Remifentanil in cardiac surgery: a meta-analysis of randomized controlled trials

CRD summary
The authors concluded that remifentanil could be beneficial in cardiac surgery, reducing mechanical ventilation time, length of hospital stay and cardiac biomarker release. This was a generally well conducted review but the limitations of the evidence (such as study variation and wide confidence intervals) reduce the reliability of the findings and suggest that the authors' conclusions should be interpreted cautiously.

Authors' objectives
To compare the effects of remifentanil versus other opioids on mechanical ventilation in patients undergoing cardiac surgery.

Searching
PubMed and BioMed Central were searched without language restrictions up to May 2010. Search terms were reported. Conference proceedings were searched. Experts in the field were contacted. Reference lists of relevant reviews and articles were searched manually.

Study selection
Eligible studies were randomised controlled trials (RCTs) that compared remifentanil versus other opioids (fentanyl or sufentanil) for anaesthesia in patients undergoing cardiac surgery. The primary outcome was time on mechanical ventilation. Secondary endpoints included cardiac biomarkers, myocardial infarction, use of inotropic drugs, intensive care unit and hospital length of stay and mortality.

Included trials were conducted between 1999 and 2009. All trials involved coronary artery bypass graft surgery; two trials also involved valvular surgery. Other anaesthetic drugs included midazolam, isoflurane and/or propofol, sevoflurane, fentanyl and thiopental. Most trials administered drugs as a continuous infusion (doses varied between 0.15 and 4 μg/kg; figures taken from the table) but some used an intravenous bolus (doses varied between 0.3 and 5 μg/kg). Length of infusion varied and lasted between 2.25 and 6.7 hours until extubation or end of surgery or up to two hours after surgery.

Four reviewers independently screened titles/abstracts. Two reviewers screened full text articles for inclusion. Discrepancies were resolved through consensus.

Assessment of study quality
Two reviewers independently assessed trial quality according to relevant Cochrane risk of bias method criteria. Discrepancies were resolved through consensus.

Data extraction
Dichotomous data were extracted to calculate odds ratios and 95% confidence intervals. Continuous data were extracted to calculate mean differences and 95% confidence intervals. Primary authors were contacted for missing data where necessary.

Four reviewers independently extracted outcome data; discrepancies were resolved through consensus.

Methods of synthesis
A fixed-effect model (or random-effects model where there was statistical heterogeneity) was used to combine odds ratios (OR) and 95% confidence intervals (CI). Mean differences were combined to calculate weighted mean differences (WMD) and 95% CI. Statistical heterogeneity was assessed using Cochran's Q and the I² statistic.

Results of the review
Sixteen RCTs containing 1,473 patients (calculated from the table as 1,402; range 26 to 304) were included in the review. Three RCTs were considered high quality (figure taken from the table), seven moderate and six low quality (full
details were reported in the review). Follow-up varied across trials and included the end of induction, end of surgery or up to extubation, end of intensive care unit stay or end of hospitalisation.

Compared to other opioids, remifentanil statistically significantly reduced postoperative mechanical ventilation (WMD -138.49 minutes, 95% CI -244.28 to -32.71 minutes; eight RCTs; $I^2=89\%$), length of stay (WMD -1.08 days, 95% CI -1.60 to -0.57 days; six RCTs; $I^2=71\%$) and cardiac troponin-I release (WMD -2.08ng/mL, 95% CI -3.93 to -0.24; three RCTs; $I^2=74\%$). There was evidence of statistical heterogeneity for all three outcomes.

There were no statistically significant differences between treatments in length of intensive care unit stay, incidence of perioperative myocardial infarction and mortality. Patients who received remifentanil statistically significantly increased use of inotropic drugs (OR 1.75, 95% CI 1.05 to 2.90; $I^2=69\%$).

**Authors' conclusions**
Remifentanil could be beneficial in cardiac surgery with reduced time of mechanical ventilation, length of hospital stay and cardiac biomarker release.

**CRD commentary**
The review question and inclusion criteria were stated clearly. A few sources were searched for published and unpublished data without language restrictions, which reduced potential for language and publication bias. Trial quality was assessed using some relevant criteria and the authors acknowledged that many of the RCTs were of suboptimal quality. Each stage of the review process was performed in duplicate which minimised potential for reviewer error and bias.

Few patient details were specified but other study details were adequately reported. There was evidence of statistical heterogeneity for some outcomes and a fixed-effect model was used for synthesis in relation to one of these outcomes, which was not appropriate. The authors acknowledged that sample sizes were limited. Confidence intervals were wide for some outcomes, which reduced the robustness of the findings.

This was a generally well conducted review but the limitations of the evidence reduce the reliability of the findings and suggest that the authors’ conclusions should be interpreted with caution.

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

**Practice:** The authors stated that the results could be particularly relevant to cardiac surgery in which early tracheal extubation might be hindered by accumulation of high dose opioids.

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

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