Dimenhydrinate for prophylaxis of postoperative nausea and vomiting: a meta-analysis of randomized controlled trials

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Authors' objectives
To evaluate dimenhydrinate in the prophylaxis of post-operative nausea and vomiting (PONV).

Searching
The Cochrane Library, MEDLINE and EMBASE were searched up to June 2001 with no language restrictions. The free text search terms employed included 'dimenhydrinate', 'diphenhydramine', 'dramamine' and 'nausea' or 'vomiting' or 'emesis'. The reference lists of retrieved reports, review articles and locally available anaesthesia journals were examined for additional reports.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion in the review.

Specific interventions included in the review
Studies that compared the efficacy of dimenhydrinate with an inactive control for the prophylaxis of PONV were eligible for inclusion. For adults, dimenhydrinate was administered as a single intravenous (i.v.) or intramuscular (i.m.) dose of 1 to 2 mg/kg, with a repetition (1 or 3 times 1.2 mg/kg rectal or i.v.) after the initial 1 mg/kg i.v. For children, dimenhydrinate was administered as either a single i.v. or i.m. dose of 0.5 to 2.2 mg/kg, or as a rectal dose of 2 to 3 mg/kg.

Participants included in the review
The participants included both adults and children in the surgical setting. Adults and children were analysed as separate subgroups.

Outcomes assessed in the review
The main outcome assessed was the number of patients that stayed completely free of PONV, which was defined as absence of any nausea, retching or vomiting. The secondary outcomes assessed were the absence of post-operative nausea (PN), post-operative vomiting (PV) and side-effects. The outcomes were assessed for two post-operative intervals: 'early' (the first 6 hours post-operatively) and 'overall' (the first 48 hours post-operatively).

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 Oxford scale of Jadad et al. (see Other Publications of Related Interest), which assigns trials a value from 1 up to a maximum of 5 points, was used to assess study validity. The authors do not state who performed the validity assessment.

Data extraction
Two of the review's authors independently extracted the data from each study.

Data were extracted on the absence of PN, PV and PONV, and what the authors refer to as 'other relevant features'. If the extracted data were conflicting they were checked, and any further disagreements were resolved through discussion with a third author. Relative benefits (RB) were calculated for each study, along with 95% confidence intervals.
methods of synthesis
How were the studies combined?
The studies were pooled statistically in a meta-analysis, using a random-effects model to calculate the combined RB with 95% CIs across the whole participant population. The pooled results were analysed for the main outcome of PONV. The number-needed-to-treat with 95% CIs was also calculated, as an estimate of the clinical relevance of any difference between the intervention and control.

How were differences between studies investigated?
The authors do not report a formal test for heterogeneity, but subgroup analyses were conducted according to three main subgroups: application modes (single versus repetitive doses), routes of application (i.m. versus i.v. versus rectal) and age (children versus adults), and also according to the ‘early’ and ‘overall’ observation interval to narrow the inter-study variety.

Results of the review
Eighteen RCTs with 3,045 participants (intervention = 1,387, control = 1,658) were included in the review.

The median Jadad score was 4 (range: 1 to 5). For the main outcome of PONV for the whole population, 8 RCTs demonstrated that dimenhydrinate was associated with a higher incidence of patients without emetic symptoms in the ‘early’ observation period (RB 1.21, 95% CI: 1.07, 1.35). Six trials found a significant benefit for PV for patients receiving dimenhydrinate versus placebo (RB 1.20, 95% CI: 1.03, 1.40). Two trials only reported PN and the results were not significant.

For the ‘overall’ first 48 hours post-operatively, 16 RCTs found a significant benefit for patients treated with dimenhydrinate versus placebo (RB 1.51, 95% CI: 1.27, 1.78). Fourteen RCTs found a significant benefit in favour of dimenhydrinate versus placebo for PV (RB 1.45, 95% CI: 1.22, 1.72), while 7 trials found a significant benefit in favour of dimenhydrinate versus placebo for PN (RB 1.32, 95% CI: 1.03, 1.70).

No major harm associated with the use of dimenhydrinate was reported by any of the studies, but owing to the sparse reporting of side-effects, no pooled statistical analysis was undertaken.

‘Overall’ first 48 hours post-operatively for the different subgroups.

For adults given a single application of dimenhydrinate (i.v. or i.m., 1 to 2 mg/kg), the pooled data from 3 RCTs gave a statistically-significant RB of 1.20 (95% CI: 1.01, 1.42) in favour of dimenhydrinate, versus placebo. A further 6 RCTs with a repetition (1 or 3 times 1.2 mg/kg rectal or i.v.) after the initial dose of 1 mg/kg gave a significant result in favour of dimenhydrinate versus placebo (RB 1.55, 95% CI: 1.05, 2.29). There was a non significant trend favouring the latter regimen.

For children, the pooled data from 3 RCTs demonstrated that a single i.v. or i.m. application of 0.5 to 2.2 mg/kg was as effective (RB 1.80, 95% CI: 1.31, 2.47) as a single rectal application of a dose of 2 to 3 mg/kg (RB 1.71, 95% CI: 1.16, 2.53).

Authors’ conclusions
Dimenhydrinate is worthwhile considering when an inexpensive anti-emetic is needed. The anti-emetic efficacy exceeds a placebo effect, and is in the range that may be considered clinically relevant. However, to obtain relevant absolute risk reduction it seems essential to limit its use to patients who are prone to suffer from PONV. While it has been in use for a long-time, the dose-response is unclear. Repeating the application of dimenhydrinate may be associated with increased benefit in adults. Serious side-effects seem to be rare.
The review question and the study selection criteria were clearly stated. The literature search seemed reasonably comprehensive, with no language restrictions being applied. The authors provided no details on the study selection and validation processes, but otherwise, gave adequate details regarding the data extraction methods. However, relevant details of the included participants (such as type of surgery) were not provided. The statistical tests employed seemed appropriate for the analyses undertaken, and there was ample and clear presentation of the findings and a good discussion of the data.

The authors’ conclusions seem appropriate in the light of the data presented.

Implications of the review for practice and research
Practice: The authors state that dimenhydrinate is worthwhile considering when an inexpensive anti-emetic is needed.
Research: The authors did not state any implications for further research.

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Other publications of related interest

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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.