Use of non-invasive ventilation to wean critically ill adults off invasive ventilation: meta-analysis and systematic review

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CRD summary
This review compared the effects of invasive and non-invasive weaning, concluding that the limited data showed that non-invasive weaning reduces mortality and ventilator associated pneumonia in critically ill mechanically ventilated adults, but further research is required. This was a well-conducted review, where the authors acknowledged the limitations with the included trials, and their conclusions are likely to be reliable.

Authors' objectives
To compare the effects of invasive and non-invasive weaning techniques on important outcomes in critically ill mechanically ventilated adults.

Searching
MEDLINE (January 1966 to April 2008), EMBASE (January 1980 to April 2008) and the Cochrane Central Register of Controlled Trials (Issue 2, 2008) were searched without language restrictions. Details of the search terms and strategy were available on request. In addition, the American Journal of Respiratory, Intensive Care Medicine, Critical Care Medicine and Chest (January 2003 to April 2008) and references of retrieved articles were manually searched. Authors were contacted for unpublished data.

Study selection
Trials comparing extubation with immediate application of non-invasive ventilation to continued invasive weaning were eligible for inclusion. The population of interest was adults with respiratory failure who required invasive mechanical ventilation for at least 24 hours. Eligible studies were required to report mortality, which was the primary outcome of interest, or one of several named outcomes. Patients who were immediately post-operative or who had received an unplanned intubation were excluded. Studies comparing non-invasive ventilation with unassisted oxygen supplementation were also excluded.

Included studies were mainly of patients with chronic obstructive pulmonary disease but studies also included patients with acute disease. Some patients had pulmonary infection or respiratory failure. Inclusion criteria for weaning varied among studies and, where reported, patients were intubated for between 36 hours to three days. The majority of studies delivered non-invasive ventilation via face or nasal mask, while the majority of controls received invasive pressure support. Mortality was reported at 30 days, 60 days, 90 days, at hospital discharge or at an undefined time.

Two reviewers independently screened studies for inclusion. Discrepancies were resolved by consensus, and referred to a third reviewer if necessary.

Assessment of study quality
Two reviewers independently assessed the quality of the studies, including items on: randomisation, allocation concealment, co-interventions, blinded outcome assessment, follow-up and intention-to-treat analysis.

Discrepancies were resolved by consensus, and referred to a third reviewer if necessary.

Data extraction
Two reviewers independently extracted data on dichotomous outcomes to calculate estimates of relative risk (RR), and weighted mean differences (WMDs) were calculated for continuous outcomes, both with their 95% confidence intervals.

Discrepancies were resolved by consensus, and referred to a third reviewer if necessary.
Methods of synthesis
A random-effects model was used to pool RRs and WMDs. Statistical heterogeneity was assessed using the Cochran Q statistic (p<0.10) and I² test. Sensitivity analyses were undertaken to assess the impact of removing quasi-randomised trials on mortality and ventilator associated pneumonia. Subgroup analyses was undertaken to compare the effects of non-invasive weaning on mortality and weaning failures in patients with chronic obstructive pulmonary disease compared with non-chronic populations, and on mortality in studies with 50% or more patients versus less than 50% patients with chronic obstructive pulmonary disease. Publication bias was assessed through visual inspection of a funnel plot.

Results of the review
Eleven randomised controlled trials (RCTs) and one quasi-randomised controlled trial (n=530) were included in the review. Sample sizes ranged from 21 to 90 patients. Included studies were of moderate to high quality.

Non-invasive weaning was more effective than invasive weaning in reducing mortality (RR 0.55, 95% CI: 0.38, 0.79, p=0.001, 12 trials) and ventilator associated pneumonia (RR 0.29, 95% CI: 0.19, 0.45, p<0.001, 11 trials). There was no evidence of statistical heterogeneity.

Non-invasive weaning reduced the length of stay in intensive care (WMD -6.27 days, 95% CI: -8.77, -3.78) and hospital stay (WMD: -7.19 days, 95% CI: -10.8, -3.58). Non-invasive weaning also reduced total duration of mechanical ventilation by 5.6 days and duration of invasive ventilation by 7.8 days but there was evidence of statistical heterogeneity. There were no significant differences in benefit between invasive and non-invasive weaning on weaning failure or weaning time. Adverse events were reported in the review.

Sensitivity analysis and post-hoc analysis did not significantly alter the results. Subgroup analysis showed a significant benefit of non-invasive weaning on mortality in studies enrolling 50% or more patients with chronic obstructive pulmonary disease (p=0.02). No statistically significant benefits were reported for other subgroup analyses.

There was evidence of publication bias on inspection of the funnel plot, which suggests that studies with non-significant results may have been missed.

Authors' conclusions
The limited data shows that non-invasive weaning has a positive effect on mortality and ventilator associated pneumonia in critically ill adults but net clinical benefits need clarification.

CRD commentary
The review question and inclusion criteria were clear. The supporting literature search was comprehensive and was conducted without language restrictions, thus reducing the potential for language. A search for both published and unpublished articles was undertaken to minimise the potential for publication bias but publication bias was evident on inspection of the funnel plot. Validity was assessed using appropriate criteria and studies were of acceptable quality.

The review process for study selection, data extraction and validity assessment were made explicit, thus minimising the potential for reviewer bias and error. Appropriate methods were used to combine the data and assess for statistical heterogeneity but there was evidence of statistical heterogeneity for some secondary outcomes. The authors acknowledged certain limitations with the included trials, including methodological heterogeneity and the potential for performance bias. They also pointed out that studies were predominantly of patients with chronic obstructive pulmonary disease, which means it remains to be determined whether similar effects would be apparent with other causes of respiratory failure. This was a well-conducted review and the authors' conclusions appear appropriate and are likely to be reliable.

Implications of the review for practice and research
Practice: The authors stated that weaning should be used preferentially in patients with chronic obstructive pulmonary disease and applied in a highly monitored environment.

Research: The authors stated that a further well-conducted RCT is required to evaluate the clinical benefits of non-invasive weaning on clinical outcomes, particularly the risks associated with extubation and the impact of re-intubation after failed extubation.
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