Case Report

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Toxic keratopathy related to antiseptics in nonocular surgery

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Abstract:

Antiseptics, especially those containing ethanol, are toxic to the ocular surface. Here, we report a 5-year-old girl with antiseptic-related eye injury following an uneventful bilateral tonsillectomy under general anesthesia. Before surgery, her eyes were protected and disinfection of perioral skin with ethanol-containing chlorhexidine followed. Whitening of the lower half of her right ocular surface was found after the surgery, and this indicated severe chemical burn. Prompt irrigation with normal saline, instillation of topical medication, and application of amniotic membrane containing device were performed, which led to a satisfactory result. Toxic eye injury could happen in head and neck surgeries under general anesthesia. Causes of ocular injury include improper eye protection, head positions leading to accumulation of excessive antiseptics, and improper usage of ethanol-containing antiseptics for skin preparation. The use of ethanol-free antiseptic solutions in the peri-ocular region and proper protection of eyes may reduce the risk of severe ocular surface injury in nonocular surgeries.

Keywords:

Antiseptics, ocular injury, chemical burn, perioperative ocular complication

Introduction

Eye injuries ranging from corneal abrasion to serious corneal edema and limbal ischemia may occur during nonocular surgeries,[1] although several ocular protective strategies during general anesthesia have been proposed.[2-4] Improper eye protection, head positions leading to accumulation of excessive antiseptics, and use of ethanol-containing antiseptics for skin preparation may increase the risks of perioperative ocular injury.[5-8]

Literature regarding toxic keratopathy related to antiseptics was scanty.[1-8] Most of the studies focused on the incidence and risk factors of eye injuries during general anesthesia. The management of toxic keratopathy has not been well described. Yu *et al*. reported that corneal abrasion and conjunctivitis were the most common perioperative ocular injuries and most were treated with topical balanced salt solution, artificial tear, steroid, and antibiotic solution and/or ointment.[1] One patient was reported to have prolonged blurred vision, but no treatment was documented. One patient was reported to have permanent blindness despite treatments with acetazolamide, carteolol eye drops, and mannitol. Anderson *et al*. reported treatment consisted of applying topical antibiotic ointments and cycloplegic solutions to prevent posterior synechiae and relieve ciliary muscle spasm.[2] Liu *et al*. reported three cases of severe toxic keratopathy following the use of alcohol-containing antiseptics in nonocular surgery.[5] One patient received fluorometholone and tetracycline, 0.1%, ointment. Another patient had topical betamethasone, 0.1% and Descemet stripping automated endothelial keratoplasty 6 months later. Topical betamethasone, 0.1%, hypromellose, 0.32%, and sodium chloride, 5%, hypertonic solution were administered in the third case who received penetrating keratoplasty and cataract surgery 2 years later.

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Here, we report a 5-year-old girl having antiseptic-related eye injury following an uneventful bilateral tonsillectomy under general anesthesia despite the fact that her eyes were protected with tetracycline ointment and transparent film dressing. Managements including prompt irrigation with normal saline, instillation of topical medication, subconjunctival injection of autologous blood, and application of a temporary amniotic membrane patch (Prokera, Bio-Tissue, Inc., Doral, FL, USA) were given timely. To the best of our knowledge, this is the first report that Prokera could be used in antiseptic-related ocular injury and the result was satisfactory.

Case Report

A 5-year-old girl with chronic tonsillitis was found to have whitening in the lower half of the ocular surface on her right eye following an uneventful bilateral tonsillectomy under general anesthesia. She also complained of pain and irritation. During that operation, the patient was kept in a position with her neck extended. Both of her eyes were protected with tetracycline ointment, 0.1%, and then covered with transparent film dressing (Tegaderm, 3M Center, St. Paul, MN, USA). The perioral area was disinfected with 2% chlorhexidine gluconate in 70% ethanol solution. The durations of anesthesia and operation were 113 and 68 min, respectively.

On initial examination, ocular whitening with corneal damage extending to the adjacent bulbar conjunctiva and lower 120° limbal ischemia was found [Figure 1]. The demarcation line between the healthy and damaged ocular surfaces was straight and apparently indicated that ocular protection was improper. The injured area happened to be the exposed area of the patient's right eye during general anesthesia. Some horizontal lines were also noted in the injured area, indicating that there were different degrees of injury and that there might be abrasion during the removal of Tegaderm. Visual acuity could not be obtained because the young patient could not cooperate well. The eye was then treated with aggressive normal saline irrigation, topical levofloxacin, 0.5%, ophthalmic solution and betamethasone, 0.1%, subconjunctival injection of autologous blood, and application of sutureless amniotic membrane device to improve wound healing. The amniotic membrane on Prokera dissolved at 2 weeks after the injury, and the ocular surface achieved complete re-epithelialization. Corneal haziness and edema improved significantly and limbal ischemia recovered [Figure 2]. *In vivo* confocal microscopy showed an endothelial cell density of 2706 cells/mm^2 without increased polymorphism. The best-corrected visual acuity (BCVA) returned to 20/22 at 1 month after the ocular injury.

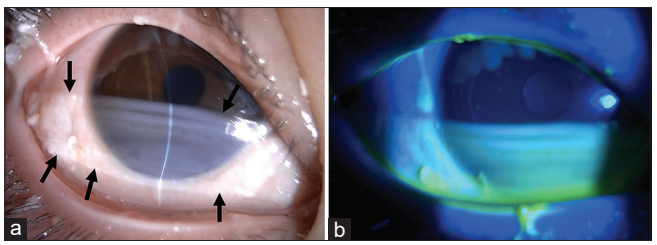

Figure 1: External eye photography of a 5-year-old girl immediately after surgery. (a) Well-demarcated corneal edema and opacity obscuring iris detail with a corresponding corneal epithelial defect, inferior limbal blanching, and necrosis of adjacent conjunctiva (arrows) were found. (b) Fluorescein staining showed a corresponding epithelial defect on the lower ocular surface

Discussion

Literature review shows only a few case reports on toxic keratopathy related to antiseptics.[1-8] The management of toxic keratopathy has not been well described. The heterogeneity of disease presentation, variations in treatment, undefined criteria for treatment success and failure, and nonuniform outcome measures are factors complicating the establishment of standard treatment for toxic keratopathy related to antiseptics. In this case, we managed toxic keratopathy related to antiseptics as acute ocular chemical burns and we did our utmost to help the young patient recover her vision. Extensive irrigation was promptly initiated to wash out toxic chemicals. Topical antibiotics, cycloplegics, corticosteroid, and autoserum were administered to prevent infection, relieve pain, reduce inflammation, and promote wound healing.

Growth factors, such as the epidermal growth factor, fibroblast growth factor, angiogenic growth factor, neurotrophic growth factor, insulin-like growth factor, and mesodermal growth factor isolated from the cornea, are known to contribute to the maintenance of a healthy epithelial surface and facilitate its regeneration.[9,10] Autologous serum, which contains a high concentration of growth factors mentioned above, has been used in the treatment of ocular surface pathologies, including severe dry eye disease, persistent epithelial defects, superior limbic keratoconjunctivitis, recurrent corneal erosions, and neurotrophic keratitis.[11] It has also been reported to promote faster healing of epithelial defect, better corneal

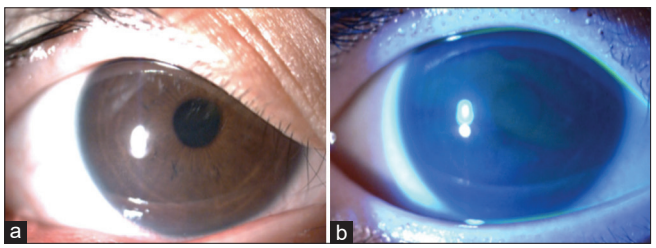

Figure 2: External eye photography at 2 weeks after injury. (a) The cornea cleared up at 2 weeks after treatment. (b) Complete re-epithelialization was achieved

clarity at 3 months, and a trend toward better BCVA for acute corneal chemical injury.[12] Subconjunctival injection of blood, which contains growth factors that promote healing, has been reported to facilitate epithelial regeneration and healing in ocular chemical burns.[13,14] Subconjunctival injection of autologous blood with or without topical autologous serum drops was preferred in this case since it was difficult to instill many eye drops frequently in an uncooperative child. Because the patient underwent aggressive irrigation under general anesthesia, subconjunctival injection of autologous blood was performed at the end of surgery.

Amniotic membrane transplantation (AMT) offers better acute pain reduction and earlier epithelialization.[15-18] This action of the amniotic membrane is by virtue of the epithelial basement membrane layer providing a mechanical support and acting as an internal splint. In addition, the amniotic membrane has beneficial biological properties such as secretion of cytokines, growth factors, and protease inhibitors which reduce surface inflammation and prevent fibrosis and symblepharon formation. AMT stabilizes the ocular surface and provides a conducive surface for further procedures such as autologous and allogeneic limbal transplantation, lamellar or penetrating keratoplasty.[17] Temporary sutureless amniotic membrane patches, such as Prokera, have been reported as an early intervention for acute alkali burns in the eyes because they ensure earlier biologic actions, which may preserve the remaining limbal stem cells for rapid extension, relieve symptoms rapidly, reduce inflammation, and promote epithelialization.[19] Prokera instead of AMT was chosen for this young patient to avoid another surgery under general anesthesia. In addition, during AMT, sutures might be required to fix the amniotic membrane, and another surgery might be required for suture removal.

Antiseptics, especially those containing ethanol, are toxic to the ocular surface.[5] Ethanol can markedly reduce corneal epithelial cell viability and increase pro-inflammatory cytokine and chemokine expression in both corneal epithelial and stromal cells.[6] Even the short-term exposure of the corneal surface to ethanol can disrupt corneal epithelium integrity and cause inflammation.[7] Corneal exposure to chlorhexidine may also cause epithelial defects and corneal edema.[20,21] Conscious patients are usually alert to trivial toxic corneal damage because corneas have the highest density of nerve innervation in the whole body.[22] The inhibition of corneal sensation under general anesthesia may lead to severe ocular damage if ocular surfaces are exposed to toxic agents. In addition, Bell's phenomenon, which is the upward and outward movement of the eye when an attempt is made to close the eyes,[23] is absent under general anesthesia. The inability of the upward movement of the eye may lead to exposure keratopathy or chemical injury of the cornea if the eyes are not properly protected during the surgery. The head position of a patient also plays an important role in the antiseptic-related eye injury during surgery. When a patient's neck is extended and the eyes are in a relatively low position, the risk of ocular toxicity caused by an improper preoperative aseptic procedure is increased. In the present case, antiseptic-related eye injury occurred despite eye protection with tetracycline ointment and Tegaderm. We speculate that the Tegaderm might have not sealed the eyes tightly because of excessive tetracycline ointment, and some antiseptic solution might have accumulated around the periocular area during skin disinfection and then seeped into the eye. In addition, improper usage of antiseptics with ethanol-based chlorhexidine increased the damage to the ocular surface.

Several methods are suggested for the prevention of toxic keratopathy related to antiseptics in nonocular surgery. First, the periocular skin should be dry and clean without oil or any other moisture-enhancing product before applying the bio-occlusive products, such as Tegaderm. The controversy remains on whether to put antimicrobial eye ointments into a patient's eyes. However, if eye ointments are used, excessive eye ointments should be avoided because it can compromise the adherence of Tegaderm. Last but not least, antiseptic agents free of alcohol or chlorhexidine are preferable for disinfection around the periocular region. At the end of the surgery, Tegaderm should be removed gently and the ocular surface should be checked grossly. If toxic keratopathy is suspected, ophthalmologists should be consulted and management should be initiated promptly. Here, we report a case of toxic keratopathy related to antiseptics that was treated successfully through aggressive irrigation, topical medications, subconjunctival injection of autologous blood, and temporary sutureless amniotic membrane patches through Prokera. Since cryopreserved human amniotic membrane and subconjunctival injection of autologous blood have been widely accepted to be the standard and safe treatment for poor corneal epithelialization problem in ocular surface diseases, we thus treated this patient with Prokera and subconjunctival injection of autologous blood. Prokera and subconjunctival injection of blood were used, for the first time, as an intervention for toxic keratopathy related to antiseptics, and visual outcomes and the ocular surface condition seemed promising in this case. Although it is difficult to conclude that these two treatments played the main role in promoting the healing process in this patient, the satisfactory results still implied that Prokera and autologous blood injection could be chosen as the treatment strategy under such conditions. Prokera may offer additional benefits for uncooperative children

because the assessment and management of eye injury in young patients are challenging.

Conclusion

Toxic eye injury could happen in head and neck surgeries under general anesthesia. Proper eye protection, selecting aseptic agents with less toxicity, and prompt response when eye damage is found are golden standards to prevent such injury.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal parents have given their consent for images and other clinical information to be reported in the journal. The parents understand that names and initials will not be published and due efforts will be made to conceal patient identity, but anonymity cannot be guaranteed.

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Conflicts of interest

The authors declare that there are no conflicts of interests of this paper.

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