Assessment of the efficacy of esmolol on the haemodynamic changes induced by laryngoscopy and tracheal intubation: a meta-analysis

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Authors' objectives
To assess the effect of esmolol on haemodynamic changes induced by laryngoscopy and tracheal intubation (LTI).

Searching
The authors searched MEDLINE, EMBASE and LILACS, all after 1982, and the Cochrane Library (Issue 1, 2000); the last search was conducted May 2000. The search terms were stated. In addition, the reference lists of identified reports and reviews were checked, and abstracts from relevant meetings published in major journals of anaesthesiology were handsearched. Studies in any language were eligible.

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

Specific interventions included in the review
Studies that compared esmolol with placebo were eligible for inclusion. The included studies compared one or more different doses of esmolol with placebo, or with placebo and an alternative. The included studies used eleven different regimens of esmolol such as intravenous bolus, infusions, bolus plus infusion, and both fixed and variable doses. The most commonly used intravenous bolus doses were 100 and 200 mg esmolol. Where stated, esmolol was administered before and after the induction agent. Some studies used opiates either as premedication or during induction.

Participants included in the review
Studies of patients undergoing LTI were eligible for inclusion.

Outcomes assessed in the review
Studies that assessed any of the following outcomes were eligible for inclusion: heart rate (HR), systolic blood-pressure (SBP), mean arterial pressure (MAP), and diastolic blood-pressure (DBP).

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
Two researchers independently extracted the data. Data were extracted on the baseline HR, SBP, MAP and DBP, and the minimum and maximum values of these variables after esmolol or placebo and after tracheal intubation; sequence of drug administration; treatment regimens; characteristics of the patients including physical status; exclusion criteria; and adverse effects. The authors extracted absolute values and standard deviations from graphs where necessary. Where the data were incomplete, the authors of the primary studies were contacted for verification and/or additional information. For each study, the percentage difference from baseline to the maximum or minimum value were estimated for each outcome to give the percentage increase and decrease, respectively.

Methods of synthesis
How were the studies combined?
The percentage increase or decrease in SBP, DBP, MAP and HR were averaged using a correction factor based on the number of patients in each study. The studies were only combined in meta-analyses where three or more studies used the same dose and/or treatment regimen. Pooled weighted mean differences and 95% confidence intervals (CIs) between esmolol and placebo were calculated for each outcome. A fixed-effect model was used where statistical heterogeneity was not found (P>0.2), while a random-effects model was used where significant heterogeneity was detected.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the chi-squared statistic. A subgroup analysis was used to explore the influence on the four outcome variables (SBP, DBP, HR and MAP) of co-administration of opiates, and different doses and regimes of esmolol (100 and 200 mg esmolol bolus; 1, 2 and 3 mg/kg esmolol doses; and four different infusion regimens). The change in HR from baseline with esmolol and with placebo was calculated for patients with coronary artery disease or at an increased risk of cardiovascular disease.

Results of the review
Thirty-eight RCTs (n=2,009) were included.

SBP (28 RCTs): the average SBP after induction decreased by 13.8% with placebo, compared with 6.1% with esmolol; the average SBP after LTI increased by 26.3% (placebo) and 9.1% (esmolol), respectively.

DBP (14 RCTs): DBP after induction decreased by 3.4% with placebo, compared with 6.8% with esmolol; DBP after LTI increased by 34.2% (placebo) and 22.8% (esmolol), respectively. MAP (16 RCTs): MAP after induction decreased by 2.6% with placebo, compared with 10.1% with esmolol; MAP after LTI increased by 21.4% (placebo) and 10.6% (esmolol), respectively.

HR (36 RCTs): HR after induction increased by 7.2% from baseline with placebo, compared with a decrease of 4.2% from baseline with esmolol; HR after LTI increased by 29.6% (placebo) and 9.3% (esmolol), respectively. The change in HR was similar for patients with coronary artery disease or at an increased risk of cardiovascular disease (6 RCTs); the minimum values were +4.8% and -2% with placebo and esmolol, respectively, while the maximum values were +23% (placebo) and +6.7% (esmolol).

Opiates (19 RCTs): the results were presented for increases and decreases in the four outcome variables, with and without opiates, for esmolol and placebo.

There was no significant difference between esmolol and placebo when esmolol was given before or after the induction agents. No data were presented.

There was no significant difference between esmolol and placebo in the minimum decrease of SBP, MAP or HR after administration of the intervention, or in the maximum increase in SBP, MAP or HR after intubation. Only the DBP results between esmolol 200 mg and placebo differed: the baseline values of patients allocated to placebo were high (P=0.01). Data were presented.

Optimal results for HR control after LTI were obtained using a bolus of 500 microg/kg per minute over 4 minutes, followed by an infusion of 200 to 300 microg/kg per minute. Using this regimen, the decrease in HR with esmolol in comparison with placebo was 20.2 beats/minute (95% CI: 15.6, 24.7). The greatest reduction in blood-pressure before LTI was obtained using a 200 mg esmolol bolus: the decrease in SBP was 18 mmHg (95% CI: 14.4, 21.5), MAP 10.2 mmHg (95% CI: 3.1, 17.2), and DBP 10.1 mmHg (95% CI: 7.3, 12.8).

The 200-mg dose of esmolol significantly decreased all outcome variables in comparison with the 100-mg dose (P<0.01).

Authors' conclusions
Esmolol attenuates the tachycardia and increase in SBP induced by LTI. However, the dose-dependent decrease in
blood-pressure during induction means that routine use of esmolol in anaesthesia cannot be recommended.

CRD commentary
The review question was clear in terms of the study design, intervention, participants and outcomes. Several relevant sources were searched, the search terms were stated, and studies in any language were eligible for inclusion. However, no attempt was made to locate unpublished studies, thus raising the possibility of publication bias. The methods used to select the studies were not described, hence the adequacy of these methods cannot be judged. Only RCTs were included but, as validity was not formally assessed, the quality of the evidence was unknown. Two reviewers independently selected and extracted the data, which reduces the potential for bias and errors. Some relevant information on the included studies was tabulated, but information on the patients' characteristics and cointerventions that would have enabled an assessment of clinical heterogeneity among studies was lacking.

The data were combined in a meta-analysis and statistical heterogeneity was assessed, although potential causes of heterogeneity were not explored in analyses where statistically-significant heterogeneity was detected. The statistical significance of the difference between esmolol and placebo was not reported for other analyses, such as the comparison of interventions with and without opiates. In view of these limitations, the conclusion should be interpreted with caution.

Implications of the review for practice and research
Practice: The authors stated that the risk of hypotension during induction prohibits the routine use of esmolol in anaesthesia. They further stated that the use of esmolol in patients at high risk has to be considered on an individual basis. The authors advise that, if esmolol is considered appropriate, a small loading dose of 500 microg/kg be given over 4 minutes followed by a continuous infusion of 200 to 300 microg/kg per minute.

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

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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.