Management of Acute Chemical Burn

By
Mario A. Di Pascuale, MD
Antonio Elizondo, MD
Edgar M. Espana, MD
V.K Raju, MD, FRCS
Scheffer C.G. Tseng, MD, PhD

INTRODUCTION

A clear vision allow us to see well during the inter-blink period, in order to maintain a healthy ocular surface, a stable tear film along with a transparent cornea are required. Cornea epithelial stem cells are located in the limbus in a unique microenvironment or niche, they are responsible to replace cornea epithelial in normal condition or during any insult to the ocular surface. The loss of the limbal epithelial stem cells or their niche may lead to limbal stem cell deficiency. The common hallmark of limbal stem cell deficiency is conjunctivalization, or the growth of conjunctiva epithelium over the cornea that results in cornea scar and subsequent loss of vision.

If acute chemical burn is not treated appropriately, it can lead to limbal stem cells deficiency. During the acute phase, persistent inflammation and the chemical insult are responsible to destroy the limbal stem cells. Therefore, the therapeutic strategy should be base on the clearance of the chemical substance along with reduction of acute inflammation. In this chapter we describe in more detail the management to reduce the inflammation, to foster collagen synthesis, to prevent tissue scar and to promote a faster epithelial healing.

Clinical History and Ophthalmic Examination

A thorough data collection, when the clinical history is taken should include the following aspects: type of chemical agent, time of the exposition to chemical
agent, place where this accident took place, a detailed initial management. Because it is more frequent that chemical burn occurs at work, a detailed information should be recorded if any primary preventive measures were taken, if not, a detailed inform of the failing preventive measures should be given including an appropriate guidelines to the employer to prevent futures accident. The clinical symptoms should be recorded such as if one eye or both eyes were affected. It is important to record if patients feel pain, in case where patient did not feel any pain, it is highly probable that ocular surface nerve are lost, thus an appropriate neurotrophic keratopathy management should be also considered when a future ocular surface reconstruction will be planned.

A complete ophthalmic examination should be taken, and some areas should be examined and recorded carefully such as: eyelid condition (lid edema, eye closure, blink rate, skin ulcer, loss of lashes, eyelid eversion-it is possible that tarsal conjunctiva is affected with ulcers that may progress to eyelid contraction and finally may lead to cicatricial entropion, such as recently reported by us in patients with acute Stevens Johnson Syndrome-4), conjunctiva inflammation measure by the grade of injection, conjunctiva ischemia size and location, early symblepharon, fornices depth, conjunctiva epithelium defect size and location. The limbus should be carefully examined to determine the present or absent the palisades of Vogt, limbal ischemia recorded in numbers of o’clock hours affected, limbal epithelial defect measured by fluorescein staining and followed by cornea examination which include detection of corneal epithelium defect, corneal edema, cornea transparency, deposit of pigment on endothelium and Anterior segment inflammation signs should be also recorded. A base line intraocular pressure should be taken and recorded before any topical anti-inflammatory therapy is use and further measures after treatment during every follow up.

CLEARANCE OF CHEMICAL SUBSTANCE

Chemical burn occurred more frequently during work activity, ether industrial or at home, therefore, the primary prevention is the first strategy that should be implemented; however when it is inevitable, such cases of chemical assault or when preventive measures failed, a swift and appropriated management are required.

According to Schrage N. et al3, a delayed of therapy or no rinsing are associated with increase of number eye surgeries, time of hospitalization, and worse visual acuity when is compared to immediate rinsing. Therefore, the rinse of eye including both upper and lower fornices with several liters of balanced salt solutions or Ringer-lactate solutions should be applied for many hours as needed, until the removal of the particle or remnants substances in ocular surface are achieved.
REDUCTION OF THE IMFLAMMATION, FOSTERING OF COLLAGEN SYNTESIS, PREVENTION SCAR FORMATION AND PROMOTING EPITHELIAL HEALING

MEDICAL THERAPY

Topical drugs can induce inflammation or lead to a condition known as "medicamentosa", in order to avoid drug related inflammation in an eye where the microenvironment or niche is very inflamed, the logical use of topical drugs are necessary to avoid further damage to the eye.

After appropriate eye rinsing, topical anti-inflammatory such as prednisolone should be used as frequently as every half hour, which dose varies depending on severity of inflammation, and later taper off, once inflammation is controlled, along with topical antibiotic therapy, preferentially newer 4th generation of fluoroquinolones, which are less toxic and achieve good concentration in lower doses. Topical antibiotic should be continued until ocular surface epithelium is totally healed.

In order to avoid further inflammation, oral delivery of drugs is the preferential mode of delivery recommended, thus, to foster collagen synthesis, and to prevent corneal scar, the use of oral vitamin C is recommended at 1 g a day, in addition to topical tetracycline such as doxycycline 100 mg bid or minocycline 50 mg qd. Only if intraocular pressure is high, oral anti-glaucomatous drugs are recommended such as acetazolamide (Diamox®) or methazolamide (Neptazane®).

AMNIOTIC MEMBRANE TRANSPLANTATION

Amniotic membrane is the innermost layer of the placenta and consists of a thick basement membrane and an avascular stromal matrix. Amniotic membrane transplantation has been used as a graft or as a patch in different surgical subspecialties [for review see6-8]. In 1940, De Rotth9 used a life fetal membrane including both amnion and chorion as a graft for conjunctiva surface reconstruction for symblepharon and conjunctiva defect, but a low success rate was achieved probably caused by the inclusion of live cells and the chorion. In 1946 and 1947 Sorsby et al10,11,11 used
chemically processed "dry" Amniotic membrane, termed "aminoplastin", as a temporary patch to treat acute ocular burns that result showed that the earlier intervention the shorter the hospitalization. Although a remarkable success was noted, amnioplastin had to be repetitively applied. For reasons still not clear, the use of amniotic membrane disappeared from the literature. Kim and Tseng\(^\text{12}\) in 1995 reintroduced amniotic membrane for ophthalmic uses in treating corneas with total limbal stem cell deficiency in a rabbit model. We attribute such a surge of interest to an improved method of processing and preservation, which maintains the inherent properties of the amnion.

The results of several studies indicate that the amniotic membrane basement membrane may support the growth of epithelial progenitor cells by prolonging their life span and maintaining their clonogenicity. Amniotic membrane transplantation can be used to expand the remaining limbal stem cells and corneal transient amplifying cells during the treatment of partial limbal deficiency\(^\text{13,14}\) and to facilitate epithelialization for persistent corneal epithelial defects with stromal ulceration\(^\text{15-18}\) and perforation\(^\text{19}\).

The stromal side of the membrane suppresses TGF-\(\beta\) signaling, and myofibroblast differentiation of normal human corneal and limbal fibroblasts\(^\text{20}\) and of normal conjunctiva fibroblasts and pterygium body fibroblasts\(^\text{21}\). This action may explain why it may also maintain the normal phenotype of keratocytes\(^\text{22}\). This action also explains why amniotic membrane transplantation reduces scars during conjunctiva surface reconstruction\(^\text{23-25}\), prevents recurrent scarring after pterygium removal\(^\text{26-27}\), and reduces corneal haze following phototherapeutic keratectomy (PTK) and photorefractive keratectomy (PRK)\(^\text{29-31}\). Amniotic membrane stroma can also exclude inflammatory cells by stimulating them into rapid apoptosis\(^\text{29,30}\), and contains various forms of protease inhibitors\(^\text{32}\). This action explains why stromal inflammation is reduced after amniotic membrane transplantation\(^\text{15,25}\) and corneal neovascularization is mitigated\(^\text{33}\).

Amniotic membrane can be used as a temporary graft or patch to reduce acute inflammation so as to prevent scarring and to facilitate epithelialization in chemical burns in a rabbit model\(^\text{34}\) and in human patients\(^\text{35,36}\), in acute Stevens Johnson syndrome/Toxic epidermal necrolysis\(^\text{4,37}\). Amniotic membrane can also be used to suppress refractory chronic inflammation in various ocular surface disorders\(^\text{38}\) including the shield ulcers in vernal keratoconjunctivitis\(^\text{39}\). Experimentally, when used as a temporary graft, it can reduce corneal haze following PRK or PTK\(^\text{29,31}\), an effect observed in human patients after LASEK or PTK\(^\text{40,41}\), and reduce chronic inflammation caused by HSV\(^\text{27,42}\).
Surgical Technique

The purpose of this technique is to reduce the acute inflammation and to promote a scar less wound healing by covering all ocular surface with amniotic membrane as a patch. The amniotic membrane is removed from the storage media, and peel off from the nitrocellulose filter paper and place over the recipient eye, thus it covers the entire ocular surface from the upper lid margin to the lower lid margin, if eyelid skin is also affected should be included and covered by the amniotic membrane such as recently reported. The amniotic membrane is secured to the conjunctiva and to the lid margin with the stromal side or sticky side facing down by using 8-0 or 9-0 Vicryl sutures with episcleral bites. At the lower and upper fornices the amniotic membrane is further secured with two double-arm 4-0 silk sutures, which are brought through the lid and tie over the skin with bolsters. (Figures are not shown, but for further review and detailed illustration please see)

TENTONPLASTY

Persistent conjunctiva or cornea defect, in eyes with chemical burn and severe ischemia, the risk of eye perforation is high, therefore, the surgical approach consist of bringing back the blood supply in which vital connective vascular tissue of the orbit is placed at the ischemic area by using a surgical technique published in 1989 by Teping C and Reim M. Herein, we further describe our tenonplasty modified surgical technique by using amniotic membrane as a substrate for the relocation of a vital vascular tenon sheet.

Surgical Technique

Peritomy is performed to separate the necrotic tissue from the remaining healthy conjunctiva by using scissors (Fig.1A and B), the following step consists of removal of the necrotic tissue over the ischemic area. The necrotic tissue is dissected off by using scissors (Fig. 1C). Once the necrotic tissue is removed (Fig. 1D), this is followed by dissecting a free pedicle tenon vascular sheet from the deep posterior part of un-burn area, thus, first a plane can be created by lifting up the conjunctiva and the subconjunctiva fibrovascular tissue using 0.12 forceps, and this plane can be further dissected the conjunctiva from subconjunctiva by using scissors (Fig. 1E). After the separation of the conjunctiva epithelial layer from subconjunctiva tissue, a second plane is identified between the deep tenon layer and subconjuntiva fibrovascular tis-
sue (Fig. 1F), this plane can be separated in the similar fashion by scissor dissection. (Fig. G and H). After separation of the tenon layer from the fibrovascular tissue, a free vascular pedicle graft can be moved from the posterior pole toward the limbus (Fig. 1I). Once an adequate size of pedicle tenon vascular sheet is obtained, the bare sclera (Fig. 1J) is further protected by using a layer of amniotic membrane, to do so, the amniotic membrane is removed from the storage media and peel off from the nitrocellulose paper (Fig. 1K), the stromal side or sticky side of amniotic membrane is faced down, and further anchored to the bare sclera by using interrupted 8-0 Vicryl sutures at the conjunctiva (Fig. 1L) and 10-0 nylon sutures at the limbus with long episcleral bites. Then, the free pedicle vascular tenon sheet is placed over the amniotic membrane (Fig. 1M), and secured it by using interrupted 8-0 Vicryl sutures with episcleral bites (Fig. 1M and N). A second layer of amniotic membrane is used to cover the vascular tenon sheet (Fig. 1O) and secured with 10-0 nylon sutures at limbus and 8-0 Vicryl sutures at conjunctiva (Fig. 1O). At the end of surgery, the entire ischemic area is now protected by a sandwiched vascular tenon sheet with amniotic membrane graft (Fig. 1P).

**Figure 1 (See Facing Page):** Key surgical steps of tenonplasty with amniotic membrane transplantation. (A and B), After peritomy, (C and D) dissection and removal of the necrotic tissue were performed. E, This was followed by a thorough dissection of the subconjunctival fibrovascular tissue. F, A second plane is identified between the deep layer of tenon and subconjunctiva fibrovascular tissue. (G and H), This second plane can be separated in the similar fashion with scissors dissection. I, A vital vascular tenon sheet is obtained, thus it can be easily moved toward the limbus. J, The denuded scleral defect at limbus is measured. K, Appropriated size of amniotic membrane is obtained and removed from the nitrocellulose paper. L, Amniotic membrane is placed stromal side down at the limbus over the bare sclera and secured with 8-0 Vicryl sutures in the conjunctiva and 10-0 nylon sutures in the limbus with episcleral bites. M, The vascular tenon sheet is moved toward limbus over amniotic membrane and secured with 8-0 Vicryl sutures in the conjunctiva side. N, The appearance of the eye after vascular tenon sheet is applied and secured. O, A second layer of amniotic membrane is applied facing stromal side down over the vascular tenon sheet so that it was sandwiched with two layers of amniotic membrane. P, The final appearance of the eye is showed at the end of surgical procedure.
Figure 1 I-P
The preoperative appearance of this patient with chemical burn and severe ischemia showed an inflamed ocular surface with severe ischemia that had affected the bulbar conjunctiva and limbal area, with total cornea epithelial defect. (Fig. 2A and B) The last follow up performed at 20 months after the first surgery, tenonplasty with amniotic membrane transplantation as a sandwich, which surgical steps were previously showed in Fig. 1, and keratolimbal allograft transplantation performed in a later stage, showed a non-inflamed ocular surface with minimal peripheral cornea scar and intact conjunctiva and cornea limbal epithelium (Fig. 2C and D).

Figure 2: A representative case with chemical burn and severe ischemia treated with tenonplasty, amniotic membrane transplantation (AMT) and keratolimbal allograft transplantation (KLAL). (A and B) Preoperative appearance showing an inflamed ocular surface with severe ischemia that affect almost 180° of nasal bulbar conjunctiva and limbal area, with total cornea epithelial defect evidenced by using fluorescein staining under cobalt blue light. (C and D) The last follow up in the same patient after tenonplaty with AMT as sandwich, previously showed in Fig. 1, and KLAL performed in a later stage, showing a non-inflamed ocular surface with minimal peripheral cornea scar with intact conjunctiva and corneal limbal epithelium.
NEW MANAGEMENT OF ACUTE CHEMICAL BURN
Sutureless Amniotic Membrane Transplantation

The use of sutures induced inflammatory cells infiltration, even with the less reactive materials such as nylon, therefore, it is now a trend in ophthalmic field to use biological adhesives such as fibrin glue or modified chondroitin sulfate. A new method to place the amniotic membrane which eliminates the need of suture is now developed, thus it will reduce inflammation, the pain, it can be safely performed in the examination room, and thus it will also reduce the cost related to the operating room.

In April of 2005, Bio-Tissue just released a new product name ProKera, which is a corneal-epithelial device consistent of an ophthalmic conformer that incorporates amniotic membrane (Amniograft). ProKera has been assembled so that the stromal side will be in contact with the patient ocular surface; it is preserved in the frozen state, thus the natural biological properties of the membrane remains. We recently used Prokera in a 54 years-old female, with acute chemical burn caused by chloride. She was seen 24 hours later after the initial event, and she complained of pain, light sensitivity, loss of vision in left eye, and her initial examination revealed that the uncorrected visual acuity was 20/20 in right eye and 20/80 in left eye, the right eye ophthalmic examination was unremarkable, but in the left eye, the eyelid was edematous, conjunctiva was inflamed with 2+ injection associated with limbic ischemia at 3 and 9 o’clock hours and in the lower limbus, including lower bulbar conjunctiva (Fig. 3A), and there was a 90% of corneal epithelial defect with corneal edema (Fig. 3B). After receiving the ProKera, the next day, the patient felt 30% better about pain, and redness (a subjective scale from 0 that represents no improvement to 100% that represents the absent of symptoms), the examination revealed that the amniotic membrane was still present and the conjunctiva injection improved (Fig. 3C) as well as corneal epithelial was healing (Fig.3D). Three days after the initial visit, the patient felt that her pain, light sensitivity and redness further improved about 50%, the amniotic membrane dissolved, and the conjunctiva was less inflamed (Fig.3E), and the corneal conjunctiva epithelial defect was only 15% (Fig. 3F), the conformer from the ProKera was removed, and a bandage contact lens was placed over the cornea. The patient was seen five days after initial visit, she did not feel pain, the only complained was residual light sensitivity, and her uncorrected visual acuity improved from 20/80 to 20/50, her conjunctiva was mild inflamed with 1+ injection and there were no conjunctiva or cornea defects. The last follow up was performed six weeks after showing that there were no symptoms, her uncorrected visual acuity further improved to 20/20 and the ocular surface was non-inflamed without epithelial defect (Fig. 3G and 3F).
**Figure 3:** A representative case with acute chemical burn in the left eye managed with ProKera. (A) In the initial visit, the conjunctiva inflammation associated with limbic ischemia located at 3 and 9 o’clock hours and in the lower limbus including lower bulbar conjunctiva, (B) the cornea had a 90% corneal epithelial defect associated with corneal edema. (C) The next day, the amniotic membrane was still present, and the conjunctiva injection improved, (D) the corneal epithelial defect improvement can be seen even with the amniotic membrane on cornea such as consistently had been reported by Kobayashi et al46, and this was further demonstrated by the healing of the epithelial edge moving down showed by black arrows. (E) Three days after the initial visit, the amniotic membrane dissolved, and the conjunctiva was less inflamed, (F) the residual corneal epithelial defect was only 15%. (G) Six weeks after initial visit, the ocular surface was non-inflamed, and (H) without epithelial defect.
References


Supported in part by an unrestricted grant from Ocular Surface Research & Education Foundation, Miami, Florida.

_________________________

Mario A. Di Pascuale, MD
Antonio Elizondo, MD
Edgar M. Espana, MD
V. K. Raju, MD, FRCS
Scheffer C. G. Tseng, MD, PhD

Ocular Surface Center and
Ocular Surface Research &
Education Foundation,
Miami, Florida
USA