Efficacy, dose-response, and adverse effects of droperidol for prevention of postoperative nausea and vomiting
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Authors' objectives
To estimate the efficacy and harm produced by droperidol in the prevention of post-operative nausea and vomiting (PONV).

Searching
MEDLINE from 1996 (last search May 1999), EMBASE from 1982 (last search March 1999), and the Cochrane Library (Issue 2, 1999), were searched using different search strategies and the following free text keywords: 'droperidol'; 'nausea' or 'vomiting' or 'emesis'; 'random'; and 'surgery' or 'anesthesia' or 'post-operative'. Studies reported in any language were considered. Additional trials were identified from the reference lists of retrieved reports, and review articles on PONV and droperidol, and by manually searching locally available journals on anaesthesia.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs). Only trials that reported end points of interest in dichotomous form were included. Data from abstracts, letters, review articles, and studies of animals were not considered. One study, where only six participants per group were analysed, was excluded.

Specific interventions included in the review
Prophylactic droperidol versus placebo or 'no treatment'. Studies looking at the efficacy of droperidol as a treatment of established PONV were excluded. Twenty-four different regimens of droperidol were used by the included studies; these included administration via oral, intramuscular and intravenous routes. The dosage used in adults ranged from 0.25 to 0.30 mg, to 5.4 mg. The dosage used in children ranged form 5 to 20 microg/kg, to 300 microg/kg.

Participants included in the review
Surgical patients who have received both general anaesthesia or combined, spinal and general anaesthesia. Studies which pooled data from adults and children were excluded.

Outcomes assessed in the review
Prevention of early nausea and vomiting (including retching), and adverse effects. The review did not take into account the following outcomes because the end points were inconsistently reported: nausea scores; the number of vomiting episodes, or the time to the first vomiting episode; the number of patients needing anti-emetic rescue medication; delay until discharge, post hoc analyses; stratified analyses (e.g. by gender); or scores of the patients' satisfaction.

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

Assessment of study quality
The 3-item, 5-point scale of Jadad et al. (see Other Publications of Related Interest no.1) was used to assess the included studies. The authors scored each included study independently and consensus was reached by discussion.

Data extraction
Data were extracted for the following categories: patients, surgery, dose and route of administration of droperidol, study end points, and adverse effects.
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction. The cumulative incidence of PONV was extracted for two time periods, within 6 hours after surgery and within 24 hours. The data were examined separately for the adults and children.

### Methods of synthesis

**How were the studies combined?**

The combined data were analysed using the relative risk (RR) and the numbers-needed-to-treat (NNT), both with 95% confidence intervals (CIs). For the pooled RR, a fixed-effect model was used to combine the data when there were no more than two trials, or when there was no significant heterogeneity (i.e. P>0.1). A random-effects model was used in all other situations, according to the DerSimonian and Laird method (see Other Publications of Related Interest no.2). If any cell of a sample was zero, then 0.5 was added to all cells of that sample to calculate the RR.

Sensitivity analyses were undertaken by calculating the RR and NNT for the nausea and vomiting outcomes separately, for the best-documented regimens within two predefined ranges of control event rates: early outcomes within 20 and 60% of the control event rate, and late outcomes within 40 and 80% of the control event rate. There was an attempt to test the evidence for dose responsiveness using pre-set criteria (see Other Publications of Related Interest no.3).

**How were differences between studies investigated?**

Heterogeneity of the data was explored graphically. This showed the scatter of the event rates (incidence of PONV) with droperidol versus the event rates with control.

### Results of the review

Seventy-six RCTs with 13,352 patients: 5,351 received droperidol, 3,372 received placebo or 'no treatment', and 4,629 received another anti-emetic intervention. Forty-seven trials were in adults, of which 29 were in women only. Twenty-nine studies were conducted in children.

The median quality score of the included trials was 3 (range: 1 to 5). The major methodological problem was the important variability in the control event rates among the trials, which may reflect differences in the underlying risk.

Qualitative analysis.

The scatter in the event rates shown for both the early and late outcomes suggested that improved efficacy was obtained with droperidol, compared with placebo. The average incidence of early nausea was 16% with droperidol and 33% with placebo. The average incidence of early vomiting was 14% with droperidol and 29% with placebo. The average incidences of late nausea were 45 and 58% with droperidol and placebo, respectively. The average incidences of late vomiting were 28 and 46% with droperidol and placebo, respectively.

Quantitative analysis.

Overall, droperidol was found to be more efficacious than placebo in preventing PONV.

In adults, the anti-nausea effect was short-lived, and there was no dose-responsiveness; for a dose of 0.25 to 0.30 mg, the NNT to prevent early nausea was 5. However, there was dose-responsiveness for both early and late anti-vomiting efficacy; the best efficacy was obtained with a dose of 1.5 to 2.5 mg, for which the NNT was 7.

In children, there was dose-responsiveness; the best efficacy was obtained with a dose of 75 microg/kg, for which the NNT to prevent early and late vomiting was 4. The next lower dose tested in children, 50 microg/kg, showed less efficacy in both the short- and long-term, although this dose was tested in a limited number of patients only. The slightly decreased efficacy at 24 hours (NNT 4.4 with 50 microg/kg versus NNT 3.8 with 75 microg/kg) may not be perceived as clinically relevant.

Adverse drug reactions.

Two children had extrapyramidal symptoms with droperidol; the NNT was 91 in children, and 408 in any patient. There
was dose-responsiveness for sedation and drowsiness; the NNT was 7.8 for a dose of 2.5 mg. Droperidol prevented post-operative headache (NNT -25).

**Authors' conclusions**

Droperidol is anti-emetic in the surgical setting. The effect on nausea is short-lived, but more pronounced than the effect on vomiting. In terms of adverse effects, sedation and drowsiness are dose-dependent, extrapyramidal symptoms are rare, and there is a protective effect against headache.

**CRD commentary**

This appeared to be a fairly well-conducted review. The aims were clearly stated. The search strategy appeared to be fairly comprehensive. However, no attempt was made to locate unpublished data and the possibility of publication bias cannot be ruled out. Information about the review process was presented, although it was not reported how the data were extracted or how many of the reviewers were involved in the process. The validity of the included trials was assessed. Details of the primary studies were not presented, but the results for all of the different regimens of droperidol used were summarised in a tabular format; this included the p-value relating to statistical heterogeneity. The review also did not report the age category used to define 'children'.

The authors' conclusions appear to follow from the results.

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

**Practice:** The authors state that for adults, repeated boluses of low doses of droperidol (e.g. 0.5 mg intravenous, 12-hourly) should be used to control post-operative nausea. They also note that for children, 50 microg/kg may be considered as the best prophylactic dose when sedation and drowsiness should be prevented.

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

**Bibliographic details**


**PubMedID**
10875717

**DOI**
10.1007/BF03018945

**Original Paper URL**
http://www.cja-jca.org/cgi/content/full/47/6/537

**Other publications of related interest**


**Indexing Status**

Subject indexing assigned by NLM

**MeSH**
AccessionNumber
12000002053

Date bibliographic record published
30/06/2002

Date abstract record published
30/06/2002

Record Status
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