The effect of positive pressure airway support on mortality and the need for intubation in cardiogenic pulmonary edema: a systematic review

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Authors' objectives
To critically appraise and summarise the trials examining the addition of continuous positive airway pressure (CPAP) or noninvasive positive pressure ventilation (NPPV) to standard medical therapy on hospital mortality, need for endotracheal intubation, and predischarge left ventricular function in patients admitted to the hospital with cardiogenic pulmonary oedema with gas exchange abnormalities.

Searching
MEDLINE was searched from 1983 to June 1997 using the following keywords: 'pulmonary edema (therapy)' and 'respiratory insufficiency (therapy)' separately, with and without 'positive pressure respiration'. In addition, relevant conference proceedings (1985 to 1997), bibliographies of retrieved papers and relevant journals (listed in the paper) (1985 to June 1997) were handsearched. The search strategy was restricted to English language only.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs). In the event of there being fewer than two RCTs, other study designs, such as case series, were to be considered for inclusion.

Specific interventions included in the review
CPAP and standard medical therapy versus standard medical therapy alone; NPPV and standard medical therapy versus standard medical therapy alone; NPPV and standard medical therapy versus CPAP and standard medical therapy.

Participants included in the review
Patients presenting to hospital with acute cardiogenic pulmonary oedema with gas exchange abnormalities.

Outcomes assessed in the review
Hospital survival, need for endotracheal intubation, predischarge left ventricular dysfunction.

How were decisions on the relevance of primary studies made?
Titles and abstracts were examined. The process of selecting studies was not described (i.e. how many reviewers involved, whether blinded to results and source, whether decisions were made independently, how disagreements were resolved).

Assessment of study quality
Randomisation concealment, objective criteria for study population, objective criteria for the need for endotracheal intubation, description of potential confounders, complete follow-up, mention of co-intervention standardisation, use of intention-to-treat analysis. Independently, by two reviewers.

Data extraction
Data were extracted independently by two reviewers.

Methods of synthesis
How were the studies combined?
If trials were found to be homogeneous, hospital mortality results were pooled using the DerSimonian and Laird
random-effects model, to obtain an overall risk reduction with associated 95% confidence intervals (CIs). As long as the 95% CIs did not cross zero, the number needed to treat was calculated with its respective CIs. Similarly, data on the need for endotracheal intubation and predischarge left ventricular function were pooled when available. For the outcomes of hospital mortality and need for endotracheal intubation, a strong trend was defined as a pooled risk reduction of 10% with 95% CI including zero. If fewer than two RCTs were available for analysis, study results were summarised qualitatively.

How were differences between studies investigated?
If two or more RCTs were available, the trials were assessed for clinical heterogeneity by the authors abstracting data, and tested for statistical heterogeneity of study results using the Breslow-Day test.

Results of the review
Overall eleven studies were included. There were three RCTs of CPAP versus standard medical therapy alone (n=180), one RCT of CPAP versus NPPV (n=27), and seven case series of NPPV versus standard medical therapy alone (n=218).

Continuous positive airway pressure (CPAP) and standard medical therapy versus standard medical therapy alone (3 RCTs): CPAP was associated with a trend toward decreased hospital mortality (risk difference -6.6% 95% confidence intervals (CI): 3, -16%), test for heterogeneity non-significant, a decreased need for intubation (risk difference -26%, 95% CI: -13, 38%), number needed to treat 4, 95% CI: 3, 8, test for heterogeneity non-significant. One of the trials assessed left ventricular function and found no statistically significant difference between groups for left ventricular ejection fraction at one year. Baseline pH values for the three trials differed and seemed to be inversely related to the risk difference in intubation rates. Clinical heterogeneity was therefore a possibility.

Noninvasive positive pressure ventilation (NPPV) and standard medical therapy versus standard medical therapy alone (7 case series): mortality rates ranged from 0 to 22%, intubation rates ranged from 0 to 44%. Left ventricular function was not reported in these studies.

CPAP and standard medical therapy versus NPPV and standard medical therapy (1 RCT): there was no between group difference for hospital mortality or rate of reintubation. Left ventricular function was not reported in these studies.

Authors' conclusions
A modest amount of favourable experimental evidence exists to support the use of CPAP in patients with cardiogenic pulmonary oedema. CPAP appears to decrease intubation rates and data suggest a trend toward a decrease in mortality, although the potential for harm has not been excluded. The role of NPPV in this setting requires further study before it can be widely recommended.

CRD commentary
Overall, this is a clearly presented review. The research question, selection criteria for primary studies, characteristics of studies, and methods of pooling data were all appropriate and clearly described. Some details were provided relating to the review process. A validity assessment was presented for the RCTs but not for the case series included in the review. It is possible that the validity of such studies will vary (e.g. range of sample size 2-158) and therefore more detail would have been useful. Only one electronic database was accessed for the search strategy, and only English language articles were sought, which means that relevant material may not have been identified. In addition, there was no mention of an attempt to identify unpublished literature, therefore publication bias is a possibility. The authors’ conclusions appear to follow-on from the presented evidence.

Implications of the review for practice and research
Practice: The authors state that there is a modest amount of evidence to support the use of CPAP in patients with cardiogenic pulmonary oedema due to its association with a decrease in the need for intubation and a trend toward a decrease in mortality. However, between-study differences suggest that the greatest benefit may be obtained in patients
with severe ventilatory failure. The decision to use CPAP for a specific patient is dependent on patient, provider, and institutional factors in addition to the reported findings of clinical trials.

Research: The authors state that RCTs are required to establish the effectiveness of NPPV in pulmonary oedema. In addition, further work is required to clarify the risks and benefits of CPAP and NPPV in such patients.

Funding
Richard Ivey Critical Care Trauma Center; London Health Sciences Centre; Program of Critical Care Medicine.

Bibliographic details

PubMedID
9792593

Original Paper URL

Other publications of related interest
This additional published commentary may also be of interest. Hughes CM. Review: continuous positive airway pressure support reduces the need for intubation in patients with cardiogenic pulmonary edema. ACP J Club 1999;130(3):58.

Indexing Status
Subject indexing assigned by NLM

MeSH
Clinical Trials as Topic; Confidence Intervals; Hospital Mortality; Humans; Intubation, Intratracheal; Positive-Pressure Respiration; Pulmonary Edema /etiology /mortality /therapy; Reproducibility of Results; Retrospective Studies; Shock, Cardiogenic /complications; Survival Rate; Treatment Outcome

AccessionNumber
11998001920

Date bibliographic record published
31/01/2000

Date abstract record published
31/01/2000

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.