

Use of Non-Invasive Ventilation as a Weaning Mode in the ICU — Should We Pull Out the Endotracheal Tube?*

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ABSTRACT

Background. Non-invasive ventilation (NIV) has been used to avoid the need for and problems associated with endotracheal intubations in acute respiratory failure, especially in patients with chronic obstructive pulmonary disease (COPD). There is increasing use of NIV as a bridge in weaning patients from mechanical ventilatory support in the intensive care unit (ICU) with earlier extubations. However, there is a need to evaluate the evidence of its use with an adequate systematic review of the literature. We aimed to study the effectiveness of NIV compared to the conventional invasive ventilation in weaning patients from mechanical ventilatory support.

Methods. Two reviewers searched electronic databases, Medline, Embase and the Cochrane Central Register of Controlled trials (The Cochrane Library, Issue 1, 2004) for prospective randomised controlled trials. The methodological quality of the relevant trials was independently assessed and the data was extracted by both reviewers. Where possible and appropriate, the data were pooled and analysed.

Results. We identified 11 studies of which only 3 studies fulfilled our inclusion criteria. None of the studies were blinded. The patient population comprised mainly patients with COPD and NIV was used to wean patients from invasive mechanical ventilation (IMV). The pooled results for the 126 patients showed significant reductions in the duration of ICU stay (WMD -6.9 , 95% CI -12.69 to -1.1 days), nosocomial pneumonia rates (RR 0.37, 95% CI 0.15 to 0.93) and mortality (RR 0.25, 95% CI 0.09 to 0.65) in the NIV group. The weaning time from mechanical ventilation was however inconsistent among the 3 studies. In 2 studies, reduction was significant in the NIV group while in the third study the reduction was significant with the conventional invasive ventilation group.

Conclusion. Earlier extubation to a period of NIV before discontinuation of mechanical ventilatory support may be an option in a select group of patients with COPD intubated for acute-on-chronic respiratory failure. More and larger studies are needed to confirm the role of NIV as a weaning mode for acute hypoxemic respiratory failure in the ICU.

Keywords: extubation, mechanical ventilation, meta-analysis, systematic review, weaning failure

INTRODUCTION

Non-invasive ventilation (NIV) refers to the provision of mechanical ventilatory support of the lungs without the use of an endotracheal tube. Initially used for the treatment of hypoventilation in patients with neuromuscular disorders, non-invasive ventilation has since been tried in a wide variety of respiratory diseases and conditions.^{1,2}

The main attractions and benefits of NIV are avoidance of endotracheal intubation and hence reductions in nosocomial pneumonia rates, shorter length of hospital stay, greater patient comfort and an improvement in overall outcome.^{3,4}

Ventilatory support provided by means of standard critical care ventilators, or portable bilevel ventilators, is usually a form of pressure-limited ventilation or pressure support ventilation. Minimum mandatory breaths can be set and ensured. Newer modes of NIV include proportional assist ventilation which can match

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Table 1. Characteristics of included trials.

Study	Nava <i>et al</i> ⁹	Girault <i>et al</i> ¹²	Ferrrer <i>et al</i> ¹³
Location	3 centres: 3 Respiratory ICUs	Single centre: Medical ICU	2 centres: Respiratory ICU, general ICU
Number of Patients	50	33	43
Age of Patients (NIV/IMV) (yrs)	68.7/67	63.6/64.9	70.3/71.0
Inclusion Criteria	Acute on chronic respiratory failure requiring endotracheal intubation	Acute on chronic respiratory failure	Intubated patients who met weaning criteria but failed spontaneous breathing trials for 3 consecutive days
Method of Randomisation	Not reported	Not reported	Computer-generated table
Concealment	Sealed opaque numbered envelopes	Not reported	Not reported
Follow-up (days)	60	90	90
Weaning Protocol	Yes	Yes	Yes
Mode of IMV	PSV	PSV	AC, PSV or both
Reintubation Criteria	Not reported	Not reported	Yes
Intention to Treat Analysis	Yes	Yes	Yes

IMV: Invasive mechanical ventilation

PSV: pressure support ventilation

AC: Assist-control ventilation

the patient's respiratory efforts rather than depend on preset pressures or volumes for greater patient comfort and hence compliance.

Since the 1980s, there has been a resurgence in the use of NIV in the form of non-invasive positive pressure ventilation (NPPV) delivered via a mask interface such as a nasal mask, facemask or a full-face mask.¹ The type of mask chosen is dependent on patient tolerance and for patient comfort. NIV is in fact the ventilatory therapy of choice in selected patients with hypercapnic respiratory failure compared to medical therapy alone.^{5,6}

The first reports of NIV for weaning from invasive mechanical ventilation (IMV) started to appear in the literature from 1992 but it was not until 1998 that Nava *et al* published a randomised controlled trial comparing NPPV to IMV.⁷⁻⁹ Furthermore, the British Thoracic Society Standards of Care Committee had, in the year 2002, included in its guideline on "Non-invasive ventilation in acute respiratory failure" a Grade B recommendation (Scottish Intercollegiate Guideline Network or SIGN criteria) for the use of NIV when conventional weaning strategies fail.¹⁰

OBJECTIVES

This systematic review was undertaken to determine objective estimates of which is the better treatment option, weaning of patients from mechanical ventilatory support using NIV or conventional IMV,

based on evidence from randomised controlled trials (RCTs) in the intensive care unit (ICU).

METHODS

Search Strategy

Two reviewers independently conducted a search of the databases, Medline from 1966 to December 2003, Embase from 1974 to December 2003 and the Cochrane Library (Issue 1, 2004). We used the search terms "non-invasive ventilation" as well as "weaning" and restricted the study design to RCTs. We also reviewed the reference lists of articles identified electronically for potentially relevant primary studies.

Selection Criteria

We included prospective, randomised controlled trials involving the use of NIV for weaning from IMV. Blinding of trials was not a prerequisite criteria for selection. The primary outcomes sought were its effects on length of stay in hospital and intensive care unit (ICU), nosocomial pneumonia rates, mortality and successful weaning at 20 days.

Study Description and Validity Assessment

Independently and in duplicate, the authors extracted the data from the identified trials. The trials were assessed for quality from the level of randomisation, concealment of allocation and intention to treat analysis.

Statistical Analysis

In pooling the data from studies, we used relative risk (RR) for dichotomous outcomes and weighted mean difference (WMD) for continuous variables and 95% confidence intervals (CI) to estimate the treatment effects where available and appropriate. Analysis was by intention to treat. Pooled effect estimates and heterogeneity between studies were tested with Rev Man 4.2.1 statistical package.¹¹ When heterogeneity was significant with the fixed effects model a random effects model was used.

RESULTS

Study Selection

We found a total of 11 studies from the electronic searches, but only 3 studies satisfied our inclusion criteria on weaning using NIV following intubation for acute respiratory failure.^{9,12,13} Further reviews of abstracts of articles contained in the reference lists did not produce any suitable studies for inclusion. One study was excluded due to its quasi-randomisation design.¹⁴ There was complete agreement between both reviewers on the selected studies.

Study Description and Validity

All the 3 studies were randomised controlled trials published in English between 1998 and 2003. Method of randomisation was by computer-generated numbers in 1 study but it was unclear in the other 2 studies.¹³ None of the studies were blinded. There was concealment of allocation in one study since they used sealed opaque envelopes but it was unclear in other studies.^{9,12} The results reported were based on intention to treat analysis. Overall, the studies were of reasonably good methodological quality (Table 1).

All patients in 2 of the studies and 44% of intubated patients in the third study by Ferrer *et al* enrolled patients with acute exacerbations of COPD; up to 77% of patients in the third study had chronic pulmonary disorders. Exclusion criteria included lack of co-operation from the patients and recent gastrointestinal surgery in all the studies.

All patients had to meet some simple weaning criteria before a 2-hour T-piece weaning trial was attempted. Patients in Ferrer study had to have an improvement or resolution of the underlying cause of acute respiratory failure as well and enrolment into the study only followed after 3 consecutive days of failed daily T-piece weaning trials. These patients were considered to be difficult to wean. All patients in the 3 studies had at least 24 to 48 hours of invasive ventilatory support before randomisation to 1 of 2 groups.

The sample sizes of the 3 studies ranged from 33 to 50 patients, with a combined total of 126 patients. In all the studies, patients randomised to the NIV group were extubated and put on NIV by mask. Weaning from NIV started on the very same day in the study by Girault *et al*, with increasingly longer periods of spontaneous breathing with nasal oxygen therapy in-between mask ventilation. In the other 2 studies, NIV was only interrupted for brief periods during meals for the first 24 to 48 hours post-extubation, following which ventilatory support was gradually reduced according to set protocols. In the control groups on IMV, patients were ventilated with pressure support ventilation (PSV) or assist control (AC) modes.

Mortality rate was assessed at 60 days in 1 study and at 90 days in the other 2 studies. The overall results show that there was a significant reduction in the mortality rates in the NIV group of patients (RR 0.25, 95% CI 0.09, 0.65) (Fig. 1). There was no significant result heterogeneity between the studies, so a fixed effects model was used (chi square=0.08, p=0.96). In view of the heterogeneity of the pooled data for the duration of ICU stay and nosocomial pneumonia rates, the random effects model was used. Duration of ICU stay was significantly reduced in favour of the NIV group (WMD -6.9, 95% CI -12.69, -1.1 days). A similar significant reduction was also observed in nosocomial pneumonia rates in favour of the NIV group (RR 0.37, 95% CI 0.15, 0.93).

The duration of mechanical ventilatory support or the time required for weaning from mechanical ventilation, both invasive and non-invasive, was inconsistent among the 3 studies. In 2 studies, reduction was significant in the NIV group while in the third study the reduction was significant with the conventional invasive ventilation group. (WMD -2.09, 95% CI -13.97, 9.79 days) (Fig. 2). Success of weaning at 20 days of ventilatory support, the threshold beyond which patients are generally considered unweanable,¹⁵ favoured the NIV group (RR 1.94, 95% CI 1.39, 2.72) using the fixed effects model (chi square=0.15, p=0.7) with available data reported in 2 of the studies.

Complications from the use of NIV in the 3 studies were minor and included nasal bridge abrasions or ulcerations and gastric distension.

DISCUSSION

This meta-analysis confirms the benefit of NIV as an extubation and weaning technique in patients with COPD compared to conventional weaning with IMV. Although this systematic review was done with scientific rigour, its limitations include the small

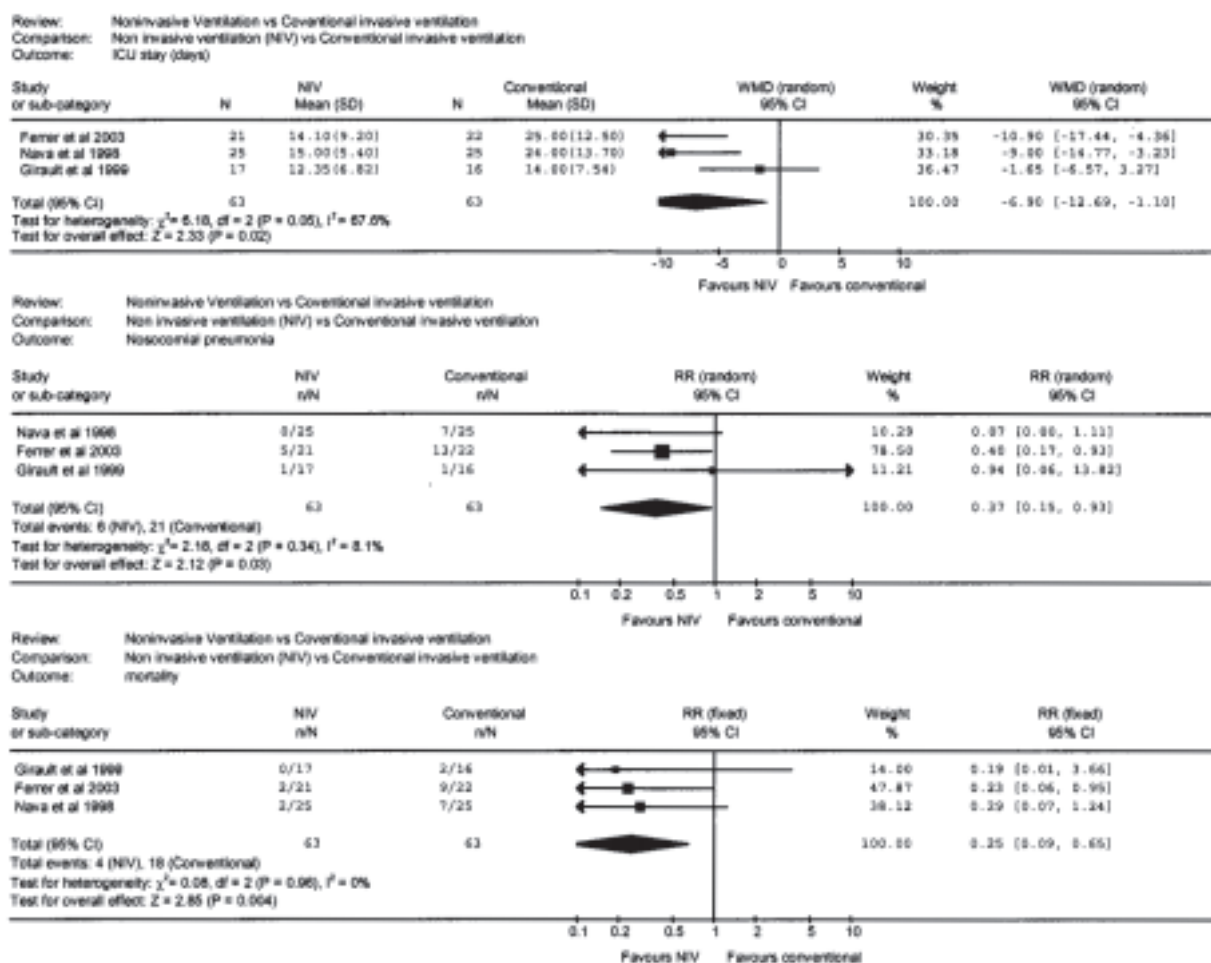


Fig. 1. Forest plots for the outcome variables duration of ICU stay, nosocomial pneumonia rates and mortality.

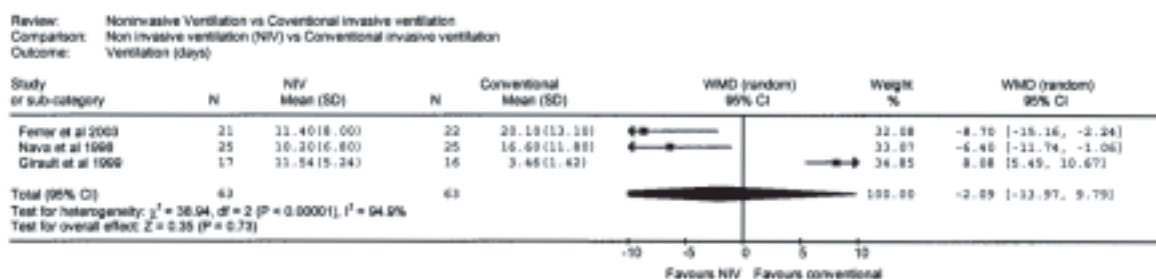


Fig. 2. Forest plot comparing the duration of mechanical ventilation between NIV and IMV.

number of randomised trials and the small sample sizes of these trials.

Much of the evidence for NIV as an alternative to intubation in acute respiratory failure is from controlled studies on patients with acute-on-chronic respiratory failure or hypercapnic respiratory failure.¹⁶⁻²¹ Use of NIV, as opposed to medical therapy alone, improves physiologic parameters, symptom relief and decreases the rate of intubations and its associated complications. Only one randomised controlled trial did not have the same positive outcome.²¹ Controlled trials also support the use of NIV in patients with acute respiratory failure

following solid organ transplantation and those who are immunocompromised to avoid endotracheal intubation.^{22,23}

Traditionally, weaning from mechanical ventilation means the initiation of stepwise reductions in invasive ventilatory support with the aim of extubation of the trachea and discontinuation of any form of positive pressure ventilation.²³⁻²⁷ Indices used to predict success of any weaning trial are similarly validated.^{28,29}

With the success of NIV in avoidance of endotracheal intubation in acute respiratory failure compared to

medical therapy alone, it is inevitable that the role of NIV would be expanded to include facilitation of earlier extubation and subsequent weaning from mechanical ventilatory support, bridged by a period of NIV. By avoiding the complications associated with prolonged intubation, it is hoped that outcomes can be improved. In addition to pressure support and T-piece wean, this third option of extubating to NIV as an alternative mode of weaning from mechanical ventilation was given a boost by the recent publication of these 3 randomised controlled trials.²⁹

In light of current evidence, should we then be pulling out the endotracheal tubes earlier?

The decision to extubate is not one to be taken lightly.³⁰ Extubation failure and reintubation not only increases the risk of nosocomial pneumonia but are also independent predictors of mortality.³¹⁻³³ Conversely, so are delayed extubation and prolonged invasive ventilation causes of increased morbidity, length of ICU and hospital stay and tracheostomy rates.³⁴

In the event of extubation failure, NIV has been shown to reduce the need for reintubation in some two-thirds of patients in uncontrolled trials.^{6,35,36} However, delays in reintubation result in deterioration in diaphragmatic and lung function, increased aspiration risk and mortality.³¹ Furthermore, the very act of intubation is often fraught with danger and is of great physiological consequence.

The patients in the 3 trials on weaning all met some simple weaning criteria and were deemed ready to begin the process of weaning from mechanical ventilatory support. Those randomised to the NIV group had failed spontaneous breathing trials and would normally have been continued on conventional IMV but were extubated instead. Hence, the patients very likely would have required intervention immediately post-extubation. Nava *et al* and Ferrer *et al* applied NIV continuously for the first 24 to 48 hours before embarking on weaning from NIV. Girault *et al* started weaning from NIV right from the day of extubation. Whether this could have been the cause of some of the differences in the study results is not apparent (Fig. 2). Reintubation rates for the non-invasively ventilated patients ranged from 14 to 23.5%, not different from the group managed with conventional weaning strategy.^{12,13}

Studies comparing invasive versus NIV are not possible to blind. Greater use of sedatives in patients in the control group receiving IMV can theoretically prolong the period of invasive ventilation by delaying

extubation as has been shown in randomised trials.³⁷ Weaning regimens are also different between the IMV or control group and the NIV group post-extubation. Other factors which can influence the study results and the interpretations include: the differing effects of different weaning criteria, thresholds for initiation of weaning, modes of ventilatory support prior to extubation and the weaning regimens employed for each weaning mode on outcome measures such as reintubation rates.²⁹

Timing of extubation is important. Too early extubations may increase the risk of failure and resultant reintubation rates; too high a threshold for extubation leads to a longer period of IMV and the benefits derived from NIV would be negated.

Indeed, these are exciting times for intensivists. With the encouraging results from the 3 studies which put a whole new perspective to the meaning of weaning from mechanical ventilatory support, even difficult to wean patients can be considered for early extubation, thereby avoiding the problems associated with prolonged intubation and hopefully the need for subsequent tracheostomies.

To leverage on the current wealth of evidence from the use of NIV in acute respiratory failure to avoid endotracheal intubation, patients who would otherwise benefit from NIV compared to medical therapy but are intubated because of haemodynamic instability or for airway protection are possible candidates for attempting weaning by NIV. Once the patients' conditions improve and the reason for keeping the endotracheal tube in-situ is solely for the purpose of providing mechanical ventilatory support, an extubation followed by weaning from NIV can be considered in the absence of contraindications.

More and larger similarly well-designed studies are needed to confirm the results of these studies on weaning using NIV and the applicability of the results on patients with acute hypoxemic respiratory failure from any cause. Risk versus benefit ratio on the timing of earlier extubation needs further in-depth study and review. Till then, one would be advised to tread cautiously in the selection of patients for early extubation and weaning, reserving the technique mainly for patients with acute-on-chronic respiratory failure.

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