Which patients with acute exacerbation of chronic obstructive pulmonary disease benefit from noninvasive positive-pressure ventilation: a systematic review of the literature

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CRD summary
This review assessed noninvasive positive-pressure ventilation (NPPV) for acute exacerbations of chronic obstructive pulmonary disease. The authors concluded that NPPV benefits patients with severe exacerbations, but studies found no benefit for milder exacerbations. The authors’ conclusions about severe exacerbation are likely to be reliable, but there may have been insufficient evidence to show an effect for nonsevere exacerbations.

Authors' objectives
To assess the effects of noninvasive positive-pressure ventilation (NPPV) in patients with acute exacerbations of chronic obstructive pulmonary disease (COPD).

Searching
MEDLINE (from 1966 to December 2002), EMBASE (from January 1990 to June 2002) and the Cochrane Library were searched without any language restrictions; the search terms were given. Abstracts of the following meetings were handsearched from 1990 to 2002: the American Thoracic Society, the American College of Chest Physicians, the Society of Critical Care Medicine, the European Society of Critical Care Medicine, and the European Respiratory Society. The reference lists of identified studies and reviews were also reviewed, as were the authors’ personal files. Experts and first authors of selected studies were contacted for details of additional published and unpublished studies.

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 NPPV plus standard therapy with standard therapy alone (or with additional alternative therapy not considered to be standard therapy) were eligible for inclusion. The included studies used different interfaces for NPPV (nasal or face mask), different types of ventilation (most used pressure cycled, others used volume cycled) and different ventilators (conventional mechanical or small portable). The participants were treated in general respiratory wards or intensive care units. In the included studies involving patients with nonsevere exacerbations, NPPV was delayed for up to 24 or 48 hours after admission. Some studies offered conventional mechanical ventilation to all patients who failed the initial allocated treatment, while others offered this only to selected patients.

Participants included in the review
Studies in patients with an acute exacerbation of COPD (as defined by the authors) were eligible for inclusion. Studies that reported the results separately for subgroups of patients with COPD were also included. The primary studies included patients with severe exacerbations defined by strict criteria, as well as poorly defined patients with less severe exacerbations.

Outcomes assessed in the review
Studies that assessed in-hospital mortality (the primary review outcome), endotracheal intubation, or length of hospital stay were eligible for inclusion.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected studies and reached full agreement on the included studies.
Assessment of study quality
Studies published in full were assessed and scored using 11 validity criteria, including a description of the study protocol, blinding, explicit description of cointerventions and outcome assessment, and definition of outcomes. The report indicated that further details are available on the journal's website, but a subscription may be required to access such information. The maximum possible score was 11 points. The reviewers were unable to assess the validity of studies published as abstracts, owing to insufficient information. Two reviewers independently assessed validity and resolved any disagreements by reaching consensus, with the aid of a third author if required.

Data extraction
Two reviewers independently assessed validity and resolved any disagreements by reaching consensus, with the aid of a third author if required. For each study, the intubation rates and mortality for each treatment group were extracted. The risk difference (RD) and 95% confidence intervals (CIs) were extracted for dichotomous data, while mean values and 95% CIs were extracted for continuous variables.

Methods of synthesis
How were the studies combined?
The studies were combined using a random-effects meta-analysis. Pooled RDs and 95% CIs were calculated for in-hospital mortality and endotracheal intubation. Data from 2 RCTs that only reported mortality in the intensive care unit were excluded from the meta-analysis of in-hospital mortality. For studies reporting the mean length of hospital stay, the pooled weighted mean absolute difference (WMD) and 95% CI between treatments were calculated. Studies reporting medians were not included in this meta-analysis. A funnel plot was used to assess publication bias.

How were differences between studies investigated?
Statistical heterogeneity was assessed visually and using the chi-squared statistic.

Two planned subgroup analyses were conducted. One analysed patients with severe exacerbations and those with less severe exacerbations separately; the other included only studies published in full. Two post hoc subgroup analyses were also conducted. The first included only studies that used endotracheal intubation or other specified criteria to define treatment failure. The second examined the influence on the results of the proportion of patients offered conventional mechanical ventilation.

Results of the review
Fifteen RCTs (636 patients with COPD) were included.

The studies scored from 4 to 10 out of 11 points. None of the studies used blinding. Most studies explicitly described cointerventions (9 RCTs), specified criteria for intubation and outcome assessment (8 of 11 RCTs) and explicitly defined outcomes (8 of 11 RCTs).

Main analyses.
NPPV significantly reduced in-hospital mortality in comparison with standard therapy alone (RD 10%, 95% CI: 5, 15), based on 11 RCTs with 629 patients. No statistically significant heterogeneity was detected (P>0.2).

NPPV significantly reduced the rate of endotracheal intubation in comparison with standard therapy alone (RD 28%, 95% CI: 15, 40), based on 13 RCTs with 654 patients. Statistically significant heterogeneity was detected (P<0.001).

NPPV significantly reduced the length of hospital stay in comparison with standard therapy alone (WMD 4.57 days, 95% CI: 2.30, 6.83), based on 9 RCTs with 340 patients. Statistically significant heterogeneity was detected (P<0.001). Two RCTs that reported the results as medians found no significant difference between treatments in the length of hospital stay.

Planned subgroup analyses. In patients with severe COPD exacerbations, NPPV significantly reduced in-hospital mortality (RD 12%, 95% CI: 6, 18), rate of endotracheal intubation (RD 34, 95% CI: 22, 46) and length of hospital stay.
(WMD 5.59 days, 95% CI: 3.66, 7.52), compared with standard therapy alone, based on 9 RCTs. Statistical heterogeneity remained but the direction of effect was consistent among studies.

In patients with nonsevere exacerbations, there was no significant difference between treatments in hospital survival (RD 2%, 95% CI: -8, 12), intubation (RD 0, 95% CI: -11, 11) or hospital stay (WMD 0.82 days, 95% CI: -0.12, 1.77), based on 2 RCTs with 72 patients.

Post hoc subgroup analyses.

The results were similar when only studies that used endotracheal intubation or other pre-specified criteria to define NPPV treatment failure were analysed.

The proportion of people offered conventional mechanical ventilation did not influence the results.

No effect of publication status on the results was found.

**Authors' conclusions**
The addition of NPPV to standard therapy benefited patients with severe acute exacerbation of COPD, but was not shown to benefit hospitalised patients with milder exacerbations of COPD.

**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 attempts were made to minimise publication and language bias. Two reviewers independently selected the studies, assessed validity and extracted the data, thus reducing the potential for bias and errors. Only RCTs were included and validity was formally assessed using defined criteria. Relevant information on the included studies was tabulated.

The data were combined in a meta-analysis and statistical heterogeneity was assessed. Clinical and statistical heterogeneity were explored using planned and post hoc subgroup analyses, and forest plots for hospital mortality and endotracheal intubation showed consistency in the direction of effect (even if not statistically homogeneous for effect size) among studies in patients with severe exacerbations. The authors' conclusions regarding patients with severe exacerbation of COPD are likely to be reliable, but there may have been insufficient evidence to show an effect in patients with nonsevere exacerbations of COPD.

**Implications of the review for practice and research**
Practice: The authors recommended that NPPV be added to standard medical therapy for patients with severe exacerbation of COPD, and that these patients should be closely monitored in a high-dependency unit. They stated that NPPV was not currently indicated for patients with initially mild exacerbations of COPD, but that these patients should be closely monitored and NPPV started should respiratory distress increase and respiratory acidosis develop.

Research: The authors stated that more research into the role of NPPV in patients with mild exacerbations of COPD is required. They also stated that large RCTs are needed to examine different methods of weaning patients from NPPV, to determine whether NPPV can help wean patients from invasive mechanical ventilation, and to determine which methods of administration minimise NPPV failure.

**Bibliographic details**

**PubMedID**
12779296
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.