Evaluation of the effective drugs for the prevention of nausea and vomiting induced by morphine used for postoperative pain: a quantitative systematic review

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Authors' objectives
To conduct a meta-analysis of the randomised controlled trials (RCTs) on the use of prophylactic drug therapy for post-operative nausea and vomiting (PONV), in patients receiving morphine for the treatment of post-operative pain.

Searching
MEDLINE (from 1966 to February 2000) and the Cochrane Library (Issue 1, 2000) were searched for relevant papers. Details of the search terms used are given in the original paper. The search was restricted to English language publications.

Study selection
Study designs of evaluations included in the review
Parallel placebo-controlled RCTs were included.

Specific interventions included in the review
Studies were included if the evaluated drug was given intravenously for the purpose of preventing PONV. The specific drugs included in the review were droperidol, metoclopramide, dexamethasone, propofol and ondansetron.

Participants included in the review
The studies had to include patients who were aged over 18 years and were given morphine to control post-operative pain. The characteristics of the participants were not reported.

Outcomes assessed in the review
Studies were included if ‘the presence or absence of nausea and/or vomiting’ was used as the end point.

How were decisions on the relevance of primary studies made?
Two of the authors assessed the papers for inclusion, and any disagreements were resolved through discussion.

Assessment of study quality
The primary studies were evaluated using the scoring system of Jadad et al. (see Other Publications of Related Interest no.1). Only studies which received a score of 3 or more points were included in the analysis. Two of the authors assessed the quality of the papers, and any disagreements were resolved through discussion.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

Data were extracted on: reference details; validity scores; setting, in terms of the type of surgery or procedure; the number of patients in each study arm; the type of opioid medication; the opioid dosage; the type of active treatment; initial and maintenance dose; the control (placebo); observation period; the number of events in each treatment arm; and the percentage of patients responding to treatment.

Methods of synthesis
How were the studies combined?
The odds ratio (OR) and 95% confidence intervals (CIs) were calculated for each study. Where studies were found to
be heterogeneous, a pooled OR and 95% CI was calculated using Peto's fixed-effect model (see Other Publications of Related Interest no.2). Studies were pooled according to the active treatment used.

How were differences between studies investigated?
Heterogeneity between studies was determined using a Q-test with a significance level set at 10%.

Results of the review
Twenty studies with 31 active drug versus placebo comparisons were included in the review. The active drug was droperidol in 11 comparisons, metoclopramide in 5 comparisons, dexamethasone in 6 comparisons, propofol in 4 comparisons, and ondansetron in 5 comparisons.

Significant heterogeneity was only found between studies which compared ondansetron with placebo (Q=18.30, d.f.=4, p<0.01). These studies were combined using a random-effects model.

The results of the meta-analysis for droperidol indicated an OR of 0.27 (95% CI: 0.21, 0.34, p<0.00001), with a highly significant decrease in nausea and vomiting when compared with the placebo group. The OR was 0.48 (95% CI: 0.30, 0.75, p<0.001) for metoclopramide, and 0.23 (95% CI: 0.15, 0.35, p<0.00001) for dexamethasone. The results for propofol indicated an OR of 1.09 (95% CI: 0.61, 1.95, p<0.8) with no significant increase in the incidence of nausea and vomiting. The results for ondansetron indicated an OR of 0.40 (95% CI: 0.13, 1.22, p<0.11), with a decreased tendency for nausea and vomiting when compared with the placebo group, although there was no significant difference in the incidence of PONV.

Authors' conclusions
The results suggested that dexamethasone, droperidol and metoclopramide were effective in prophylactic treatment for PONV. Of these three, dexamethasone provided the best results.

CRD commentary
The literature search covered more than one database, but the failure to identify studies through other sources and the exclusion of non-English language papers may have led to publication bias. The inclusion criteria were appropriate and were applied by more than one reviewer. The validity of retrieved studies was assessed, with only higher quality studies being included in the meta-analysis. The data extracted were appropriate, although it was unclear how many reviewers performed the data extraction. The authors duplicated some information: e.g. Gan, 1995 (wrongly presented as Gon, 1994 in the tables) was reported as 3 separate trials with 20 treatment participants and 20 controls; the actual number of participants in the study was 80 (3 treatment groups of 20, plus 20 control individuals). Thus, some of the tests for heterogeneity were incorrect. In addition, the pooling of this data were incorrect, thus invalidating the results for droperidol, metoclopramide and dexamethasone. The authors have also wrongly reported a p-value of 0.00001 for ondansetron. A re-analysis of this data using RevMan software produced a p-value of 0.11. The results and conclusions of this review should be treated with extreme caution, given that the data were not analysed correctly.

Implications of the review for practice and research
Practice: The authors state that dexamethasone was shown to be the agent with the best evidence, and that a dose of 1.25 to 10 mg dexamethasone was able to decrease the incidence of PONV from 56 to 80%, to 16 to 50% (OR 0.23). They also appear to state that the adverse events associated with each anti-emetic should be considered when choosing such prophylactic agents in PONV. The adverse events highlighted were delayed post-operative wound healing or infection due to a steroid dexamethasone, over sedation due to droperidol, and parkinsonism due to metoclopramide.

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

Bibliographic details
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