The impact of prophylactic dexamethasone on nausea and vomiting after laparoscopic cholecystectomy: a systematic review and meta-analysis

Karanicolas PJ, Smith SE, Kanbur B, Davies E, Guyatt GH

CRD summary
This review concluded that prophylactic dexamethasone decreased the incidence of postoperative nausea or vomiting after laparoscopic cholecystectomy (gallbladder removal) compared with placebo, and may decrease the severity of postoperative pain, whilst not increasing the incidence of headaches or dizziness. These conclusions reflected the results of the review and appear likely to be reliable.

Authors' objectives
To assess the effect of prophylactic corticosteroid administration on postoperative nausea, vomiting, pain and complications in patients undergoing laparoscopic cholecystectomy (gallbladder removal).

Searching
MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL) and Web of Science were searched without language restrictions from 1966 to April 2007. Search terms were reported. References of identified studies, reviews and major textbooks were checked. Two indices of conference proceedings and www.clinicaltrials.gov were searched and experts in the field were contacted.

Study selection
Randomised controlled trials (RCTs) or quasi-RCTs that compared perioperative corticosteroid administration with placebo or other treatment in patients undergoing laparoscopic cholecystectomy who did not regularly take corticosteroids were eligible for inclusion. Eligible trials had to assess at least one of the following outcomes: nausea, vomiting, pain, quality of life, postoperative complications, and/or length of hospital stay. Trials including other surgical procedures were included if data were reported separately for patients undergoing laparoscopic cholecystectomy. Corticosteroids could be administered orally, intravenously or rectally, but administration had to include at least one dose taken within 24 hours of surgery and not given in response to symptoms.

Most included trials enrolled relatively healthy patients (American Society of Anaesthesiologists class I or II) undergoing general anaesthesia for laparoscopic cholecystectomy. Most of the included patients were female and relatively young. All the included trials used a single intravenous dose of dexamethasone (2mg to 16mg), administered between 90 minutes before induction of anaesthesia and the end of the procedure. Comparators were placebo, metoclopramide, ondansetron, granisetron or a combination of these. The use of rescue emetics and analgesia was also evaluated in addition to the outcomes detailed above.

Two reviewers assessed the studies for inclusion and disagreements were resolved through discussion.

Assessment of study quality
Two reviewers assessed the studies for validity using the criteria of allocation concealment, blinding of patients, clinicians and assessors, and losses to follow-up. Disagreements were resolved through discussion.

Data extraction
Data were extracted to permit the calculation of relative risks (RR) with 95% confidence intervals (CI) for dichotomous outcomes. For the continuous outcome of pain, mean differences with 95% confidence intervals were extracted or calculated. Where trials reported medians and ranges, the authors estimated means and standard deviations. Where event occurrence was divided into time intervals, the interval between zero to six hours postoperatively was considered "early", and that approximating closest to 12 to 24 hours was considered "late". Authors were contacted for additional data, where necessary.

Two reviewers extracted the data using standardised forms. Disagreements were resolved through consensus.
Methods of synthesis
Random-effects model meta-analyses were used to calculate pooled relative risks with 95% confidence intervals and the ratio of means for the outcome of pain. The standardised mean difference (SMD) was also calculated for pain and back-translated to a scale from 0 to 100. Where trials contained more than two arms, data were analysed without repeated use of any group. Statistical heterogeneity was assessed using the Breslow-Day test and the $I^2$ statistic.

A sensitivity analysis excluding a trial over which there were methodological concerns was performed.

Publication bias was assessed using funnel plot analysis.

Results of the review
Sixteen trials were included in the review. Sample sizes ranged from 43 to 5,199 (although this large trial included only 397 patients undergoing laparoscopic cholecystectomy); 2,174 patients were included in the analysis. The quality of the trials was generally high, with all except two trials reporting blinded outcome assessment, and all except one trial reporting no or minimal loss to follow-up. Most trials also used blinding.

The dexamethasone groups had a statistically significantly lower rate of nausea (RR 0.59, 95% CI 0.48 to 0.72), vomiting (RR 0.41, 95% CI 0.30 to 0.55) and postoperative nausea or vomiting (RR 0.55, 95% CI 0.44 to 0.67) compared to placebo. There was moderate heterogeneity in the nausea and vomiting analysis ($I^2$=32.7%), which was partly explained by the dose of dexamethasone but not explained by concomitant anti-emetics. There were reductions in the rates of nausea and vomiting in both the early and late postoperative periods. Patients in the dexamethasone groups also required less anti-emetics than those in control groups (RR 0.40, 95% CI 0.19 to 0.88), although there was a high degree of unexplained heterogeneity ($I^2$=81.9%).

Doses of 8mg to 16mg were statistically significantly more effective in reducing postoperative nausea or vomiting than doses of 2mg to 5mg (p = 0.002).

Patients in groups treated with dexamethasone experienced a moderate reduction in postoperative pain compared with placebo groups (ratio of means 0.87, 95% CI 0.78 to 0.98), although there was no statistically significant difference in the requirement for rescue analgesia. There was significant heterogeneity for both measures.

There were no statistically significant differences between dexamethasone and placebo groups in the incidence of headache and dizziness (the most commonly reported adverse events) or in any other adverse events.

Results of comparisons between dexamethasone and other anti-emetics were also reported for trials that assessed individual comparisons.

Authors’ conclusions
Prophylactic dexamethasone decreased the incidence of postoperative nausea or vomiting after laparoscopic cholecystectomy compared with placebo and may decrease the severity of postoperative pain. Dexamethasone did not increase the incidence of headaches or dizziness.

CRD commentary
The review question and inclusion criteria were clear. The authors searched several relevant databases and other sources without language restrictions and made systematic attempts to locate unpublished studies. These measures reduced the chances of relevant studies being omitted or selection biases introduced into the review. The authors reported using methods designed to reduce reviewer bias and error at all stages of the review process.

Trial quality was assessed using appropriate criteria. The use of meta-analysis appeared appropriate and measures to assess and explore heterogeneity were undertaken.

The authors’ conclusions reflected the results of the review and appear likely to be reliable.
Implications of the review for practice and research

**Practice:** The authors stated that surgeons should consider the prophylactic administration of corticosteroids to patients undergoing laparoscopic cholecystectomy, particularly those at high risk of postoperative nausea or vomiting.

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

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