Meta-analysis of intravenous lidocaine and postoperative recovery after abdominal surgery

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CRD summary
The review evaluated continuous intravenous lidocaine versus placebo during and after abdominal surgery in adults and found that it significantly decreased the duration of postoperative ileus, pain intensity 24 hours after operation, nausea/vomiting, and time in hospital. This was a generally well-conducted review, but limited evidence and the presence of heterogeneity make the reliability of the authors' conclusions unclear.

Authors' objectives
To evaluate the effectiveness of intravenous lidocaine on recovery after abdominal surgery.

Searching
MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched from inception to December 2007 for publications in any language. Search terms were reported. Biographies of retrieved articles and correspondence were handsearched and hyperlinks were also checked.

Study selection
Randomised controlled trials (RCTs), with a double-blind design and an Oxford quality score of at least 3, evaluating intravenous lidocaine versus placebo during and after abdominal surgery, were eligible for inclusion. All the included studies were of patients scheduled for abdominal surgery alone. Trials were excluded if: they included children; they only compared intravenous lidocaine with epidural analgesia; lidocaine was only administered by bolus and with no continuous infusion; there was no perioperative lidocaine administration. Literature reviews and letters were also excluded.

The primary eligible outcome was time to recover bowel function, i.e. the duration of postoperative ileus (time to flatus, faeces or bowel movement). Other eligible outcomes included: length of hospital stay; 24 hour and 48 hour postoperative pain scores (measured on a Visual Analogue Scale); opioid consumption; incidence of opioid side effects (e.g. nausea, vomiting, sedation); and systemic lidocaine toxicity. The incidence of complications was also recorded, if reported.

In all but one of the included trials a lidocaine bolus of (1.5 to 2mg/kg) was given before surgical incision, followed by continuous infusion during and for up to 24 hours after the operation. In the RCT with no lidocaine bolus, infusion was started 30 min before surgical incision. The control patients in all the RCTs received an intravenous infusion of isotonic saline. The types of surgery in the included trials were described as cholecystectomy, colectomy, radical retropubic prostatectomy, colorectal and major abdominal surgery, including open surgery and laparoscopy. All the included patients were American Association of Anesthesiologists grade I-III. No details of the age or sex of patients were given. The opioids used for postoperative pain relief in the included trials were morphine, mepiridine or piritramide.

The authors gave limited details of how the papers were selected for the review, but did not state how many reviewers performed the selection.

Assessment of study quality
Study quality was assessed by two reviewers using the Oxford quality score (Jadad scale), a 5 point scale for randomisation, blinding and follow-up (withdrawals and drop-outs). Disagreements were resolved by discussion with co-authors.

Data extraction
Continuous data were extracted as means and standard deviations in order to calculate weighted mean differences (WMDs). Dichotomous data was extracted as event rates and used to calculate odds ratios (ORs). Authors were contacted for additional information on methods and results, particularly when numerical results were not provided; if the authors did not respond, the data was extrapolated from figures. Similarly, authors were contacted, if data for
nausea and vomiting were reported separately, in order to find the total number of patients with nausea and vomiting; if there was no response, the greater of the two numbers was used.

Methods of synthesis
An intention-to-treat analysis of the original data was carried out. For dichotomous data, odds ratios and 95% confidence intervals (CI) were calculated using a fixed-effect model, but if the Cochrane Q test for between study heterogeneity was significant (p<0.1), a random-effects model was used. For continuous data weighted mean differences and 95% confidence intervals were calculated. Forest plots were produced and numbers needed-to-treat were calculated where possible. Sensitivity analyses were performed to assess the effect of lidocaine in different situations (cholecystectomy versus colonic resection and laparoscopic versus open surgery).

Results of the review
Eight relevant RCTs were identified (n=320 patients, range 20 to 60). The median Oxford quality score was 4 points (range 3 to 5).

Continuous intravenous lidocaine significantly reduced: the duration of ileus (WMD -8.36 hours, 95% CI -13.24 to -3.47; \( I^2 = 90.6\%, p<0.001 \) for heterogeneity; seven RCTs); the length of hospital stay (WMD -0.84 days, 95% CI -1.38 to -0.31; \( I^2 = 46.7\%, p=0.11 \) for heterogeneity; five RCTs); postoperative pain intensity at 24 hours after surgery on a 0 to 100mm Visual Analogue Scale (WMD -5.93mm, 95% CI: -9.63 to -2.23; \( I^2 = 63.6\%, p=0.02 \) for heterogeneity; six RCTs); and the incidence of nausea and vomiting (OR 0.39, 95% CI 0.20 to 0.76; \( I^2 = 0\%, p=0.85 \) for heterogeneity; five RCTs). The number-needed-to-treat to avoid one instance of nausea and vomiting was 5 (95% CI 3 to 17). All but one trial also showed a significant 30 to 50% reduction in opioid consumption during the postoperative period with lidocaine infusion.

Subgroup analyses found that continuous intravenous lidocaine significantly reduced duration of ileus in: cholecystectomy patients (WMD -1.23 hours, 95% CI -2.12 to -0.34; two RCTs); after colonic resection (WMD -12.00 hours, 95% CI -14.86 to -9.13; three RCTs); where laparoscopy was performed (WMD -1.06, 95% CI -2.00 to -0.13; two RCTs); and where laparoscopy was not performed (WMD -7.90 hours, 95% CI -9.88 to -5.91; five RCTs).

Details of the dosage and timing of intravenous lidocaine were given for each trial. Details of the postoperative recovery programmes for fast track surgery used in some trials were also given. The authors noted that the side effects of opioids were not consistently reported, precluding a pooled analysis.

Authors' conclusions
Continuous intravenous administration of lidocaine during and after abdominal surgery improved patient rehabilitation (reduced postoperative ileus, the severity of pain, nausea and vomiting) and shortened hospital stay.

CRD commentary
The review addressed a well-defined question in terms of participants, interventions, study design and relevant outcomes. Relevant databases were searched in any language and reference lists were reviewed. Unpublished studies were not considered and publication bias was not assessed. Study quality was assessed using suitable criteria and the resulting trial quality grades were reported. The paper implies that two reviewers independently assessed trial quality, with any disagreements resolved by consensus with the other authors. The number of reviewers involved in the search, study selection and data extraction were not reported, so reviewer error and bias could not be ruled out. Some details of the trial participants were not extracted, for example age and sex. Statistical heterogeneity was assessed and there was evidence for heterogeneity with some outcomes; the heterogeneity remained in subgroup analyses. The review was generally well-conducted, but the author's conclusions regarding the efficacy of treatment may be too firm considering the presence of heterogeneity and that the total number of trial participants was relatively small.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice that were based on the results of the review.

Research: The authors recommended that future research on the safety of continuous intravenous lidocaine in abdominal surgery should include a large cohort of surgical patients. They also recommended that a direct comparison
of epidural analgesia and intravenous lidocaine in patients with an active rehabilitation protocol should be made with respect to length of hospital stay.

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