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Amniotic Membrane Transplantation for Ocular Surface Reconstruction

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A B S T R A C T

The purpose of this study is to analyze the clinical experience and the effect of human amniotic membrane transplantation on pterygium excision and bullous keratopathy. From January 1999 to January 2001 at University Hospital »Sestre milosrdnice« amniotic membrane transplantation was performed consecutively in 21 eyes: 11 eyes with bullous keratopathy and 10 with recurrent pterygia. In the group with bullous keratopathy epithelization took place in 19.6 days in 72.7% and the reduction of pain was satisfactory. Recurrence rate in group with recurrent pterygia was 20%. Based on the presented results it could be concluded that amniotic membrane transplantation can be considered as an effective alternative for treating severe ocular surface diseases and as an alternative for penetrating keratoplasty if there is a lack of grafts.

Introduction

Management of ocular surface disturbances still remains a therapeutically problem despite various conservative and surgical treatments. For some of them previously there was no effective management and they caused a loss of vision.

The aim of this study is to evaluate the effectiveness of application of amniotic membrane in patients with bullous keratopathy and pterygium. Pires, Prabhasawat and Tseng have first reported about reconstruction of corneal surface in symptomatic bullous keratopathy and pterygium[1,2].

Bullous keratopathy is a disease characterized by corneal stromal edema with or without epithelial bulla. Breakdown of endothelial function leads to increased hydration and intraepithelial edema which could lead to recurrent or persistent erosions. Patients with bullous keratopathy may suffer from ocular pain and reduced vision. Bullous keratopathy caused by various intraocular surgical procedures and non-surgical causes can be treated with bandage contact lens, anterior stromal punctures, epikeratoplakia, conjunctival flap, excimer laser phototherapeutic karatectomy and annular keratotomy[3,4].

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Pterygium is a degenerative ocular disease characterized by fibrovascular tissue proliferation involving the cornea. Because of a strong tendency to aggressive recurrence after surgical therapy, numerous methods of pterygium surgery have been developed. The main procedure involves excision of the pterygium down to bare sclera. After excision the defect can be left exposed (bare sclera excision), covered by surrounding conjunctiva (primary closure) or covered by various grafts (conjunctival autograft, buccal mucous membrane grafts, lamellar keratoplasty, penetrating keratoplasty or sclerokeratoplasty[5]. An additional treatment includes application mitomycin C or irradiation[6].

Material and Methods

From January 1999 to January 2001 at the Department of Ophthalmology, University Hospital »Sestre milosrdnice« amniotic membrane surgery was performed consecutively in 21 eyes: 11 female and 10 male. The patients were between 25 and 78 years old. An informed consent was obtained from each patient before the surgery. Based on the underlying causes of ocular diseases they were divided into 2 groups: 11 eyes had bullous keratopathy and 10 recurrent pterygia. The same surgeon performed all surgical procedures.

Human amniotic membrane was prepared and preserved as previously described[7–9]. Amniotic membrane with an attached placenta was obtained shortly after Cesarean section. By serological testing human immunodeficiency virus (HIV), hepatitis virus type B and C and syphilis infections have been excluded. The placenta was cleaned by washing with BSS containing penicillin (50 g/ml), streptomycin (50 g/ml), neomycin (100 g/ml), and amphotericin B (2.5 g/ml). The amniotic membrane was separated from the chorion and was flattened over a nitro-cellulose filter paper with epithelial surface up and the stromal matrix down. Prepared amnion was placed in a plastic container and stored at –80 °C.

All surgeries were performed with application of laterobulbar anesthesia (2% lidocain). In the eyes with bullous keratopathy the whole epithelium was removed. The amniotic membrane was peeled from the nitro-cellulose filter pape. and placed on the surface of the cornea with the epithelial surface up. The amniotic membrane was secured to the edge of the defect by interrupted 10.0 nylon sutures. After the transplantation, a bandage contact lens was applied in 5 eyes. In the postoperative period topical Maxitrol (neomycin sulfate, ploymyxin B sulfate and dexamethason) was administrated 4 times daily.

All patients with recurrent pterygium had one or more previous surgeries. After the pterygium body was removed, the amniotic membrane with stromal side down was used to cover conjunctival defect. The amniotic membrane was secured to the episclera with 10.0 nylon interrupted perilimbal sutures and to the cornea as well. Postoperatively, all patients were treated with topical corticosteroid for 4 to 6 weeks. Sutures were removed during the second or third postoperative week.

Results

Amniotic membrane transplantation was performed in 11 eyes with bullous keratopathy. All patients suffered from ocular surface pain associated with poor visual potential (Table 1). Their average age was 65.9 years (range 51–78 years) and most of them had pseudophacic eyes (N = 6) caused by extracapsular cataract extraction (ECCE) (N = 4) and phacoemulsiphication (PHACO) (N = 2). On three eyes (3/6) underwent additional oc-

TABLE 1
BULLOUS KERATOPATHY – DEMOGRAPHIC AND CLINICAL DATA BEFORE AMNIOTIC MEMBRANE TRANSPLANTATION

Age (years)	65.9 (51–78)
Number of eyes (Male/Female)	11 (6/5)
Causes	Pseudophakia (N = 6)
	PHACO (N = 2)
	ECCE (N = 4)
	Aphakia (N = 2)
	Failed graft (N = 2)
Duration (weeks)	41.3 (18–73)
Associated diagnosis	Glaucoma (N = 2)
(ocular/systemic)	Diabetes mellitus (N = 3)
	Nonproliferative diabetic retinopathy (N = 2)
Previous surgery	Trabeculectomy (N = 2)
	Second implantation IOL (N = 1)
	Vitrectomy (N = 1)
	Anterior vitrectomy (N = 1)
Previous treatment	Artificial tears, lubricants, prophylactic antibiotics (N = 5)
	Soft contact lens (N = 4)

ular surgery (trabeculectomy, secondary implantation of intraocular lens (IOL) and vitrectomy was previously performed. In two cases of aphakic bullous keratopathy both (N = 2) were caused by ECCE and one of them previously had partial anterior vitrectomy and secondary developed glaucoma. In those with failed corneal grafts both were pseudophacic (ECCE) and one of them had had trabeculectomy. Additional ocular diseases included glaucoma in 2 eyes, nonproliferative diabetic retinopathy in 2 eyes. All eyes had been treated with artificial teardrops, lubricants, 5 eyes with prophylactic antibiotics and bandage contact lens was applied in 5 eyes. The duration of bullous keratopathy before operation varied from 18 to 73 weeks (mean 41.3 weeks). Epithelization took place in 19.6 days (8–35 days) in 8 eyes (72.7%) (Table 3). Amniotic membrane transplantation was repeated in 3 eyes with residual pain. Amniotic membrane transplant failed in one eye and after repeated procedure the eye become pain-free. In two eyes the pain remained in one eye the pain was reduced and it was unchanged in one eye. Visual acuity was improved in 1 eye from finger counting to 0.05, and in others it remained unchanged.

In the second group amniotic membrane was applied in 10 eyes with recurrent pterygia. Age range was 25–74 years and the mean age was 51.2 years (Table 2). All patients have had already at least one or more pterygium operations. In 2 eyes glaucoma was noted as pre-existing ocular disease, and one of them had previous surgery (laser iridotomy). All eyes had one or more previous pterygium surgeries (bare sclera excision and excision primary closure). Epithelization was complete in 20.1 days (range 11–34 days) (Table 3). Recurrence with fibrovascular tissue invading the cornea occurred after 4.5 months in 2 eyes (20%). The visual acuity was improved in 5 eyes (1–3 lines),

TABLE 2
RECCURENT PTERYGIA – DEMOGRAPHIC AND CLINICAL DATA BEFORE AMNIOTIC MEMBRANE TRANSPLANTATION

Age (years)	51.2 (25–74)
Number of eyes (Male/Female)	10 (4/6)
Duration (weeks)	27.3 (16–54)
Associated diagnosis (ocular/systemic)	Glaucoma (N = 2)
Previous surgery	YAG laser iridotomy (N = 1)
Previous treatment	Bare sclera excision (N = 5) Excision primary closure (N = 6)

TABLE 3
OUTCOME AFTER AMNIOTIC MEMBRANE TRANSPLANTATION

	Associated treatment	Epithelization (days)	Healing (%)	Follow up (months)
Persistent corneal ulcus	Soft contact lens (N = 5) Partial tarsoraphy (N = 2)	23.1 (7–39)	12/16 (75%)	8.9 (5–14)
Bullous keratopathy	Soft contact lens (N = 9)	19.6 (8–35)	8/11 (72.7)	7.8 (2–15)
Reccurent pterygia		20.1 (11–34)		11.2 (7–14)

it remained unchanged in 4 eyes and decreased in 1 eye (cataract development). Pyogenic granuloma was the postoperative complication in one eye and it was treated with excision of the granuloma and topical corticosteroid drops.

Discussion

In this study we have evaluated the efficacy and safety of amniotic membrane transplantation in two ocular surface disorders: symptomatic bullous keratopathy and recurrent pterygia. The amniotic membrane transplantation has been used since 1910. when Davis introduced it in general surgery for skin transplantation[10]. In ophthalmology amniotic membrane transplantation as a part of fetal membrane transplantation was first reported by De Rötth in the reconstruction of conjunctival defects in 1940[11]. Kim and Tseng first reported a new dimension of preserved and dissected amniotic membrane using it for ocular surface reconstruction in rabbits after epithelium removal and limbal lamellar keratectomy[7]. Amniotic membrane transplantation has recently became very popular surgical technique and it is used for ocular reconstruction following chemical or thermal burns[12], advanced ocular cicatricial pemphigoid and Steven-Johnson syndrome[13], for pterygium excision[2], conjunctival surface reconstruction[14,15], sterile corneal ulceration[9,10] and symptomatic bullous keratopathy[1].

The amniotic membrane is composed of monolayer epithelial cells, a basement

membrane, and an avascular stromal matrix. The membrane permits rapid epithelization due to various actions: it facilitates migration of epithelial cells, reinforces adhesion of basal epithelial cells, promotes epithelial differentiation and prevents epithelial apoptosis[8,18]. The stromal side of the membrane also contains a component that suppresses TGF- signaling, and the proliferation and differentiation of myofibroblast of normal corneal and limbal fibroblasts and normal human corneal and limbal fibroblasts[18]. This action explains why amniotic membrane transplantation prevents recurrent scarring after pterygium removal[2]. Furthermore amniotic membrane produces basic fibroblast growth factor, hepatocyte growth factor and transforming growth factor ; while stromal matrix excludes inflammatory cells and contains several forms of protease inhibitors[19]. These mechanisms are the reason why stromal inflammation is reduced after amniotic membrane transplantation and corneal neovascularization is mitigated.

In accordance with the previous report from Kruse at al we have noted that ocular surface inflammation was reduced after amniotic membrane transplantation[20]. These finding supports recent studies showing that the stromal matrix of the amniotic membrane excludes inflammatory cells, contains various forms of protease inhibitors, and suppresses transforming growth factor (TGF) signaling and proliferation and differentiation of myofibroblast of normal human corneal and limbal fibroblasts[21].

Patients with symptomatic bullous keratopathy suffer from ocular pain associated with reduced vision. As result of histopathological changes in cornea, poor epithelial adhesion may persist and lead to recurrent or persistent epithelial defect. We performed amniotic membrane transplantation in 11 eyes refractory to conventional treatment. Eight eyes (72.7%) became pain-free during the following period of 19.6 days (8–35 days), which is accordance with the results of other similar studies[1,22].

Pain relief after amniotic membrane transplantation is associated with restoration of corneal epithelial integrity and can be contributed to therapeutic amniotic membrane effect whose properties have been already mentioned.

Surgical removal of pterygium is still a challenge. Numerous methods of surgical excision have been reported and they all have the same goal: to achieve low recurrence rate associated with lack of postoperative complications. The complications in our study were minor and included pyogenic granuloma in one eye. It has to be stressed that in this study we have treated only recurrent pterygia defined by re-growing of the fibrovascular tissue across the cornea.

Recurrence rate in our study was 20% and it varies for recurrent pterygia from 9.5% to 37.5% as reported by Solomon and Prabhasawat[2]. Conjunctival autograft yields lower recurrence rate for recurrent pterygia varying from 0 to 25% different reports[2,23,24]. This advantage may be explained by the fact that conjunctival autograft includes the limbal tissue with stem cells that could create a limbal barrier.

Although, conjunctival autograft achieves lower recurrence rate, amniotic membrane transplantation can be considered as the treatment of first choice in cases in which the conjunctiva might be needed for possible glaucoma filtering operations, for large pterygia with large defect that should be covered or scared bulbar conjunctiva.

It could be concluded that the amniotic membrane transplantation can be useful in treatment of severe ocular surface diseases. It may be considered as alternative method for ocular surface reconstruction which is refractory to conventional treatment.

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REKONSTRUKCIJA POVRŠINE ROŽNICE TRANSPLANATCIJOM AMNIJSKE MEMBRANE

SAŽETAK

Cilj ovog rada bio je izvijestiti o kliničkom iskustvu i rezultatima transplantacije amnijske membrane kod operacije pterigija i bulozne keratopatije. U razdoblju od siječnja 1999. do siječnja 2001. godine, na Klinici za očne bolesti KB »Sestre milosrdnice« transplantirali smo amnijsku membranu u 21 očiju: 11 očiju s buloznom keratopatijom i 10 očiju s rekurentnim pterigijem. U grupi s buloznom keratopatijom epitelizacija je postignuta u 19,6 dana u 72,7% očiju. Postotak recidiva u grupi s pterigijem bio je 20%. Transplantacija amnijske membrane predstavlja djelotvorno alternativno liječenje teških bolesti prednjeg očnog segmenta i dobra je alternativa keratoplastici u slučaju nedostatka transplantata.