Section: Ophthalmology

Review Article

EXPOSURE KERATOPATHY – AN UPDATED CLINICAL REVIEW OF LITERATURE

Harshita Dabral[1], Minakshi Dalal[2], Anindya Anuradha[3], Rushali Khanna[4], Arya Karan[5], Darshankumar Picha[6]

[1]Department of Ophthalmology, Government Doon Medical College, Dehradun, Uttarakhand, India
[2]Department of Ophthalmology, Indira Gandhi Hospital, Dwarka, New Delhi, India
[3]Department of Ophthalmology, Bhagwan Mahavir Medica Super specialty Hospital, Ranchi, Jharkhand, India
[4]Department of Ophthalmology, Rockhampton Hospital, Queensland, Australia
[5]Department of Ophthalmology, Rajendra Institute of Medical Sciences, Ranchi, Jharkhand, India
[6]Government Medical College and District Hospital, Akola, Maharashtra, India

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Corresponding Author:
Dr. Minakshi Dalal,
Email: drmin27@gmail.com

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Abstract

Background: Exposure Keratitis (EK), also known as exposure keratopathy is a disease in the outermost layer of the eye, leading to inflammation of the cornea. The disease is a commonly observed condition in any patient routinely exposed to the environment, due to pathological conditions. The ocular surface exposure is a substantial ground for various infections. It may eventually lead to opacification of the cornea and further succumbs to loss of vision, either partially or sometimes, complete. Exposure keratitis can also lead to ulceration, microbial keratitis, and permanent vision loss from scarring. The given review article conceptualizes the underlying factors that lead to EK, the associated risks, diagnosis, management, and prevention of the disease. Also, the genetic mechanisms that enunciate the progression of EK have been summarized as a whole.

INTRODUCTION

The health of the cornea, which is exposed and vulnerable to the environment depends on its functional abilities that is to blink, produce tears, and maintain moisture in the eyes, thus preventing dryness or infections. Sight is one of the most vital human senses for cognition. Lack of proper eye care, especially in anaesthetized patients can lead to serious ocular complications, resulting in vision loss sometimes. The cornea serves as a major refracting surface in our eye and focuses the light on the retina for the integrity of vision. Though the cornea is well protected by the eyelids, one cannot deny its proximity to the external environment and thereby, the stresses that are encountered mainly result in ulcers and keratitis. The microbiological causes of keratitis such as bacterial, viral, and fungal have been studied immensely, and required therapies and medications have been formulated for the benefit of the patients globally. However, not much has been said or devised about exposure keratitis, the silent impairment that eventually may cause blindness to the patient. Exposure keratitis is a progressive keratopathy where the cornea is covered insufficiently by the lids, and it is further complemented by the loss of the protective mechanism of blinking. This has been observed by the patients usually admitted to Intensive Care Units who have decreased or no consciousness. In such patients, the major aim of the treatment has been to treat the life-threatening conditions; while not much attention is paid to the superficial problems. Therefore, such patients are more prone to eye disorders and damage as compared to others. The EK rate in critically ill patients has been reported as low as 10% to as high as 55-60 %. In the worst-case scenario, EK precipitates microbial keratitis leading to acute perforation, endophthalmitis, and permanent visual impairment.

Although ICU in-patient care requires support for all body systems, most nursing care focuses on life-threatening problems; this can reduce the healthcare team's focus on other organs, including eyes so that even a simple procedure such as eye care (EC) by nurses is easily neglected.[1]

Most ICU patients, on the other hand, need nursing care to maintain the natural and pathophysiological health of their eyes and should not experience complications associated with a lack of standard care.[2]

RISK FACTORS

As suggested by the article,[3] the cornea may be at risk in the following cases:

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- Inadequate eyelid closure, e.g. due to facial nerve palsy or cicatricial damage to eyelids due to chemicals
- Any neuropathic drug/anesthetic
- Proptosis
- Poor or infrequent blinking

Also, in a variety of cases, the causes have been different. These may be:

- Severe degree of ectropion
- Symblepharon
- Lagophthalmos during sleep(occasionally)

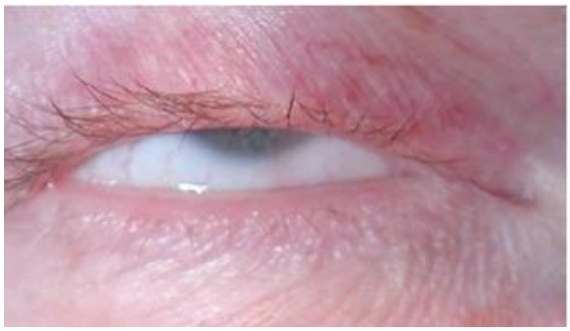
Another risk factor that may be associated with EK is mainly due to the use of sedatives and muscle relaxants that affect the eye muscles, lead to blink reflex disorder, and lead to partial eye closure, which may cause evaporation of tears. Other drugs (antihistamines, atropine, etc.) and prolonged eye closure cause hypoxia, hypercapnia, slow repetition of blinks, dryness, and damage to the eye, all due to reduced tear production.[4] It should be noted that in these patients, the use of ventilation with positive pressure and firm fixation of the endotracheal tube leads to increased venous pressure, followed by increased intraocular pressure and conjunctival edema, and increases the chances of eye disease. On the other hand, patients admitted to the ICU often suffer from fluid imbalance, which increases capillary permeability leading to edema and eye damage.[4] Studies have shown that 60% of patients who have endotracheal tubes in which eyelids do not close completely are at risk for ocular complications.[5]

Identifying the risk of corneal injuries

Assessment of eye closure must be done in a patient during his/her stay in the hospital time to prevent any keratopathy or its worsening. To assess the risks of corneal injuries, the degree of lagophthalmos must be judged to identify the severity of the disease.

Grade 0: Eyelids closed completely

Grade 1: Any conjunctival exposure (any white of the eye being visible) but no corneal exposure



Grade 2: Any corneal exposure, even a small one

Actions Required:

Grade 0 exposure requires no action.

Grade 1 exposure requires lubrication. Taping is also preferred in some cases.

Grade 2 exposure needs lubrication and taping of the lids with Micropore tape along the lash margin.

For Grade 1 and 2, the following steps need to be performed:

Step 1: Warm water is used for bathing of eye to remove any dried ointment, if present.

Step 2: The eye should be examined with a bright light to look for redness, dullness, opacity, or chemosis. If any such finding is present, the patient should immediately be referred to an ophthalmologist.

Step 3: New ointment is then applied to the surface of the eye: The lower lid is pulled down with a finger. The ointment is inserted over the top of the lower eyelid into the gap between the lid and conjunctiva every 4 hours.

If taping is required for the given situation, the eyes are closed after putting the ointment. The outer eyelid must be free of any quantity of lubricant for the tape to stick properly. Micropore tape is then applied horizontally across the lids to seal them shut.

In prone and unconscious patients, the eyelids and face can become edematous, and conjunctival swelling (chemosis) is common. Direct eye compression can occur and can be avoided using a 3-pin head holder as is used for prone spinal surgery. The eyes should always be re-lubricated every 4 hours, and taped shut. Where there is severe

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edema and the swollen conjunctiva prolapses through the closed eyelids, the medical staff should be contacted as the eyelids may need to be temporally closed with a suture.[7]

Corneal Abrasion versus EK

Being exposed to the environment in a case of lagophthalmos, the cornea is always at substantial risk of facing injuries, especially in ICU patients. This appears in the form of corneal abrasion. It causes the eye to become red and is best seen using fluorescein eye drops and a blue light. Any epithelial defect appears bright yellow here.

EK represents a dryness of cornea due to incomplete eyelid closure allowing excess tear evaporation and failure of tears to spread adequately across the eye surface. It also manifests as red eye. This can be investigated by using fluorescein drops which reveal smaller or larger epithelial defects (which look very similar to corneal abrasion). It affects 20-42% of ICU patients, and 60% of those sedated for > 48 hours develop corneal epithelial defects (42% within the first week) as a result. Prolonged epithelial defects can cause scarring or even, in severe cases, perforation of the cornea.[8] Some articles also stated that EK that develops on air exposure may be a consequence of defective epithelial renewal.[9,10] Thus, internal complications may intertwine with exposure keratopathy and may further result in chemosis, corneal erosion, melting, infectious keratitis, and corneal perforation.

Reasons why ICU patients are at greater risk of developing EK

The most obvious factor that contributes to the above fact is that the ICU is a pathogen-rich environment. Thus, the risk of infection to the ocular surface is greater.

- An alteration in the level of consciousness, impacting the blink reflex and incomplete eye closure (lagophthalmos)
- Metabolic derangements
- Immunosuppression
- Mechanical ventilation
- Medications, such as sedatives and muscle relaxants
- Paralysis
- Respiratory pathogens from open suction technique
- Systemic disease
- Prone positioning

Eye Care (EC) In Clinical Practice

A lot of studies illustrate the fact that eye care protocols are not followed in the majority of hospitals, if followed, there are completely different procedures practiced at different hospitals, with some major steps missing.

One of the common EC methods in the ICU is rinsing the eyes with normal saline solution in patients with a decreased level of consciousness, but various EC methods have been reported that can be used with eye ointments such as tetracycline, gentamicin, methylcellulose, liposuction ointment, simple eye closure, use of polyethylene coating, use of swimming goggles, paraffin gas, and artificial tear drops.[5]

In particular muscle relaxants reduce the tonic contraction of the orbicularis muscle around the eye which normally keeps the lids closed, and sedation reduces blink rate and impairs (and can eliminate) the blink reflex. Whatever the cause, those unable to close the eye for themselves, or in whom blinking rates are substantially reduced, are at increased risk of damage to the front of the eye, and this risk is higher in those mechanically ventilated, due to greater length of stay, use of sedative/paralyzing drugs and the effects of positive pressure ventilation.

The provision of regular and proper eye care has proved to be a keystone in the prevention or even cure of EK in critically ill populations. This is true in both the adult and pediatric populations. When clinicians have received focused clinical education on eye care for the critically ill and are increasingly compliant with eye care guidelines, this has led to reduced exposure to keratopathy for patients.[11-15]

Specific eye care practice has included the following:

- Regimens of cleaning the eyes with sterile water or normal saline every two to four hours, twice daily or daily
- Instillation of a lubricating liquid, such as methylcellulose eye drops
- Applying eye ointment for high-risk patients, or where evidence of eye injury may be apparent, such as when conjunctival edema is present
- Polyethylene film with artificial tear drops has been shown to be more effective than polyethylene film alone. For conditions of conjunctival or corneal exposure, methods such as passive eye closure, eye taping, padding with gel membranes, and creation of moisture-closed chambers using polyethylene film or goggles have been described.[16-18]

Etiopathogenesis of EK

As etiology and pathogenesis of the disease are grossly related. Air exposure to the corneal epithelial cells may lead to endoplasmic reticulum stress. This may further advance to activation of autophagy via the P13K/AKT/mTOR signaling pathway. Here, the studies of macro autophagy revealed that it is mediated through both (mTOR)-dependent autophagy and non-mTOR-dependent autophagy pathways. The protein kinase B controls the activation of mTOR which further regulates autophagy by modification of phosphorylation of Unc-51-like autophagy activating kinase 1 (ULK1). The air exposure down-regulates the levels of p-mTOR in conjunction with the levels of p-AKT and p-PI3K as illustrated in the article.[19]

The etiology of exposure keratopathy can be placed under categories such as:

- Proptosis and various associated factors, mainly anatomical malformations, physiological

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malfunction, glandular or endocrine under secretion, tumors in the bony orbit, or any optic neuropathy.
    - Nocturnal lagophthalmos
    - Ectropion
    - Traumatic defect in the eyelid margin
    - Floppy eyelid syndrome
- Palpebral pathology-related causes: due to trauma during surgery or excessive scar effect
- Cranial dysinnervation syndromes, such as Mobieus syndrome and congenital facial palsy.
- Eyelid coloboma
- 7th cranial nerve palsy:
    - Stroke
    - Tumor (e.g.: Acoustic neuroma, meningioma, choristoma, parotid, nasopharyngeal)
    - Demyelination
    - Sarcoidosis
    - Otitis
    - Ramsay Hunt Syndrome
    - Guillan Barre Syndrome
    - Lyme disease

It is also important to investigate potential thyroid eye disease, especially in female patients. A lot of systemic manifestations, most importantly some neurological conditions, have been linked to Exposure keratopathy.

The facial nerve innervates facial muscles, thus affecting the facial features and may have a profound impact on the functioning of the eyelid. This may manifest as paralytic lagophthalmos. Exposure keratopathy is a subsequent consequence. Also, the trigeminal nerve that sends sensory inputs to the cornea may succumb to lesions resulting in neurotrophic keratitis. This inhibits blink reflex, and the patient is at a potential risk of exposure keratitis.

Signs and Symptoms

Symptoms of exposure keratopathy include blurred vision, irritation, redness, dry eyes, foreign body sensation, photophobia, and tearing. In severe cases, the condition may lead to corneal ulcer, perforation, and microbial keratitis.[20,21]

Common signs include incomplete/decreased frequency of blinking, lagophthalmos, reduced tear meniscus, reduced tear film breakup time, corneal filament formation, punctate epithelial erosion (usually inferior if underlying lagophthalmos and central if due to proptosis), and epithelial defects.[22,23] There may be impairment of corneal sensation, loss of corneal lustre, irregularity of corneal surface, ectropion, lid abnormalities and Neurotrophic Keratopathy in severe cases.

Differential Diagnosis

- **Dry Eye Syndrome:** Dry eye syndrome is a disease where the cornea becomes dry as a result of endocrinal dysfunction, infection, or irritability in the eyes. However, the causative factor of EK is exposure itself. The cornea on being exposed to the surroundings in semi-conscious or unconscious patients leads to corneal dysfunction, manifested as inflammation, and further involves various ocular complications.
- **Sjogren Syndrome:** Sjögren syndrome is a chronic inflammatory disorder characterized by exocrine gland dysfunction and a variable systemic course. Lymphocytic infiltration of the lacrimal and salivary glands results in the classic sicca complex characterized by dry eyes (keratitis sicca or keratoconjunctivitis sicca [KCS]) and dry mouth (xerostomia). Severe dry eyes can cause corneal scarring, ulceration, infection, and even perforation; thus, although the prognosis is good for most patients with Sjögren syndrome and ophthalmologic features, individuals with complications have a guarded prognosis.
- **Neurotrophic Keratopathy:** Neurotrophic keratitis (NK) is a degenerative disease characterized by corneal sensitivity reduction, spontaneous epithelium breakdown, and impairment of corneal healing. Management of NK should be based on clinical severity, and aimed at promoting corneal healing and preventing progression of the disease to stromal melting and perforation. Concomitant ocular diseases, such as exposure keratitis, dry eye, and limbal stem cell deficiency, negatively influence the outcome of NK and should be treated.
- **Medicamentosa:** Even for the most experienced clinician, ocular surface medicamentosa (OSM) can be a challenging diagnosis. Patients often see multiple providers and try various eyedrops to alleviate their symptoms with no success. The most common causes for OSM are preservatives in eye medications, contact lens solutions, and artificial tears with preservatives. Slit lamp examination will reveal conjunctival hyperemia and chemosis, bulbar conjunctival papillae and/or follicles, mild eyelid edema, and watery discharge. There can be punctate keratitis or epithelial erosions in more severe cases.
- **Blepharitis:** Blepharitis is a common disease of the eyelids characterized by redness, thickening, and flakey or scaly crusting along the eyelids and eyelashes. It is sometimes known as "eye dandruff." Over time, a sticky plaque, or biofilm, forms along the lids, causing lash loss, clogged glands, infections, and other complications.

Management

The silver lining of the treatment involves treating the underlying conditions that led to exposure keratitis.

- **Medical Therapy:** This includes the usage of Preservative-free artificial tears hourly with lubricating ointment. A literature review indicated that the use of ocular lubrication was significantly more effective than passive eyelid closure, basic eye toilet, or Geliperm but equally effective to the use of lid taping in the critical care setting. The use of moisture chambers or

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polyethylene films provided the greatest amount of protection.[24,25]

- **Surgery:** Surgical treatments are often useful to verify the pathophysiology of the disease. However, it is reserved for the refractory cases of EK. In the case of lagophthalmos, temporary or permanent tarsorrhaphy has been used as well as gold weight implantation (also for facial nerve palsy). If the exposure is secondary to lid malposition, canthoplasty, lid tightening procedures, and lid suspension may be considered. Eyelid reconstruction (for ectropion) and orbital decompression (for proptosis) can also be considered when applicable.[26,27]

Tarsorrhaphy is the joining of part or all of the upper and lower eyelids to partially or completely close the eye. Temporary tarsorrhaphies are used to help the cornea heal or to protect the cornea during a short period of exposure or disease.[28] A temporary central tarsorrhaphy with a drawstring that allows it to be repeatedly opened and closed for examining the eye.

Permanent tarsorraphies are used to permanently protect the cornea from a long-term risk of damage. A permanent tarsorrhaphy usually only closes the lateral (outer) eyelids, so that the patient can still see through the central opening and the eye can still be examined.[29]

Indications for tarsorrhaphy:

- Inadequate eyelid closure
- Marked protrusion of the eye causing corneal exposure
- Poor or infrequent blinking (as in ICU patients or those with brain injuries)

Some other techniques that may be used are:

Botulinum toxin tarsorrhaphy (the upper lid elevator muscles are paralyzed with the toxin)

Cyanoacrylate glue tarsorrhaphy (used to join the lids and place a weight in the upper eyelid)

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