Esmolol reduces perioperative ischemia in cardiac surgery: a meta-analysis of randomized controlled studies


CRD summary
This review evaluated the effectiveness of esmolol in emergency and high-risk cardiac surgery patients. The authors concluded that esmolol reduced incidence of myocardial ischaemia and arrhythmias in cardiac surgery and that an increase in bradycardia was noted. Overall the authors' conclusions reflect the evidence presented and are reliable.

Authors' objectives
To evaluate the effectiveness of esmolol in emergency and high-risk cardiac surgery patients.

Searching
BioMed Central and PubMed were searched up to April 2008. Search terms were reported. Conference proceedings of five relevant conferences were searched from 2006 to 2007. References of retrieved articles and relevant studies were scanned. International experts were contacted. There were no language restrictions.

Study selection
Randomised controlled trials (RCTs) that compared esmolol (any dose or time of administration) to placebo or control treatment in patients who underwent cardiac surgery and that reported data on clinical outcomes were eligible for inclusion.

The primary outcome of interest was the rate of perioperative ischaemia as defined by the study authors. Additional primary outcomes of interest included perioperative use of inotropic drugs and the incidence of arrhythmia after cardiopulmonary bypass. Secondary outcomes included perioperative incidence of myocardial infarction, length of hospital stay and intensive care unit stay, mortality, cardiac events and possible adverse effects (such as bradycardia).

Most surgery was coronary artery bypass graft (CABG). Dose of esmolol varied between studies and was administered as a single bolus (500μg/kg to 2mg/kg) followed by a continuous infusion (0.5μg/kg/minute to 300μg/kg/minute). The timing of administration of esmolol varied between studies: it was administered before the induction of anaesthesia, before cardiopulmonary bypass, in cardioplegic solution, as a cardioplegic agent and after diagnosis of atrial fibrillation in the postoperative period. Controls included placebo, cardioplegia, potassium in blood in cardioplegia, oral beta blockers, usual antihypertensive medication and diltiazem.

Two reviewers independently selected studies for inclusion in the review. Any disagreements were resolved by consensus.

Assessment of study quality
Two reviewers independently assessed study quality using an adapted version of Cochrane Collaboration risk of bias assessment tool, which assessed sequence generation, allocation concealment, blinding, similar concomitant medication, incomplete outcome data addressed, uniform and explicit outcome definitions, free from selective outcome reporting and freedom from other biases. Any disagreements were resolved by consensus.

Data extraction
Data were extracted in order to calculate odds ratios (OR), mean differences (MDs) and their associated 95% confidence intervals (CI).

Three reviewers independently extracted data. Any disagreements were resolved by consensus.

Methods of synthesis
Fixed-effect models were used to estimate summary odds ratios and mean differences in the absence of heterogeneity ($I^2<25\%$); otherwise a random-effects models were used. Heterogeneity was assessed using the Cochran Q test and the $I^2$ statistic. In the case of moderate or substantial heterogeneity, odds ratios or mean differences were combined in a random-effects model. Publication bias was assessed using funnel plots and Egger's test. Sensitivity analysis were performed by excluding one study at a time from the meta-analysis and by comparing the fixed-effect and random-effects models.

**Results of the review**

Twenty RCTs (778 patients) were included in the review. Sample sizes ranged from 20 to 72 patients. Allocation sequence generation and allocation concealment were unclear in all but one study. Ten studies were reported to be blinded. There was no evidence of publication bias.

Compared to control, esmolol was associated with a statistically significant reduction in rate of perioperative ischaemia (OR 0.42, 95% CI 0.23 to 0.79; seven studies) and also with a statistically significant increase in bradycardia (OR 5.49, 95% CI 2.21 to 13.62; six studies). Although not statistically significant, esmolol was associated with a a trend towards a reduction in arrhythmias after cardiopulmonary bypass (OR 0.42, 95% CI 0.18 to 1.01; six studies). There was no statistically significant difference between esmolol and control in the use of inotropic drugs in the perioperative period, mortality, incidence of myocardial infarction, hypotension or low output cardiac syndrome.

There was no statistically significant difference between esmolol and control in length of stay in the intensive care unit and in length of hospital stay. However, there was evidence of statistically significant heterogeneity for these two outcomes (intensive care unit $I^2 = 71.6\%$ and hospital $I^2=53.0\%$).

Subgroup analyses suggested that the results were robust.

**Authors' conclusions**

Esmolol reduced the incidence of myocardial ischaemia and arrhythmias in cardiac surgery. An increase in bradycardia was noted.

**CRD commentary**

This review addressed a clear research question and was supported by adequate inclusion criteria. The search was performed with no language restrictions, which reduced the risk of language bias. There was an attempt to locate unpublished studies by searching conference proceedings, although the search was limited to 2006 to 2007. However, publication bias was assessed and found to be absent. The study quality assessment tool was appropriate to the included study designs. Adequate details of primary studies were provided and the synthesis methods was appropriate. The review process was carried out with sufficient attempts to minimise reviewer error and bias. Overall the authors conclusions reflect the evidence presented and are reliable.

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

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that more studies with a large cohort of patients were required.

**Funding**

Not stated

**Bibliographic details**


**PubMedID**

19297196
Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.