Effects of postoperative, nonsteroidal, antiinflammatory drugs on bleeding risk after tonsillectomy: meta-analysis of randomized, controlled trials

Marret E, Flahault A, Samama C M, Bonnet F

CRD summary
This review assessed the risk of bleeding associated with non-steroidal anti-inflammatory drugs given to relieve pain after tonsillectomy. The authors concluded that these drugs increase the risk of needing an operation to stop bleeding and should not be used after tonsillectomy. Though a small number of studies may potentially have been missed, the conclusions appear appropriate.

Authors' objectives
To evaluate the risk of bleeding after tonsillectomy in patients treated post-operatively with non-steroidal anti-inflammatory drugs (NSAIDs).

Searching
PubMed (from 1966 to May 2001), the Cochrane Controlled Trials Register, and the references of retrieved papers were searched for relevant RCTs published in English. The search terms were reported in the review.

Study selection
Study designs of evaluations included in the review
Only double-blind randomised controlled trials (RCTs) were included in the review (studies that scored less than 3 on a 5-point validity scale were excluded).

Specific interventions included in the review
Studies that evaluated NSAID therapy after surgery were included. The specific NSAIDs included were intravenous (i.v.) or intramuscular ketorolac (30 mg and 1 mg/kg), oral ibuprofen (5 mg/kg every 6 hours), or i.v. ketoprofen (3.5 mg/kg). The control groups received saline (3 studies), paracetamol plus codeine (2 studies), or either morphine or meperidine (2 studies).

Participants included in the review
The authors selected studies that included children (under 16 years old) or adults who underwent tonsillectomy with or without adenoidectomy. The participants were aged from 1 to 57 years, although 71% of them were younger than 16 years.

Outcomes assessed in the review
The primary outcome was the need for surgical electrocautery to stop the bleeding. The secondary outcome was post-operative bleeding requiring a change in post-operative management: i.e. admission to the emergency department, readmission to the hospital, or blood transfusion. Bleeding was defined as primary if it occurred within 24 hours after surgery, and as secondary if it occurred later.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Each article was scored using a 5-point scale that evaluated randomisation, blinding and completeness of patient follow-up (see Other Publications of Related Interest). Two reviewers who were not blinded to the authors or results assessed the validity of each study. Any disagreements were resolved by discussion.
**Data extraction**
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. Data were extracted on: author, year, patient age range, number of patients in each study arm, surgical dissection technique, NSAID type and dosage, route of administration, duration of treatment or number of doses, and time of onset for NSAID treatment.

**Methods of synthesis**
How were the studies combined?
The Mantel-Haenszel procedure was used to pool odds ratios (ORs) that were assigned weights proportional to the inverse of the within-study OR variance. Analyses were conducted on an intention-to-treat basis wherever possible. The primary and secondary outcomes were analysed separately.

How were differences between studies investigated?
Statistical heterogeneity was investigated using the chi-squared statistic.

**Results of the review**
Seven RCTs (n=505) were included in the review.

Thirteen (5.43%) of 243 patients who did not receive NSAID therapy had primary or secondary post-operative bleeding, compared with 24 (9.2%) patients who did receive NSAID therapy (OR 1.8, 95% confidence interval, CI: 0.9, 3.4).

Eleven (4.2%) of 262 patients who received NSAID therapy required reoperation for haemostasis, compared with 2 (0.8%) of 243 patients who did not receive NSAID therapy. This difference was statistically significant (OR 3.8, 95% CI: 1.3, 11.5). This equates to a number-needed-to-harm of 29.

No statistical heterogeneity was found in either the meta-analysis of post-operative bleeding outcomes (chi-squared 3.07, d.f.=6, P=0.7) or that of reoperation (chi-squared 1.32, d.f.=6, P=0.95).

The validity scores for the individual studies included in the meta-analysis were not reported.

**Authors’ conclusions**
Post-operative use of conventional NSAIDs such as ketorolac, ibuprofen, or ketoprofen increases the risk of reoperation for haemostasis after tonsillectomy.

**CRD commentary**
This was a reasonably well-conducted and reported meta-analysis of the effects of post-operative NSAIDs on bleeding risk after tonsillectomy. The inclusion criteria were brief but fairly clear, and inclusion was limited to double-blind RCTs with high internal validity. Relevant databases were searched and references were followed up, but since inclusion was limited to English language studies, this might have introduced language or publication bias (though the authors argued that the potential for publication bias could be small in this field, the identification of any further non-English RCTs might still have increased the power of their meta-analysis). Two reviewers scored studies for validity, but no other attempts to minimise bias in the review process were mentioned.

Statistical heterogeneity was assessed in the meta-analysis, and sufficient study characteristics were presented in the text and tables to allow the reader some insight into the clinical heterogeneity of the included studies. Though the review has some potential for bias, the authors' conclusions appear appropriate given the findings of their meta-analysis.

**Implications of the review for practice and research**
Practice: The authors stated that the use of NSAID therapy after tonsillectomy should be abandoned, both at the
hospital and at home.

Research: The authors stated that additional strategies (e.g. local anaesthetic infiltration or dissection with high-frequency ultrasound) that may decrease post-operative pain should be investigated. Studies of cyclooxygenase-2 inhibitors after tonsillectomy may also be in order.

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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.