SERIES "NONINVASIVE VENTILATION IN ACUTE AND CHRONIC RESPIRATORY FAILURE"

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Noninvasive ventilation after intubation and mechanical ventilation

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ABSTRACT: Patients with chronic airflow obstruction who are difficult to wean from mechanical ventilation are at increased risk of intubation-associated complications and mortality because of prolonged invasive mechanical ventilation. Noninvasive positive pressure ventilation may revert most of the pathophysiological mechanisms associated with weaning failure in these patients.

Several randomized controlled trials have shown that use of noninvasive ventilation to achieve earlier extubation in difficult-to-wean patients or in patients who develop respiratory failure after apparently successful extubation can result in reduced periods of endotracheal intubation and complication rates and improved survival. However, this is not a consistent finding, and the currently available published data with outcome as the primary variable are exclusively from patients who had pre-existing lung disease. In addition, the patients were haemodynamically stable, with a normal level of consciousness, no fever and a preserved cough reflex.

It remains to be seen whether noninvasive positive pressure ventilation has a role in other patient groups and situations, such as prevention of postextubation failure or unplanned extubation. The technique is, however, a useful addition to the therapeutic armamentarium for a group of patients who pose a significant clinical and economic challenge.

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Mechanical ventilation using an artificial airway is probably the most frequently life-saving procedure used in the management of critically ill patients with severe respiratory failure. However, it is associated with multiple complications [1], primarily increased risk of nosocomial pneumonia with a high mortality rate [2–4], but also generalized myopathy, possibly related to the sedation or curarization necessary for invasive mechanical ventilation [5]. In the majority of cases, mechanical ventilation can be withdrawn after resolution or significant improvement of the underlying indication for mechanical ventilation. However, it is estimated that ~20–30% of patients require gradual withdrawal of ventilatory support, namely weaning [6]. The process of discontinuing mechanical ventilation may be a major challenge, especially in patients with chronic respiratory disorders, in whom

weaning is particularly difficult. It is estimated that the proportion of intubated and ventilated chronic obstructive pulmonary disease (COPD) patients needing a weaning procedure ranges 35–67%, depending on the mode of ventilation used and the definition of weaning [7–9]. Persistent weaning failure is associated with prolonged mechanical ventilation [10], a major risk factor for nosocomial pneumonia [11, 12], as well as with increased morbidity and mortality, especially in patients with a background of pre-existing chronic respiratory failure [13, 14]. It is also an expensive use of a valuable resource, namely intensive care unit (ICU) bed days. As a result, any intervention which shortens the weaning period is to be welcomed. This article particularly focuses on the role of noninvasive positive pressure ventilation (NPPV) as a supportive measure during weaning from mechanical ventilation.

The clinical approach to weaning

In patients in whom the underlying indication for mechanical ventilation has resolved or significantly improved, daily screening of the functioning of the respiratory system is recommended. Before weaning can be considered, there should be a normal level of consciousness, haemodynamic stability, exclusion of significant anaemia [15] and correction of arterial hypoxaemia (arterial oxygen tension ≥ 8.0 kPa, using an inspiratory oxygen fraction of ≤ 0.4 and a positive end-expiratory pressure (PEEP) of ≤ 0.67 kPa). If all of these criteria are fulfilled, then a spontaneous breathing trial is recommended to confirm that the patient is capable of unassisted spontaneous breathing [16, 17]. This should be carried out using either a Venturi oxygen source connected to the endotracheal tube through a T-piece or low levels of pressure-support ventilation (PSV), ≤ 8 – 10 cmH₂O, to compensate for the additional work of breathing imposed by the endotracheal tube and the circuits and valves of the ventilator [18, 19] and reproduce the expected work of breathing necessary once the patient has been extubated [20]. If the patients tolerate this, they can be extubated, and, if no ventilatory support is needed within 48–72 h, they can be considered to have been weaned successfully (weaning success). However, if ventilatory support is needed within 48–72 h after extubation, this is defined as extubation failure. If signs of poor tolerance occur during the spontaneous breathing trial, defined as weaning failure, patients must be reconnected to the ventilator and gradual withdrawal of ventilatory support is recommended.

A distinction must be made between dependence on the ventilator and an ongoing need for endotracheal intubation. When the weaning process is initiated, it is necessary to evaluate: 1) the need for ventilatory support *via* a spontaneous breathing trial; and 2) whether or not the artificial airway is needed. The beneficial effects of noninvasive ventilation as a wean-supporting technique can be expected only when an initial weaning attempt has failed (ventilator dependence) but there is no need for an artificial airway.

The optimal ventilatory mode for the management of patients during weaning remains controversial. Although one study showed that, compared with PSV and intermittent mandatory ventilation (IMV), once-daily or multiple daily trials of spontaneous breathing were the fastest methods of liberating patients from the ventilator [21], others have shown that patients were weaned earlier using progressively decreasing levels of PSV, compared with assisted controlled ventilation and intermittent mandatory ventilation [6]. Both studies concluded that, regardless of the ventilatory mode used during weaning, age and underlying disease, particularly a diagnosis of COPD, were the main determinants of outcome in those patients. The conventional approach to weaning is summarized in figure 1.

Pathophysiological mechanisms of weaning failure

Patients who cannot be weaned immediately from mechanical ventilation are likely to develop a rapid

Fig. 1.—Algorithm for the clinical management of discontinuation of mechanical ventilation. MV: mechanical ventilation; P_{a,O_2} : arterial oxygen tension; F_{i,O_2} : inspiratory oxygen fraction; PEEP: positive end-expiratory pressure; f_R : respiratory frequency; V_T : tidal volume. *: procedures supported by a grade A level of evidence (the highest), *i.e.* several randomized controlled trials. (1 mmHg=0.133 kPa.) (Adapted from [16].)

and shallow breathing pattern during the spontaneous breathing trial (table 1) [22]. In COPD patients, failure during the transition from positive pressure ventilation (PPV) to spontaneous breathing is associated with an increased workload for the respiratory muscles, with progressively higher levels of dynamic lung elastance, intrinsic PEEP (PEEP_i), inspiratory

Table 1.—Pathophysiological bases of weaning failure during transition from positive pressure ventilation to spontaneous breathing

Rapid and shallow breathing pattern
Increased workload of respiratory muscles
Increased PEEP _i
Increased elastance and resistance of respiratory system
Increased work of breathing
Increased effective inspiratory impedance
Increased load/capacity balance
Inappropriate cardiovascular response
Increased venous return to right ventricle
Increased negative deflections in intrathoracic pressure
Increased left ventricular afterload
Fall of P_{v,O_2} and S_{v,O_2}
Impaired neurological status

PEEP_i: intrinsic positive end-expiratory pressure; P_{v,O_2} : mixed venous oxygen tension; S_{v,O_2} : mixed venous oxygen saturation.

resistance and work of breathing [23]. Because of worsening hyperinflation, the respiratory muscles work at an increased mechanical disadvantage with consequent reduction in capacity, which can be reduced further by the development of acidosis [24]. In ventilator-dependent patients, the presence of a high drive to breathe and imbalance between the increased workload and reduced inspiratory muscle capacity causes respiratory distress and hypercapnia [25]. These changes are not present when patients successfully tolerate a spontaneous breathing trial. Consequently, the most accurate clinical predictors of weaning outcome during a spontaneous breathing trial are the presence of a rapid and shallow breathing pattern during the first minutes of spontaneous breathing [26], an increased neuromuscular drive to breathe, measured by the airway opening pressure at 0.1 s ($P_{0.1}$) [27], or a combination of the two [28].

The cardiovascular response to the switch from PPV to spontaneous breathing is also important in achieving successful weaning. An increase in venous return to the right ventricle and, consequently, the leftward shift of the ventricular septum caused by the ventricular interdependence and large negative deflections in intrathoracic pressure due to the inspiratory threshold load, increases left ventricular afterload [29]. Inappropriate cardiovascular response to these changes with left ventricular dysfunction and increased pulmonary artery occlusion pressure occurs during weaning failure [29, 30]. Weaning failure is also associated with decreased mixed venous oxygen saturation during spontaneous breathing [31], reflecting the inability of the cardiovascular system to compensate for the increased systemic oxygen demands when spontaneous breathing is instituted. Conversely, in successfully weaned patients, mixed venous oxygen tension or saturation has been shown to remain unchanged or increase during spontaneous breathing, compared with PPV [31–33].

Physiological basis for the use of noninvasive ventilation during unsuccessful weaning

The rationale for the use of noninvasive ventilatory support to facilitate weaning lies in the ability of NPPV to offset several pathophysiological mechanisms associated with unsuccessful weaning, particularly the increased workload of the respiratory muscles (table 2).

In nonintubated COPD patients with acute hypercapnia, NPPV is effective in reducing work of breathing and the large negative deflections in intrathoracic pressure [34]. In the present study, an additive effect of PPV (as inspiratory support) and external PEEP (to counterbalance PEEPi) was shown. The mechanisms of short-term improvement of hypoxaemia and hypercapnia with NPPV in these patients appear to be related to increased alveolar ventilation secondary to attainment of a slower and deeper breathing pattern, with no changes in the ventilation/perfusion mismatch, assessed using the multiple inert gas elimination technique [35]. Similarly, in intubated patients without COPD and a spontaneous breathing

Table 2.—Physiological effects of noninvasive positive pressure ventilation

Effect on respiratory mechanics
Decreased negative deflections of intrathoracic pressure
Decreased work of breathing
Additive effects of positive pressure ventilation and external PEEP
Effects on gas exchange
Improvement of hypoxaemia and hypercapnia secondary to slower and deeper breathing pattern
No effects on ventilation/perfusion mismatch

PEEP: positive end-expiratory pressure.

trial failure, the rapid and shallow pattern of breathing improved after extubation with noninvasive ventilatory support [36]. Recent data in patients affected by chronic respiratory disorders who are not ready to sustain spontaneous breathing, have shown that PSV delivered through the endotracheal tube and noninvasively after extubation are equally effective in reducing the work of breathing and improving arterial blood gas levels, compared with spontaneous breathing during a T-piece trial [37].

Noninvasive ventilation after intubation and mechanical ventilation

The primary aim of NPPV should be to shorten weaning time and avoid reintubation [38]. During the early 1990s, in several uncontrolled trials, NPPV was applied in patients who had been intubated and ventilated for a long period, usually with a tracheotomy [39–41]. These studies suggested that NPPV could facilitate liberation from the ventilator in these patients. The first randomized controlled trial of the application of NPPV in weaning was carried out in a very particularly selected group of 50 intubated COPD patients with severe hypercapnic respiratory failure, who had recovered from an exacerbation within 48 h after mechanical ventilation was initiated, but had failed a 2-h spontaneous breathing trial with a T-piece [42]. In this study, patients were randomly allocated to be extubated and supported with noninvasive PSV or to remain intubated and ventilated with PSV, both of which followed a conventional weaning approach. Patients who were extubated and received noninvasive ventilatory support remained ventilated (10.2 ± 6.8 versus 16.6 ± 11.8 days) and in the ICU (15.1 ± 5.4 versus 24.0 ± 13.7 days) for significantly shorter periods, had a lower incidence of nosocomial pneumonia (no (0%) versus seven (28%) patients) and a higher 60-day survival rate (23 (92%) versus 18 (72%) patients). Moreover, noninvasive PSV was as effective as invasive PSV in maintaining arterial carbon dioxide tension and pH levels in both groups. The authors concluded that the reduction in the period of endotracheal intubation was the main cause of the decreased incidence of ventilator-associated complications and mortality.

Another randomized controlled trial assessing the efficacy of NPPV during weaning was performed in 33 intubated patients with acute-on-chronic respiratory

failure after a single weaning trial failure, with hypercapnic respiratory failure [43]. Patients were randomly allocated to remain intubated with PSV or to be extubated and receive noninvasive PSV. This study showed that NPPV permitted a reduction in the endotracheal mechanical ventilation period (4.6 ± 1.9 versus 7.7 ± 3.8 days), but the total duration of ventilatory support related to weaning was longer in patients extubated with NPPV. In this study, a few days after extubation, NPPV was administered in most patients, especially during the night-time, more as a "preventive" tool than out of confirmed necessity. There was a trend towards a lower incidence of complications in the NPPV group. However, these differences were not significant, partly because of the small sample size. No improvement in length of ICU stay or survival was shown. As in the prior study, both noninvasive and endotracheal PSV achieved a similar improvement in gas exchange compared to the spontaneous breathing trial. Several reasons can be put forward to explain the modest benefits obtained with NPPV in this study: 1) the authors used intermittent periods of NPPV separated by scheduled periods of spontaneous breathing after extubation, instead of continuous delivery immediately after extubation for as much time as possible, as in the study of NAVA *et al.* [42]; and 2) patients from this study did not require prolonged mechanical ventilation, as assessed by the moderate mean length of ventilatory support in the group of patients who remained intubated, hence limiting the expected efficacy of NPPV in shortening the ventilatory period.

A preliminary report of another study comparing NPPV with conventional weaning suggested there was a significant benefit to the noninvasive approach in a group of patients who were confirmed as being difficult to wean [44]. This study also showed a reduction in the need for tracheotomy, which may have helped to reduce the incidence of infectious complications, because the presence of such a device increases the period of use of an artificial airway and the patient's susceptibility to further respiratory infections, even when the patient is already breathing spontaneously. Because tracheotomy may interfere with swallowing, a nasogastric tube is often needed, which is associated with gastro-oesophageal reflux and aspiration of gastric contents and feed into the airways [45–48], another major risk factor for nosocomial pneumonia [11, 49].

All patients included in the two published randomized controlled studies [42, 43] and 77% of patients from the other study [44] had underlying chronic pulmonary disorders, and most of them developed hypercapnic respiratory failure during the failed spontaneous breathing trials. There is little information regarding the role of NPPV in patients with respiratory failure due to other causes, such as acute respiratory distress syndrome, postsurgical complications or cardiac failure. In patients undergoing lung resection, compared with conventional therapy consisting of oxygen therapy alone, the use of NPPV increased the efficiency of gas exchange, assessed by a decreased alveolar-to-arterial oxygen gradient, without noticeable effects on haemodynamics, ventilatory

pattern, dead space ventilation or pleural leaks [50], although no clinical outcomes were evaluated in this study. In patients undergoing aortocoronary bypass surgery, the use of continuous positive airway pressure after weaning improved pulmonary gas exchange, but failed to modify the prevalence of postsurgical atelectasis [51]. In intubated trauma patients, noninvasive PSV delivered after extubation was as effective as invasive PSV prior to extubation in maintaining arterial blood gas levels, with excellent subjective compliance and acceptance by the patients [52]. In this uncontrolled study, however, the rate of reintubation following this procedure was 41%, thereby challenging the safety of extubation with noninvasive ventilatory support in these patients.

Noninvasive ventilation for extubation failure and after unplanned extubation

Postextubation respiratory failure is one of the major clinical problems in patients admitted to the ICU. It is estimated that 15–20% of patients extubated after a successful spontaneous breathing trial are reintubated within 48–72 h [53, 54]. Although patients aged >65 yrs, increased severity of illness, as quantified by the Acute Physiology And Chronic Health Evaluation-II score [55], and cardiac failure as the cause of intubation have been identified as risk factors for extubation failure [53], no valid predictors have been identified in clinical studies. The most frequent causes of extubation failure are airway aetiologies (aspiration, excessive secretions and vocal cord oedema) and nonairway aetiologies (respiratory failure, congestive heart failure, atelectasis and encephalopathy) [56, 57]. Reintubation is an independent risk factor for nosocomial pneumonia and mortality in mechanically ventilated patients, and those patients with extubation failure are up to seven times more likely to die in the hospital compared with those who are successfully weaned [53, 58]. Moreover, extubation failure is associated with increased length of ICU and hospital stay. A retrospective study using a historical control group showed that NPPV decreased the need for reintubation and the duration of mechanical ventilation [59]. However, no randomized controlled trials have been published assessing whether or not NPPV is effective in preventing the development of postextubation respiratory failure after a spontaneous breathing trial that has been well tolerated or whether NPPV can prevent reintubation once postextubation respiratory failure has occurred.

Another potential field of application for noninvasive ventilation could be during unplanned extubation, which occurs in 3–13% of intubated patients [60]. Again, however, no prospective data are available to assess the efficacy of noninvasive ventilation in preventing reintubation in this clinical situation.

Limitations of noninvasive ventilation after invasive mechanical ventilation

The main reasons for failure of noninvasive ventilation are lack of cooperation, excessive secretions,

severe strength/load imbalance and haemodynamic instability, which can be corrected by protection of the airways and proper medical therapy. In general, it is estimated that ~30–35% of intubated COPD patients with hypercapnic respiratory failure needing progressive withdrawal of mechanical ventilation are unlikely to benefit from noninvasive ventilation, but large-scale studies are needed to confirm these estimates. It is important to stress the significance of identifying the need for assisted ventilation or for an artificial airway as the cause of weaning difficulty. Clearly, NPPV may have a role in the former but not in the latter situation.

Conclusion

Although randomized controlled trials show that use of noninvasive ventilation to advance extubation in difficult-to-wean patients or patients who develop respiratory failure after apparently successful extubation can result in reduced periods of endotracheal intubation and complication rates and improved survival, this is not a consistent finding. The published data with outcome as the primary variable are exclusively from patients who had pre-existing lung disease. In addition, the patients were haemodynamically stable, with a normal level of consciousness, no fever and a preserved cough reflex. It remains to be seen whether noninvasive positive pressure ventilation has a role in other patient groups and situations. The technique, however, is a useful addition to the options available for liberating a group of patients who pose a significant clinical and economic challenge from assisted ventilation.

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