Topical nonsteroidal anti-inflammatory drugs for corneal abrasions: meta-analysis of randomized trials

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CRD summary
This review assessed topical non-steroidal anti-inflammatory drugs (NSAIDs) for pain relief for traumatic corneal abrasions. The authors concluded that topical NSAIDs can provide effective analgesia for patients with traumatic corneal abrasions. This was a good-quality systematic review and the conclusions are likely to be reliable.

Authors' objectives
To assess whether topical non-steroidal anti-inflammatory drugs (NSAIDs) provide effective analgesia in traumatic corneal abrasions.

Searching
MEDLINE (1966 to February 2004), EMBASE (1980 to week 10, 2004), the Cochrane CENTRAL Register (Issue 1, 2004) and the Cochrane Database of Systematic Reviews (Issue 1, 2004) were searched; the search terms were reported. The authors also checked the reference lists of all retrieved clinical trials and reviews. Four relevant journals were handsearched from 1995 to 2004. Pharmaceutical companies that manufacture topical NSAIDs were contacted to identify industry-sponsored trials. No language restrictions were applied. The authors included published and unpublished trials, including those identified in conference proceedings, abstracts and letters.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Studies of any type of topical NSAID were eligible for inclusion. Studies of oral NSAIDs were not eligible for inclusion. The included studies assessed the following NSAIDs: indomethacin 0.1% or 1%, flurbiprofen 0.03%, ketorolac 0.5%, diclofenac 0.1% and piroxicam 0.5%. Cointerventions included gentamicin, chloramphenicol, polytrim, cyclopentolate, phenylephrine, polysporin, netilmicin, oral analgesia, eye patch, and bandage contact lens. Control groups received the cointervention only, liquifilm tears, placebo drops or cointervention drops and eye patch.

Participants included in the review
Studies of patients with traumatic corneal abrasions set in the emergency department or an ophthalmology clinic were eligible for inclusion. Studies of patients with corneal ulcers were excluded, as were studies conducted in the peri-operative setting. Where stated, the median proportion of participants that were male was 82.5% and the mean age of the participants was 37 years.

Outcomes assessed in the review
Studies that used a scale to assess pain were eligible for inclusion. The primary outcome of interest was the mean pain scale score at 24 hours, while the secondary outcome was the rate of adverse events. Where stated, the pain scales used in the included studies were a 10-cm visual analogue scale (VAS), VAS 0-5, verbal pain scale 0-10 or verbal pain scale 0-3. The times when the outcomes were measured ranged from 30 minutes to 10 days after dosing; all of the trials took measurements at 24 hours after dosing.

How were decisions on the relevance of primary studies made?
Two reviewers independently screened studies for inclusion, and any disagreements were resolved by discussion until agreement was reached.
Assessment of study quality
The studies were assessed for validity using the Jadad scale. Studies that achieved a score of 3 or 4 were described as high quality.

Two reviewers independently assessed the validity of the included studies. No attempt was made to blind the reviewers to the authors, journal or results of the trials.

Data extraction
Two reviewers independently extracted the data from the included studies onto a standardised and piloted data collection form. Any disagreements were resolved by discussion until agreement was reached. Efforts were made to contact the authors of the included studies to confirm the reported findings and to determine any unreported details. Pain scales were standardised to a 0 to 10 scale, converting scores where necessary.

Methods of synthesis
How were the studies combined?
Trials that reported adequate data and were homogeneous in terms of the population, design and outcome were pooled using a random-effects model. The overall weighted mean difference and 95% confidence interval (CI) were calculated. The authors intended to assess publication bias using a funnel plot but too few studies reported adequate data.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the Q statistic. Sensitivity analyses were planned to test the impact of the following variables: type of pain scale, trial quality, type of control, language, country of origin, type of topical NSAID, and any other sources of clinical or methodological heterogeneity.

Results of the review
Eleven RCTs were included in the review; the total number of participants was not reported. Sample sizes in the included studies ranged from 22 to 347. Only 5 studies were included in the meta-analysis.

Five trials were high quality. Nine trials did not report methods of randomisation. Four trials were not double-blinded; four described themselves as double-blinded but did not report methods of blinding. Six trials did not report withdrawals or losses to follow-up for each group; 2 trials had large losses to follow-up. None of the trials reported that their methods of allocation were concealed, however, two authors responded to correspondence and indicated that their method of allocation was concealed.

Pain scale score at 24 hours.
Five of the 11 included RCTs reported adequate data to be pooled (three of which were high quality). Three used verbal pain scales and two used a VAS. The standardised mean difference suggested a statistically significant reduction in pain favouring treatment with topical NSAIDs (-0.52, 95% CI: -0.91, -0.13).

When only the 3 high-quality trials were pooled (n=299), the standardised mean difference was -0.22 (95% CI: -0.45, 0.00).

When the 3 RCTs (n=459) that used verbal pain scales were pooled, the overall weighted mean difference suggested a statistically significant reduction in pain favouring treatment with topical NSAIDs (-1.30, 95% CI: -1.56, -1.03, P<0.00001). There was no evidence of significant heterogeneity (Q=1.57, P=0.46).

Sensitivity analyses for placebo-controlled trials, language and country of origin did not change the statistical significance of the overall estimate.

Adverse events.
Eight RCTs reported data on adverse events. There were insufficient data to conduct a formal meta-analysis. Two trials
reported that no adverse events occurred, while four reported that some patients experienced transient stinging with instillation of the eye drops. In one trial there were three recurrent corneal erosions: two in the control group and one in the NSAID group. In one trial a patient in the control group developed a corneal abscess and three patients in the NSAID group developed urticaria; since patients in this trial also received gentamicin, the cause of the urticaria was unclear.

The authors stated that few of the trials were suitable for analysis using a funnel plot, therefore the results were not reported.

**Authors’ conclusions**
Topical NSAIDs can provide effective analgesia for patients with traumatic corneal abrasions.

**CRD commentary**
The review question was clear in terms of the study design, participants, intervention and outcomes of interest. The authors searched several relevant sources for studies, and attempts were made to identify unpublished data. The authors intended to assess publication bias using a funnel plot; however, there were insufficient data. Two reviewers independently screened studies for inclusion, assessed validity and extracted the data onto a standardised and piloted data collection form, thus reducing the potential for reviewer bias and error. The studies were assessed for validity using an appropriate validated scale.

Apart from the omission of sample size for all included studies, adequate details of the included studies were presented. Appropriate measures of effect were calculated, statistical heterogeneity was assessed, and sensitivity analyses were performed. This was a good-quality systematic review and the conclusions are likely to be reliable. However, as the authors acknowledged, the exclusion of 6 trials from the meta-analysis, owing to inadequate reporting of outcome data, was a limitation of the review.

**Implications of the review for practice and research**
Practice: The authors did not state any implications for practice.

Research: The authors stated that future research should explore the effectiveness of topical analgesia versus oral analgesia for traumatic corneal abrasions.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.