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Original Research Paper

Ophthalmology

CHEMICAL BURNS : ROLE OF AMNIOTIC MEMBRANE-MOTHER'S OWN REMEDY

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KEYWORDS :

INTRODUCTION :

Nuclear Chemical Biological Warfare is the most dreaded weapon of mass destruction garnered through the violent terrorist acts . The increasing lethal and seemingly random incidents of these acts are posing a substantial threat to the mankind due to their forlorn and permanent deleterious effects on the demographic profile causing a harrowing impact like never before.[1,2]

Chemical injury is the most brutal entity in NBC warfare due to its rapid action owing to easy dissemination and persistence in the body. The chemical weapon being both accessible and affordable easily catches the eye of insurgents.

Out of all the organs involved, eye is the commonest organ affected in a chemical injury accounting for a significant portion of ocular trauma in the acute setting, requiring prompt recognition and treatment.[3-5] Therefore, an explicit discernment of the extent of damage and the treatment of chemical eye injuries is mandatory for both war and the peacetime scenario.

HISTORICAL PERSPECTIVE:

The history of chemical eye burns and their relative treatments is still an unwritten chapter in the history. But the first author who has written about burns in a didactic way is Wilhelm Fabry von Hilden.[1,7-8] In 1607, the author classified burns in three grades, and mentions the best treatment to apply for each case.[9] In the twentieth century, the treatment of chemical burns became a bigger necessity during World War I. Combat gas burst into the battle provoking very severe lesions and a terrifying anxiety among fighters.

First systematic therapeutic strategies were introduced by Passow who recommended rinsing with water and releasing the toxic secret from the conjunctiva via the "Passow incisions."[10] A new systematic approach started with the classification of eye burns introduced by Roper Hall in 1978, giving hints from the initial clinical presentation to the later outcome.[11] The modified classification from Reim reflected the observation that limbus affection and circulation in the limbus area in the early post-traumatic phase gives major information on the later outcome of eye burns. Thus, Reim et al. introduced early treatment options for eye burns starting with a concept of corneal opacity, limbal ischemia, and conjunctival damage. Thus a prognostic and therapeutic concept existed that made the prognosis more certain. Modifications of this concept are all based on this fundamental work. Today an equilibrated concept of modern first aid with steroids, vitamin C, antibiotics and defined surgical techniques is the common repertoire of specialists in the field of ocular reconstruction after eye burns.

EPIDEMIOLOGY:

Ocular burns constitute true ocular emergencies and chemical burns represent potentially blinding ocular injuries representng between 11.5%-22.1% of ocular traumas [12]. Chemical burns may be caused by either alkaline or acidic agents. Alkali injuries occur more frequently than acid injuries. Common causes of alkali and acid injuries are:

ACIDS:

Sulphuric Acid, Sulphurous Acid, Hydrofluoric Acid, Acetic Acid, Hydrochloric Acid.

Acids are generally less harmful than alkali substances. They cause damage by denaturing and precipitating proteins in the tissues they contact. The coagulated proteins act as a barrier to prevent further penetration. The one exception to this is hydrofluoric acid, where the fluoride ion rapidly penetrates the thickness of the cornea and causes significant anterior segment destruction

ALKALIS:

Ammonia, Potassium Hydroxide, Lye, Lime. Alkali agents are lipophilic and therefore penetrate tissues more rapidly than acids. They saponify the fatty acids of cell membranes, penetrate the corneal stroma and destroy proteoglycan ground substance and collagen bundles. The damaged tissues then secrete proteolytic enzymes, which lead to further damage.

PATHO-PHYSIOLOGY:

Ocular chemical burns cause extensive limbal and conjunctival cell destruction. Persistent inflammation with leucocytic infiltration in the acute stage causes further gradual stem cell loss, preventing epithelialization and accelerates ulceration and melting with globe perforation. It also contributes to scarring sequelae like symblepharon and lid shortening, tear film deficiency, and inflammatory granuloma in the chronic stage. In addition, in severe burns ischaemic changes result in anterior segment necrosis and sterile corneal ulceration at an early stage after the injury.

The severity of ocular injury depends on four factors: the toxicity of the chemical, how long the chemical is in contact with the eye, the depth of penetration, and the area of involvement. It is therefore critical to take a careful history to document these factors. The most common symptoms are severe pain, epiphora, blepharospasm and reduced visual acuity.

Two major classification schemes for corneal burns are the **Roper-Hall (modified Hughes) classification** and the **Dua's classification**.

The Roper-Hall classification is based on the degree of corneal involvement and limbal ischemia.

The Dua classification is based on an estimate of limbal involvement (in clock hours) and the percentage of conjunctival involvement.

MANAGEMENT:
While there is variability in treatment strategies of chemical burns, most Ophthalmologists recommend a graded approach depending on the severity of injury. Mild burns (Roper-Hall grade I) respond well to medical treatments and lubrication, while more severe burns necessitate more intensive medical therapies and surgery.

Early irrigation is critical in limiting the duration of chemical exposure. The goal of irrigation is to remove the offending substance and restore the physiologic pH.

ANTIBIOTICS-
A topical antibiotic ointment like erythromycin ointment four times daily can be used to provide ocular lubrication and prevent superinfection.

Cycloplegic agents such as atropine or cyclopentolate prevent ciliary spasm.

ARTIFICIAL TEARS-
and other lubricating eye drops, preferably preservative free, should be used generously for comfort.

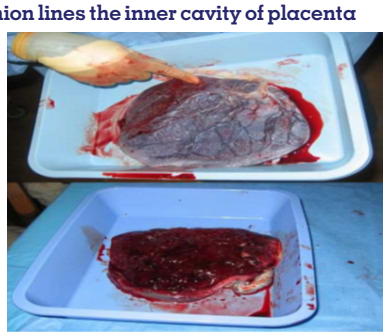
STEROID DROPS-
topical steroids can help calm inflammation and prevent further corneal breakdown.

ASCORBIC ACID-
is a cofactor in collagen synthesis and may be depleted following chemical injury. Ascorbic acid can be used as a topical drop or orally to promote collagen synthesis and reduce the level of ulceration.

SURGICAL TECHNIQUES:
AMNIOTIC MEMBRANE TRANSPLANTATION (AMT) -
the purpose of AMT is to rapidly restore the conjunctival surface and to reduce limbal and stromal inflammation. Amniotic membrane, the outermost portion of foetal membranes possesses anti-inflammatory, anti-scarring, stem cell proliferating and epithelialization promoting effects on the ocular surface (Fig 1)[13,14]

The benefits are thought to be two fold : Physical and Biological.

Fig 1: Amnion lines the inner cavity of placenta



Physically, AMT has been shown to improve patient comfort by reduction of eyelid friction. Throughits physical actions, AMT may also prevent symblepharon formation.

Amniotic membrane is also felt to have biologic effects. It expresses TGFB1 and epidermal growth factor, which have roles in wound healing. The basement membrane of the AM contains collagen types IV, V and VII, in addition to fibronectin and laminin. The laminins are very effective in facilitating corneal epithelial cell adhesion. Type V collagen helps in the epithelial cell anchorage to the stroma. The AM stromal matrix, rich in foetal hyaluronic acid suppresses TGF B signalling, proliferation and myofibroblastic differentiation of normal conjunctival, corneal and limbal fibroblasts .The stromal matrix also suppresses expression of certain inflammatory cytokines that originate from the ocular surface epithelia, including interleukin 1a, IL -2, IL-8, interferon , tumour necrosis factor- , basic fibroblast growth factor and platelet derived growth factor. The AM attracts and sequesters inflammatory cells infiltrating the ocular surface and contains various forms of protease. Taken together, these biological effects may dampen inflammation, promote epithelial growth, prevent scarring and prevent neovascul arization.

GRAFT PROCUREMENT AND PRESERVATION:
Amniotic membrane is obtained from prospective donors undergoing Caesarean section, who are negative for communicable diseases including HIV, hepatitis and syphilis.. Dulbecco Modified Eagles Medium/glycerol (1:1) is used for cryopreservation and the tissues are frozen at -80 degrees until further use[3].(Fig 2) Amnion stored in 50-85% glycerol is reliable and effective for over a year, with the added advantage of antibacterial properties. Human AM deprived of amniotic epithelial cells by incubation with EDTA when freeze dried, vacuum packed and sterilized with gamma-irradiation at 25kGy retained most of the physical, biological and morphologic characteristics of cryopreserved AM.

Fig 2: Amnion on nitrocellulose paper

SURGICAL TECHNIQUE:
The main objectives of AMT are ocular surface reconstruction, promotion of epithelialization, providing symptomatic relief and reducing inflammation. There are three basic principles upon which the final technique is individualized.

INLAY OR GRAFT TECHNIQUE:
When the AMG is tailored to the size of the defect and is meant to act as a scaffold for the epithelial cells, which then merges with the host tissue, it is referred to as a graft.

OVERLAY OR PATCH TECHNIQUE:
When the AM is used akin to a biological contact lens in order to protect the healing surface defect beneath, it is referred to as a patch. A patch also reduces inflammation by its barrier effect against the chemical mediators from the tear film.

FILLING-IN OR LAYERED TECHNIQUE:
the entire depth of an ulcer crater is filled with small pieces of AM trimmed to the size of the defect. A larger graft is sutured to the edges of the defect in an inlay fashion and an additional patch may help in preserving the deeper layers for a longer duration.

COMPLICATIONS:
In the immediate postoperative period one may come across hematoma formation under the membrane. Premature degradation of the membrane and cheese wiring may need frequent repeat transplantations. Occasionally, a residual sub epithelial membrane may persist in some cases and inadvertently opacify the visual axis.

The incidence of post -AMT microbial infections is as low as 1.6%. Gram-positive organisms are the most frequent isolates. The key to reducing postoperative complications is meticulous selection of both donor and recipient and maintaining high

standards of quality assurance.

OTHER TREATMENT MODALITIES:
LIMBAL STEM CELL TRANSPLANT-

Limbal autografts can be used from the healthy contralateral eye if only one eye is injured in chemical burn.

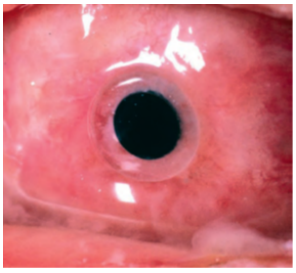
CULTIVATED ORAL MUCOSAL EPITHELIAL TRANSPL ANTATION (COM ET) -

can also be used to promote re-epithelialization and reduce inflammation in corneal burns. The cells are harvested from the patient's own buccal mucosa so that systemic immunosuppression is not necessary.

BOSTON KERATOPROSTHESIS-

Severe chemical injury leads to chronic inflammation and scarring, making visual recovery challenging. In these most difficult cases, the Boston Keratoprosthesis can be used.(Fig 3) Because it is independent of stem cell function, it does not require systemic immunosuppression.

Fig 3: Boston Keratoprosthesis



CONCLUSION:

The success of AMT depends upon the severity of chemical eye burns. However, AMT has certainly gained an acceptable position in Ocular surgical armamentarium. The relative ease of the procedure, freedom from intra ocular intervention and low rate of intra- op and post- op complications make it an attractive surgical option .

Shimazaki et al reported successful reconstruction of the ocular surface with AMT in seven eyes with severe chemical burns [4]. However, Dua et al reported failure of AMT to restore ocular surface or preserve the integrity of eye in severe acute burns [16-20]. A recent report by Kobayashi et al also emphasized that immediate amniotic membrane transplantation is useful for mild to moderate acute chemical burns and preserves ocular surface integrity. Experience cautions against the overenthusiasm in the use of amniotic membrane alone in acute chemical burns with extensive limbal ischaemia and conjunctival involvement as the amniotic membrane was not very successful in establishing the ocular surface. It mainly plays an adjunctive role in limbal stem cell deficiency in severe chemical burns with near total limbal ischaemia.

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