Non-invasive ventilation in acute exacerbations of COPD

There is currently great interest in the use of non-invasive ventilation (NIV), particularly in the management of acute exacerbations of COPD. The technique differs from invasive mechanical ventilation in that the patient is ventilated via a well-fitting face or nasal mask rather than an endotracheal tube or tracheostomy. It has a number of potential advantages, but concerns have been voiced that it may delay endotracheal intubation (ETI) and mechanical ventilation, resulting in a worse outcome,\(^1\) that it is time-consuming\(^2\) and unpleasant for patients. These concerns need to be set in context; patients with an acute exacerbation of COPD and a respiratory acidosis (pH < 7.25) have a 30% mortality;\(^3\) the outcome of ETI and ventilation is disappointing, with reported survivals of between 20 and 50%.\(^4\) In two large European multicentre studies,\(^5,6\) 20% of patients who had been intubated and mechanically ventilated were difficult to wean. ETI is associated with a range of complications of which the most important is ventilator-associated pneumonia (VAP). For every day intubated, there is a 1% risk of developing VAP, which results in a high morbidity and mortality.\(^7\)\(^-\)\(^10\)

With NIV, paralysis and sedation are not needed, and ventilation outside the Intensive Care Unit (ICU) is an option; given the considerable pressure on Intensive Care beds in the UK and the high costs, this is attractive. Patients with severe COPD are often functioning close to the point at which the respiratory muscle pump can no longer maintain effective ventilation. The load is high due to airway obstruction and hyperinflation, and the capacity of the respiratory muscle pump is reduced as the inspiratory muscles are working at a mechanical disadvantage due to hyperinflation.\(^11\) In an exacerbation, as the load increases the respiratory muscle pump begins to fail. Hypoxia and hypercapnia worsen and impair muscle function.\(^12\) The patient develops a pattern of rapid shallow breathing, in an attempt to protect the muscles against ‘fatigue’,\(^13\) but at the expense of alveolar ventilation, further worsening hypercapnia and acidosis. Ventilatory support can be introduced at an earlier stage in the evolution of ventilatory failure than would be usual when a patient is intubated, and it is possible with NIV to give very short periods of ventilatory support, which in some cases may be sufficient to reverse the downward spiral into life-threatening ventilatory failure. Finally, patients are able to eat and drink and speech is unaffected, allowing them to participate in decisions about their own management.

However, NIV does have limitations. Some 13–29% of patients are unable to tolerate the mask, and persuading patients to keep the mask on can take considerable nursing time.\(^2,14\)\(^-\)\(^19\) Facial pressure sores occur in 2% of patients,\(^20\) and with NIV the upper airway is not protected and the lower airway cannot be accessed. This therefore limits the technique’s applicability to those who are unconscious or have a secretion retention sufficient to require suctioning. To date, all trials of NIV in COPD have excluded patients requiring emergency intubation.

There have been five prospective randomized controlled trials of NIV in acute exacerbations of COPD, two performed in, and three outside of, the ICU.\(^14,15,20\)\(^-\)\(^22\) Brochard et al. showed that NIV (pressure support of 20 cmH\(_2\)O, in the ICU, reduced the intubation (11/43 vs. 31/42, \(p < 0.001\)) and mortality rates (4/43 vs. 12/42, \(p = 0.02\)) compared to conventional medical therapy.\(^20\) NIV also improved pH, PaO\(_2\), respiratory rate and encephalopathy score at 1 h, and was associated with a shorter hospital stay (23 days vs. 35 days, \(p = 0.005\)) and a lower complication rate (16% vs. 48%, \(p = 0.001\)). Most of the excess mortality and complications, particularly pneumonia, were attributed to ETI. In a smaller study (\(n = 31\)) in two North American ICUs, Kramer et al.,\(^21\) using modest levels of pressure support (mean 11 cmH\(_2\)O) showed a marked reduction in intubation rate, particularly in the subgroup with COPD (\(n = 23\)) (all patients 31% vs. 73%, \(p < 0.05\); COPD 67% vs. 9%, \(p < 0.05\)). However, mortality, hospital stay and charges were unaffected. The benefits in both studies were seen with relatively modest daily use of NIV (Brochard et al. 6 h per day, Kramer et al. 14.4 h in first 2 days). Both studies had similar inclusion criteria—an exacerbation of COPD, respiratory acidosis (pH < 7.35) and tachyp-
noea. Those enrolled had a severe exacerbation, as evidenced by a mean pH of 7.28, but patients deemed to warrant immediate intubation were excluded in both studies.

In a cohort study (n = 24, mean pH = 7.29) with carefully matched historical controls, Confalonieri et al. showed a more rapid improvement in blood gases with NIV, a reduction in intubation rate (2/24 vs. 9/24) and a reduced hospital stay (16 vs. 31 days). In-hospital mortality was not affected. However, on longer-term follow-up, a survival advantage to NIV was seen (6 months, 71% vs. 54%; 1 year, 71% vs. 50%; p < 0.05) as well as reduction in the number and days of hospital admission (0.6 vs. 1.4 admissions/year; 7 vs. 25 days in hospital/year). It has been suggested that this difference is explained by poor matching between the two groups, but similar results were also seen in another retrospective study comparing NIV with historical controls. This observation needs to be validated in prospective randomized controlled trials, but there are a number of possible explanations. Patients who have been intubated for more than 7 days show electrophysiological and biopsy evidence of myopathy. Weakness of the expiratory muscles reduces the capacity to clear secretions and weakness of the inspiratory muscles reduces the ventilatory reserve, such that if there is another exacerbation severe ventilatory failure is more likely. It is also possible that patients and/or their doctors may be reluctant to embark on a further period of intensive care if the last episode was prolonged or difficult. NIV is easier, and it is noteworthy that 6/14 readmissions in the study of Confalonieri et al. resulted in a further period of NIV.

All these studies were performed on ICUs, and their generalizability to the UK, where NIV is usually performed on general wards, is uncertain. Although in mainland Europe and North America, some ICUs may have lower staffing levels (1:3 to 1:5), these ratios are better than on most general wards, and in addition the ICUs have high-quality monitoring and the facility for immediate intubation and ventilation. What these studies do show is that NIV is possible and that the prevention of ETI is advantageous. In addition, Nava et al. have shown in a prospective costings study that NIV is no more expensive and does not take up more nursing time than ETI and mechanical ventilation. This finding supports the observation of Kramer et al. that hospital charges were no different in the two arms of their randomized controlled trial.

There have been three prospective randomized controlled studies of NIV outside the ICU. Bott et al. randomized 60 patients to either conventional treatment or NIV. NIV was initiated by research staff who spent 15 min to 4 h initiating it (average 90 min). NIV led to a more rapid correction of pH and PaCO₂. In the conventional treatment group, 9/30 died compared to 3/30 of the NIV group. On an intention-to-treat analysis, these figures were not statistically significant, but when those unable to tolerate NIV were excluded, a significant survival benefit was seen (9/30 vs. 1/26, p = 0.014). Patients with acute exacerbations of COPD are usually very breathless, and some find even a loose-fitting oxygen mask claustrophobic. Despite a more intrusive nasal mask, held tightly in place, patients reported less breathlessness on visual analogue scales during NIV than in the conventional group, suggesting that the technique is not unpleasant for patients. Generalizability from this study, although performed on general wards, to routine practice is again difficult given that staff additional to the normal ward complement set up the NIV. The high mortality rate (30%) in the control group was surprising considering that the mean pH was only 7.34. In addition, the low intubation rate, while probably reflecting UK practice, has been criticized.

Barbe et al. initiated NIV in the emergency department, and continued it on a general medical ward. To ease some of the problems of workload and compliance NIV was administered for 3 h twice a day. In this small study (n = 24) there were no intubations nor deaths in either group, and arterial blood gas tensions improved equally in both the NIV group and in the controls. However, the mean pH at entry in each group was 7.33, and at this level of acidosis significant mortality is not expected; in other words it was unlikely that such a small study would show an improved outcome when recovery would be expected anyway.

Wood et al. randomized 27 patients with acute respiratory distress to conventional treatment or NIV in the emergency department. Intubation rates were similar (7/16 vs. 5/11) but there was a non-significant trend towards increased mortality in those given NIV (4/16 vs. 0/11, p = 0.123). The authors attributed the excess mortality to delay in intubation, as conventional patients requiring invasive ventilation were intubated after a mean of 4.8 h compared to 26 h in those on NIV (p = 0.055). It is difficult to draw many conclusions from this study about the place of NIV in acute exacerbations of COPD, given its small size; only six patients had COPD and they were not severely ill on pH criteria (mean pH at entry 7.35). Finally the level of ventilatory support was very modest (inspiratory positive airway pressure 8 cmH₂O).

No studies have compared NIV with ETI and mechanical ventilation. NIV is less likely to be successful in patients with more severe acidosis at presentation, coma or confusion, significant comor-
bidity, radiological evidence of consolidation or orofacial abnormalities that interfere with the fitting of the nasal or face mask. Furthermore early correction of pH and other physiological variables correlates with success in a number of studies.\(^1\) In the study of Brochard et al., only 30% of patients were deemed suitable candidates for the non-invasive approach, the rest requiring immediate ETI.\(^2\) Nava et al.\(^3\) performed a prospective multicentre randomised controlled trial of the use of NIV as a means of weaning patients with COPD who had failed a T-piece weaning trial after 48 h of ETI, controlled mechanical ventilation and aggressive suctioning to clear secretions. Of these patients, 56% had required ETI on presentation and 44% after a failed trial of NIV (mean pH at presentation = 7.18). If patients failed the weaning trial they were randomized to further intubation and mechanical ventilation or NIV. NIV was associated with a shorter duration of ventilatory support (10.2 days vs. 16.6 days), a shorter ITU stay (15.1 days vs. 24 days), less nosocomial pneumonia (0.25 vs. 7.25) and an improved 60-day survival (92% vs. 72%). In patients not suitable for NIV from the outset or those who failed, ETI for 24 to 48 h to gain control and then early extubation on to NIV had significant advantages over prolonged endotracheal intubation.

In conclusion NIV is feasible, under ‘ideal conditions’, i.e. on an ICU with a particular interest in NIV or on a general ward using extra research staff. Within ICU, intubation rates, and the consequent complications, particularly ventilator-associated pneumonia, are reduced. NIV should be considered as a means of preventing, rather than a direct alternative to, ETI and mechanical ventilation. When ETI is deemed necessary, a strategy of early extubation onto NIV should be considered.

Current data do not support the use of NIV, as part of a standard service, in mildly acidotic patients on general medical wards. However, UK HDUs with nurse staffing ratios of 1:2 and adequate monitoring equipment are comparable in many respects to Continental European and North American ICUs and these or other appropriately staffed and resourced units are an appropriate setting for NIV, provided that ETI is readily available when deemed appropriate. Further studies are needed to determine the optimal threshold for initiating NIV, to assess the feasibility, safety and effectiveness in lower intensity settings, and to determine the cost-effectiveness both in the short and long term.

P.K. Plant
M.W. Elliott
Department of Respiratory Medicine
St James’s University Hospital
Leeds

References


