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ORIGINAL PAPER

Efficacy of fixation of the amniotic membrane on a symblepharon ring with continuous suturing in acute ocular chemical burn patients

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Abstract

Purpose To describe a modified non-traumatic amniotic membrane transplantation (AMT) technique and evaluating its efficiency for the ocular surface injury after chemical burn were aimed.

Methods Twenty eyes of 20 patients (F: 6, M: 14) with acute chemical burn for whom modified non-traumatic AMT was utilized were evaluated retrospectively. In this technique, amniotic membrane (AM) was fixated onto a symblepharon ring with continuous suturing. The healing time of the corneal epithelial defect due to ocular surface chemical injury and melting duration of AM were evaluated. Development of infection or symblepharon, recurrence or persistence of epithelial defect, corneal perforation and the ring falling out with AM were evaluated as complications.

Results Mean age of the patients was 24.7 ± 11.7 years old (14 months–40 years). Mean duration of applying the non-traumatic AMT after contact with the chemical agent was 8.4 ± 6.2 days (2–21 days). The mean duration of the epithelial defect healing was 27.8 ± 8.8 days (11–40 days) in the grade II, III, and IV (n = 12) cases, while in the grade V and VI (n = 8) cases, a persistent epithelial defect developed, and the mean duration of the epithelial defect healing was 83 ± 23.1 days (42–120 days) (p = 0.0002). The mean melting duration of the AM was 22.7 ± 10 days (10–42 days).

Conclusion By using this modified AMT technique, AM can be utilized efficiently, easily, and non-traumatically in every center for the treatment of the ocular surface injury due to chemical burn.

Keywords Amniotic membrane · Ocular surface · Symblepharon ring · Chemical burn

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Introduction

The treatment of ocular surface injuries due to chemical burns is a time-consuming and challenging issue. Acute ocular chemical burns are among the ophthalmological emergencies in which a rapid diagnosis and treatment are necessary. The aims of acute ocular chemical burn treatments are to accelerate epithelial healing, decrease inflammation, and prevent corneal thinning and cicatricial complications. Several options are available for the treatment of ocular burn injuries, and an amniotic membrane transplantation (AMT) is one of them [1].

An AMT is used for the treatment of ocular burns as a therapeutic bandage. The biological properties of the amniotic membrane (AM) provide re-epithelization and help relieve pain during the acute period. After an

AMT, a prominent decrease in the inflammatory activity on the ocular surface has been shown in chemical burn cases [2] by inducing apoptosis of the inflammatory cells, such as neutrophils and macrophages [3]. In addition, the AM contains multiple growth factors which play important roles in the healing and repair of corneal epithelial injuries [4–7].

An AMT is generally performed with sutures or fibrin glue for the treatment of ocular surface injuries [8–10]. However, the use of sutures increases the duration of the surgery, may cause postoperative discomfort, and can lead to inflammation and infection [8, 11, 12].

The sutureless AMT techniques have been developed to reduce the disadvantages of the technique with suture. In these techniques, the AMs have been stabilized around a symblepharon ring (SR) or another similar plastic/titanium ring [13–16]. In our study, the AM was also applied onto the ocular surface like a contact lens after suturing the membrane around a SR. The SR used here is an easy to access product worldwide, and the amniotic membrane was fixed around the SR with continuous suturing. In this study, we evaluated the results of this simple non-traumatic AMT technique in 20 eyes of 20 patients with acute chemical burns.

Methods

This study included patients with histories of chemical burns in which a modified AMT technique was applied between November 2015 and December 2017. The medical records of the patients were investigated retrospectively. The study was conducted according to the Declaration of Helsinki, and it was approved by the local ethical committee of Cerrahpasa Medical Faculty. Informed consent was obtained from all of the patients or their legal guardians after explanation of the nature and possible consequences of the AMT. Additional informed consent was obtained from all individual participants for whom identifying information is included in this article. Those patients with acute chemical burns were included in this study, and a maximum of 3 weeks after exposure to the chemical agent was accepted as an acute ocular surface burn. The patients with chemical burns after 3 weeks and the patients with thermal burns were excluded from the study. The patients were asked to describe the name of the chemicals causing the burn, and its ingredients were searched for their pH.

All of the patients with acute chemical burns were classified according to the Dua classification [17]. The AM was placed onto the eye like a contact lens after its sutured stabilization around a SR (Fig. 1). The SR is made of polymethylmethacrylate (PMMA), with clear and smooth edges, and it comes in three different sizes (20, 22, and 25 mm). Before the AM stabilization, the ring was placed onto the eye, and the fit was checked; the best fitting ring was selected for use.

Postoperatively, moxifloxacin was administered four times, a preservative-free eye lubricant was administered six times, and dexamethasone eye drops were administered three times a day, which was gradually decreased over 3 weeks.

The healing rate of the corneal epithelial defect secondary to the ocular surface chemical injury, the healing process duration, and the AM melting duration were determined. The development of an infection or symblepharon, recurrence or persistence of an epithelial defect, corneal perforation, and the ring falling off together with the AM were evaluated as complications. Symblepharon was classified as mild (less than 1 quadrant), moderate (between 1 and 2 quadrants), or severe (more than 2 quadrants) depending on the dial position affected [18]. Cryopreserved AM from the eye bank was used for all of the patients.

Placement of the AM onto the SR

After maintaining the cryopreserved AM at room temperature for 10 min, the membrane was spread onto a smooth surface. The down-facing surface (stromal surface) was the surface that would come in contact with the ocular surface. The SR (FCI Ophthalmics Inc., Pembroke, MA, USA) was placed on the AM (Fig. 1a). After measuring the edge thickness of the SR with a compass, that distance was marked with a surgical pen on the AM from the border of the ring. The AM was marked circumferentially around the ring (Fig. 1b, c). While the SR was on the AM, the marked area was cut with scissors and the remaining part was removed (Fig. 1d). Starting from the border of the ring, an AM as large as the edge thickness was obtained (Fig. 1d). Continuous suturing was performed circumferentially on the edges of the membrane using 10-0 nylon suture (Fig. 1e). When both ends were pulled toward each other, the amniotic

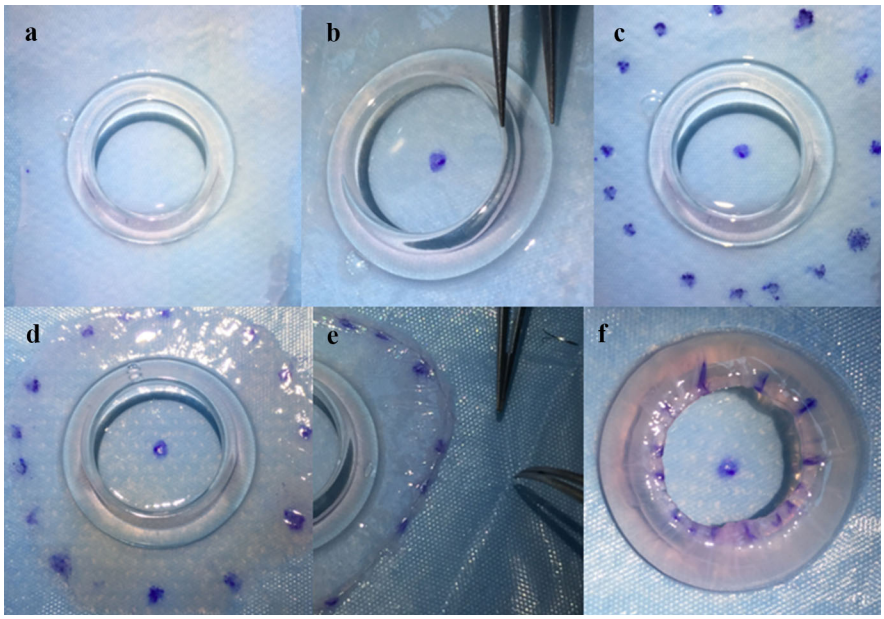

Fig. 1 **a** The symblepharon ring is placed on the amniotic membrane with the stromal surface facing down. **b** The edge thickness of the ring is measured with a compass. **c** Starting from the border of the ring, an area as large as the edge thickness is marked 360° around the ring. **d** The amniotic membrane is cut away from the marked part. **e** The amniotic membrane is continuously sutured around the edge with 10-0 nylon suture. **f** The two ends of the continuous suture are pulled and tied to each other. In this manner, the amniotic membrane slides through the edges of the ring and is ready for the ocular surface application

membrane slid through the suture and was installed on the SR. After sliding the membrane on the ring, the suture ends were tied (Fig. 1f). At this point, the SR covered with the AM was ready to be applied onto the eye. The SR–AM complex was placed on the eye first on the upper fornix by pulling the upper eyelid and then on the lower fornix by pulling the lower eyelid under topical anesthesia; this was very similar to the placement of a contact lens. The SR–AM complex was placed on the eye in such a way that it covered the ocular surface almost completely. The SR–AM complex was removed from the eye after the membrane melted by pulling the lower lid to remove the lower part of the ring and grasping the ring with forceps.

Mann–Whitney U test was used for the comparison of the independent samples. SPSS (version: 21.0) was used for the biostatistical analysis.

Results

This study included twenty eyes of 20 patients (6 females, 14 males) with acute ocular chemical burns. The mean age of the patients was 24.7 ± 11.7 years old (14 months–40 years). The etiological agent was alkaline in 14 patients and acidic in six patients. The mean duration for the application of the non-traumatic AMT after contact with the chemical agent was 8.4 ± 6.2 days (2–21 days). Among the cases at an acute stage, six cases were grade II, two cases were grade III, four cases were grade IV, six cases were grade V, and two cases were grade VI according to the Dua classification (Table 1). A tenon advancement together with the non-traumatic AMT was performed in only two patients (grade II and grade III cases with scleral necrosis) with acute ocular chemical burns.

The mean duration of the epithelial defect healing was 27.8 ± 8.8 days (11–40 days) in the grade II, III, and IV (n = 12) cases, while in the grade V and VI (n = 8) cases, a persistent epithelial defect developed, and the mean duration of the epithelial defect healing was 83 ± 23.1 days (42–120 days). Comparison of these groups resulted with statistically significant difference (p = 0.0002) which might mean that the epithelial defects of the patients with lower grades of ocular burn tend to heal more rapidly. In addition, the

Table 1 Demographics and characteristic of patients

	Total number of eyes (*n*: 20)
Unilateral	20
Bilateral	–
Time of presentation (days)	
0–2	6
3–6	4
6+	10
Agent	
Acid	6
Alkali	14
Dua classification	
I	–
II	6
III	2
IV	4
V	6
VI	2

healing duration of the corneal epithelial defect and the melting duration of the AM were detected. The healing was followed via a biomicroscopic examination and fluorescein staining. The mean follow-up time was 8.2 ± 2.3 months (5–13 months), and the mean AM melting duration was 21.1 ± 8.5 days (10–42 days). The mean number of repeats of AMTs was 2.5 ± 1.9 times (1–9 times). Complete corneal epithelization and conjunctival inflammation regression were observed in all the patients (Figs. 2, 3).

The development of superficial corneal vascularization was evaluated as limbal stem cell failure, which developed in 16 of the 20 cases. Total limbal stem cell failure was present in eight of those 16 cases. There were no cases of corneal perforation, and microbial keratitis was not observed in terms of a complication. None of the patients reported ocular discomfort necessitating the removal of the ring. A ring falling out was observed in two patients, and this was prevented by applying medical adhesive on the eyelid. Two of the patients developed symblepharon during the follow-up. One of these cases was a grade III ocular burn (the case with scleral necrosis, moderate symblepharon), and the other case was a grade VI ocular burn (symblepharon at a mild level).

Discussion

Suturing the AM on the conjunctiva is the most commonly used AMT technique to date. However, suture-related complications, such as conjunctival edema, conjunctival hemorrhage, conjunctival epithelial defects, and scar formation, may occur [19–21]. For the solution of this issue, AMT techniques utilizing a SR, or another plastic/titanium ring [15], have been reported where they stabilized the AM to the edges of the eyelids with sutures [16] or fixed the AM around the SR with fibrin glue [13] or prepared personalized rings resembling SR using feeding tubes [22] or a plastic dual clip ring system (AmnioClip) [23]. Contrary to the above-mentioned studies, our technique is a noninvasive technique that can be applied easily with high reproducibility and with a short duration of preparation by using a well-known SR.

Liang et al. [5] applied sutureless amniotic membrane to 39 acute chemical burn patients with modified

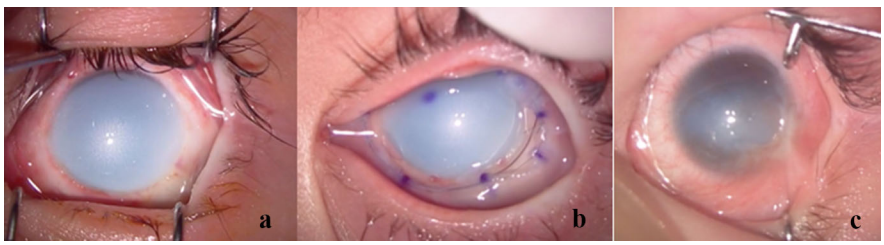

Fig. 2 An acute ocular surface chemical burn in a 14-month-old patient secondary to drain opener exposure (grade VI). **a** 360° limbal ischemia and total corneal opacity were observed, but the anterior chamber was not visible. **b** The non-traumatic AMT applied on the second day after contact with the chemical agent. **c** The non-traumatic AMT was applied eight times in 4 months; a 360° limbal stem cell deficiency and lower temporal prominence were observed, and the corneal opacity regressed. Symblepharon was observed in the lower temporal area where the chemical agent first made contact with the eye. All the interventions were done under general anesthesia with a surgical microscope

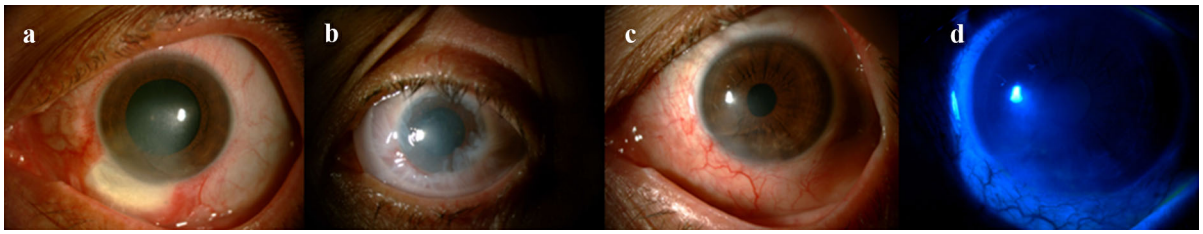

Fig. 3 Acute chemical burn case. **a** An alkaline chemical agent caused scleral necrosis, scleral melting, and corneal melting at the 6–8 o'clock level. **b** Tenon advancement and a non-traumatic AMT were performed during the same session. **c**, **d** At the postoperative first month examination, vascularization in the scleral melting area and regression in the corneal melting area were seen

symblepharon ring (MSR) and compared their results with the conventional AMT. The MSR had been designed similar to the production of the ocular prostheses and filled the fornix with an outer diameter of 35–40 mm. In our opinion, this technique has some disadvantages. Firstly, since their MSR filled the fornix without any ability of movement, the debris produced from the inflamed ocular surface will not be cleaned away properly from the ocular surface. For this reason, as they have also indicated in their report, they needed to replace the amniotic membrane every other day for three to five times in the early period. Secondly, the distribution of the postoperative topical ocular medications through the ocular surface may be blocked by the AM since this technique may block also the normal circulation of the natural tear. In our technique, because the AM moved similar to the contact lenses, the distribution may be more natural. We did not observe accumulation of any debris under the amniotic membrane. Secondly, in our technique, we preferred a well-known SR that has been used for years for the prevention of the formation of symblepharon. Although we did not observe accumulation of any debris below the AM, in case of any accumulation, one can easily wash the debris without any need for removal. Similar issues might also be encountered in the techniques in which the AM-fixing material fills the fornix totally (MSR [5], feeding tube [22] etc.). In addition, in slit lamp examination, the anterior segment can be easily observed, and the epithelial defect can be followed with staining while the patient has the SR–AM complex.

An AM linked to a SR has been introduced as a commercial product (Prokera; Bio-Tissue, Inc., Miami, FL, USA), in which the AM is fixed onto two rings similar to SR. Prokera has contact with the perilimbal conjunctival area, and the AM reaches to this border. The outer radius of Prokera's polycarbonate ring is 21 mm [14]. However, the outer radius in our modified AMT technique is more patient specific with its different available sizes (20–21–25 mm); therefore, it fills the fornix better. This characteristic allows it to reach the deeper fornices and provide a larger contact area, making it a possibly more efficient option for the treatment of ocular surface burns.

Some of these techniques [14, 15, 23] have been developed as commercial products, and the others were only case series. The most important problem of the other products or techniques is the high price of the products causing low reproducibility of the techniques because of the price. The other reported techniques were case reports or case series with a very low number of patients. In our study, only the cases with acute chemical injury (n = 20) were included, and the most important advantage of the technique is its high reproducibility with being an easy-to-apply, noninvasive, and practical technique.

The risk of developing symblepharon is very high in advanced stage ocular surface burns. In cases of acute chemical burns in the study by Liang et al., the rate of the formation of symblepharon was 35.9% in the sutureless group for whom the AM was applied with the MSR and 57.1% in the sutured group [5]. In our study, two of the 20 patients developed symblepharon and those two patients were grade III and VI. Lower rate of symblepharon formation in our study might be related with the use of the well-known SR that has been designed specifically for the prevention of symblepharon and the low efficiency of the MSR for the prevention of symblepharon formation in their study. Because even though the design of their MSR was good for covering the ocular surface, it may not be efficient for the prevention of symblepharon formation. The MSR was compatible with the forniceal

anatomy; however, it was not designed to prevent the contact between the bulbar and palpebral conjunctiva. Besides, the MSR is not a real SR. In our opinion, the MSR technique can be used in the other ocular surface disorders successfully rather than for the prevention of symblepharon formation in the patients with acute chemical burns.

None of the patients in our study reported any complaints that necessitated the removal of the ring. Noticeable symptomatic relief was observed in the patients after applying the SR–AM complex. In developing countries, fresh AMs are still in use, and with the help of this technique, a fresh AM can be applied onto the ocular surface inexpensively and non-traumatically. Low number of patients and retrospective nature of the study were the limitations of the study.

In conclusion, despite low number of cases, in this pilot study, we showed that this modified technique for an AM stabilized into a SR with continuous suturing is an easy, inexpensive, and most importantly, non-traumatic treatment for ocular surface burns that can be performed in any health center. Application of this technique can be further extended for the treatment of the other ocular surface pathologies.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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