Acute Chemical Injuries

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Chemical burns account for 11.5-22.1% of traumatic ocular injuries, a majority of which occur in young males because of exposure to acid or alkali in the setting of industrial accidents. These injuries also occur frequently as a result of exposure to chemicals at home and in association with criminal assaults. Alkali injuries occur more frequently than acid injuries, with lime (chuna particle) injury being the commonest.

Aetiology
Alkali injury is more common than acid injuries, because of their frequent use in many household cleaning agents and building materials. A few common acids and alkalis responsible for acute chemical burns are described below.

Acids
The most common etiological agent responsible for acid injuries is sulphuric acid, which is commonly used in inverter batteries. Sulphuric acid is a strong acid used in car batteries, fertilisers, in the manufacturing of dyes, explosives and refining petroleum. Nitric acid is also a strong acid used in manufacturing of fertilisers, rocket propellants and nylon products. It leads to a yellowish corneal opacity. Chromic acid is used in electroplating, ceramic glazes and wood preservation, and causes brownish discoloration of conjunctiva, often simulating chronic conjunctivitis.

Hydrofluoric acid, though a weak acid in itself, gives the most reactive anion. It is used in etching glass, semiconductor production and rust removal. It acts like alkali to saponify lipids, causing deep rapid penetration, extensive ischemia and calcific plaques in corneal stroma.

Alkalis
Ammonia is a common cause of alkali injury, and is found in fertilisers, refrigerants and cleaning solutions. It combines with water to form ammonium hydroxide with very rapid penetration in ocular tissues. Lye or sodium hydroxide is a common constituent of drain cleaners, with almost as rapid penetration as ammonia. Potassium hydroxide, also known as caustic potash causes similar injuries as lye. Magnesium hydroxide is a constituent of sparklers, and results in combined thermal and chemical injuries. Lime is the most frequent cause of chemical injury at workplace. It is a constituent of plaster, mortar, cement and whitewash. Though it has poor penetration, the toxicity is increased by retained particulate matter causing prolonged severe damage.

Pathophysiology
Alkali burns cause corneal damage by three main mechanisms-

pH changes
The rise in pH leads to saponification of fatty acids of cell membranes leading to cell destruction. Collagen is more susceptible to enzymatic degradation by hydrolysis of protective glycosaminoglycans.

Ulceration and proteolysis
Alkalis cause stromal ulceration at two to three weeks post injury due to various proteolytic enzymes (glycosidases, elastases, and cathepsins) that are released by polymorphonuclear leucocytes (PMNL) and epithelial cells.

Collagen synthesis defects
Alkali burns damage ciliary body to reduce aqueous ascorbate levels. Ascorbate is necessary for conversion of proline and lysine to hydroxylysine, and also plays an important role in the synthesis of glycosaminoglycans.
Acid burns lead to coagulation and precipitation of proteins. It reacts with collagen leading to shrinkage of collagen fibres associated with a rapid rise in intraocular pressure. No defects in collagen synthesis are usually noted. Severe acid burns lead to ciliary body damage and decreased aqueous ascorbate levels.

**Classification**

Various classification systems have been proposed over the years, each with its own limitations and advantages.

Roper-Hall classification\(^3\) originally described in 1965 has been the most widely used classification system (Table 1). It is a modification of the Ballen classification\(^4\) (1964), which is based on the original Hughes classification\(^5\) (1946). It classifies all burns with more than 50% limbal ischemia as grade IV burns. However, the prognosis of burns with just over 50% limbal ischemia is much better than those with total limbal ischemia, warranting the need for a better classification.

Dua\(^6\) in 2001 gave a new classification for ocular burns, based on the clock hours of conjunctival and limbal involvement (Table 2). It also prognosticated each grade of injury. This classification has the added advantage that it can be presented in an analogue manner rather than in the stepped progression of a graded classification.

**Clinical course**

The clinical course following an acute chemical injury can be characterised in three stages:

- **Acute stage (immediate to one week)**
  In mild burns, corneal and conjunctival epithelial defects with sparing of limbal blood vessels are found. In severe burns, destruction of corneal and conjunctival epithelium with immediate limbal ischemia (Figure 1,2) is observed. Increase in pH of aqueous humor with decreased glucose and ascorbate levels further aggravates ischemia, and leads to alteration of nutrients and cell death. A bimodal rise in intraocular pressure is observed, with the initial peak due to compression of globe because of hydration and longitudinal shortening of collagen fibrils. The second peak is a result of impedance of aqueous humor outflow.

- **Early reparative stage (one to three weeks)**
  It is characterised by the replacement of destroyed cells and extracellular matrix. In grade I/II burns, epithelium regeneration begins, along with corneal neovascularisation, clearing of stroma and synthesis of collagen glycosaminoglycans. In grade III/IV burns, epithelium regeneration may not start and progress. Stroma remains hazy, and endothelium may be replaced by retrocorneal membranes. Stromal ulceration takes place due to action of digestive enzymes such as collagenases, Matrix

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Table 1: Roper-Hall classification (1965)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Prognosis</th>
<th>Cornea</th>
<th>Conjunctiva/ limbus</th>
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</thead>
<tbody>
<tr>
<td>I</td>
<td>Good</td>
<td>Corneal epithelial damage</td>
<td>No limbal ischemia</td>
</tr>
<tr>
<td>II</td>
<td>Good</td>
<td>Corneal haze, iris details visible</td>
<td>&lt; 1/3 limbal ischemia</td>
</tr>
<tr>
<td>III</td>
<td>Guarded</td>
<td>Total epithelial loss, stromal haze, iris details obscured</td>
<td>1/3-1/2 limbal ischemia</td>
</tr>
<tr>
<td>IV</td>
<td>Poor</td>
<td>Cornea opaque, iris and pupil obscured</td>
<td>&gt; 1/2 limbal ischemia</td>
</tr>
</tbody>
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Figure 1: Acute chemical injury with severe limbal ischemia

Figure 2: Acute chemical injury with epithelial defect, stromal haze and limbal ischemia
metalloproteinases (MMP) and other proteases released from regenerating corneal epithelium and PMNLs.

Late reparative stage and sequelae (≥ three weeks)

Grade I/II burns achieve completion of the healing process usually, with good prognosis. Grade III/IV burns usually have a variety of complications (Figure 3) such as corneal scarring, xerophthalmia, symblepharon, ankyloblepharon, glaucoma, uveitis, cataract, lagophthalmos, cicatricial entropion or ectropion, trichiasis, dry eye etc.

Management

The primary goals of treatment are

• Restoration of intact epithelium
• Control of acute inflammatory reaction
• Support of reparative process
• Prevention of complications

Management can be divided into four stages

Immediate emergency treatment

Immediate treatment should be instituted as soon as possible, within first few minutes of injury. Immediate irrigation (Figure 4) of the eye with any non toxic liquid for a minimum of thirty minutes is recommended. pH should be measured from the cul-de-sac 5-10 minutes after completion of irrigation, and further irrigation should be carried out if pH is less than 7, till pH approaches normal level. Eyelid speculum or Morgan lens (sclera irrigating lens) may be used to keep the eye open while irrigating solution is delivered through i.v. tubing.

Various solutions may be used for irrigation, including tap water, normal saline, ringer’s lactate, balanced salt solution, Cedderoth eye wash (borate buffer solution) or diphoterine (high buffer capacity amphoteric hypertonic polyvalent compound). No therapeutic differences have been identified between normal saline, normal saline with bicarbonate, lactated Ringer’s, and balanced salt solution (BSS), or BSS Plus7. Use of acidic solution to neutralise alkali is dangerous and NOT recommended.

After irrigation, a thorough examination should be carried out by double eversion of lids to examine the fornices under proper ocular anaesthesia (Figure 5). Any embedded particulate matter should be removed. Chuna particles should be removed with cotton tipped applicator.
Early acute phase treatment

- Treatment with broad spectrum antibiotics to prevent secondary bacterial infection and cycloplegics to relieve ciliary spasm should be instituted. Antiglaucoma drugs, both topical and systemic may be needed to control IOP spikes. Further drugs are added to-

  - Control of inflammation
    a) Topical corticosteroids
      Topical steroids used in the initial ten days after injury have been shown to reduce inflammatory cells infiltrating the corneal stroma, which are a source of proteolytic enzymes responsible for corneal ulceration. Steroids should be rapidly tapered after ten days if the epithelium is not intact, as it slows repair process.
    b) Progestational steroids
      Medroxyprogesterone acetate 1% inhibits collagenase and ulceration, and suppresses corneal neovascularisation with minimal suppression of stromal wound repair. It can be used 10-14 days post injury instead of corticosteroids.
    c) Topical nonsteroidal anti-inflammatory drugs
      should be used cautiously due to the possibility of corneal melting in conjunction with epithelial defects.
      A simple sweeping of the glass fornices daily with ointment coated glass rod may go a long way in prevention of symblepharon formation. Additionally, scleral lenses and symblepharon rings may be used, to aid symblepharon prevention.
      The benefit of paracentesis and irrigation of the anterior chamber following a severe chemical injury is uncertain. It may be therapeutic by allowing rapid normalization of pH, and buffered phosphate solution or balanced salt solution may be used for anterior chamber reformation.
    - Support repair and minimize ulceration
      a) Ascorbate
      Dose: oral ascorbate 2g/day (500 mg QID), topical 10% solution in artificial tears administered hourly
      A decreased incidence of corneal ulceration and perforation has been observed in rabbit studies when aqueous ascorbate levels are >15mg/dl. It acts by replenishing ascorbic acid to the scorbatic fibroblasts of cornea.
    b) Tetracycline
      Doxycycline 100 mg BD inhibits MMP through restriction of gene expression of neutrophil collagenase and epithelial gelatinase. It suppresses alpha-1 antitrypsin mediated degradation and causes scavenging of reactive oxygen intermediates.
    c) Collagenase inhibitors
      10% sodium citrate drops made in artificial tears, instilled hourly also play a role in supporting repair. Other collagenase inhibitors include cysteine, acetylcysteine, EDTA and penicillamine.
  - Promote re-epithelialization and transdifferentiation
    a) Tear substitutes- they promote re-epithelialization, ameliorate persistent epitheliopathy, decrease risk of recurrent erosions and accelerate visual rehabilitation
    b) Autologous serum eye drops 20-40% contain growth factors that may aid in establishing epithelial integrity.
    c) Bandage contact lens prevents the ocular surface from windshield-wiper effect of the eyelids. The promote basement membrane regeneration.
    d) Fibronectin has shown a favourable effect in animal models. It is still under investigation.
    e) Epidermal growth factor favourably influences epithelial migration in human studies. However recurrent erosions have been seen after discontinuation.
    f) Retinoic acid is theoretically useful in promoting goblet cell recovery, tear film stabilisation and improved ocular surface wetting.

Intermediate term treatment

a) Debridement
A careful excision of all necrotic tissues should be carried out, as necrotic tissue acts as a store for inflammatory mediators that elicit a PMNL response and further hasten ulceration.
b) Conjunctival/tenon advancement (tenoplasty) can be undertaken to improve the vascular supply of the anterior segment\(^1\). It involves excision of the necrotic conjunctiva and cornea, followed by the advancement of Tenon’s over the cornea employing careful dissection to preserve the vascular supply of capsule located posteriorly.

c) Tissue adhesives such as cyanoacrylate glue may be used in conjunction with a bandage contact lens, in the eventuality of a small corneal perforation.

d) Large perforations may need emergency patch graft or therapeutic penetrating keratoplasty, depending on the size of the perforation.

e) Amniotic membrane transplantation (Figure 6) has seen a revival of interest for use in acute chemical injuries, with several studies showing a beneficial effect in grade II-III chemical burns\(^12\). Amniotic membrane facilitates epithelialisation, reduces inflammation, and prevents symblepharon formation, vascularisation and scarring. It also provides a fast and dramatic relief from pain and photophobia.

Late rehabilitation treatment

a) Ocular surface rehabilitation

Symblepharon lysis, fornix formation, entropion or ectropion surgery may be needed.

b) Limbal stem cell deficiency (Figure 7).

Limbal stem cell transplantation may be needed, especially in high grade chemical injuries with extensive perilimbal ischemia. Sources for limbal stem cell transplants range from conjunctival limbal autografts, living related and cadaveric donors, to ex-vivo culture expanded limbal epithelium. Large diameter lamellar keratoplasty provides corneal tissue for tectonic support in addition to limbal stem cells.

c) Visual rehabilitation

Penetrating keratoplasty, if needed, should be delayed for 18 months-2 years, as keratoplasty in acute inflammatory stage is fraught with a high failure rate. The ocular surface problems that arise as sequelae of chemical injury may be a potential contraindication for keratoplasty, and may necessitate the need for a keratoprosthesis.

d) Glaucoma is a frequent complication, and should be appropriately managed.

References