Dexamethasone for the prophylaxis of postoperative nausea and vomiting associated with neuraxial morphine administration: a systematic review and meta-analysis

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CRD summary
The authors concluded that a single dose of intravenous dexamethasone 5mg to 10mg was an effective antiemetic in women receiving neuraxial morphine for caesarean delivery or abdominal hysterectomy. Possible publication bias suggested the findings should be interpreted with caution. The evidence base was generally small and the authors’ recommendation to interpret the findings with caution seems appropriate.

Authors' objectives
To assess the prophylactic efficacy of an antiemetic (dexamethasone) in patients receiving neuraxial anaesthesia with neuraxial morphine.

Searching
MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) and Web of Science were searched up to February 2011 without language restrictions. The search strategy was reported. Reference lists of retrieved articles were searched manually.

Study selection
Eligible studies were randomised controlled trials (RCTs) that compared the efficacy of a single dose of intravenous dexamethasone with placebo in patients receiving neuraxial anaesthesia with neuraxial morphine. The main outcome was postoperative nausea and vomiting. Other outcomes included pruritus and/or need for rescue antipruritic treatment, pain scores assessed at four hours (early) and 24 hours (late) or the closest reported time interval and/or the need for rescue analgesics. Patients who received another antiemetic alone or in combination with dexamethasone were excluded from analysis.

Included trials were conducted in Taiwan and the UK in female patients only. Patients received neuraxial morphine (epidural or intrathecal) for abdominal hysterectomy or caesarean delivery. Dexamethasone was given at doses between 2.5mg and 10mg. Six trials administered dexamethasone at the end of surgery before neuraxial morphine and two trials administered dexamethasone after neuraxial morphine. All trials administered postoperative rescue antiemetics and analgesics. Six trials also administered postoperative rescue antipruritics. Placebo groups received saline. Treatment-related side effects were reported.

The authors did not explicitly state how many reviewers screened studies for inclusion. They mentioned that they followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations.

Assessment of study quality
Two reviewers independently assessed trial quality using the Cochrane risk of bias tool. Discrepancies were resolved through referral to a third reviewer.

Data extraction
Dichotomous data were extracted to calculate relative risks and 95% confidence intervals. For continuous outcomes means and standard deviations were extracted or estimated to calculate mean differences and 95% confidence intervals. Where trials reported postoperative nausea and postoperative vomiting at different time intervals, the highest incidence was extracted for both outcomes.

Pain scores recorded using zero to 100mm visual analogue scales were converted to an 11-point scale from zero (no pain) to 10 (worst pain). Authors were contacted for clarification on data where necessary.

One reviewer extracted data and two reviewers independently checked the extraction for accuracy.
Methods of synthesis
Where appropriate, a fixed-effect model was used to pool relative risks (RRs) and mean differences and their 95% confidence intervals (CIs). The number needed to treat (NNT) was calculated for dichotomous data for the primary outcomes.

Statistical heterogeneity was assessed using the I² statistic (>50% represented significant heterogeneity). Subgroup analyses were performed on different dexamethasone doses, surgical procedures and route of administration of neuraxial morphine where reported by two trials or more. Meta-regression was performed to assess whether there was a dose-response relationship for dexamethasone.

Where data could not be synthesised quantitatively, data were presented as a narrative synthesis. Publication bias was assessed for primary outcomes using funnel plots and Egger’s test.

Results of the review
Eight RCTs (768 patients) were included in the review. All trials were blinded and were free of selective reporting. Seven trials addressed incomplete data, one trial had adequate allocation concealment and seven had inadequate allocation concealment. Six trials had adequate sequence generation and two were unclear.

Postoperative vomiting and nausea: Dexamethasone statistically significantly reduced the incidence of postoperative nausea compared to placebo (RR 0.57, 95% CI 0.45 to 0.72; eight RCTs; NNT=six) and postoperative vomiting compared to placebo (RR 0.56, 95% CI 0.43 to 0.72; seven RCTs; NNT=seven). Dexamethasone doses of 5mg, 8mg and 10 mg showed statistically significant reductions for both outcomes but the 2.5mg dose did not. There was no evidence of statistical heterogeneity for either outcome.

Meta-regression showed no evidence of a dose-response relationship for either outcome. Subgroup analyses did not significantly alter the findings except for studies in which intrathecal morphine was administered which showed no statistical difference between treatment groups for either outcome.

Postoperative rescue treatment: Dexamethasone statistically significantly reduced use of postoperative rescue antiemetic therapy compared to placebo (RR 0.47, 95% CI 0.36 to 0.61; eight RCTs; figures as reported in the text) and postoperative rescue analgesics compared to placebo (RR 0.76, 95% CI 0.62 to 0.93; eight RCTs). There was no evidence of statistical heterogeneity.

Other secondary outcome and subgroup analyses results were reported in the review. There was evidence of publication bias for both postoperative vomiting and nausea according to funnel plots and Egger’s test.

Authors’ conclusions
The evidence indicated that a single dose of intravenous dexamethasone 5mg to 10mg was an effective antiemetic in women receiving neuraxial morphine for caesarean delivery or abdominal hysterectomy. Dexamethasone improved postoperative analgesia compared to placebo but was not an effective antipruritic. In light of possible publication bias, the findings need to be interpreted with caution.

CRD commentary
The review question and criteria were reported clearly. It appeared that a satisfactory literature search was undertaken without language restrictions. Assessment of publication bias in fewer than 10 studies may not be robust (as acknowledged by the authors). Data extraction and quality assessment was performed in duplicate but the process was not explicitly stated for screening of studies. Trial quality was assessed and all except one of the included trials appeared to be at high risk of bias due to inadequate allocation concealment.

There was clinical and methodological heterogeneity between trials. The authors went some way to investigate this using subgroup analyses but statistical heterogeneity was not reported for some of these outcomes so it was unclear whether a fixed-effect model was appropriate to pool data and whether use of a random-effects model would have altered the findings significantly. The evidence base was generally small and in women only. The authors highlighted that seven studies seem to have been performed at the same institution which limited the generalisability of the findings.

The authors’ recommended interpreting the findings with caution and this seemed appropriate.
Implications of the review for practice and research

Practice: The authors stated that the results from the review may not be applicable to men and populations of different ethnicity.

Research: The authors stated that future research should accurately report dexamethasone side effects and further research should be undertaken to determine the role of dexamethasone as an antiemetic in patients who received intrathecal morphine after neuraxial anaesthesia, particularly in populations at risk. Further recommendations included assessing the role of dexamethasone in combination with other antiemetic treatments.

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