

# Topical anaesthetic in the treatment of corneal epithelial defects

## *What are the risks?*



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### Background

Recent publications have suggested that topical anaesthetic eye drops can be used safely and are effective in providing pain relief for the treatment of corneal abrasions. Complications resulting from the injudicious prescribing of topical anaesthetic eye drops are seen with some frequency in the Royal Victorian Eye and Ear Hospital's (RVEEH's) emergency department.

### Objective

The aim of this article is to review the literature and provide a clinical perspective to challenge the safety of topical anaesthetic eye drops for corneal abrasions.

### Discussion

The literature relevant to this clinical question is reviewed, with an emphasis on a critical evaluation of the publications in question. Cases from the RVEEH are used for illustrative purpose. An alternative option for analgesia is suggested.

**PATIENTS WITH** ocular symptoms commonly present to general practitioners (GPs), with one study estimating they account for approximately 1.4% of all presentations.<sup>1</sup> One of the most common symptoms is pain, which, when associated with diseases or injury affecting the cornea, can be severe. A small number of publications suggest that topical (local) anaesthetic (LA) drops can safely be used for short periods for pain management following a corneal abrasion or removal of a corneal foreign body.<sup>2,3</sup> We review the current literature and highlight the risks of prescribing LA drops in the primary care setting, where assessment of the 'painful, red eye' can be challenging.

### Local anaesthetic drops impair corneal healing

The corneal epithelium normally heals quickly after an injury, repairing at a rate of approximately 1 mm<sup>2</sup>/hr.<sup>4</sup> The complex cascade of events involves epithelial cells, corneal nerves, stromal keratocytes and a stable tear film with adequate eyelid cover. Any disease or treatment that affects these factors can potentially slow the healing response. Even at very low concentrations, LA drops exert toxic effects that delay corneal healing.<sup>5,6</sup> Overuse of LA drops can cause persistent epithelial defects,

stromal/ring infiltrates, corneal oedema, endothelial damage, peripheral anterior synechiae formation, elevated intra-ocular pressure, and ocular and periorbital inflammation, among other side effects.<sup>7</sup>

### Wrong diagnosis: When a simple corneal abrasion is not so simple

A man aged 55 years presented to the Royal Victorian Eye and Ear Hospital (RVEEH) emergency department with a two-day history of a painful, photophobic, red eye. He had previously been seen in a general emergency department, diagnosed with a corneal abrasion and discharged with chloramphenicol 0.5% eye drops four times daily and multiple oxybuprocaine 0.4% as needed. On examination, his visual acuity in the affected eye was 6/24. He had a dendritiform corneal epithelial defect, corneal stromal infiltrate and moderate anterior chamber inflammation, consistent with a diagnosis of herpes simplex keratouveitis. Ten weeks after the initial presentation and as a result of appropriate treatment, his visual acuity improved to 6/9.

The potential for misdiagnosis is a significant risk when prescribing LA drops for corneal pain, and review of referrals to an eye centre showed

a diagnostic accuracy of 39% by emergency physicians and 33% by GPs.<sup>8</sup> In a second study, concordance between non-ophthalmologists and ophthalmologists for acute anterior segment conditions was 54%.<sup>9</sup>

### Treating the symptom risks masking the disease

A woman aged 46 years presented with a painful, red right eye to the RVEEH emergency department. She had been prescribed tetracaine 0.5% eye drops with five repeats by her GP, and had been using these drops to treat her painful eye over the preceding three weeks. Examination showed a corneal epithelial defect and stromal infiltrate consistent with bacterial keratitis. Visual acuity was 'hand movements' in the right eye, and 6/9 in the left. Resolution of the infection was achieved after prolonged inpatient treatment. Soon after discharge, she was referred again to the RVEEH for bacterial keratitis in the left eye, once again following the use of LA drops, and again requiring inpatient management. At last follow-up, her visual acuity was 6/36 in the right eye and 6/12 in the left.

This case illustrates misdiagnosis and a misuse of LA drops, and highlights another risk implicit in their prescription: that use may become extended and unsupervised. This use resulted in the delayed diagnosis of bacterial keratitis, a serious corneal infection that can lead to corneal scarring and permanently decreased vision, as was unfortunately the outcome in this case. Similarly, poor visual outcomes have been reported elsewhere from abuse of LA drops.<sup>10-12</sup>

### Limited efficacy data on treating the pain from corneal abrasions

Three prospective, randomised, placebo-controlled trials investigated the safety and effectiveness of LA drops in the setting of acute corneal injury.<sup>2,3,13</sup> All three trials were undertaken in emergency department settings, with conclusions in support of brief courses of LA drop use for analgesia, most often following traumatic corneal abrasions. This contrasts with

ophthalmologists' practice, in which these conditions are treated without LA drops.<sup>14</sup>

Only one of these studies (Ball et al) showed a statistically significant difference in pain relief with LA drops when compared with placebo, and the authors concluded that dilute LA drops (proparacaine 0.05%) were effective at providing analgesia for patients with corneal injuries.<sup>2</sup> Waldman et al reported no significant difference in pain scores between the control and treatment groups.<sup>3</sup> The third study by Ting et al was insufficiently powered to draw conclusions regarding efficacy of analgesia through use of LA drops.<sup>13</sup>

However, while Ball et al reported that LA drops were effective for pain relief in corneal injuries, there was no significant difference in the amount of oral analgesia used between the group of patients using the LA drops and the control group, suggesting that the analgesia offered by LA drops was so short-lived as to be clinically insignificant. Additionally, the authors did not address the possibility that the patients may have been inadvertently unmasked, or at the very least biased, to their treatment group, as LA drops usually sting on instillation, whereas placebo drops would not.

The results from this study are further limited in their applicability in the local context in that neither the fourth-generation fluoroquinolone antibiotic eye drop used (gatifloxacin 0.3%) nor the 10-fold diluted concentration of proparacaine 0.05% is commercially available in Australia.

### What did these studies reveal about the safety of local anaesthetic drop use?

In the study by Waldman et al, the primary outcome was whether LA drops were safe for short-term use following a corneal abrasion.<sup>3</sup> However, in studying this, the authors excluded post facto cases that were not typical abrasions, thereby excluding the very cases in which inappropriate LA use could be most harmful.<sup>3</sup> Re-analysis of their data suggested that the prescription of tetracaine for more serious pathologies occurred in six of 122 patients (4.9%).<sup>3,14</sup>

Their conclusion that LA drops are safe when used for abrasions was also made in part on the poorly defined criterion of 'fluorescein uptake'. Not measuring the size of an epithelial defect precludes assessment of corneal healing. In addition, the absence of slit lamp examination by an experienced clinician may have led to missed diagnoses such as toxic keratopathy or corneal infiltrates.<sup>14</sup> This limitation was also present in the study by Ting et al.<sup>13</sup> All three studies suggested that there was no significant increase in adverse events in the LA group, but the sample sizes in the studies by Ball et al and Ting et al were too small to draw meaningful conclusions,<sup>2,13</sup> and there was also a non-significant trend to persistence of epithelial defects in the treatment group in the study by Ting et al.<sup>13</sup>

### Poor compliance and follow-up

The study by Ting et al highlighted the poor follow-up rate that is typical in this setting, with two out of three participants failing to attend for review despite involvement in a research trial.<sup>13</sup> Similarly, in the larger Waldman et al study, 30.2% of participants did not attend their follow-up appointment and 9.5% of participants were identified as having been 'non-compliant' with the study protocol.<sup>3</sup> Ball et al reported that eight patients (24.2%) were either non-compliant or lost to follow-up.<sup>2</sup>

While it has been argued that LA drops have been used without detriment after elective surgical procedures such as photorefractive keratectomy (PRK),<sup>3</sup> these procedures are performed in day surgery centres with meticulous sterile technique and instrumentation, and close monitoring post-operatively by an ophthalmologist. As such, the risk of misdiagnosis or lack of follow-up in this context is negligible, and any extrapolation from this to a general concept of safety of LA drop use for other corneal conditions is not supported.

A thorough examination of the medicolegal implications of severe visual morbidity resulting from imprudent prescription of LA drops is beyond the scope of this article, but such issues are clearly implicit.

## Alternative options for analgesia in patients with corneal pain

In our collective clinical experience, use of an ice or cold pack can be very effective in relieving the pain associated with corneal abrasion or following procedures such as PRK and corneal collagen cross-linking. This is supported by results from a randomised controlled trial by Zeng et al.<sup>15</sup> In this study, the simple application of a cold patch was found to be effective in reducing pain on a visual analogue scale as well as significantly reducing the use of LA drops and non-opioid oral analgesia following PRK.

## Conclusion

While appreciating the need for primary care physicians to provide analgesia, prescribing LA drops for any corneal lesion assessed in the primary care setting carries too many risks to be justified. It can mask diagnosis, has questionable efficacy and safety data, risks developing dependence and has the potential for blinding consequences to the patient.

## Key points

- High-quality data on the safety of LA drop use in the management of pain caused by corneal abrasions remain absent.
- LA drops are toxic to the cornea and slow epithelial healing.
- Poor visual outcomes from LA drop use are possible, as reported in this article and elsewhere.
- There is no compelling evidence to suggest LA drops are effective in treating pain from corneal abrasions, with studies supporting its use limited by flawed methodology.
- Ice packs have been shown to be a safe, effective method of adjunct analgesia for pain caused by corneal epithelial damage.

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Competing interests: None.  
Funding: None.  
Provenance and peer review: Not commissioned, externally peer reviewed.

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