 3-4 mm away from the limbus and to the lid margin with 8-0 vicryl/ethilon sutures. To ensure the depth of the newly created upper and lower fornices, the amniotic membrane was secured with two/three fornix deepening sutures of 5-0 mersilk and brought out from the eyelid skin. A confirmer of adequate size was placed, if fornix was reconstructed.

2.2 Post operative care

Post operatively, the eye was padded for 24 hours. Systemic antibiotics and analgesics (tab amoxicillin 50 mg/kg/day in three divided doses & Ibuprofen 15 mg/kg/day in three divided doses) were given orally for 5 days. Topically antibiotic (tobramycin 0.3%) six times a day and topical steroid eye drops (prednisolone acetate 1%) six times a day, for 7-10 days, ascorbic acid (10%) in preservative free lubricating eye drops 8 times a day. Atropine eye ointment 1% was prescribed twice a day. Patients were admitted for 7-10 days and evaluated daily for, subjective relief from pain, lid edema, and amniotic membrane graft was evaluated for any premature detachment or loss, persistence of the epithelial defect was evaluated through the semitransparent membrane. Steroid eye drops were discontinued after 7-10 days. Re-amniotic membrane was performed in cases of premature loss of the membrane. Antibiotic eye drops were continued till the epithelial defect had healed.

2.3 Follow Up Protocol

Patients were evaluated every week, for the first month or till the epithelial defect was healed. Patients were evaluated in details for visual acuity, lid edema, amniotic membrane graft for any displacement or loss, size of the epithelial defect, congestion of the eye, symblepharon, conjunctivalization and vascularization of cornea, scleral necrosis, ischemia in perilimbal zone, corneal melting, IOP (assessed digitally), pupil size and reaction, iris pattern, lens for any evidence of cataract and schirmer test was performed

3. Observations and results

Table 1: Time lapse between injury and presentation

Time lapse	No. of cases	% of cases
Within 8 hours	12	30
8-16 hours	14	35
16-24 hours	4	10
1 day-1 week	6	15
1 week-1 month	4	10
Total	40	100

Table 2: Extent of AMT

Extent of AMT	No. of cases	% of cases
Entire cornea and limbus	12	30
Entire ocular surface	28	70
Total	40	100

Table 3: No. of times AMT was repeated

AMT done	No. of cases	% of cases
Once	22	55
Twice	14	35
Thrice	4	10
Total	40	100

Table 4: Indication for repetition of AMT

Indication for repetition of AMT	No. of cases	% of cases
Persistent epithelial defect	10	45.5
Symblepharon lysis	8	36.4
Premature detachment of the membrane	4	18.1
Total	22	100

Table 5: Additional procedure performed

Additional procedures	No. of eyes
Symblepharon lysis	14
Autolimb transplantation	2
Penetrating keratoplasty	2

Table 6: Epithelial defect healing time

Grade of injury	Average epithelial defect healing time (days)
II	14.25
III	31.83
IV	45.55

Table 7: Change in the visual acuity

Change in the visual acuity	No. of cases	% of cases
Gained 6 or more lines	2	5
Gained between 4 and 5 lines	12	30
Gained between 1 and 3 lines	2	5
No improvement in vision	8	20
Vision deteriorated	2	5
Visual acuity could not be tested because the patients were underage	14	35
Total	40	100

Table 8: Corneal vascularisation

Grade of injury (no. of patients)	Corneal vascularisation (no. of patients)		
	Nil	Mainly superficial	Superficial and deep
Gr. II (8)	8	0	0
Gr. III (14)	0	6	8
Gr. IV (18)	0	0	18

Table 9: Limbal deficiency

Grade of injury (no. of patients)	Limbal deficiency (clock hours)					
	Nil	1-3	4-6	7-9	10-11	12
Gr. II (8)	8	0	0	0	0	0
Gr. III (14)	0	6	4	4	0	0
Gr. IV (18)	0	0	0	0	6	12

4. Discussion

As conventional methods in the management of ocular burns have met with only a limited success, it remains one of the most challenging entities facing the clinician today. In the present study, 75% of the patients presented within first 24 hours and 90% of patients presented within the first week as shown in Table 7. Thus it was possible to evaluate and treat these injuries in the acute phase. Remaining 10% of the patients presented a little later (from 8 days to 1 month).

The extent to which the ocular surface was grafted with amniotic membrane is shown in Table 2. In 28 patients (70%), there was extensive injury to the ocular surface following the chemical or thermal burns, and hence the entire ocular surface from upper eyelid margin to the lower eyelid margin, covering the entire conjunctiva, cornea and the limbus was grafted with amniotic membrane. Number of times AMT was done on the same eye is shown in table 3. AMT was repeated for a total of 22 times in 18 (45%) eyes. It was repeated once in 14 (35%) and repeated twice in 4 (10%) eyes. Out of the 22 times AMT was repeated, it was repeated 10 times (45.5%) for persistent epithelial defects, 8 times (36.4%) for symblepharon lysis and 4 times (18.1%) because the membrane got detached prematurely as shown in Table 4. In the study conducted by Meller *et al*[7], AMT was repeated in 38.46% of the case, for persistent epithelial defect (7.69%) and because the membrane got detached (7.69%) and along with limbal stem cell transplantation in 23.08% cases for limbal deficiency. Dua HS *et al*[8] repeated AMT by itself or in combination with other procedures in all (n=4) of grade IV ocular burns for persistent epithelial defect. In addition to AMT, the additional surgical procedures, which were performed in this study, are shown in Table 5. Out of the total 40 patients, symblepharon lysis was performed in 14 patients (35%). Autolimb stem cell transplantation was

performed in 2 (5%) cases and penetrating keratoplasty for visual rehabilitation was performed in 2 (5%) cases.

The epithelial defect healing time following AMT performed in the first week following injury is shown in Table 6. The average epithelial defect healing time in grade II ocular burns was 14.25 days, in grade III ocular burns was 31.83 days and in grade IV ocular burns was 45.55 days. Meller *et al*[7], in their study found a significantly faster healing rate, with the mean of 18.8 days in grade II and grade III burns, and 23.7 days in grade IV burns and 15.37% patients had persistent epithelial defects. Dua HS *et al*[8] studied 4 eyes with grade IV chemical (n=3) and thermal (n=1) injuries. AMT was performed in the 2nd and 3rd week following injury. All the four eyes had persistent epithelial defects, progressive corneal melting and developed symblepharon, in spite of AMT, by itself or in combination with other procedures. Out of the four eyes, one eye developed progressive corneal melting and hypopyon, two eyes auto eviscerated and one eye went into phthisis bulbi.

Change in the visual acuity following AMT in chemical and thermal ocular burns is shown in Table 7. Out of the 40 cases, in 14 cases (35%) visual acuity could not be tested because the patients were underage. Out of these 14 cases, 10 cases developed total macular corneal opacity but stable ocular surface epithelium. These eyes can potentially gain vision following penetrating keratoplasty with or without limbal stem cell transplantation. The remaining 4 eyes developed total symblepharon and became phthisical.

In this study, number of patients developing corneal vascularisation and limbal deficiency is shown in Table 8 and Table 9 respectively. No eyes (0%) with grade II injuries developed corneal vascularisation and limbal deficiency. All the patients with grade III and grade IV injuries developed corneal vascularisation and limbal deficiency. Out of the 14 eyes with grade III injury, 6 eyes (42.85%) developed only superficial vascularisation of cornea; while the remaining 8 eyes (57.15%) developed both superficial and deep corneal vascularisation. All the 18 patients with grade IV ocular injuries developed superficial as well as deep corneal vascularisation (Table 8). Out of the 14 eyes with grade III injury, 6 eyes (42.8%) developed limbal deficiency involving 1-3 clock hours, 4 eyes (28.6%) had limbal deficiency of 4-6 clock hours, and 4 eyes (28.6%) had 7-9 clock hours of limbal deficiency. Out of the 18 eyes with grade IV injury, 6 eyes (33.3%) developed limbal deficiency

involving 10-11 clock hours, 12 eyes (66.6%) had total limbal deficiency.

Meller *et al*[7] found in their study, observed that only grade IV ocular burns developed limbal stem cell deficiency with superficial corneal vascularisation and conjunctivalization; which was also observed in our study. However, in their study, none of the patients with grade III burns developed corneal vascularisation or conjunctivalization. In contrast in our study, we found that all patients with grade III burns developed limbal deficiency with corneal vascularisation and conjunctivalization.

5. Conclusion

AMT is an effective way of treating ocular and thermal injuries in the acute stage. Such an acute intervention can break the vicious cycle leading to the progressive melting or scarring sequelae in the chronic stage. AMT is more effective in preserving the anatomical as well as the functional structure of the conjunctival and corneal surface in terms of decreased corneal vascularisation, preventing conjunctivalization of the cornea, improved tear film status and preventing fibrosis in mild grade II to moderate (grade III) burns but cannot do so in severe (grade IV) burns with total limbal deficiency.

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