Effect of systemic steroids on post-tonsillectomy bleeding and reinterventions: systematic review and meta-analysis of randomised controlled trials


CRD summary
The authors concluded that systemic steroids did not appear to increase bleeding events after tonsillectomy, but were associated with increased incidence of operative reinterventions for bleeding episodes, which may be related to increased severity of bleeding events. The authors' conclusions reflect the evidence presented and suggest the effects of systemic steroids on post-tonsillectomy bleeding and reinterventions remains uncertain.

Authors' objectives
To evaluate the risk of postoperative bleeding and reintervention with the use of systemic steroids in patients undergoing tonsillectomy.

Searching
Eight databases (including MEDLINE, EMBASE and The Cochrane Library) were searched to March, 2011; Google Scholar and Intute search engines were also accessed. Search terms were reported. No language restrictions were applied. References of included studies and relevant reviews identified through the searches were scanned to locate further studies. Google Scholar was accessed to identify authors who had cited any of the included studies; additional studies identified were considered for inclusion in the review.

Study selection
Eligible studies were randomised controlled trials (RCTs) of tonsillectomy (any indications) that compared the administration of any systemic steroids with any comparator (other intervention, no intervention or placebo). The primary outcome was incidence of postoperative bleeding from the tonsillar fossa. Eligible secondary outcomes included incidence of admission for bleeding episodes, operative reinterventions for bleeding episodes, red blood cells transfusion and mortality. Studies that included patients with bleeding disorders, patients on chronic steroid therapy, or patients in whom steroids were injected or sprayed on the tonsillar bed were excluded.

Most trials were conducted in the United States; others were conducted in Asia, Europe, Australia and Africa. Nineteen trials were performed in children only, six in adults only and four included both. Patient age ranged from one to 70 years (where reported). Trial procedures were mainly tonsillectomy alone, or tonsillectomy with adenoidectomy; equal proportions employed hot, cold or combined dissection techniques. Bleeding outcome definitions were only reported by two trials. Steroid drugs administered were dexamethasone (28 trials) and prednisolone (one trial); single or repeated doses were administered prior to induction/surgery, during surgery, or up to eight days post-operation. Eight trials reported use of nonsteroidal anti-inflammatory drugs among patients. Active comparator drugs included paracetamol, tropisetron, ondansetron, droperidol, piroxicam, pregabalin and bupivacaine.

Two reviewers independently selected studies for inclusion; any disagreements were resolved by discussion with a third reviewer.

Assessment of study quality
Risk of bias was assessed using the Cochrane Collaboration’s risk of bias tool. Studies with considerable loss to follow-up and those with a short follow-up period (less than 24 hours) were considered to have increased risk of bias due to their potential for missing bleeding events. Studies with more than 10% loss to follow-up were assigned an "unclear" overall risk of bias.

Two reviewers independently performed the quality assessment; the authors did not state how any disagreements were resolved.

Data extraction
Outcomes were extracted to calculate odds ratios and 95% confidence intervals for treatment and control groups.
For comparison purposes, all steroid doses were converted in dexamethasone equivalents. Fixed doses were converted to mg/kg, using mean weight, standard weights (adults) or weight charts (children). Bleeding episodes within the first post-operative 24 hours were considered to be primary; all episodes beyond this time frame were considered secondary. Authors were contacted for any missing data or for clarification of methods.

Two reviewers independently extracted the data; any disagreements were resolved by discussion with a third reviewer.

**Methods of synthesis**

Odds ratios (ORs) and 95% confidence intervals (CIs) from individual studies were pooled using a Peto fixed-effect model. A continuity correction of 0.5 was applied to trials that reported no events in both groups. Statistical heterogeneity was assessed using the I² statistical test.

Pre-planned sensitivity analyses based on clinical and methodological characteristics were performed. Publication bias was assessed using a funnel plot for the bleeding episodes outcome.

**Results of the review**

Twenty-nine RCTs (2,674 patients; calculated 2,669 patients) were included in the review. Follow-up duration ranged from six hours to four weeks (where specified). Eleven trials had high risk of bias and eleven trials had unclear risk of bias.

**Post-tonsillectomy bleeding episodes**

The difference in odds of bleeding with steroid treatment versus control groups was not statistically significant (OR 0.96, 95% CI 0.66 to 1.40, 29 trials). No statistical heterogeneity was observed (I²=0%). Sensitivity analyses yielded similar results (reported fully in paper). According to GRADE criteria, this was evidence of very low quality.

**Hospital admission**

No significant statistical difference in hospital admission (due to a bleeding episode) was found between steroid and control groups (OR 1.16, 95% CI 0.68 to 2.00, 17 trials). Very low statistical heterogeneity was shown (I²=19%). All sensitivity analyses yielded similar results (data not reported). This evidence was rated as being very low quality (GRADE).

**Reintervention for a bleeding episode**

The incidence of operative reintervention for bleeding episodes was statistically significantly increased in the steroid treatment groups, compared with control groups (OR 2.27, 95% CI 1.03 to 4.99, 12 trials). No statistical heterogeneity was indicated (I²=0%). This evidence was rated as high quality (GRADE).

Sensitivity analyses revealed a statistically significant increase in reinterventions among children (OR 3.43, 95% CI 1.29 to 9.13, eight trials, I²=0%), among trials containing less than one hundred patients (OR 3.85, 95% CI 1.13 to 13.17, seven trials, I²=0%) and among those with a steroid dosage regimen of 0.5 mg/kg or less (OR 2.45, 95% CI 1.04 to 5.76, eight trials, I²=0%). A borderline statistically significant increase in reintervention among patients receiving non-steroidal anti-inflammatory drugs was shown (OR 4.10, 95% CI 0.99 to 16.97, three trials, I²=0%).

No significant differences in reintervention incidence were observed in any of the other sensitivity analyses (reported in paper); double blinded trials and trials with longer follow-ups suggested strong (non-significant) trends towards increased incidence among steroid groups.

**Allogenic transfusion and mortality**

None of the included trials reported transfusion of red blood cells or mortality.

**Publication bias and quality of evidence**

The authors stated that publication bias was not present.
Authors' conclusions
Systemic steroids did not appear to increase bleeding events after tonsillectomy, but their use was associated with increased incidence of operative reinterventions for bleeding episodes. Increased incidence of these operative reinterventions may be related to increased severity of bleeding events.

CRD commentary
The review question was clear and inclusion criteria appeared sufficiently replicable. Relevant databases were searched and efforts were made to minimise error and bias during the review process. The included studies were published in a range of different languages, suggesting that presence of language bias was unlikely. The authors stated that publication bias was not present but the funnel plot suggested that publication bias was possible. Suitable quality assessment criteria were employed; the authors stated that the majority of included trials were of limited quality.

Methods of synthesis seemed appropriate for the data presented. Efforts were made to explore potential sources of clinical and methodological heterogeneity through various sensitivity analyses; no substantial statistical heterogeneity was indicated. Findings that related to the re-intervention outcome were of borderline statistical significance and the authors stated that the review outcomes were not the primary outcomes within the original trials. This, along with the high loss to follow-up and short follow-up durations for some trials suggested that numbers of some events may have been underestimated. Overall, this appeared to be a well-conducted review and the authors' conclusions reflect the evidence presented and highlight the remaining uncertainty regarding the effect of systemic steroids on post-tonsillectomy bleeding and reinterventions.

Implications of the review for practice and research
Practice: The authors stated that steroids should be used with caution and the risks and benefits weighed. Steroids should not be used routinely for such purposes, especially in children.

Research: The authors stated that further studies should be designed to answer concerns about the safety of the perioperative use of steroids in tonsillectomy procedures.

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