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# A Review of the Effectiveness and Safety of Topical Anesthetics in Corneal Abrasions

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## Abstract

Corneal abrasions are known to be extremely painful and are a commonly seen eye condition. Topical anesthetic drops used for diagnosis of corneal abrasions provide immediate pain relief for most patients, but their use for outpatient use has been controversial. There is lack of consensus regarding ideal management of pain associated with corneal abrasions, with some physicians prescribing nonsteroidal anti-inflammatory drugs or opioids which both can have serious side-effects and/or abuse potential. In recent years, several studies have been conducted to assess the efficacy and safety of short term topical anesthetic use for the treatment of acute corneal abrasions. For this review, four published randomized controlled trials were identified that focused on the effectiveness and safety of various topical analgesics used in treating corneal abrasions. These showed varying degrees of efficacy depending on the outcomes measured without any significant difference in complication rates. Additionally, we reviewed an observational study that investigated whether routinely sending corneal abrasion patients home with a 24-hour supply of topical tetracaine is safe. They found no increased risk of ED revisits, fluorescein uptake at follow up, or ophthalmology clinic referrals. Larger prospective studies are still required to establish definitive safety, but the current available evidence suggests use of topical anesthetics for simple corneal abrasions is efficacious and safe.

## Introduction

Corneal abrasions are extremely painful and are one of the most common ocular injuries. These ocular injuries are seen in all age groups, but the highest rates of occupational eye-related injuries are seen in young, working males[1]. Topical anesthetic drops are routinely used before slit-lamp examination for diagnosis of corneal abrasions and often provide immediate pain relief. The use of topical anesthetics for outpatient treatment of corneal abrasions has previously been discouraged because of concerns over safety. Case reports of abuse and misuse, as well as animal studies, have suggested that long-term use of topical anesthetics may lead to rare complications and delay healing[2-7]. Anesthetic overuse seen in case reports and case series have shown delayed wound healing, and rarely keratopathy, ulceration, perforation, or scarring[8-10].

Ocular pain associated with corneal abrasions can be incapacitating, and thus pain control is essential in the management of these patients. Current treatment options include nonsteroidal anti-inflammatory drugs (NSAIDs) or opioids, both with potential for significant side effects. If topical anesthetics could be safely prescribed for short-term use in the management of corneal abrasions, it could decrease use of systemic opioids for this purpose.

More recently, several studies have demonstrated the safety and efficacy of topical anesthetics for treatment of pain associated with corneal abrasions. However, the recommendation for routine outpatient use remains controversial, and the benefit to potential risk is still uncertain for many physicians. In this review, we provide a summary of all the available evidence investigating this clinical quandary.

## Data Acquisition

A comprehensive search of the literature was performed in March 2021 using the Medline (Ovid), Embase (Ovid), and Scopus databases. Relevant results were limited to abstracts and/or papers in the English language and human studies published from January 1st 2005-February 28th 2021. A total of 21 citations were identified by this search. Of those 21 citations and abstracts, 5 were deemed relevant for review. Of the 16 studies excluded, 5 were post-operative studies, 5 were review articles, 4 were animal studies, and 2 were case series.

## Review of Randomized Control Trials

Four double-blind randomized controlled trials have assessed the effectiveness of short-term topical anesthetics for the treatment of pain caused by corneal abrasions. These results are demonstrated in Table 1. In 2009, Ting et al. published the first randomized controlled trial assessing the efficacy and safety of topical amethocaine compared to placebo (saline) in the management of corneal abrasions[11]. The trial was held at the Mater Adult Hospital Emergency Department (ED) in Raymond, South Brisbane, Australia. 47 patients for this pilot study were recruited over 12 months, and were required to have either: (1) traumatic superficial corneal abrasion(s), (2) superficial corneal

**Table 1:** Study Characteristics and Outcomes of Topical Anesthetic Trials

| Paper Title | Author | Design | # of Patients | Intervention | Outcomes | Follow-up | Results |
|---|---|---|---|---|---|---|---|
| Management of Ocular Trauma in Emergency (MOTE) Trial: A pilot randomized double-blinded trial comparing topical amethocaine with saline in the outpatient management of corneal trauma | Ting et al.[10] | Randomized controlled trial | 47 | 1 drop of 0.4% amethocaine applied once hourly | Healing of corneal defect, use of oral analgesics, pain using 10 cm VAS | Evaluation before treatment, 36-48 hours after; patient diary; 2-week telephone interview | No difference in healing or amount of oral analgesia between treatment groups. Satisfaction with their management similar between groups. Saline group recorded a higher mean pain burden, but not statistically tested because of small # of diaries returned |
| Dilute proparacaine for the management of acute corneal injuries in the emergency department | Ball et al.[11] | Randomized controlled trial | 33 | 2-4 drops of 0.05% proparacaine as needed over 7 days | Pain reduction using 10 cm VAS, wound healing, corneal complications | Evaluation before treatment and 5 minutes after treatment; ophthalmologist follow-up 1, 3, 5 days afterwards | Efficacious for pain reduction, no complications or delayed wound healing in either group. |
| Topical tetracaine used for 24 hours is safe and rated highly effective by patients for the treatment of pain caused by corneal abrasions: A double-blind, randomized clinical trial | Waldman et al.[12] | Randomized controlled trial | 116 | 1 drop 1% tetracaine every 30 minutes during first 24 hours of presentation | Corneal healing; pain reduction using 10 cm VAS, overall effectiveness of study drug using NRS. | VAS recorded every 2 hours while awake for first 48 hours after treatment, 1 week and 1-month telephone interviews by clinical investigator | No differences in groups in corneal healing, adverse safety events, or pain scores. Tetracaine perceived to be more effective. |
| Short-term topical tetracaine is highly efficacious for the treatment of pain caused by corneal abrasions: A double-blind randomized clinical trial | Shipman et al.[13] | Randomized controlled trial | 118 | 1 drop 0.5% tetracaine every 30 minutes as needed for first 24 hours | Overall NRS pain score; amount of hydrocodone for breakthrough pain, any adverse events | 24-48-hour ED follow-up, 1-week ophthalmologist follow-up, study conclusion text follow-up to those not attending both follow-ups | Efficacious for pain reduction, decreased hydrocodone use in treatment group, no difference in healing or complication rates. |

abrasion(s), or (3) keratitis from welding flash exposure. Their exclusion criteria included the following: more than 36 hours elapsed since the initial event, patient age less that 18, history of adverse effects to topical anesthetics or underlying eye pathology not including refractive error, contact lens usage, pregnant or lactating, presence of conjunctival infection, functionally one-eyed, or requiring urgent ophthalmologic referral (including penetrating eye injury). Patients were randomly assigned to the control group (0.9% saline solution, n=25) or the treatment group (0.4% amethocaine solution, n=22), with both groups applying 1 drop once hourly as needed for pain relief. Both groups were offered the option of adjunctive oral analgesics. Wound healing and persistent corneal defect between groups were inconclusive due to small sample size. There was no statistically significant difference between the 2 groups in regards to use of oral analgesics, self-reported visual problems, need for unscheduled medical follow-up, or patient satisfaction. Of the patients who completed pain diaries, the treatment group reported lower pain burdens (n=12, M=404±75 mm) compared to the control group (n=9, M=629±172) on VAS 0mm (no pain)-100mm (worst pain) pain rating scale. Scores were to be recorded every 3 hours for 36 total hours. However, these could not be statistically tested (and thus lack clinical significance) due to the small number of diaries that were returned.

A second pilot study investigating topical anesthetic use for treatment of corneal abrasions was published in 2010 by Ball et al.[12]. This study investigated the use of dilute proparacaine in the management of acute corneal injuries in 33 patients recruited in 2005. It was performed at two tertiary care EDs in London, Ontario, Canada. Excluded patients were: unable to consent, had an allergy to proparacaine, were unable to follow-up, or had any pre-existing eye pathology. 18 patients were randomly assigned to the control group (color and smell matched placebo), and 15 patients were randomly assigned to the treatment group (0.05% proparacaine). Patients were instructed to use 2-4 drops of the study drops as needed for 7 days. Participants were given a pain log, topical gatifloxacin, as well as tablets of 325 mg acetaminophen/30 mg codeine to be taken every 4 hours for breakthrough pain. Their sample size was small and predominately male, but the treatment group did obtain a median improvement of 3.9 (IQR =1.5-5.1) while the control group only demonstrated a median improvement of 0.6 (IQR=0.2-2.0, p=0.007) on the 10 point VAS. Patient satisfaction was also measured on a 10 point VAS, and the treatment group had a median satisfaction of 8.0 (IQR=6.0-9.0), compared to the control group median satisfaction of 2.6 (IQR=1.0-8.0, P=0.027). The study found dilute proparacaine was effective at short-term pain reduction and was additionally perceived to be more efficacious by patients.

A larger, double-blind randomized controlled trial was published in 2014 by Waldman et al., studying the use of tetracaine in the management of uncomplicated corneal abrasions[13]. The trial took place in an ED in Invercargill, New Zealand over the course of 12 months, with 116 patients completing the trial. 59 patients were randomized to receive 1% tetracaine hydrochloride and 57 randomized to receive saline. The study drops were applied every 30 minutes while awake for the first 24 hours after enrollment. Patients were excluded if they met any of the following criteria: presentation more than 36 hours after their initial injury, under age 18, previous eye surgery/cataracts, contact lens use, deafness, inability to consent, injury to bilateral eyes, co-existing ocular conditions or infections, allergy to tetracaine or similar medications, injury requiring urgent ophthalmologic follow-up (including penetrating injury), or inability to follow-up. In addition to the study drops, both groups received 500 mg acetaminophen tablets and preservative-free 1% chloramphenicol antibiotic eye ointment. The study's primary outcome was to assess the safety and corneal healing for short-term use of topical anesthetics for corneal abrasions. Secondary outcomes were pain reduction (recorded every 2 hours while awake) using a 100-mm VAS and overall effectiveness of the study drug on a numeric rating scale (NRS) of 0 (no pain)-10 (worst pain) assessed during 1 week and 1 month telephone interviews. The study found that there was no difference in corneal healing between the two groups (p=0.761) at the 48-hour recheck. Additionally, no difference in persistent symptoms between groups was found at 48 hours (p=0.957). No complications specifically attributed to the topical anesthetic were identified (2 patients in the tetracaine group and 3 patients in the saline group required additional examination and treatment). The study failed to show a clinically significant difference in VAS pain scores at any given time between the tetracaine and saline group, however, only 85 subjects returned pain questionnaires and some were not fully completed. During the telephone interview, the patients in the tetracaine group did rate their drops significantly more effective compared to patients in the saline group (NRS 7.7 vs. 3.9, p<0.0005).

In 2020, Shipman et al. published another double-blind, randomized trial of tetracaine versus placebo set in the ED in Oklahoma City, OK[14]. 118 adults with uncomplicated corneal abrasions were enrolled over a 33-month period, with 59 patients randomized to each group (tetracaine 0.5% or balanced artificial tear solution). Patients were instructed to apply 1 study drop every 30 minutes as needed for pain for a maximum of 24 hours. Patients were excluded if they met any of the following criteria: presented more than 36 hours after their injury, under age 18, previous corneal/transplant surgery, wore contact lenses, had a grossly contaminated/retained foreign body, coexisting ocular

infection, pregnancy, immunosuppression, allergy to study medication, any injury requiring urgent ophthalmologic evaluation (lacerations, vision loss, penetrating injury), or inability to attend follow-up, consent, or fluently read and speak English or Spanish. All patients received an antibiotic ophthalmic solution (polymyxin B sulfate/ trimethoprim sulfate) to be used routinely and a prescription for hydrocodone/acetaminophen 7.5/325 mg number 12, to be used as needed for breakthrough pain. The primary endpoint of the study was the overall NRS pain score measured at the patient's initial follow-up ED visit at 24 to 48 hours. Secondary endpoints were the amount of hydrocodone needed for breakthrough pain, and any adverse events. The study found there was a significantly lower overall NRS pain score after use of the study drops in the tetracaine group (1) compared with that of patients in the placebo group (8), with a difference of 7 (95% CI 6 to 8; P<.001). Additionally, they found the tetracaine group recorded using less hydrocodone, 1 tablet versus 7 in the placebo group (difference=6; 95%CI 4-9). The number of patients found to have any adverse event was similar between groups, 3.6% in the tetracaine group and 11% in the placebo group (95% CI -2.9 to 18.6), and patients with a small residual corneal abrasion on their repeat ED slit-lamp examination was also similar between groups, 18% in the tetracaine group and 11% in the placebo group (95% CI –6.4 to 20.4).

## Review of Safety Measures

None of the randomized trials investigating topical anesthetic use for the treatment of pain caused by corneal abrasions were powered to establish safety for rare adverse events. Waldman et al. performed a retrospective cohort study to determine whether routinely sending patients home with a 24-hour supply of topical tetracaine from the emergency department for simple corneal abrasions is potentially safe[15]. This study took place in the ED of a tertiary referral center in Invercargill, New Zealand. The charts of patients from February 2014 to October 2015 with acute corneal abrasions were reviewed. All patients were given chloramphenicol eye ointment and 2 paracetamol 500-mg tablets every 4 hours as needed for pain. At the discretion of the treating physician, 459 of the 1,980 study patients with corneal abrasions were given 1.5 mL of undiluted 1% tetracaine and asked to apply 1 drop every 30 minutes while awake as needed for pain for up to 24 hours. Simple corneal abrasions (SCAs) were defined as abrasions not deemed large by the treating physician, occurring within 48 hours of presentation to the ED, and caused by a simple traumatic mechanism (not from penetrating injury, chemicals, thermal burns, contact lenses, or infection). This ED had a policy change allowing physicians to use short term topical tetracaine only for SCAs. However, the review found that some patients with non-simple corneal abrasions (NSCAs) were inappropriately prescribed topical tetracaine as well. There were no serious complications or uncommon adverse events attributed to tetracaine for all SCAs and NSCAs combined (0/459; upper 95% confidence interval [CI] 0.80%). For SCAs, they found no difference between the fraction of patients requiring a subsequent ED visit in the patients who received tetracaine versus those who did not (13.5% vs 10.5%). In addition, there was no difference in persistent fluorescein uptake at follow up between the 2 groups (47% tetracaine, 53% no tetracaine). Ophthalmology clinic referrals were made on a case-by-case basis at the ED recheck only if there were concerning features. Very few patients had ophthalmology clinic referrals, 1 (0.3%) in the tetracaine group and 4 (1.8%) in the no tetracaine group. None of the 459 patients who received tetracaine experienced an uncommon adverse event. The number of overall complications reported were too small to prove definitive safety, and larger prospective studies are still required. Overall, they found that topical tetracaine used in a limited supply for 24 hours is a safe and effective means of controlling pain for SCAs.

## Summary

In conclusion, we found 4 randomized controlled trials investigating the use of topical anesthetics for corneal abrasions, enrolling a total of 314 patients. These showed varying degrees of efficacy depending on the outcomes measured without any significant difference in complication rates. A retrospective study of 459 patients receiving tetracaine for SCAs addressing safety found no increased risk of ED revisits, fluorescein uptake at follow up, or ophthalmology clinic referrals. Current management guidelines for treatment of acute corneal abrasions include topical antibiotics to prevent infection and pain control. Most small abrasions can be treated with NSAIDs, but topical NSAIDs can be painful to apply and expensive, thus offering little advantage over oral NSAIDs[1,16]. Large corneal abrasions may require oral opioids to provide adequate pain control. Current recommendations do not recommend routine home use of topical anesthetics without more evidence to establish safety[17].

## Limitations and Future Directions

None of the studies included in this review were powered to demonstrate topical anesthetic safety for rare complications. Further research with larger randomized trials would be needed to study these rare but important adverse events. Right now, available evidence suggests use of topical anesthetics for SCAs is efficacious and safe. This is practice changing and may reduce the need for opiate prescribing for this painful condition.

## Conflict of Interest

The authors have no conflicts of interest to declare.

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