Effect of non-invasive positive pressure ventilation (NIPPV) on mortality in patients with acute cardiogenic pulmonary oedema: a meta-analysis


CRD summary
The review investigated the effects of noninvasive positive pressure ventilation in patients with acute cardiogenic pulmonary oedema. The authors concluded that, compared with standard therapy, continuous positive airway pressure (CPAP) and bilevel ventilation reduce the need for subsequent mechanical ventilation and that CPAP reduces mortality. The conclusions appear reliable.

Authors' objectives
To determine the effect of noninvasive positive pressure ventilation (NIPPV), including continuous positive airway pressure (CPAP) and bilevel ventilation, on clinically relevant end points in patients with acute cardiogenic pulmonary oedema

Searching
MEDLINE, EMBASE, CINAHL, EBM Reviews, the Cochrane CENTRAL Register, the Cochrane Database of Systematic Reviews, DARE and ACP Journal Club were searched (1966 to May 2005) without language restrictions for studies on adult human populations; the search terms were reported. The bibliographies of retrieved papers and reviews were checked. The American Journal of Respiratory and Critical Care Medicine, American Heart Association, Chest, Critical Care Medicine, European Heart Journal, European Respiratory Journal, Intensive Care Medicine and Thorax were handsearched for additional studies.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials were eligible for inclusion. The follow-up period was not stated in the report.

Specific interventions included in the review
Studies comparing CPAP or bilevel ventilation with standard therapy and those comparing CPAP with bilevel ventilation were eligible for inclusion. The standard therapy was a combination of oxygen by face-mask, diuretics, nitrates and other supportive care.

Participants included in the review
Studies of adult patients with acute cardiogenic pulmonary oedema were eligible for inclusion. The mean age of the patients in the study groups ranged from 71.4 to 74.5 years and 46% of the patients were female.

Outcomes assessed in the review
Studies reporting data on hospital mortality or the need for invasive mechanical ventilation were eligible for inclusion. The other outcomes of interest in the review were length of hospital stay, duration of NIPPV procedure, occurrence of new myocardial infarction, author-defined failure of treatment and composite failure of treatment.

How were decisions on the relevance of primary studies made?
The authors stated that one reviewer screened the retrieved articles, while three reviewers further assessed the subset of papers which were potentially eligible for inclusion. However, they did not state how the papers were selected, or how any disagreements were resolved.

Assessment of study quality
The authors stated that they assessed the validity of trials according to modified criteria used by a previous study (see
Other Publications of Related Interest). The total quality score a study could achieve ranged from 0 (minimum) to 11 (maximum). The authors did not provide further data on the criteria used. Two reviewers performed the validity assessment and any disagreements were resolved by consensus.

Data extraction
Two reviewers independently extracted the data using a standardised data extraction form, and four reviewers checked the abstracted data before analysis. The number of events in each group was extracted for the binary outcomes of interest, while the mean and standard deviation (SD) were extracted for continuous variables. It was unclear whether the data were extracted in an intention-to-treat format.

Methods of synthesis
How were the studies combined?
DerSimonian and Laird random-effect models were used to compare the relative risk (RR) and 95% confidence interval (CI) for hospital mortality, need for invasive mechanical ventilation, new myocardial infarction and treatment failure. Pooled mean weighted differences were calculated for the length of hospital stay and the duration of NIPPV (where mean and SD were available). Separate analyses for the effect of CPAP and bilevel ventilation on mortality and the need for invasive mechanical ventilation were conducted using the quality score to weight the studies (fixed-effect estimator). The rank correlation test of Begg, the regression-based test of Egger and the non-parametric trim-and-fill method of Duval and Tweedie were used to assess publication bias.

How were differences between studies investigated?
The authors stated that they assessed the heterogeneity of treatment effects using the Q statistic and the I-squared measure. Meta-regression was used to assess the potential effects of the predefined confounders age, gender, quality score, partial arterial carbon dioxide pressure (PaCO2), pH and arterial oxygen tension (partial arterial oxygen pressure, PaO2) at admission on mortality and the need for mechanical ventilation, and to assess predictors of new myocardial infarction in bilevel ventilation. A cumulative meta-analysis was performed to investigate possible time trends in treatment effects. Bayesian meta-analysis regression was used to determine the effect of underlying population risk on the treatment effects.

Results of the review
Twenty-three studies were included. Twelve studies (n=583) compared CPAP with standard therapy, 7 studies (n=345) compared bilevel ventilation with standard therapy, and 10 studies (n=433) compared CPAP with bilevel ventilation. The total number of study arms was 29 since some studies had 3 arms. The overall number of participants was not reported.

CPAP was associated with a statistically significant lower risk of hospital mortality compared with standard therapy (RR 0.59, 95% CI: 0.38, 0.90, P=0.015), but there was no statistically significant difference between bilevel ventilation and standard therapy and between CPAP and bilevel ventilation.

There was a statistically significant reduction in the need for invasive mechanical ventilation with CPAP (RR 0.44, 95% CI: 0.29, 0.66, P=0.0003) and with bilevel ventilation (RR 0.50, 95% CI: 0.27, 0.90, P=0.02), compared with standard therapy, but there was no statistically significant difference between CPAP and bilevel ventilation.

There was a statistically significant decrease in composite failure rates with CPAP (RR 0.42, 95% CI: 0.27, 0.65, P=0.0005) and with bilevel ventilation (RR 0.51, 95% CI: 0.30, 0.87, P=0.01), compared with standard therapy, but there was no statistically significant difference between CPAP and bilevel ventilation.

CPAP was associated with statistically significant lower author-defined failure rates compared with standard therapy (RR 0.45, 95% CI: 0.25, 0.82, P=0.009), but there was no statistically significant difference between bilevel ventilation and standard therapy and between CPAP and bilevel ventilation.

There was an increased risk of myocardial infarction with bilevel ventilation compared with CPAP, but this difference was not statistically significant (RR 1.49, 95% CI: 0.92, 2.42, P=0.11).
There was no statistically significant difference in length of hospital stay and duration of NIPPV across the patient groups. The authors did not find any statistically significant heterogeneity for hospital mortality (P>0.34, I-squared: 0 to 11%), but reported mild heterogeneity for invasive mechanical ventilation (P>0.27, I-squared: 0 to 21%).

The Bayesian analysis found no substantial effect of underlying risk on hospital mortality and need for invasive mechanical ventilation when comparing CPAP or bilevel ventilation with standard therapy.

The quality scores of the trials included in the review ranged from 4 to 9. No evidence of publication bias was found.

Authors' conclusions
In patients with acute cardiogenic pulmonary oedema, CPAP had a favourable effect over standard therapy on reducing mortality and failure rates, while bilevel ventilation had a favourable effect over standard therapy on reducing invasive mechanical ventilation and composite failure rates.

CRD commentary
The review question, selection criteria, and methods of data extraction and analysis were appropriate and clearly described, although the use of intention-to-treat analysis was unclear and there was mild heterogeneity in some treatment effects. The search strategy was reasonably broad and comprehensive. The authors used the quality scores to weight the outcomes of interest, but they did not provide explicit data about the criteria used for the validity assessment.

The authors stated that the number of participants with some outcomes of interest (e.g. mortality) might have been too small to detect possible differences between the study groups. They also pointed out that the primary studies included only a proportion of patients with cardiogenic pulmonary oedema, so the findings of the review may not be generalisable to all patients with such a disorder.

Overall, this was a reasonably well-designed and clearly presented review. The authors' conclusion about the effect of CPAP and bilevel ventilation seem to be supported by the evidence presented.

Implications of the review for practice and research
Practice: The authors stated that the British Thoracic Society guidelines on the use of CPAP and bilevel ventilation seem appropriate.

Research: The authors stated that further studies on the use of positive end-expiratory pressure and the role of bilevel ventilation in the hypercapnic cohort of patients with acute cardiogenic pulmonary oedema would add insight into the pathology and management of the disorder.

Bibliographic details

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Other publications of related interest
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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.