Sandwich Technique and Amniotic Membrane Transplantation as an Effective Method in Repairing Corneal Perforations

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Research Article

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Abstract

Purpose
To evaluate effectiveness of human amniotic membrane (hAM) transplantation in patients with non-traumatic corneal perforation.

Methods
This retrospective chart review included the patients who were underwent hAM transplantation with sandwich technique between March 2020 to January 2023 at Ege University Hospital, Turkey. Medical records of the patients including demographic data, best corrected visual acuity (BCVA) that was measured with Snellen chart, detailed ophthalmological examination and the need for additional surgical intervention after hAM transplantation were evaluated. Complications, anatomical and functional results were presented.

Results
A total 9 eyes of 9 patients with non-traumatic corneal perforations were evaluated between 2020 and 2023. Size of perforation was ≤ 3 mm in all the eyes. The mean age of the patients was 67.77 ± 15.52. Female to male ratio was 1/8. Sandwich technique was used in all patients for hAM transplantation. Five of cases (55.55%) had infectious etiology and 4 of them (44.44%) had inflammatory etiology. Of the infectious corneal perforations, 3 (33.33%) were herpes simplex virus-induced neurotrophic keratopathy and 2 (22.22%) were bacterial keratitis. The mean residence time of the amniotic membrane on the ocular surface was 21 ± 8.05 days. Tectonic keratoplasty was needed in 1 eye (11.11%). Corneal patch grafting was required in 1 of eyes (11.11%). Evisceration was performed in 1 eye (11.11%) of a patient with no light perception who had no visual prognosis. Amniotic membrane detachment was observed in one patient as a surgical-related complication associated with hAM transplantation.

Conclusions
hAM transplantation is one of the successful treatment methods in treatment of relatively small corneal perforation. Considering the difficulty of finding a donor cornea and the easier access to the amniotic membrane, it seems like a good alternative treatment to reduce or postpone the need for tectonic keratoplasty.

Introduction
Corneal perforation is an ocular emergency caused by traumatic, infectious or inflammatory reasons. The priority in the treatment of this pathology, which has important complications such as cataract formation, glaucoma development, and endophthalmitis, is to ensure ocular integrity.

The treatment method is decided according to the size and location of the perforation area. Conservative treatments such as bandage contact lenses and pressure patch can be used to buffer the leak, and in cases where
these treatments are insufficient, surgical treatments such as hAM transplantation, patch grafting of conjunctival flaps and tectonic penetrating keratoplasty can be applied.⁴

hAM transplantation is one of the most successful alternative methods in the treatment of small-medium corneal perforations.⁵,⁶,⁷ hAM is the deepest of the three layers of fetal membranes and composed of a single layer of epithelial cells, a basement membrane, and an avascular stromal matrix. hAM has antiangiogenic, anti-inflammatory and wound healing properties.⁹ hAM, which has applications in many medical fields, is frequently applied in ophthalmology, especially in ocular surface healing. The use of the amniotic membrane in corneal perforations is thought to be effective due to its ability to promote epithelialization and reduce inflammation, in addition to acting as a tissue substrate replacement.⁵ Besides the prominent physical advantages, easier access to the tissue for grafting is an important advantage of the hAM.

Three main techniques are used in the ocular surface surgical application of the amniotic membrane: overlay, inlay, and sandwich method. The method used for corneal deep stromal defects is the sandwich technique. This technique uses two or more hAM layers, the inner acts as the graft and the outer acts as the patch.⁹

The aim of this study is to report patients with corneal perforation managed with hAM using the sandwich technique. Complications, anatomical and functional results of the treatment applied in this patient group are presented.

**Material And Methods**

This retrospective chart review included the patients who were underwent hAM transplantation for the management of non-traumatic corneal perforation with sandwich technique between March 2020 to January 2023 at Ege University Hospital, Turkey. Medical records of the patients including age, gender, underlying etiology of perforation, BCVA at preoperatively and last follow-up, resistance time of hAM on ocular surface, need for additional surgical intervention and complications after hAM transplantation were reviewed. Size of perforations > 3 mm were excluded from the study. Cryopreserved hAM was used with sandwich technique by the same surgeon. Surgery was performed under topical anesthesia. Amniotic membrane was cut according to ocular surface and its edges were sutured to conjunctiva with 8/0 vicryl sutures. Each of the patient was followed-up at least once a week until amniotic membrane disappears from the ocular surface.

The study was approved by the Institutional Ethics Review Board of Ege University, Turkey, and conducted in agreement with the tenets of the Helsinki Declaration. Each participant signed a written informed consent form for the use of their medical data.

**Results**

A total 9 eyes of 9 patients with non-traumatic corneal perforations were evaluated between March 2020 and January 2023. Size of perforation was ≤ 3 mm in all the eyes. The mean age of the patients was 67.77 ± 15.52 (30–82). Female to male ratio was 1/8. Sandwich technique was used in all patients for hAM transplantation. Five of corneal perforations (55.55%) had infectious etiology and 4 of them (44.44%) had inflammatory etiology. Of the infectious corneal perforations, 3 (33.33%) were herpes simplex virus-associated neurotrophic keratopathy and 2 (22.22%) were bacterial keratitis. Two (22.22%) of the inflammatory corneal perforations were due to dry eye and 2 (22.22%) were due to bullous keratopathy. Figure 1 shows pre-operative and post-operative anterior
segment photography in a patient with herpes simplex virus-associated neurotrophic keratopathy. The mean residence time of the amniotic membrane on the ocular surface was 21 ± 8.05 (7–28) days. Mean BCVA at last follow-up was 2.48 ± 0.49 (1.3-3) logMAR. Mean follow-up time of the patients was 15.61 ± 10.3 (2.5–32) months.

Fibrin tissue glue application is the most common additional intervention (6 of eyes, 66.66%). Tectonic keratoplasty was needed in 1 eye (11.11%). Corneal patch grafting was required in 1 of eyes (11.11%). Unfortunately, evisceration was performed in 1 eye (11.11%) of a patient with no light perception who had no visual prognosis. In the light of these information, it can be said that the success rate of hAM transplantation with the sandwich technique in controlling corneal perforations smaller than 3 mm is 66.66%.

Surgical complications associated with cryopreserved amniotic membrane transplantation consist of hemorrhage, infection, and premature detachment of the membrane.

In present study, re-suturing was required in 1 eye (11.11%) due to detachment of the amniotic membrane. Clinical data, including patient demography, surgical procedures and final outcomes are summarized in Table 1.

Table 1
Clinical and Demographic Data of The Patients

<table>
<thead>
<tr>
<th>Patient No</th>
<th>Age/Gender</th>
<th>Cause</th>
<th>Diagnosis</th>
<th>Additional Surgical Intervention</th>
<th>Resistance Time of hAM (days)</th>
<th>Final BCVA (logMAR)</th>
<th>Follow-up Time (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>65/M</td>
<td>Infectious</td>
<td>Herpetic keratitis</td>
<td>Fibrin glue</td>
<td>7</td>
<td>2.8</td>
<td>32</td>
</tr>
<tr>
<td>2</td>
<td>59/M</td>
<td>Inflammatory</td>
<td>Bullous keratopathy</td>
<td>Fibrin glue, tectonic keratoplasty</td>
<td>28</td>
<td>2.3</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
<td>75/M</td>
<td>Inflammatory</td>
<td>Dry eye</td>
<td>Fibrin glue, evisceration</td>
<td>1</td>
<td>3</td>
<td>28</td>
</tr>
<tr>
<td>4</td>
<td>79/M</td>
<td>Infectious</td>
<td>Herpetic keratitis</td>
<td>-</td>
<td>28</td>
<td>1.3</td>
<td>24</td>
</tr>
<tr>
<td>5</td>
<td>30/M</td>
<td>Infectious</td>
<td>Herpetic keratitis</td>
<td>Fibrin glue</td>
<td>21</td>
<td>2.8</td>
<td>3</td>
</tr>
<tr>
<td>6</td>
<td>82/M</td>
<td>Inflammatory</td>
<td>Dry eye</td>
<td>-</td>
<td>21</td>
<td>2.8</td>
<td>13</td>
</tr>
<tr>
<td>7</td>
<td>63/M</td>
<td>Infectious</td>
<td>Bacterial keratitis</td>
<td>Fibrin glue</td>
<td>28</td>
<td>2.3</td>
<td>2.5</td>
</tr>
<tr>
<td>8</td>
<td>82/E</td>
<td>Inflammatory</td>
<td>Bullous keratopathy</td>
<td>-</td>
<td>21</td>
<td>2.3</td>
<td>20</td>
</tr>
<tr>
<td>9</td>
<td>75/K</td>
<td>Infectious</td>
<td>Bacterial keratitis</td>
<td>Fibrin glue, corneal patch grafting</td>
<td>28</td>
<td>2.8</td>
<td>12</td>
</tr>
</tbody>
</table>

BCVA: best-corrected visual acuity, M: male, F: female

Discussion
The treatment chosen generally depends on the size, location, and etiology of the corneal perforation, as well as the surgeon's experience and the availability of donor tissues. One of the most successful alternative methods in the treatment of relatively small corneal perforations is hAM transplantation. Because of its antifibrotic, anti-inflammatory and antiangiogenic properties, hAM is considered to be superior to alternatives in corneal perforation repair. Thanks to these properties, it not only fills the defect and restores the integrity of the sphere, but also prevents further tissue loss. The hAM application technique is also important in the success of the repair of corneal perforations. Single or multiple hAM transplantation with the overlay technique cannot effectively occlude the perforation site, while the sandwich technique is more effective in this occlusive function.

Although hAM application in corneal perforations is a known method, there are publications in the literature in the form of case series that generally include a limited number of patients. Amniotic membrane roll-in filling technique reported by Fan et al. in a 46-eyed study involving a relatively large number of patients. The combined success rate of C3F8 gas filling into the anterior chamber was found to be 100%. Again, the success rate is reported almost completely in a limited number of publications. In present study, we reported the success rate as 66.66%. The most important factors in the success of hAM transplantation for corneal perforations are the size and localization of the perforation site and the underlying etiology. As the perforation area widens, it is inevitable that the sealing efficiency of hAM, which has low resistance, decreases. Again, in infectious etiologies, it is obvious that procedures such as patch grafts, which also allow corneal debridement, may be more advantageous than hAM application.

Differences in surgical procedure may also affect prognosis and success rate in the treatment of corneal perforations with hAM transplantation. In a study in which the anterior chamber was filled with C3F gas in addition to hAM transplantation, the success rate was reported to be 100%. Meduri et al. reported the efficacy of sutureless amniotic membrane transplantation in 12 eyes with inflammatory pathologies. They defined the surgical procedure in their study as two layers of hAM and the application of a therapeutic contact lens on two layers, followed by striated seamless tarsorrhaphy, and reported resolution in all patients. In this study, the fact that the inflammation was not triggered by seamless surgery in the patient group with significant ocular inflammation, especially consisting of Sjögren's syndrome and ocular cicatricial pemphigoid, may have increased the surgical success.

Solomon et al. reported the clinical outcomes of hAM transplantation in 34 eyes with non-traumatic corneal perforations, desmatoceles, and deep ulcers. In this study, the success rate was reported as 82.3%. The inclusion of desmatocele and corneal ulcers in this study may be a reason for the higher success rate compared to our study.

In the presented study, while the relatively long follow-up period can be counted as a strength of the study compared to the literature, its retrospective design is one of the limitations of the study.

This study clarifies the importance of a relatively easy intervention in the emergency treatment of non-traumatic corneal perforations. hAM transplantation performed by the sandwich method is an effective and easy treatment option in the repair of perforations that develop due to many etiological factors, with the contribution of anti-inflammatory and antimicrobial properties.

Declarations
STATEMENTS AND DECLARATIONS

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Author Contributions: All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Mukaddes Damla Ciftci and Ozlem Barut Selver. The first draft of the manuscript was written by Mukaddes Damla Ciftci and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics Approval: The study was approved by the Institutional Ethics Review Board of Ege University, Turkey, and conducted in agreement with the tenets of the Helsinki Declaration.

Consent to Participate: Each participant signed a written informed consent form for the use of their medical data.

Consent to Publish: The authors affirm that human research participants provided informed consent for publication of the images in Figures 1a and 1b.

References


Figures

Figure 1

(a) Anterior segment photography showing corneal perforation secondary to neurotrophic keratopathy (b) Postoperative photography demonstrating successful closure of the perforation area with hAM transplantation with the sandwich technique