

Article Appraisal

**Article:** Shipman S *et al.* Short-Term Topical Tetracaine is Highly Efficacious for the Treatment of Pain Caused by Corneal Abrasions: A Double-Blind, Randomized Clinical Trial. Ann Emerg Med 2020. [PMID: 33121832](https://pubmed.ncbi.nlm.nih.gov/33121832/)

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**Background and Study Objective(s):**

Corneal abrasions are the most common cause of ocular trauma, representing 10% of all ocular complaint presentations to the emergency department (ED). They typically heal spontaneously within 24-72 hours, but can be quite painful. Achieving adequate analgesia can be difficult. Previous options have included oral analgesics and topical NSAIDs. The use of topical tetracaine has typically been avoided due to concerns around poor wound healing and subsequent corneal ulceration, scarring or blindness. There is a concern that it’s use may discourage patients from seeking care for persistent or worsening symptoms. However, some recently ophthalmology literature has emerged showing safety in short term usage amongst post-operative patients.

In light of this, this study attempted to answer the following question: how effective is 24-hour home use of topical tetracaine in patients with uncomplicated corneal abrasions compared to placebo? The primary outcome was overall numeric rating scale pain score measured at 24-48 hours during ED follow-up (on a scale from 0-10 cm). Secondary outcomes were the amount of hydrocodone ingested for breakthrough pain, and occurrence of any adverse events.

**Study Design:**

This was a single-center, prospective, double-blind, placebo-controlled, randomized trial of adults with uncomplicated corneal abrasions. Enrollment occurred at an urban community ED in Oklahoma from January 2015 to September 2017.

Inclusion criteria were age 18 to 80 years, suspected acute corneal abrasion and written informed consent. Exclusion criteria were use of contact lenses, previous corneal surgery or transplant, greater than 36 hours after injury, grossly contaminated foreign body, retained foreign body, coexisting ocular infection, penetrating eye injury, pregnancy, immunosuppression, allergy, inability to follow-up, non-fluent English or Spanish speaker or injury requiring urgent ophthalmology assessment.

ED physicians and residents enrolled patients into the study through convenience sampling. Enrollment could occur at any time of day, seven days a week. Both ED physicians, ophthalmologists and patients were blinded to randomization. Patients were sequentially randomized in a 1:1 fashion to receive either one ampule of topical tetracaine 0.5%, or four ampules of topical placebo (artificial tears). In either case they were instructed to use one drop every 30 minutes as needed for 24 hours. Allocation occurred using a computer random-number generator.

In addition, all patients received polymyxin B sulfate/ trimethoprim sulfate drops with instructions to instill 2 drops q4hrs into the affected eye, as well as hydrocodone/ acetaminophen 7.5/325mg (12 tablets) with instructions to use 1 or 2 tablets PRN q6hrs for breakthrough pain.

Patients were brought back to the ED at 24-48 hours for repeat evaluation, and were asked to follow-up with ophthalmology at 7 days. Additional follow up at the conclusion of the study included telephone contact and electronic medical record review focused on eliciting any subsequent adverse events related to the patient’s corneal abrasion.

**Results:**

One-hundred and eighteen patients were randomized, from a total of 283 patients assessed for eligibility. A total of 111 patients were included in the final analysis (56 in the tetracaine group, 55 in the placebo group). Baseline numeric rating scale pain score was the same (7) across both groups. On repeat assessment at 24-48 hours, the overall pain score was significantly lower in the tetracaine group with a mean of 1 out of 10, as compared to the placebo group with a mean of 8 out of 10 (Absolute Difference: 7; 95% CI 6 to 8; p <0.001).

Secondary outcome of median hydrocodone tablet usage showed that the tetracaine group used a median of one tablet, as compared to median usage of seven tablets in the placebo group. The study was not powered to detect adverse events, but did show a complication rate of 3.6% (2/56)in the tetracaine group versus 11% (6/55) in the placebo group. On repeat assessment at 24-48 hours, the percentage of patients with small residual corneal abrasion was similar across groups (18% in the tetracaine group, 11% in the placebo group). This difference was not statistically significant (95% CI -6.4 to 20.4).

**Validity of Results:**

This study addressed a clearly focused clinical question, by conducting a well done randomized controlled trial that followed an intention to treat protocol. No competing interests or funding conflicts were identified; however, this study was registered on clinicaltrials.gov only after its completion. Although patient enrollment was allowed at all hours and days of the week, further details around the specifics of enrollment was unclear (i.e. consecutive vs convenience sampling). Randomization was successful, as evidenced by multiple balanced baseline characteristics in Table 1, most importantly the initial pain rating between groups. Despite a reasonable attempt to blind both patients and physicians, the burning nature of tetracaine application and the different number of ampules allocated between groups may have unblinded patients and enrolling physicians, respectively. Follow up of patients for primary outcome data collection was excellent at greater than ninety-two percent. Safety of tetracaine application was taken seriously by the authors as evidenced by the incorporation of multiple assessment points in their study, including ophthalmology specialist and phone call follow-up, and electronic medical record examination of adverse events at the conclusion of the study. Despite this prudent study design, these safety follow-ups saw low records of attendance by patients, raising the possibility that complications were missed. Furthermore, there was no standardized approach utilized by the emergency physicians conducting follow-up slit lamp exams to evaluate healing corneal abrasions, which makes this secondary outcome subjective and lack reliability. Regardless, this study was not powered to detect safety outcomes. Finally, although the study was marginally underpowered to meet their predetermined minimal clinical difference in pain scores, the study’s primary outcome did show an impressively precise and large difference between groups.

**Generalizability of Results:**

Although this study was conducted at a single centre in the USA, it was a busy community ED with a residency program seeing upwards of 80,000 patients per year thereby broadening its generalizability. The results of this study are only applicable to patients with simple, uncomplicated corneal abrasions. We believe the exclusion criteria utilized to isolate this specific patient population is representative of how the majority of emergency physicians practice. The degree of follow-up implemented in this study (repeat 24-48 hour ED visit, ophthalmologist follow-up within 1 week, and telephonic follow-up) to act as a safety net for detecting adverse events may not be a realistic strategy for every ED or patients themselves, particularly those that do not have prompt specialist accessibility. This is further evidenced by the fact that 90 out of 111 patients did not return for their ophthalmology follow-up in the study. Furthermore, this study was capable of establishing a robust method of limiting tetracaine eye drop usage by discarding the topical anesthetic at the 24-48 hours follow up visit. Given the significant safety concerns with prolonged use, a lack of a fail-safe method for practitioners to limit the amount of topical anesthetic prescribed and prevent overuse may make prescribing this drug impractical. Lastly, the additional pain control and treatment offered to every patient in this study included an opioid analgesic and an antibiotic drop, which does not appear to be representative of local practice in British Columbia. From our experience, opioids are infrequently used to treat corneal abrasions and more often an antibiotic ointment, as opposed to a drop, is preferred given its enhanced lubricating effects that help limit pain.

**The Bottom Line:**

This randomized controlled trial clearly demonstrated that twenty-four hours of topical 0.5% tetracaine utilized every thirty minutes as needed for uncomplicated corneal abrasions significantly reduced pain scores at twenty-four to forty-eight hours compared to a topical balanced artificial tear solution. Although this result may have been expected by most clinicians, it is also interesting to note the associated observation that patients receiving only opioids and artificial tears still had average pain scores of 8/10 at their follow-up visit. This further corroborates that opioids are likely ineffective at alleviating pain associated with corneal abrasions and should not be used for this injury. Lastly, this specific study implemented multiple safety mechanisms to monitor for adverse effects of applying short-term topical tetracaine, however it was not powered for safety outcomes and should not be used as evidence supporting the safety of topical tetracaine.