The efficacy of landiolol for suppressing the hyperdynamic response following laryngoscopy and tracheal intubation: a systematic review

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CRD summary
The review found that a continuous infusion of landiolol can suppress heart rate and blood pressure responses following laryngoscopy and tracheal tube intubation. Insufficient information was presented about the conduct of the review, included patients and the results, which made it difficult to draw any conclusions about the reliability of the authors’ conclusions.

Authors' objectives
To evaluate the effects of landiolol on haemodynamic responses to laryngoscopy and tracheal tube intubation.

Searching
MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched from inception to February 2009; search terms were reported. The database of journals from Japan Medical Abstract Society and reference lists and bibliographies of related articles and of surgical and anaesthesia journals were searched.

Study selection
Randomised controlled trials that compared landiolol to placebo in adults who underwent laryngoscopy and tracheal tube intubation and reported on any haemodynamic variable and or heart rate at baseline and within five minutes of endotracheal intubation were eligible for inclusion. Trials of hypertensive patients were excluded and results for patients within the included trials who received alternative therapeutic agents were excluded from the analysis.

Haemodynamic variables analysed across the trials included heart rate, mean blood pressure and systolic blood pressure. Incidence of adverse events was evaluated. Five trials used a continuous infusion of 0.125mg/kg/minute landiolol for one minute followed by 0.04mg/kg/minute landiolol. The remaining two trials used a 0.1mg/kg or 0.3mg/kg bolus dose of landiolol. The timing of administration varied between 1.5 and seven minutes before laryngoscopy and tracheal tube intubation. None of the studies included concomitant use of opiates during induction of anaesthesia.

The authors did not state how many reviewers performed the study selection.

Assessment of study quality
Methodological quality was assessed with the Jadad scale. A score of 5 indicated a high-quality study. The assessment included randomisation, blinding and completeness of follow-up.

The authors did not state how many reviewers performed the assessment. Any disagreements were resolved by consensus.

Data extraction
Data were extracted to calculated weighted mean differences (WMD) with corresponding 95% confidence intervals for changes in haemodynamic variables between placebo and landiolol groups. In the event of incomplete data, study authors were contacted.

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
Pooled weighted mean differences and 95% CIs were calculated using a Mantel-Haenszel fixed-effect model. The $I^2$ test and Q-statistic were used to evaluate statistical heterogeneity. If the Q-statistic test was significant (p<0.10), pooled
weighted mean differences and 95% CIs were derived using a DerSimonian and Laird random-effects model.

**Results of the review**

Seven trials (n=325) were included in the review. Sample sizes ranged between 22 and 64 patients. Three studies were given a Jadad score of 3, two studies were given a score of 4 and one study received a Jadad score of 5 points.

After laryngoscopy and tracheal tube intubation, groups that received continuous infusions of landiolol showed significant reductions in heart rate (WMD -21.18, 95% CI -28.17 to -14.20; five studies), systolic blood pressure (WMD -23.03mmHg, 95% CI -43.59 to -2.47; two studies) and mean blood pressure (WMD -16.26mmHg, 95% CI -23.96 to -8.55; three studies). There was significant statistical heterogeneity across studies for heart rates after intubation ($I^2=68.3\%$) and systolic blood pressure ($I^2=74.6\%$), but not for mean blood pressure after intubation.

There were no differences in heart rates and blood pressure between landiolol and placebo groups after bolus doses of landiolol. Analysis of adverse events showed no increases in incidence of brachycardia and hypotension for administration of landiolol compared with placebo.

There was a discrepancy in the paper for one of the confidence intervals; here we used the figures from the table.

**Authors' conclusions**

Administration of a continuous infusion of landiolol of 0.125mg/kg/minute for one minute followed by infusion at 0.04mg/kg/minute can safely and effectively suppress increases in heart rates and blood pressure caused following laryngoscopy and tracheal tube intubation. Further studies were required to investigate the effectiveness, optimal doses and timing of bolus dose regimens of landiolol.

**CRD commentary**

The review addressed a clear question. Criteria for study inclusion were broad in scope. Appropriate databases were searched, but the decision of the reviewers to restrict other searches to Japanese-only databases meant that there was a possibility other studies may have been missed. The search for unpublished studies appeared to be limited and so there was a risk of publication biases. Some steps were taken to minimise errors and biases during the quality assessment of the included studies; no such steps were reported for study selection and data extraction. There was little information on the included patients in the studies. The included studies were small. There was significant statistical heterogeneity reported for blood pressure and systolic blood pressure; therefore, it was unclear whether it was appropriate for the authors to combine the results in a meta-analysis. There were no attempts to explore reasons for statistical heterogeneity.

Methodological flaws and the limited evidence base mean that the results from this review should be interpreted with a substantial degree of caution. The overall reliability of the authors' conclusions is unclear.

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

**Practice:** The authors recommended that landiolol be administered by continuous infusion to counteract haemodynamic changes as a result of laryngoscopy and tracheal tube intubation due to its short acting properties. The authors stated that continuous landiolol administration did not appear to have a synergistic effect on haemodynamics when combined with anaesthetic agents.

**Research:** The authors stated that more research was required to establish the optimal dose, timing and effectiveness of bolus dose of landiolol for patients who undergo laryngoscopy and tracheal tube intubation.

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