A comparison of continuous and bi-level positive airway pressure non-invasive ventilation in patients with acute cardiogenic pulmonary oedema: a meta-analysis

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CRD summary
This well-conducted review concluded that, based on the limited data available, bi-level positive airways pressure (BiPAP) does not offer any substantial clinical advantage over continuous positive airways pressure in patients with acute cardiogenic pulmonary oedema, regardless of whether BiPAP support is titrated or whether patients have marked hypercapnia. The authors’ conclusions are likely to be reliable.

Authors’ objectives
To evaluate the effects of continuous positive airway pressure (CPAP) compared with bi-level positive airway pressure (BiPAP) noninvasive ventilation in the treatment of patients with cardiogenic pulmonary oedema.

Searching
MEDLINE and EMBASE (to December 2005) and the Cochrane CENTRAL Register (Issue 3, 2005) were searched; the search terms were reported. The reference lists of relevant reviews and retrieved articles were also searched, as were the websites of the International Network of Agencies of Health Technology Assessment and the International Society of Technology Assessment in Health Care.

Study selection
Randomised controlled parallel-group trials (RCTs) comparing CPAP with BiPAP were eligible for inclusion. The included studies either used fixed levels of CPAP (10 cmH₂O) and BiPAP (15 and 5 cmH₂O), or titrated the level of peak inspiratory pressure in the BiPAP group in order to achieve a tidal volume of 400 mL or titrated both CPAP (5 to 20 cmH₂O) and BiPAP (peak inspiratory pressure range 10 to 25 cmH₂O).

The participants in eligible studies had to have acute cardiogenic pulmonary oedema. Studies that included patients with other causes of respiratory failure were excluded unless outcomes for those with acute cardiogenic pulmonary oedema were reported separately. The mean age of the patients in the included studies ranged from 61 to 77 years and their mean Acute Physiology and Chronic Health Evaluation II scores, where reported, ranged from 17 to 20. In some studies all participants had hypercapnia (mean arterial carbon dioxide tension >45 mmHg).

Studies were eligible that reported hospital mortality or the need for invasive ventilation or intubation (primary outcomes). Other outcomes of interest were new-onset myocardial infarction, duration of noninvasive ventilation to resolution of pulmonary oedema and length of hospital stay.

In the included studies there was wide variation in the criteria for initiating invasive ventilation and for weaning off noninvasive ventilation.

Two reviewers independently selected studies for inclusion, with any disagreements resolved by consensus.

Assessment of study quality
Risk of bias was evaluated using the Jadad scale (which addresses randomisation, blinding and withdrawals) and allocation concealment. In order for a study to qualify as double-blinded, the physician making decisions about initiation of invasive ventilation or discontinuation of noninvasive ventilation was required to be blinded to the study intervention. Two reviewers independently assessed the validity of the included studies, with any disagreements resolved by consensus.

Data extraction
For binary outcomes, risk ratios (RRs) and 95% confidence intervals (CIs) were calculated. For continuous outcomes, the mean difference between the groups and the 95% CI were reported. Two reviewers independently extracted the
data, with any disagreements resolved by consensus.

**Methods of synthesis**
The studies were grouped according to outcome and pooled RRs or weighted mean differences were calculated, along with 95% CIs, using a random-effects analysis. Statistical heterogeneity was assessed using the $\chi^2$ and $I^2$ statistics. Differences between the studies were evident from the text and tables; sensitivity analyses were conducted to further investigate the effects of hypercapnia. The studies were also subgrouped according to whether they used fixed or variable level airway pressure. Publication bias was assessed using funnel plots and hospital mortality as an end point.

**Results of the review**
Seven RCTs (n=290) were included.

Allocation concealment was clearly adequate in 4 studies, but only one used double-blinding. The mean Jadad score was 3 (range: 2 to 5). The meta-analysis may have been underpowered to show a modest difference in effect between the interventions (e.g. 40% difference in risk of requiring intubation).

There was no statistically significant difference between the groups for hospital mortality, requirement for invasive ventilation, duration of noninvasive ventilation required until resolution of pulmonary oedema, length of hospital stay or new-onset myocardial infarction (7 RCTs, n=290). Based on limited data (4 RCTs, n=167), there was a non significant trend towards increased risk of new-onset myocardial infarction in the CPAP group (RR 2.10, 95% CI: 0.91, 4.84, p=0.08; $I^2=25.3\%$). Stratification by level of airway pressure had little effect on the results, nor did sensitivity analyses including only studies of patients with marked hypercapnia. There was no statistically significant heterogeneity in any of the analyses.

The funnel plot showed some potential for publication bias, but it was of a small degree deemed unlikely to affect the overall findings.

**Authors’ conclusions**
Based on the limited data available, BiPAP does not offer any substantial clinical advantage over CPAP in patients with acute cardiogenic pulmonary oedema, regardless of whether BiPAP support is titrated, or whether patients have marked hypercapnia.

**CRD commentary**
The objectives and inclusion criteria were clear and the literature search was adequate. The study selection, validity assessment and data extraction processes were undertaken by two reviewers independently, thus reducing the risk of reviewer error and bias. Suitable statistical methods were used to combine the studies, and both heterogeneity and publication bias were assessed in an appropriate manner. The review was well-conducted and the authors’ conclusions are likely to be reliable.

**Implications of the review for practice and research**
Practice: The authors stated that BiPAP does not appear to offer any substantial clinical benefits over CPAP for treating patients with acute cardiogenic pulmonary oedema. On the basis of current evidence, it is appropriate to base the choice of modality mainly on the equipment available.

Research: The authors stated that a large RCT is needed to confirm whether BiPAP is equivalent or superior to CPAP for the treatment of patients with acute cardiogenic pulmonary oedema. Outcomes should include cost-effectiveness. Noninvasive ventilation studies should blind the attend physician to the intervention.

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