Prophylaxis of postoperative vomiting in children undergoing tonsillectomy: a systematic review and meta-analysis

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CRD summary
This review evaluated interventions to reduce the incidence of post-operative vomiting in children after tonsillectomy, with or without adenoidectomy. It reported good evidence for the effectiveness of dexamethasone and certain serotonergic antagonists; some evidence for metoclopramide, perphenazine and midazolam; but insufficient evidence for dimenhydrinate, droperidol, gastric aspiration or acupuncture. These conclusions appear largely reliable.

Authors' objectives
To systematically review the available literature on interventions to reduce the incidence of post-operative vomiting (POV) in children after tonsillectomy, with or without adenoidectomy.

Searching
The Cochrane Central Register of Controlled Trials, MEDLINE and EMBASE databases were searched for relevant studies, from 1966 to September 2003. Search terms were reported. In addition, conference proceedings in Anesthesia and Analgesia, Anesthesiology, and the British Journal of Anaesthesia were searched, along with the reference lists of retrieved studies. Studies had to be published in English.

Study selection
Randomised, double-blind, placebo-controlled trials (RCTs) were eligible for inclusion in the review. RCTs had to evaluate the prophylactic reduction of post-operative vomiting in patients aged 18 years or less, who had undergone tonsillectomy, with or without adenoidectomy. Studies were eligible for inclusion if they reported the primary outcome measure of post-operative vomiting in the first 24 hours. Among the included studies, post-operative vomiting, where reported, was defined as either vomiting or retching/vomiting. Both pharmacological and non-pharmacological interventions were eligible for inclusion.

Pharmacological interventions evaluated in the selected studies included metoclopramide (0.15 to 0.5 mg/kg), dimenhydrinate (0.5 mg/kg), droperidol (0.075 mg/kg), perphenazine (0.07 mg/kg), ondansetron (0.1 to 0.3 mg/kg), granisetron (0.01 to 0.08 mg/kg), tropisetron (0.1 or 0.2 mg/kg), dolasetron (0.5 mg/kg), and midazolam (0.075 mg/kg). Most drugs were given intravenously. Non-pharmacological interventions included gastric aspiration and P6 acupoint stimulation.

Two authors independently performed the study selection.

Assessment of study quality
The authors did not state that they assessed validity, but they did address the potential impact of study quality on outcomes in their analysis. Only double-blind RCTs were included and these were assessed as to whether they were analysed on an intention-to-treat or per-protocol basis.

Data extraction
Study interventions, dose and data required to calculate odds ratios (ORs) were extracted from the included studies. In trials where more than one dose of a drug was administered, the overall effect of the drug was derived from combining all groups receiving the drug. The authors did not state how data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
Fixed-effect summary ORs were calculated for the effect of each drug, using the Mantel-Haenszel method. Statistical heterogeneity was assessed using the $I^2$ and $Q$ statistics. Publication and other biases were investigated with the use of funnel plots and the regression test proposed by Egger et al.

Sensitivity analyses were performed by excluding trials with methodological flaws (significant losses to follow-up and inappropriate early termination) or with protocols that varied from other included studies. Regression analysis was used to examine the effect of drug-dose on treatment effect.

**Results of the review**
A total of 22 trials (n=4112) were included in the review.

Statistically significant prophylactic anti-emetic effects were observed for dexamethasone (OR 0.23, 95% CI: 0.16, 0.33, nine trials) and also for the serotonergic antagonists: ondansetron (OR 0.36, 95% CI: 0.29, 0.46, 10 trials); granisetron (OR 0.11, 95% CI: 0.06, 0.18, three trials); tropisetron (OR 0.15, 95% CI: 0.06, 0.35, two trials); and dolasetron (OR 0.25, 95% CI: 0.10, 0.59, one trial). Significant effects were also observed for metoclopramide (OR 0.51, 95% CI: 0.34, 0.77, four trials).

Significant heterogeneity was found for ondansetron ($I^2=57.2\%, p=0.013$). Regression analysis showed a dose-response effect of ondansetron.

Significant reductions in post-operative vomiting were reported by one trial of perphenazine (OR 0.50, 95% CI: 0.31, 0.82) and one trial of midazolam (OR 0.54, 95% CI: 0.31, 0.93).

No significant anti-emetic effects were observed for dimenhydrinate (one trial) or droperidol (one trial). Similarly, no significant effects were found for gastric aspiration (one trial) or acupuncture (three trials).

**Authors' conclusions**
There is good evidence that dexamethasone and the serotonergic antagonists ondansetron, granisetron, and tropisetron are effective agents for the prophylactic control of post-operative vomiting in children after tonsillectomy, with or without adenoidectomy. There is also evidence that metoclopramide is effective. Some evidence supports the effectiveness of perphenazine and midazolam, but this has not been corroborated. There is currently insufficient evidence to support the effectiveness of dimenhydrinate, droperidol, gastric aspiration or acupuncture in this setting.

**CRD commentary**
The review question was clearly defined in terms of study designs, participants, interventions and outcomes. The search for relevant literature covered the major electronic databases and other sources. Data from the included studies were provided in adequate detail. As inclusion was limited to English language publications, the potential for missing non-English publications could not be entirely ruled out. Also, it is not clear if attempts were made to minimise error and bias in the data extraction process (as they were in the selection of studies). The authors synthesised the studies using appropriate statistical methods, taking into account clinical and statistical heterogeneity. Although validity was not assessed using a formal checklist, only double-blind RCTs were included in the review and key aspects of study quality were investigated in sensitivity analyses. Given the evidence presented, the authors' conclusions appear reliable.

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

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