How much does pharmacologic prophylaxis reduce postoperative vomiting in children?
Calculation of prophylaxis effectiveness and expected incidence of vomiting under treatment
using Bayesian meta-analysis
Engelman E, Salengros J C, Barvais L

CRD summary
The authors apparently concluded that combination treatments to prevent postoperative vomiting in children were superior to single-drug treatments and that a 5-hydroxytryptamine-receptor antagonist combined with dexamethasone or droperidol reduced vomiting by about 80%. Given the methodological problems in the review, including the limited search, failure to assess study quality and use of indirect comparisons, the results may not be reliable.

Authors' objectives
To estimate the relative effectiveness of different pharmacological interventions for preventing postoperative vomiting in children.

Searching
PubMed was searched for studies. Search terms were reported. Reference lists of studies retrieved and four recent systematic reviews were handsearched.

Study selection
Controlled trials in a postoperative setting of single-drug or combination treatments for management of postoperative nausea and vomiting in children (aged up to 18 years) were eligible for inclusion if the treatment was listed in the Guidelines for the Management of Postoperative Nausea and Vomiting (Gan 2007) and the comparator was placebo or (for combination treatments) one of the drugs in the combination.

Participants in the included studies were surgical patients aged from one month to 18 years (where reported). The type of surgery varied, but was most commonly tonsillectomy or strabismus. Interventions used included ondansetron (0.1 to 0.3mg/kg), tropisetron (0.5 to 0.2mg/kg), granisetron (40µg/kg), dolasetron (0.35 to 0.5mg/kg), dexamethasone (0.05 to 0.25mg/kg) and droperidol (5 to 25µg/kg), alone or in combination. Studies that used doses not recommended in the Guidelines (Gan 2007) were excluded. In most cases the drugs were administered intravenously during surgery; some were given orally preoperatively. The review outcome was vomiting, which included a range of emetic events (vomiting, retching, nausea and need for antiemetics) if these were part of the endpoint in the primary study. Some studies explicitly excluded events such as retching from analysis. Several studies excluded from analysis children with a history of travel sickness, previous nausea or vomiting, or preoperative emesis. Duration of follow up was 24 hours in most studies.

The authors stated neither how the papers were selected for the review nor how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Data were extracted on the number of events in the control and intervention groups of each study. The authors stated neither how the data were extracted for the review nor how many reviewers performed the data extraction.

Methods of synthesis
Studies were combined in a Bayesian meta-analysis. This was sequential: the study with the earliest publication data was assumed to have a non-informative prior probability and then the log odds ratios of successive studies were added in one at a time. The updated odds ratios and 95% credible intervals (CrI) were reported after the inclusion of each trial. Odds ratios were converted to relative risks and these were used to estimate the risk of vomiting for children in the
baseline risk categories of a published paediatric risk scale (Eberhart 2004) by estimating the lowest and highest risk values for a child from a given category. An indirect comparison was used to estimate relative risks for combination treatments that were not tested against a placebo. Sensitivity analyses were used to check the robustness of the choice of the initial prior distribution by repeating analyses using a sceptical prior probability based on the relative risk reduction reported in trials with adult patients.

**Results of the review**

Fifty controlled trials were included (n=approximately 6,437).

**Intervention versus placebo:** All except six trials showed a statistically significant reduction in vomiting symptoms for the study drug compared with placebo. The pooled odds ratio (OR) for each of the drug versus placebo comparisons also showed statistically significant reductions in the odds of vomiting when compared with placebo. The final ORs from the Bayesian models were: ondansetron 0.37 (95% CrI: 0.35 to 0.39; 14 trials); tropisetron 0.17 (95% CrI: 0.13 to 0.22; five trials); dolasetron 0.16 (95% CrI: 0.09 to 0.27; two trials); granisetron 0.16 (95% CrI: 0.10 to 0.20; three trials); dexamethasone 0.31 (95% CrI: 0.28 to 0.34; 13 trials); droperidol 0.48 (95% CrI 0.37 to 0.61; three trials).

**Combination treatments:** The lowest risk of vomiting was associated with combination treatments, with relative risks as follows: ondansetron plus droperidol 0.22 (95% CrI: 0.10 to 0.45 direct comparison; one trial), ondansetron plus dexamethasone 0.22 (95% CrI: 0.07 to 0.61 direct comparison) 0.17 (95% CrI: 0.14 to 0.21, indirect comparison) (five trials); granisetron plus dexamethasone 0.10 (CrI: 0.02 to 0.47, direct comparison; one trial); tropisetron plus dexamethasone 0.20 (95% CrI: 0.14 to 0.30, indirect comparison; two trials); dolasetron plus dexamethasone 0.21 (95% CrI: 0.12 to 0.39, indirect comparison; one trial).

Sensitivity analyses that used a sceptical prior probability showed almost identical results for ondansetron and dexamethasone, but increased the OR for other comparisons. The review also reported the most optimistic and the most pessimistic estimated risk of vomiting associated with each intervention at specific paediatric risk categories.

**Authors’ conclusions**

The authors apparently concluded that combination treatments to prevent postoperative vomiting in children were superior to single-drug treatments and that a 5-hydroxytryptamine-receptor antagonist combined with dexamethasone or droperidol reduced vomiting by about 80%.

**CRD commentary**

The objectives and inclusion criteria of the review were clear, but the reason for the exclusion of a number of studies was not explained clearly. The search was limited to one database and it did not appear that efforts were made to locate unpublished studies, so studies may have been missed and the review may have been prone to publication bias. It was unclear whether the search was restricted by language. The search dates were not reported. The processes used to select studies and extract data were not described and so it was unclear whether steps were taken to minimise the risk of reviewer bias and error by having more than one reviewer make decisions independently. It did not appear that study validity was assessed. These factors make it difficult to evaluate the reliability of the evidence presented. The authors used a Bayesian meta-analysis, but did not appear to have used standard Bayesian meta-analysis techniques or software, and without presenting forest plots or results for each individual study it was difficult to assess the appropriateness of the methods. There was no assessment of statistical heterogeneity. Indirect comparisons were used, although the authors acknowledged the limitations of these methods. No clearly stated conclusion was reported. Given the methodological problems in the review, including the limited search, failure to assess study quality and use of indirect comparisons, the results may not be reliable.

**Implications of the review for practice and research**

**Practice:** The authors stated that tables in the review could be used with baseline risk values from any source to guide cost-effectiveness evaluation of different drugs for the prevention of postoperative vomiting in children.

**Research:** The authors did not state any implications for further research.
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