Tetracaine Challenges Old Dogma for Emergency Department Management of Corneal Abrasion Pain and Beckons a Definitive Study

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Corneal abrasions account for a large portion of eye-related injuries treated in the emergency department (ED), with an incidence of approximately 3 in 1,000.1 If not diagnosed and treated properly, there may be permanent sequelae.2 Traditional management has been to remove the foreign body and send patients home with systemic (oral) pain medication such as nonsteroidal anti-inflammatory drugs and opiates, or topical nonsteroidal anti-inflammatory drops, as well as topical antibiotics.3-5 The use of topical antibiotics has greatly reduced the incidence of infection-related complications, but there is still a lack of consensus in regard to the proper management of pain in corneal abrasions.6 The efficacies and safety profiles of these therapeutic options remain unclear mainly because the existing literature is limited by a number of factors, including small sample sizes.7,8

In this issue of Annals, Waldman et al9 introduce a retrospective cohort study designed to assess the outcomes and safety of routine topical tetracaine use to manage pain in patients with simple corneal abrasion. This editorial will place their article in historical and clinical context by introducing the study design, results, and limitations; reviewing the existing clinical literature about management of corneal abrasion pain; and suggesting a definitive clinical trial to help reach a consensus in regard to the proper management of pain in corneal abrasions.

The study was conducted at the ED of Southland Hospital in New Zealand, where policy change allowed physicians to use topical tetracaine hydrochloride 1% eyedrops for 24 hours for pain treatment for patients with corneal abrasions. Tetracaine-treated patients were sent home with 1.5 mL of preservative-free, undiluted, 1% tetracaine hydrochloride in addition to the ED standard treatment for corneal abrasions, which consists of chloramphenicol eye ointment and a prescription for 2 paracetamol 500-mg tablets every 4 hours as needed. Tetracaine was supplied in a premade take-home pack consisting of 3 plastic 0.5-mL commercially available vials, or approximately 50 drops. Patients were instructed to place tetracaine in their eye as often as every 30 minutes while awake, for up to 24 hours. Outcome measures were ED rechecks, persistent fluorescein uptake, ophthalmology clinic referrals, or complications. ED rechecks were chosen as a surrogate marker for prolonged symptoms or delayed healing. Persistent fluorescein was also chosen as a marker for delayed healing. Ophthalmology clinic referrals were chosen to look for potential minor or temporary complications, major or permanent complications, and uncommon adverse events.

There were no serious complications or uncommon adverse events attributed to tetracaine for the 459 patients who received tetracaine at the initial ED visit or at a recheck visit in the ED or ophthalmology clinic. The relative risk (RR) of ED recheck (RR 1.67) and persistent fluorescein staining (RR 1.65) was increased overall among patients who received tetracaine. The RRs for only simple corneal abrasions receiving tetracaine were 1.16 for ED recheck and 0.77 for persistent fluorescein staining, which more accurately represents the population for whom tetracaine is believed to be appropriate. Referrals to ophthalmology were significantly decreased for all patients in the tetracaine group (RR 0.33). The fraction requiring a subsequent ED recheck was 13.5% in the simple corneal abrasion—tetracaine group and 10.5% in the standard treatment group. At ED rechecks, the group that received tetracaine on the initial visit had fluorescein uptake 47.1% of the time, whereas the standard treatment group had fluorescein uptake 52.9% of the time. These results suggest that the appropriate use of tetracaine for simple corneal abrasion pain is safe. However, even when sizeable clinical trials with high-level scrutiny are conducted, many adverse
drug effects are not noted until postmarketing studies. Given the low but not absent risks inherent in topical tetracaine use, extensive continuous safety monitoring throughout the life cycle of the drug will likely be required to thoroughly clarify the risk-benefit ratio, and it is far beyond the scope of this study to do so.10

The study did have some key limitations. First, the retrospective nature of the study limits the conclusions that can be drawn from observations. The chart reviewers were not blinded to the study hypothesis and could have biased the data collection. It was not verified whether patients received their medications as directed. Only patients who returned for rechecks were assessed, and it is possible that some patients developed scars or defects in their vision but did not return to either the ED or the ophthalmology clinic. The 95% confidence intervals for the RRs are generally wide in the simple corneal abrasion group, so it is possible that clinically important effects were not detected in this study. Standard ED examination was limited to fluorescein staining to define the corneal injuries or to detect healing abnormalities on a microscopic level.

Measures of ED rechecks were unable to be reliably determined because it was not always possible to ascertain from the medical record whether the recheck was planned or unexpected. Patients returning for unexpected rechecks were experiencing symptoms, whereas those returning for planned rechecks may or may not have had symptoms. It is possible that recheck numbers for the treatment group were higher because of an overcautiousness in planned rechecks among new physicians adopting the practice, which would have inflated recheck numbers in the treatment group.

The literature defending the controlled use of a limited supply of topical anesthetics for simple corneal abrasions is increasing. Four studies have examined the use of topical anesthetics after photorefractive keratectomy surgery, and these topical therapies were shown to effectively treat pain and not delay wound healing.11-14 Subsequently, 3 ED studies15-17 examined the treatment of pain caused by simple corneal abrasion. The results of the first 2 studies15,16 showed no serious complications and a reduction of pain. In 2014, a larger randomized controlled trial also supported the safety of topical tetracaine.17 Swaminathan et al18 summarized the evidence for the safety of topical tetracaine and proparacaine for pain relief in patients with corneal abrasions. Their literature search produced 2 ED-based, randomized, double-blind, placebo-controlled studies on human patients with corneal abrasions and 4 studies that investigated the application of topical anesthetics in patients who underwent photorefractive keratectomy. All 6 studies demonstrated that a short course of dilute topical tetracaine or proparacaine provided efficacious analgesia without adverse effects or delayed epithelial healing.

There is disagreement about the use of topical nonsteroidal anti-inflammatory agents, one suggested treatment for corneal abrasion pain, and this controversy affords additional reason for further study. A systematic review by Wakai et al19 identified randomized controlled trials comparing the use of topical nonsteroidal anti-inflammatory agents with placebo or any alternative analgesic interventions in adults with traumatic corneal abrasions to reduce pain and the effects on healing time. Their findings did not provide strong evidence to support the use of topical nonsteroidal anti-inflammatory agents in traumatic corneal abrasions. In contrast, a systematic review by Thiel et al9 opined that topical nonsteroidal anti-inflammatory agents produced reductions in pain symptoms, whereas topical anesthetics did not demonstrate significant improvements in either healing rates or pain control. The authors’ conclusions are surprising, in light of the enthusiasm laser vision correction surgeons have for the use of topical anesthetics in surface laser ablation.

Use of topical anesthetics has long been discouraged because of concerns over safety.20,21 Case reports of preserved topical anesthetic abuse and misuse, coupled with animal studies, suggest that the use of topical tetracaine could lead to uncommon adverse events.22,23 Waldman et al found these claims to be unjustified because they were not based on clinical trials, involved preserved anesthetics used during long periods, and suggested a favorable profile for topical tetracaine, and they cited that there was no strong evidence of short-term topical tetracaine toxicity when used for controlling pain of simple corneal abrasion. Additional reasons to consider a topical anesthetic are to reduce clinical trials, involved preserved anesthetics used during long periods, and suggested a favorable profile for topical tetracaine, and they cited that there was no strong evidence of short-term topical tetracaine toxicity when used for controlling pain of simple corneal abrasion. Additional reasons to consider a topical anesthetic are to reduce pain and the effects on healing time. Their findings did not provide strong evidence to support the use of topical nonsteroidal anti-inflammatory agents in traumatic corneal abrasions. In contrast, a systematic review by Thiel et al9 opined that topical nonsteroidal anti-inflammatory agents produced reductions in pain symptoms, whereas topical anesthetics did not demonstrate significant improvements in either healing rates or pain control. The authors’ conclusions are surprising, in light of the enthusiasm laser vision correction surgeons have for the use of topical anesthetics in surface laser ablation.

A well-designed clinical trial should help illuminate the answer to the above concern. Waldman et al believe a shorter-term supply of tetracaine should become routine practice in the ED to treat simple corneal abrasion; however, a prospective study on safety and efficacy with nonpreserved tetracaine is first needed. To this end, we recommend a Food and Drug Administration–approved, prospective,
randomized, triple-blind, controlled, clinical trial to help determine safety and efficacy for the use of topical anesthetic (tetracaine) versus nonsteroidal anti-inflammatory for analgesia in corneal abrasions. Such a study could suffice in demonstrating comparable efficacy of tetracaine and, if so, would allow Food and Drug Administration–approved new labeling of tetracaine for pain control as an approved indication. Within the trial, we suggest the following: (1) preservation-free, limited-dose vials of medication to prevent complications resulting from abuse of medication beyond recommendations; (2) follow-up with an ophthalmologist for evaluation within 1 to 2 days after administration of topical tetracaine or nonsteroidal anti-inflammatory to allow standardized evaluation; (3) validated pain scoring; and (4) identification of adverse effects.

In summary, the current evidence about the use of tetracaine for analgesia in corneal abrasion is moving away from the “do not use” dogma, and this study suggests that potential safe and effective use is possible for appropriate patients, namely, those with simple corneal abrasions. The study by Waldman et al has limitations, however, and is unable to provide definitive evidence of safety and efficacy, thus necessitating an appropriate prospective study to accomplish these ends.

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REFERENCES


