

# Amniotic membrane transplantation in 20 patients with disorders of ocular surface

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## Abstract

• **AIM:** To determine the effect of amniotic membrane transplantation (AMT) on the disorders of ocular surface.

• **METHODS:** From May 2002 to July 2007, twenty patients (20 eyes), who had an previous experienced methods of sorts, including contact lens or tarsorrhaphy, underwent AMT.

• **RESULTS:** The disorders were healed after the first AMT in 10 eyes (50%) within an average of 20 days after surgery and recurred in 1 eye (10%).

• **CONCLUSION:** AMT is helpful in the treatment of the disorders of ocular surface.

• **KEYWORDS:** amniotic membrane; transplantation; ocular surface; epithelial defects

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## INTRODUCTION

Ocular surface disorders, such as neurotrophic keratitis, chemical injury, thermal burn, keratohectosis, exposure keratitis, keratoconjunctivitis sicca, or Stevens-Johnson syndrome, are very difficult to treat. Such disorders sometimes cause prolonged inflammation of the ocular surface, damaging the corneal stem cells and epithelial basement membrane (BM), and resulting in persistent corneal epithelial defects (PED), such as corneal scarring<sup>[1]</sup>, neovascularization<sup>[2]</sup>, or even with the risk of corneal perforation. Previous studies have shown that the epithelial BM facilitates migration of epithelial cells<sup>[3]</sup>, reinforces adhesion of basal epithelial cells<sup>[4,5]</sup>, and militates against epithelial apoptosis<sup>[6,7]</sup>. Human placental amnion is composed of a single epithelial cell layer, a BM, and an avascular stroma<sup>[8]</sup>. Amniotic epithelium produces basic fibroblast growth factor, hepatocyte growth factor, and

transforming growth factor  $\beta$ <sup>[9]</sup>. Both collagens IV and VII, components of corneal epithelial BM, are present in the BM of amniotic membrane<sup>[10]</sup>. Amnion prevents inflammatory cell infiltration and reduces apoptosis in keratocytes after transplantation onto the corneal surface<sup>[11]</sup>. Davis<sup>[12]</sup> first reported the use of amniotic membrane for skin transplantation in 1910. Kim *et al*<sup>[13]</sup> then showed in 1995 that preserved amniotic membrane facilitated corneal surface reconstruction in rabbits after epithelium removal and limbal lamellar keratectomy. In recently, amniotic membrane transplantation (AMT) has been used for ocular surface reconstruction in patients after chemical burn<sup>[14]</sup>, in patients with Stevens-Johnson syndrome<sup>[15]</sup>, and for sterile corneal ulceration<sup>[16]</sup>, pterygium excision<sup>[17]</sup>, and conjunctival surface reconstruction<sup>[18]</sup>. In this study, we evaluated the effect of human amniotic membrane grafts on PEDs with or without stromal ulcers of cornea.

## PATIENTS AND METHODS

**Patients** A total of 20 eyes of 20 patients who underwent AMT for PED with or without stromal ulcers of cornea between May 2002 and July 2007 were studied. The duration of corneal epithelial defects varied from 2 to 8 weeks. In these patients, there were 6 patients (6 eyes) with chemical burn, five patients (5 eyes) with thermal burn, three patients (3 eyes) with keratoconjunctivitis sicca, one patient (1 eye) with Stevens-Johnson syndrome, two patient (2 eyes) with herpes simplex keratitis, one patient (1 eye) with atopic keratoconjunctivitis, and 2 patients (2 eyes) with exposure keratitis (Table 1). All eyes studied were with PED and stromal edema. Informed consent was obtained from each patient before the surgery.

**Methods** The surgery was performed by 1 surgeon using a similar surgical technique. After peribulbar or topical anesthesia, the base of the epithelial defect or stromal ulcer was debrided with a microsponge, forceps, or a blade. And the loose epithelium surrounding the defect or ulcer was removed. The preserved amniotic membrane was removed from the storage medium and cut to the same size as the debrided corneal surface with the basement membrane surface up in all cases. The side of the basement membrane could be distinguished from the stromal side by touch with a sponge. The former was not sticky, while the latter was and could be caught by the sponge. This fashioned membrane was then sutured to the edge of the defect by interrupted 10-0 nylon sutures. Make sure that the membrane flattened tightly onto the corneal surface and approximate to the epithelial edge. Postoperatively, the patients were treated with topical dexamethasone

**Table 1 Clinical data of 20 patients with disorders of ocular surface**

	Chemical burn	Thermal burn	Keratoconjunctivitis sicca	Stvens-Johnson syndrome	Herpes simplex keratitis	Atopic keratoconjunctivitis	Exposure keratitis	Total
Patients	6	5	3	1	2	1	2	20
Male/Female	4/2	3/2	2/1	1/0	0/2	1/0	2/0	13/7
Age (yr)	32.3(17-62)	30.6(8-50)	57.7(53-62)	48.0	55.5(50-61)	46.0	47.0(45-49)	41.0(8-62)
Contact lens use (yes/no)	3/3	2/3	1/2	0/1	1/1	0/1	2/0	9/11
Visual change (better/same/worse)	3/3/0	5/0/0	1/2/0	1/0/0	2/0/0	1/0/0	2/0/0	15/5/0
Duration of epithelial healing(wk)	3.6	2.4	2.2	2.5	2.1	2.3	2.6	2.53
Follow-up(wk)	20.1(8-30)	23.2(10-40)	24.8(12-38)	21.2	22.4(21.6-23.2)	23.6	22.8(20-25.6)	22.6(8-40)

and tobramycin solutions four times a day for 2 weeks, and a bandage contact lens was applied in some cases. The bandage contact lens was removed when the amniotic membrane dissolved.

### RESULTS

These 20 patients were comprised of 13 men and 7 women. The patients with chemical burn and thermal burn, were relatively younger( 31.4 ± 6.4 years ). The mean follow-up time after AMT was 22.6(range 8-40) weeks. Their preoperative visual acuity were all worse than or equal to finger counting: finger counting ( 10 eyes ), hand movement ( 4 eyes ) and light perception ( 6 eyes ). And the mean visual acuity after the surgery, scilicet the mean visual acuity while the epithelial defect healed, was 0.08 ( range 0.01-0.4,  $P = 0.0087$  ). The average duration of epithelial healing, underwent first or repeated AMT, was 17.7(range 5-38) days after surgery. The epithelial defect healed after the first AMT in 10 eyes(50%). In 10 eyes (50%), especially in eyes with chemical burn and thermal burn, the defect persisted after the first AMT. The epithelial defect recurred after the first AMT in 1 (10%) of 10 eyes. During the follow-up, AMT was repeated in 11 patients. The AMT was accompanied by tarsorrhaphy in 2 eyes( Table 1 ).

### DISCUSSION

In this study, the epithelial defects healed after the first AMT in 50% (10/20) of all eyes. It was obviously lower than that Lee *et al* [16] reported, in success rate, of 90% (10/11). This might impute to the difference in cause of the epithelial defects. In our study, there were 11 eyes (55%) with chemical burn and thermal burn, which defeated the entire ocular surface and with PED. Shimazaki *et al* [9] claimed that the epithelium of the amniotic membrane may survive up to 70 days after cryopreservation. Their study showed that living epithelium of amnion produces basic fibroblast growth factor  $\beta$  [9]. AMT can improve visual acuity by both corneal surface restoration and improvement of corneal transparency [16]. In our study, the average visual acuity improved visibly after AMT ( $P = 0.087$ ).

The stromal side of the membrane contains a unique matrix component that suppresses transforming growth factor  $\beta$

signaling, and proliferation, and myofibroblast differentiation of normal human corneal and limbal fibroblasts [19]. This action explains why amniotic membrane transplantation reduces scars during conjunctival surface reconstruction [18], and prevents recurrent scarring after pterygium removal [17]. The stromal matrix of the membrane also contains various forms of protease inhibitors [20], important for promoting epithelial healing and reducing stromal inflammation and ulceration. We therefore believe that AMT for PEDs, with or without stromal ulcers, should be used as first- or second-line therapy, especially in eyes with chemical burn or thermal burn. Meanwhile, medications toxic to the epithelium, and aggressive lubrication should be removed. Further studies are required to confirm our results, to compare AMT in more cases in treatment of PED and stromal ulcers.

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## 羊膜移植在20例眼表疾病中的应用

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### 摘要

**目的:**研究羊膜移植在眼表疾病中的疗效。

**方法:**曾经历过眼睑缝合、角膜接触镜等各种方法治疗的20例20眼接受羊膜移植。

**结果:**在术后平均20d内,第一次羊膜移植后有10眼(50%)治愈,1眼(10%)复发。

**结论:**羊膜移植有助于眼表疾病的治疗。

**关键词:**羊膜;移植;眼表;上皮缺损