

Update

An update on recurrent corneal erosions

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Corneal erosions are a common cause of disabling ocular symptoms and can resolve with simple medical therapy. Corneal erosions can be problematic if the episode of erosion does not resolve with simple therapy and/or further episodes occur in recurrent corneal erosion syndrome^{1,2}.

Pathophysiology of corneal erosions

Corneal erosions occur when corneal epithelial cells detach². The corneal epithelium is a multi-layered squamous epithelium that is richly innervated. The epithelial cells are attached to each other via desmosomes and to their underlying basement membrane via hemi-desmosomes. The reasons the cells detach include abnormal hemi-desmosomes³, matrix metalloproteinase degradation³, tear film dysfunction leading to a lack of lubrication⁵ and lid malfunction such as exposure.

Corneal erosions may occur spontaneously, with a superficial corneal injury^{6,7}, associated with corneal dystrophies such as epithelial basement membrane (map-dot-fingerprint) dystrophy and lattice dystrophy or in association with systemic disease such as epidermolysis bullosa and cystinosis. Recently, corneal erosions have been reported in association with cancer treatments. Gefitinib, is a selective epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor that has been used in the treatment of locally advanced or metastatic non-small cell lung carcinoma and is generally well tolerated systemically. Ocular adverse events of Gefitinib therapy have been reported including corneal ulceration and perforation; these may be associated with expression of epidermal growth factor receptor on limbal and conjunctival epithelium⁸.

Corneal dystrophies associated with recurrent erosion

Epithelial Basement Membrane Dystrophy (Cogan's, Map-Dot-Fingerprint)

Epithelial basement membrane dystrophy is not uncommon with increasing age; with most patients

asymptomatic. For those who develop symptoms are from recurrent erosions which can begin in the 30's. This dystrophy is usually not inherited, but autosomal dominant (AD) (TGFBI) inheritance has been reported.

Bowman's layer corneal dystrophies

The Bowman's layer corneal dystrophies are bilateral, symmetric and may present with irritation and/or photophobia in childhood due to recurrent erosions. As the dystrophies progress visual loss occurs due to scarring and irregular astigmatism.

Lattice dystrophy onsets in the first or second 1st or 2nd decade of life and reduced vision may be severe by the 50's. Corneal erosions typically occur frequently and vision progressively reduces from the lattice stromal deposits and scarring. Corneal sensation is decreased on examination.

Avellino corneal dystrophy is an uncommon dystrophy associated with in which recurrent erosions can occur but are infrequent. As the dystrophy progresses vision may be reduced. The clinical and pathological findings are a combination of granular and lattice dystrophies.

Epidemiology of recurrent corneal erosion

One in 150 corneal abrasions have been reported to become recurrent⁹. In patients with recurrent corneal erosion, half have been reported to have a history of trauma and one third have a corneal dystrophy¹⁰.

In a retrospective cohort study conducted over a 5-year period at Moorfields Eye Hospital, London, 487,690 emergency department attendances were reviewed. The study found that 3623 patients had a new diagnosis of recurrent corneal erosion out of 330,684, giving a crude annual incidence of recurrent corneal erosion syndrome estimated at 25.4 per 100,000 giving a crude prevalence rate of 0.96%¹¹. The annual incidence was stable over the 5-year period.

Overall though it is highly likely that recurrent corneal erosion syndrome is underdiagnosed and under-reported as many cases heal quickly.

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Diagnosis of recurrent corneal erosion

History of the presenting and past symptoms is an important part of the diagnosis of recurrent corneal erosion as on examination there maybe few signs if the erosion heals quickly. Typical symptoms include; eye pain, blurred vision watering and light sensitivity on waking¹². The pain can be acute and wake the patient from sleep.

The signs sought on examination include visible erosions or an epithelial defect, Shaninians sign (corneal valance) and localised tear break up¹³. Signs of an associated disease may also be present such as those of a corneal dystrophy with the changes of map-dot-fingerprint dystrophy most common.

Prevention of recurrent corneal erosion

Prevention encompasses preventing recurrent cornea erosion occurring following a traumatic corneal abrasion and prevent further episodes once recurrent corneal erosion has been diagnosed.

Therapies to prevent recurrent corneal erosion include the use of lubricating ointment at night, hypertonic saline eyedrops or ointment, oral tetracyclines along with the use of topical lubricants¹.

Treatment of recurrent corneal erosion

A range of treatments are available to treat the episodes of corneal erosion once an erosion has occurred and are shown in Table 1.

Table 1. Treatment options for recurrent corneal erosion¹

Standard therapy (topical ointment, eyepad, cycloplegics, topical antibiotics)
Tetracyclines and topical steroids
Bandage contact lens
Phototherapeutic keratectomy (PTK)
Stromal puncture
Superficial keratectomy – Diamond Burr
Autologous serum eye drops

A systematic review assessing the effectiveness and safety of prophylactic and treatment regimens for recurrent corneal erosion included 8 randomised and 2 quasi-randomised controlled trials, encompassing 505 participants. The review reported that oral

tetracyclines for at least 6 weeks and ‘week’ topical steroids were beneficial for patients with meibomian gland dysfunction^{14,15}. The main risk of this treatment regime was gastrointestinal upset and steroid induced glaucoma^{1,16}.

A bandage contact lens maybe used in acute episodes as it can act as a protective shield and promote cell survival. The contact lens is generally worn continuous which carries with it the risk of microbial keratitis. A bandage contact lens was found to be inferior to lubricant drops and ointment and have a high complication rate, though these findings were not with modern high water-content hydrogel lenses¹⁷. In a 2-centre study conducted in the UK with 29 participants both groups experienced resolution of symptoms at four months (RR 0.97, 95% CI 0.62 to 1.53. Overall, there was a low-certainty evidence on resolution of symptoms after treatment and a very low-certainty evidence on recurrence after partial/total resolution at 7 months’ (RR 1.07, 95% CI 0.07 to 15.54). No evidence of an important difference in pain score and there were no adverse effects reported¹⁸.

In a prospective, randomized, masked, 3-arm clinical study of 66 patients presenting with superficial corneal foreign bodies¹⁹. Traumatic corneal abrasions were managed via pressure patching, bandage contact lens or ointment alone with equal efficacy in reducing the abrasion area or reducing pain¹⁹.

Phototherapeutic keratectomy

Phototherapeutic keratectomy is an excimer laser ablation that can be used in the management of recurrent corneal erosion. This procedure has the risk of inducing a change in the patient’s refraction with a hyperopic shift in refraction more likely than a myopic shift and the risk of infection.

In a systematic review, with searches on Cochrane, Embase, PubMed, Scopus, and the Web of Science the recurrence rate for corneal erosions after PTK was found to be 18% (95% CI, 13%-24%) (129/700 eyes). The recurrence rate in cases of recurrent corneal erosion after trauma was 17% (95% CI, 9%-24%) and after corneal dystrophy 22% (95% CI, 11%-32%). Treatment-related adverse events included sub-epithelial haze 13% (95% CI, 6%-21%), hyperopic shift 20% (95% CI, 11%-28%) and a decrease in best spectacle corrected visual acuity in 11% (95% CI, 5%-16%). Overall PTK was found to be a valuable treatment option for patients with recurrent corneal erosions²⁰.

Anterior stromal puncture

In anterior stromal puncture a small needle (eg 25 gauge) is used to puncture the cornea in order to

produce scar tissue that is thought to promote the adherence of epithelial cells to the basement membrane.

Superficial keratectomy

Removal of the corneal epithelium (superficial keratectomy) with a Diamond burr or alcohol has been reported in recurrent corneal erosion.

A study including 97 eyes from 73 patients compared PTK vs stromal puncture vs Diamond burr and had a mean follow up of 474 days²¹. The patients had recurrent corneal erosions secondary to epithelial basement membrane dystrophy (80% n=78 of 97), trauma 15%, n=15 of 97, and idiopathic 4%, n=4 of 97. In the Diamond burr and PTK groups there was significantly lower recurrence: 9.1%, p=0.031 and 10%, p=0.048, respectively compared with epithelial debridement with stromal puncture (recurrence 29.4%) and a higher rate of complete epithelialization at 1 week (p<0.05).

Autologous serum

Autologous serum has also been investigated for recurrent corneal erosion however the mechanism of action not fully elucidated. Autologous serum has similarities to tears in terms of their contents, with both containing albumin, IgA, epidermal growth factor, and vitamin A²¹. Their use may be limited as some patients may have a medical contraindication eg anaemia and they are time-consuming to prepare. Non-autologous serum drops are also available but may be problematic due to the risk of blood borne infections (new variant CJD, HIV, hepatitis).

A prospective single-centre study included 33 eyes of 33 recurrent corneal erosion patients who had failed other treatments. The mean age of the patients was 49.3 ± 9.8 SD (range 24-73) years and they received autologous serum drops 6 times daily for first 3 months and then 4 times daily for next 3 months. The mean follow-up: 30 ± 6.3 SD (range 12-48) months. During treatment no recurrence was reported with complete healing reported in 85%. After treatment there was a single recurrence in 5 (15%) patients at 3 to 12 months. No sight-threatening complications occurred²³.

Artificial intelligence and corneal erosions

A fully automated system has been developed to detect corneal position and grade staining severity for a corneal fluorescein staining. For punctate staining grading model achieved a classification accuracy of 76.5% was achieved with the Area under receiver operating characteristic curve 0.940 (95%CI 0.932 to

0.949). The average time for processing a single stained image 0.58 s²⁴. Such systems may have utility in clinical trials of recurrent erosion and residency training procedures.

Future directions

To establish the benefits of new and existing prophylactic and treatment regimes for recurrent corneal erosion well-designed masked randomised controlled trials using standardised methods are needed.

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