Chemical Burns of the Eye

Quresh B Maskati*
Department of Ophthalmology, Maskati Eye clinic, India

Abstract
Chemical injuries are increasing in the modern world. Acids and alkalis are the main chemicals implicated. In this review article, the author has outlined the pathogenesis of the damage inflicted by acids as well as alkalis. Emergency treatment has been described as well as treatment to be used in the acute, subacute and chronic phases to reduce morbidity in these cases. Modern methods of managing post-burns corneal problems such as AMT, stem cell transplant and finally Keratoprosthesis of various types have been reviewed.

INTRODUCTION
Among the ocular hazards that modern day humans face, the incidence of chemical injuries has been forever on the rise. Causes range from industrial and agricultural accidents, domestic accidents, assaults and chemical warfare. Uncommon causes are self inflicted injuries and improper use of drugs [1,2]. The eye is exposed to a wide variety of chemicals of diverse nature, either by accident or design. The injuries so caused vary considerably, from the most trivial causing transient irritation to the most severe, causing complete loss of integrity of the visual apparatus. The protective mechanisms of the eye are generally of not much help in these types of injuries. The bony orbit protects against large size objects, but offers no barrier to liquids and gases. The eyelids may suffer extensive damage themselves in cases of chemical injury. Liquids mix with tears and spread rapidly, extending the area of contact. Reflex lid closure and blepharospasm may trap solid particles, especially lime, beneath the lids, leading to prolonged contact [1,2].

PATHOGENESIS
The commonest types of chemicals are acids and alkalis. Most chemical injuries have a striking similarity in their pathogenesis, following the pattern of acid or alkali burns.

Acids
They cause their damage within the first few hours. Acids dissociate into hydrogen ions in the cornea. This usually occurs when a strong acid has a pH of less than 4. The hydrogen molecule damages the ocular surface by altering the pH, while the anion causes protein denaturation, precipitation, and coagulation. Protein coagulation creates a barrier of insoluble acid albuminates and thus generally prevents deeper penetration of acids. This is responsible for the ground glass appearance of the corneal stroma following acid injury. Therefore the damage is restricted and the lesions are sharply demarcated and non-progressive.

The only exception is hydrofluoric acid which behaves like an alkaline substance because the fluoride ion has better penetrance through the stroma than most acids, leading to more extensive anterior segment disruption.

Alkalis
Alkaline substances are lipophilic and can penetrate cell membranes. They dissociate into a hydroxyl ion and a cation in the ocular surface. The hydroxyl ion causes a saponification of cellular barriers such as the fatty acids in cell membranes, while the cation interacts with stromal collagen and glycosaminoglycans, causing denaturation of mucoids, swelling of collagen and severe disruption of stromal mucopolysaccharides. Thus they are able to progressively penetrate deeper into the stroma and even into the anterior segment. Alkali injuries are hence considered to have a poorer prognosis as compared to acid injuries [3].

CLASSIFICATION
Several classifications have been in vogue in the past.

A. Hughes’ classification: Mild, moderate and severe. This depended on the visibility of anterior chamber details and the blanching of the surrounding conjunctiva. However, it did not assess the area of surface involvement.

B. Thoft’s classification: 4 grades of severity from grade 1 to grade 4 based on area of perilimbal conjunctival necrosis and amount of corneal epithelial loss [4].

However, in those days, the concept of limbal stem cells and their role in regeneration of the conjunctival and corneal epithelium was not well understood. Modern classifications such as that proposed by Dr. Harminder Dua of Nottingham, UK (Table 1) fill in that lacuna and hence give the reviewer a better idea of the prognosis of such cases [5].

MANAGEMENT - GENERAL PRINCIPLES
First Aid
This consists of immediate and thorough removal of the chemical to the extent possible. Ideally the antidote of the chemical...
can be used – for example a much diluted acid for alkali injury and a much diluted alkali for acid injuries. Practically this is usually not feasible – the easiest way is a liberal washing of the eye with lactated Ringers solution or Normal Saline or even tap water, if nothing else is available, for 30 to 60 minutes.

**Examination**

A thorough examination of the involved structures is then carried out with a good illumination (slit lamp, if possible) and the extent of damage assessed. Any particles, especially in cases of lime – calcium hydroxide - injuries (the commonest cause of accidental injury in India) are picked up with a forceps or a cotton bud. The fornices must be searched well, with double eversion of the lids, which will reveal trapped lime particles. If the patient is a child this may require examination under general anaesthesia as soon as the general condition of the patient permits. The author has discovered lime particles deep in the fornix even months after the injury, which have been missed by others because the child was not examined under general anaesthesia with double eversion. Special attention is paid to examination of the adnexa, as their involvement will considerably worsen prognosis. Also, the lesions are graded according to Dua’s or any other classification.

**Medication**

Topical anaesthetics should be sparingly used, as they tend to retard epithelial healing. Systemic analgesics can be administered. A cycloplegic like atropine should be instilled to reduce the pain and discomfort of Cyclitis. Topical antibiotics should be used to prevent infection. Acetazolamide should be started in cases with moderate to severe burns to prevent secondary glaucoma. This is a wise precaution, as intra-ocular pressure cannot be taken in the early stages of chemical injuries.

**Surgical manoevers**

Early paracentesis has been recommended, especially in cases of alkali burns, though its advantages have not been proved. Mechanical removal of contaminated, necrotic tissue will promote faster healing. According to a study done at L.V. Prasad Eye Institute, Hyderabad, India, use of amniotic membrane grafts in the early stages significantly reduced overall morbidity of chemical burns lesions [6]. Sweeping of a glass rod around the fornices should be done daily, especially in the areas where symblepharon is threatening to develop. A conformer or moulded scleral contact lens can also be inserted to prevent symblepharon.

**Role of vitamin C**

Topical ascorbic acid has been advocated to promote corneal regeneration as it has been found that the aqueous in most cases of chemical injuries, especially alkali are markedly scorbutic (very low to unrecordable levels of vitamin C). Ascorbic acid is very necessary for fibroblasts to lay down healthy collagen [7]. This reparative process starts soon after the injury occurs. This is a cheap and freely available drug. It is sold as ampoules of 500mg in 5 cc or as 1000mg in 10cc. This is the exact concentration that is required of topical vitamin C i.e. 10%. It does not need any further dilution. All you have to do is break an ampoule of vitamin C, pour into a sterile, empty bottle, put an eyedropper on the mouth of the bottle and dispense. In case ampoules of vitamin C are not available, tablets of Vitamin C, 500mg can be dissolved in distilled water -5cc- and dispensed. The drops should be used frequently – every few minutes for the first 2 hrs, and then hourly for the first 48 hours. They can be continued 4-6 times a day for the first couple of weeks. Studies have shown this significantly reduces the risks of perforations and cornel melts.

**Autohaemotherapy**

Many researchers have tried the use of blood and blood products in the treatment of chemical injuries and some of the earliest results of this technique were reported by Dubrovina (1951). In fact it is even mentioned in the early Duke-Elder volumes on ophthalmology, now sadly no longer looked at by most postgraduates! In this technique, 0.5 to 1.5ml of the patient’s own venous blood drawn from the ante-cubital vein is injected under the conjunctiva in the perilimbal region and in the fornices. This is repeated every other day or as required. The aim of this therapy is manifold. Blood acts as a buffer, ensures more intimate contact with the diffusing chemical, than that achieved by surface irrigation. It thus causes a dilution of the chemical, besides ensuring separation of the tissues and acting as a barrier against deeper penetration. This is of great advantage, especially in severe alkali burns. Also, its fibrinolytic action tends to inhibit the formation of symblepharon and it acts as a cushion in between the superficial and deeper tissues. Platelets fill the gaps on the denuded surface. They also adhere to collagen by changing their shape from the usual oval to an amoeboid shape. Antiproteases in the blood inhibit collagenases, preventing the breakdown of newly formed collagen.

**Newer drugs**

There is increasing research on the use of citrates, progesterone, epidermal growth factors and some other medications to promote healing. It may be a few years before they attain mainstream status for use in all cases.

**RECENT ADVANCES IN THERAPY**

**Stem cells**

It is now well established that stem cells for the cornea as well as conjunctival epithelium are located in the limbal palisades of Vogt. In chemical injuries one or more clock hours of the limbus may be affected, causing destruction of these cells. These stem cells, in normal circumstances, divide into daughter cells, which undergo transformation into ‘transient amplifying cells’ then into ‘terminally differentiated cells’ as they move into the cornea, finally forming healthy corneal epithelial cells. If the stem cells are destroyed, healthy corneal epithelium will not fill the surface defects. This causes persistent epithelial defects. These invite vascularisation and ‘conjunctivalisation’ or growth of cells of conjunctival phenotype on the corneal surface. Penetrating keratoplasties in cases with stem cell deficiency are doomed to failure for cast off corneal epithelium cannot be replaced from the depleted stem cell reservoir. Diagnosis of stem cell deficiency can be made by direct observation of loss of the limbal palisades and limbal ischaemia and by indirect evidence such as persistent epithelial defects, conjunctivalisation and vascularisation of the cornea in cases of chemical burns [8].
If there is a partial stem cell deficiency, it can be treated by scraping of the conjunctivalised area of the cornea and amniotic membrane grafting. This gives a chance for the distal, unaffected stem cells to grow down and populate the areas of stem cell loss. This process may have to be repeated several times [7].

If however, there is a total or near total stem cell deficiency, the stem cells need to be transplanted to the affected eye. The donor stem cells can be taken from the other eye in unilateral burns (ideal). One to 2 clock hours can be taken from superior and inferior limbus of the donor eye and transplanted into a niche created in the affected eye. Dr. Sangwan et al. [9], have also published a simplified technique where a much smaller area of donor tissue is used, cut into 6-8 tiny pieces and stuck to the recipient cornea in the mid periphery with fibrin glue (SLET or Simple limbal epithelial transplant).

In bilateral burns, there are several options. If there is an unaffected area, a small piece of limbal tissue can be cultured in vitro and the cultured stem cells can be transplanted to one or both eyes (CLET or cultured limbal epithelial transplant). The other option is use of stem cells donated by living related donors. If these are not possible, one can use cadaveric stem cells from eye bank eyes. In all these cases however, it is mandatory to give prolonged systemic immunosuppressive therapy for a period of at least 6 months. Several authors are in favour of much longer dosages regimens, over years. Stem cell transplant is usually always done in association with amniotic membrane transplantation after 3-6 months of the chemical injury. An exception is use of cadaveric tissue used earlier in the period after chemical injury with a SLET technique. The authors, Dr. Sangwan, Basu et al., say early results are encouraging. Though the cadaveric tissue does not survive too long, it helps reduce the inflammation in the early post injury phase so that definitive treatment such as SLET can have better results later.

Cultured Autologous Oral Mucosal Transplant: Kohji Nishida and co-workers have also published very promising results in a small series harvesting a small piece of the patient's own oral mucosa and growing it in a lab. The epithelial sheet, devoid of any carrier is then transplanted onto the denuded patient's cornea after all symblephara have been excised. The sheet grows into a 4-5 layer transparent epithelial cover, resembling the human corneal epithelium and equally transparent. The advantage is that we do not have to touch the patient's good eye in unilateral burns and it can be performed in bilateral cases too as no donor corneal epithelium is required. Since it is the patient's own tissue, no immunosuppression is required. However, it does require a laboratory setting which makes it difficult to practice for the vast majority of corneal surgeons in small private practices.

Amniotic membrane transplant

As said earlier, in partial stem cell deficiency, it may be sufficient to repeatedly scrape the diseased epithelium and place a large piece of amniotic membrane tissue (AMT) over the cornea. Amniotic membrane is the innermost lining of the foetus and is obtained from healthy donors who are HIV free, delivered by caesarian section. Ideally, the membrane is preserved in liquid nitrogen after mounting on specially treated nitrocellulose paper for 6 months. The mother is then re-tested for HIV to eliminate the window period effect. If negative, the AMT can be used in the manner described above. AMT has several properties, which make it an ideal tissue – it down regulates inflammatory processes and up regulates healing processes. It also provides an ideal substrate for epithelial cells to grow over it and populate the areas of epithelial defects. AMT has 2 sides – a smooth side, which is the epithelial side and a sticky side, which is the stromal side. It has increasingly wider applications in anterior segment surgeries, such as in pterygium repair, which are outside the scope of this chapter. It is occasionally used in acute chemical burns management for its anti-inflammatory properties. The greater the inflammation, the faster the AMT gets absorbed, but not before down regulating the existing inflammation. However, it is more commonly used in ‘cold’ cases, in partial stem cell deficiency and in total stem cell loss (in combination with stem cell transplants). It handles fairly easily and can be sutured using either 8/0 polyglycolic acid sutures or 10/0nylon. It can be sutured directly on the cornea. It can also be put using fibrin glue in a sutureless technique. AMT works well for symblephara release and fornix reconstruction. Here, after release of the symblephara, the AMT is pushed deep into the fornices. Sutures passed through the AMT are brought out through the eyelid and sutured over small cut pieces of rubber tubing on the outside [10,11]. Results are amazing – patients with moving body vision can regain 6/6 vision with a combination of stem cells and AMT!

Keratoprosthesis

In cases where there is total stem cell loss and bilateral blindness with disfigured anterior segments with or without gross tear deficiency, the above 2 treatments will not help. These are the cases where Keratoprosthesis surgery (KP) has a role. This surgery is reserved for those who have good perception of light with accurate projection in the better eye and a B-scan showing attached retina. There are several types of KPs available in the world. The commonly used ones are the Dohlmann’s, the Pintucci and the MOOKP (Modified osteo-odonto-KP). The largest number of KPs implanted is the Singh-Worst KPs. The author has till date (2017) done 90 Pintucci KPs with a 20 year follow up. 65% of operated patients regained useful vision i.e. they were able to carry out activities of daily living independently. This is the largest series of such KPs in Asia. In cases where the tear secretion is not severely affected and there is no melting of cornea with mild to zero adnexal involvement, the Boston Keratoprosthesis which is done as a single stage procedure works well [12].

CONCLUSION

Chemical injuries are increasing in the modern world. Acids and alkalis are the main chemicals implicated. Emergency treatment if reported early may make all the difference between saving the eye and irreversible blindness. Early use of cheaply and freely available treatments such as topical Vitamin C and auto-haemotherapy can reduce morbidity in these cases. Modern methods of managing post-burns corneal problems such as AMT, stem cell transplant and finally Keratoprosthesis have considerably improved overall prognosis in these unfortunate patients.

REFERENCES


