Oxybuprocaine keratopathy: a preventable disease

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SUMMARY Topically applied anaesthetics may lead to a serious keratopathy. Three patients presented to us with disciform keratitis, peripheral corneal ring, and stromal infiltration following the topical use of oxybuprocaine. All three patients developed marked decrease in vision secondary to corneal scarring. In all three patients oxybuprocaine was dispensed over the counter by a pharmacist. Legislation for the restriction of over-the-counter sale of topical anaesthetics, steroids, and antibiotics is essential in the prevention of many of the self-induced ocular disorders seen in developing countries.

Topical anaesthetics are commonly used by ophthalmologists for minor procedures and ocular examinations. The adverse side effects of their longterm topical use have been previously reported.^{1,2} Fuchs¹ showed that intensive use of topical anaesthetics produced severe changes in the corneal epithelium and delayed recovery from corneal diseases.

The indiscriminate use of topical eye drops, the lack of control of prescription drugs, and the availability of over-the-counter topical anaesthetic eye drops are common factors in the predisposition to abuse of topical anaesthetics in developing countries. We present here three cases of oxybuprocaine keratopathy.

Case reports

CASE 1

A 42-year-old Saudi male presented with a history of pain, photophobia, and redness of the eyes for two days. He had sustained a welding arc flash injury three days earlier, and a pharmacist gave him a bottle of oxybuprocaine 0.4% (Novesin), which he used every half-hour without ophthalmological surveillance. On examination he was found to have a visual acuity of 20/200 in each eye. A large central epithelial defect was noted in each eye. Oxybuprocaine was discontinued and both eyes were patched.

Despite the discontinuation of the topical anaesthetic the patient persisted in having corneal epithelial

defects and developed corneal oedema and a sub-epithelial peripheral ring infiltrate. He was admitted to hospital and put on topical dexamethasone 0.05% eye drops without preservative to both eyes every three hours and topical atropine 1% eye drops once daily.

The corneal epithelial defects showed slow but progressive improvement and evidence of re-epithelialisation. The peripheral corneal ring infiltrate persisted in the left eye and partially resolved in the right eye (Fig. 1). The patient was discharged from hospital, and over the next six days the right corneal epithelial defect healed, leaving residual stromal oedema. The left cornea showed a central corneal ulcer, and corneal scrapings contained *Staphylococcus epidermidis*. Steroids were discontinued and the ulcer responded to topical antibiotics. His final best corrected vision was counting fingers at 5 feet (1.5 m) in the right eye and 20/80 in the left eye.

CASE 2

A 39-year-old Saudi male presented with a history of foreign body in the left eye. He had gone to a pharmacy where he received a bottle of oxybuprocaine 0.4% (Novesin). He instilled the eye drops in the left eye once every hour. On examination his vision was 20/25 in the right eye and 20/100 in the left. The right eye was normal. The left eye showed conjunctival injection. There was a central epithelial defect involving approximately one-third of the corneal surface with superficial stromal infiltration near the limbus at 5 o'clock (Fig. 2). The anterior chamber showed no cells or flare. Gram stain showed occasional polymorphonuclear cells but no organisms.

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Fig. 1 Left eye of a 42-year-old male with self-induced oxybuprocaine keratopathy showing epithelial defect and 360° peripheral ring infiltrate.

The patient was treated with oral analgesics and topical balanced salt solution eye drops every two hours, 2% homatropine twice daily, and 0.5% chloramphenicol four times daily. The epithelial defect healed and the stromal infiltrate resolved. Two weeks later he presented with diffuse epithelial oedema and two areas of elevated bullae. Healing was associated with superficial corneal scarring, and his final best corrected vision was 20/100.

CASE 3

A 42-year-old Saudi male was admitted with a history of excruciating photophobia, and redness in both eyes of one week's duration. After being exposed to a welding arc flash for a period of one and a half hours he used topical oxybuprocaine 0.4% (Novesin) once every hour for a period of four days.

Fig. 2 Large central epithelial defect with severe stromal infiltration in a patient with self-induced oxybuprocaine keratopathy.

On examination the patient was found to have a visual acuity of counting fingers at 3 feet (1 m) in each eye. Biomicroscopy revealed bilateral corneal oedema, with peripheral ring infiltrates and 360° pannus. The anterior chamber reaction could not be assessed.

He was given gentamicin ointment to both eyes twice daily and homatropine 2% eye drops twice daily. Culture of corneal scrapings was negative. Dexamethasone 0.05% (without preservatives) four times daily was added to the therapeutic regimen.

The corneal peripheral infiltrates subsided and the epithelial and stromal oedema resolved in two weeks. Four days after healing he developed a large central epithelial defect in the right cornea that healed over the next six days. Diffuse superficial corneal scarring and vascularisation were noted, and his final acuity was 20/100 in both eyes.

Discussion

Loss of corneal epithelium and stromal opacity resulting from acute or chronic overuse of topical anaesthetics have been previously reported.²⁻⁶

Klima and Ruckerova² reported on a patient receiving long-term topical applications of 0.4% oxybuprocaine (Novesin) who developed severe degenerative keratopathy with total shedding of the epithelium associated with oedema, haziness, and neovascularisation of the stroma, striae in Descemet's membrane, and decrease in vision. Henkes and Waubke⁷ reported on three patients with severe keratitis resulting from the abuse of topical anaesthetics (oxybuprocaine, Novesin). Two of the three patients presented with centrally located epithelial erosion, stromal infiltration, and keratitic precipitates. One patient who continued to use oxybuprocaine (Novesin) for six weeks developed contact dermatitis of the skin of the eyelid. A large corneal epithelial defect, stromal oedema, and superficial and deep vascularisation were noted. The patient also had a mild anterior uveitis.

Several mechanisms could be involved in the pathogenesis of the keratopathy. A slowly developing eczematous contact dermatitis of the eyelids and nearby skin suggests a delayed hypersensitivity reaction.⁴

The toxic effects of topical anaesthetics on the corneal cellular metabolism lead to depressed cellular respiration and glycolysis and to accumulation of lactic acid. Ultrastructural alterations in desmosomes, intracellular proteins, and cell membrane permeability have been reported following the use of topical anaesthetics. Inhibition of cell mitosis and migration were demonstrated by Smelser and Ozanics,⁸ causing delay in healing of corneal epithelium.

Three topical anaesthetics are commonly used, namely, proparacaine, tetracaine, and benoxinate or oxybuprocaine. They are considered to be of low cellular toxicity, and there is no clinically significant difference in potency among them.⁹ It is interesting to note that most of the previously reported cases of topical anaesthetic keratopathy were due to the misuse of oxybuprocaine or benoxinate, and not to proparacaine or tetracaine.^{2-4 10} All three of our cases had received oxybuprocaine. Oxybuprocaine is a para-aminobenzoic acid ester. Used topically in the eye it has a duration of anaesthetic action similar to that of tetracaine, 28 minutes.⁹ The majority of topical anaesthetics have preservatives, and Novesin has chlorhexidin 0.01% as a preservative.

When the anaesthetic diffuses deep into the stroma, it may inhibit the cellular metabolism of the keratocytes and posterior layers of the cornea. Inhibition of the endothelial cell metabolism may lead to corneal oedema.⁸ Weekers,⁶ in a study of the influence of cocaine, lidocaine, and benoxinate on the corneal epithelium of rabbits, concluded that the topical anaesthetic caused alteration of the Na⁺/K⁺ endothelium pump, resulting in increased osmotic pressure in the cornea and subsequent increased hydration of the stroma. The anaesthetic may penetrate to the anterior chamber, exerting its toxic effects on intraocular structures.^{6 11 12}

Loss of corneal sensation would decrease the blinking reflex and predispose the corneal surface to further desiccation. Prolonged use of anaesthetic may damage the corneal nerves and lead to neurotrophic ulcers.^{6 11}

We strongly believe that visual loss from the abuse of topical anaesthetics can be prevented by restricting over-the-counter dispensing of topical medications in certain developing countries as happens in Saudi Arabia.

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