The comparative effects of postoperative analgesic therapies on pulmonary outcome: cumulative meta-analyses of randomized, controlled trials


Authors' objectives
To assess the effect of analgesic therapies on respiratory function in post-operative patients.

Searching
The search strategy initially involved 12 databases (including nursing, sociological, psychological and pharmacological databases) as part of a broader search for evidence relating to the treatment of acute pain. For the purpose of analyses of pulmonary function, all of the articles that met the inclusion criteria came from MEDLINE. Therefore, only MEDLINE was searched, from 1966 to 1995, using the following search terms and MeSH: 'random', 'pain-postoperative', 'respirat', 'ventilat', 'atelectasis', 'carbon dioxide', 'forced expiratory volume', 'oxygen', 'lung', 'peak expiratory flow rate', 'pulmonary' and 'vital capacity'. The references of retrieved articles were also examined for relevant papers.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were included.

Specific interventions included in the review
Seven analgesic therapies were included: epidural opioid; epidural local anaesthetic; epidural opioid with local anaesthetic; thoracic versus lumbar epidural opioid; intercostal nerve block; wound infiltration with local anaesthetic; and intrapleural local anaesthetic.

Participants included in the review
Post-operative patients who had had one of the following types of surgery: thoracotomy; C-section and lower abdominal; upper abdominal; thoracotomy and upper abdominal; cholecystectomy; upper abdominal and hip; laparoscopic cholecystectomy; and coronary artery bypass graft.

Outcomes assessed in the review
The following outcomes were assessed: forced expiratory volume in 1 second (FEV1); forced vital capacity (FVC); vital capacity (VC); peak expiratory flow rate (PEFR); partial arterial oxyygen pressure (PaO2); and incidence of atelectasis, pulmonary infection, and pulmonary complications in general.

How were decisions on the relevance of primary studies made?
Two investigators read all of the studies identified.

Assessment of study quality
A cross-section of the available trials was assessed for quality using the methods of Chalmers et al. (see Other Publications of Related Interest no.1) and Liberati et al. (see Other Publications of Related Interest no.2). This involved a standardised checklist that considered internal and external validity. The articles were read and scored by two blinded readers.

Data extraction
All data were extracted by one investigator and verified by a second.
Methods of synthesis
How were the studies combined?
The random-effects model of DerSimonian and Laird (see Other Publications of Related Interest no.3) was used to combine data for both continuous and dichotomous outcomes. The overall risk ratios and 95% confidence intervals (CIs) are reported.

A random-effects weighted mean difference method was used to pool continuous data for each of the relevant outcomes (FEV1, FVC, PEFR and PaO2). The difference between treatment means and the correlated standard error of the difference were extracted from the original studies, or calculated using a method described by the authors in an appendix.

How were differences between studies investigated?
The authors performed a sensitivity analysis to determine whether the exclusion of low-quality studies affected the results.

Results of the review
Forty-eight articles were used in the meta-analysis. The total number of participants was not reported. However, the numbers of participants for some of the individual comparisons were reported: incidence of atelectasis for epidural opioids versus systemic opioids (n=769); incidence of pulmonary infection for epidural local anaesthetics versus systemic opioids (n=215); incidence of pulmonary complications for epidural local anaesthetics versus systemic opioids (n=247); and incidence of pulmonary complications for epidural opioids versus systemic opioids (n=148).

The sensitivity analyses indicated that the exclusion of low-quality studies did not change the results, and quality ratings were therefore not taken into account when combining the studies.

A significant decrease in the incidence of atelectasis was found when epidural opioid was compared with systemic opioid (relative risk 0.53, 95% CI: 0.33, 0.85). There was also significant decreases in the incidence of pulmonary infection (relative risk 0.36, 95% CI: 0.21, 0.65) and of pulmonary complications overall (relative risk 0.58, 95% CI: 0.42, 0.80). The greater PaO2 concentration observed when epidural local anaesthetic was compared with systemic opioid (difference -4.57 mmHg, 95% CI: -0.06, -9.07) was also significant.

Differences also occurred that were not statistically significant, but may be clinically important: epidural opioids, compared with systemic opioids, had a weak tendency to reduce the incidence of pulmonary infection; intercostal nerve blockage tended to reduce the incidence of atelectasis and the incidence of pulmonary complications overall.

There were no clinically or statistically significant differences in other measures of pulmonary function (FEV1, FVC, PEFR).

Authors’ conclusions
Clinical measures of pulmonary outcome (incidence of atelectasis, infection, and other complications) were significantly improved by epidural opioid and epidural local anaesthetic treatments. Differences in physiological (surrogate) measures of pulmonary function did not reach statistical significance, but this could have been due to either the small number of patients analysed, or the failure of the chosen methods to reflect pulmonary outcome. These reasons could also explain why no significant differences were found for treatments other than epidural opioid and epidural local anaesthetics.

CRD commentary
The authors presented a well-defined review question.

The search strategy was fairly narrow. No unpublished material was included and, therefore, publication bias cannot be ruled out. The authors could have extended their search to include EMBASE, Cancerlit and handsearching.

The inclusion criteria were not clearly stated.
Details of the individual studies were lacking, e.g. there were no details of the age and gender of the participants, or the duration of follow-up. A quality assessment was carried out on a cross-section of the available trials. It was unclear how the authors used quality in their sensitivity analysis if not all the studies were assessed.

The authors stated that the principal weakness of their approach was that they were forced to combine heterogeneous studies in order to pool sufficient data for meaningful analyses. For this reason, the results and conclusions should be treated with caution.

**Implications of the review for practice and research**

Future research could help to outline possible correlations between pulmonary function and factors such as doses, volumes, and mixtures of drugs used; segmental level of anaesthetic blockade; type of nerve block used; and area of peripheral neural blockade.

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