Analgesic efficacy of intravenous naloxone for the treatment of postoperative pruritus: a meta-analysis

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CRD summary
This review concluded that intravenous naloxone was associated with decreased postoperative pruritis and nausea, without increasing pain scores. No significant differences were found between naloxone and control groups for opioid consumption, or risk of sedation or emesis. These conclusions reflect the evidence, but methodological limitations of the review and its evidence base suggest that they may not be reliable.

Authors' objectives
To evaluate the analgesic efficacy of intravenous naloxone for treatment of postoperative pruritus.

Searching
PubMed and EMBASE were searched with no language restrictions. Search terms and dates of the searches were not reported.

Study selection
Randomised controlled trials (RCTs) that evaluated the analgesic efficacy of intravenous naloxone following surgical procedures were eligible for inclusion. Naloxone could be administered as a continuous infusion or as part of an intravenous patient-controlled analgesia (PCA) regimen. The primary outcome of interest was the incidence of pruritis. Secondary outcomes included: incidence of postoperative nausea, emesis or sedation; and changes in opioid consumption and visual analogue pain scores. Eligible control groups did not receive intravenous naloxone (no further details specified).

The included trials were conducted in the USA, Columbia, Australia, China, Turkey and Taiwan. Surgery types were described as gynaecologic, hysterectomy, abdominal, orthopaedic and neurosurgical, or mixed. Most trials administered naloxone as part of an intravenous patient-controlled analgesia regimen; doses of naloxone varied. Morphine was the opioid used in all trials. All control groups received saline.

One reviewer selected studies for inclusion in the review; any uncertainties were resolved by discussion with another reviewer.

Assessment of study quality
The authors stated that they did not perform a quality assessment of the included trials.

Data extraction
Data on outcomes were extracted as means for continuous outcomes (changes in opioid consumption or visual analogue pain scores), or number of events for dichotomous outcomes (postoperative nausea, emesis or sedation). These were used to calculate weighted mean differences or odds ratios, with corresponding 95% confidence intervals.

The authors did not report how many reviewers extracted the data.

Methods of synthesis
Effect estimates and 95% confidence intervals from individual trials were pooled using random-effects models. Statistical heterogeneity was measured using the $\chi^2$ test (p values of ≤0.05 indicated significance) and $I^2$.

Results of the review
Eight RCTs were included in the review (838 patients, as reported in Table 1 in the paper, range 30 to 265 per study).

Compared with saline, intravenous use of naloxone was associated with a statistically significant decrease risk of pruritis (OR 0.40, 95% CI 0.21 to 0.77; eight RCTs; $I^2=52\%$) and postoperative nausea (OR 0.62, 95% CI 0.43 to 0.89;
eight RCTs; I²=18%).

No statistically significant differences were found between groups for the risk of emesis (eight RCTs; I²=0%) or sedation (three RCTs; I²=0%), mean opioid consumption (five RCTs; I²=62%) or mean visual analogue pain scores (six RCTs; I²=89%).

Authors' conclusions
Intravenous naloxone was associated with decreases in pruritus and nausea, without an increase in pain scores. No significant differences were found between naloxone and control groups for opioid consumption or for risks of sedation or emesis.

CRD commentary
The review question and inclusion criteria were clearly defined. Only a small number of databases were searched and no attempts were made to locate unpublished or grey literature, so relevant studies may have been missed. Search terms and search dates were not reported in sufficient detail, so it was not possible to judge how appropriate they were regarding the review question.

No quality assessment was performed, so it was not possible assess whether bias within the individual included trials had influenced the pooled results. Limited trial details were presented; further details on patient characteristics, length of follow-up and treatment regimens would have shown whether there was any additional between-study heterogeneity. Nevertheless, the statistical methods of synthesis were appropriate. The authors acknowledged that the results should be interpreted with caution due to the small number of included trials, and their small sample sizes.

The authors' conclusions reflect the evidence presented. Methodological limitations of the review and the paucity of the evidence base suggest that these conclusions may not be reliable.

Implications of the review for practice and research
Practice: The authors did not state any implications for clinical practice.

Research: The authors stated that larger RCTs investigating the analgesic efficacy of intravenous naloxone were required.

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