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Noninvasive ventilation in acute exacerbations of COPD

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ABSTRACT: Noninvasive ventilation has been a major advance in the management of acute exacerbations of chronic obstructive pulmonary disease, reducing the need for endotracheal intubation, thereby reducing complications and hospital costs, as well as improving survival. It has been used in a variety of different clinical environments including the emergency room, on general wards, in intermediate respiratory care units and in the intensive care unit. It should now be regarded as part of standard therapy for patients who continue to have a respiratory acidosis after standard medical therapy.

KEYWORDS: Acute exacerbation, chronic obstructive pulmonary disease, noninvasive ventilation, obstructive lung disease, positive pressure ventilation, respiratory failure

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Noninvasive ventilation (NIV) has been shown to be an effective treatment for ventilatory failure resulting from acute exacerbations of chronic obstructive pulmonary disease (COPD) [1–16]. It has been used in a variety of settings and in exacerbations of differing degrees of severity. These are summarised in table 1.

In the ICU studies [1–4] the most striking finding was a reduction in the need for endotracheal intubation (ETI) and mechanical ventilation (MV), which in the largest study translated into improved survival, reduced complication rates and length of both intensive care unit (ICU) and hospital stay [1]. Because paralysis and sedation are not needed with NIV, ventilation outside the ICU is an option; given the considerable pressure on ICU beds in most countries, the high costs and that for some patients admission to ICU is a distressing experience [17] this is an attractive option. NIV can be instituted at an earlier stage in the natural history of the condition before mechanical ventilation would normally be considered necessary. There have been a number of prospective randomised controlled studies of NIV outside the ICU either on general wards or in the Accident and Emergency Department [5–11]. NIV was instituted at a higher pH than that reported in the ICU studies and most failed to show any significant advantage to NIV when analysed on an intention-to-treat basis. These studies were all relatively small and may have lacked sufficient statistical power to show a difference in the need for intubation and mortality given that most patients with a mild exacerbation of COPD (defined by the degree of acidosis) would not be expected to need ETI and MV anyway [18]. In a large (n=236) multicentre randomised controlled trial (RCT) of NIV in acute exacerbations of COPD on general respiratory wards in 13 centres [10] ''treatment failure'', a surrogate for the need for intubation, defined by *a priori* criteria, was reduced from 27% to 15% by NIV ($p<0.05$). In-hospital mortality was also reduced from 20% to 10% ($p<0.05$). Subgroup analysis suggested that the outcome in patients with pH <7.30 after initial treatment was inferior to that in the studies performed in the ICU. NIV was applied by the usual ward staff, most of whom had had little or no previous experience of NIV, using a bilevel device in spontaneous mode, according to a simple protocol. This study suggests that, with adequate staff training, NIV can be applied with benefit outside the ICU and that the early (pH <7.35 on admission to the ward) introduction of NIV on a general ward results in a better outcome than providing no ventilatory support for acidotic patients outside the ICU. The results in the more severely affected patients (pH <7.30 after initial management) were not as good as those seen in the ICU studies, suggesting that this simple approach is not appropriate in these patients and that they are best managed in a higher dependency setting with a more sophisticated ventilator individually adjusted to their requirements.

A number of studies have suggested that NIV is less likely to be successful in more severely affected patients [1, 19, 20] and all the studies reported to date have excluded patients who required immediate ETI and MV. The study of

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TABLE 1 Summary of randomised controlled trials of noninvasive ventilation in acute exacerbations of chronic obstructive pulmonary disease (COPD)

Study	Disease (n)	Setting	Baseline pH	ETI or surrogate	Mortality	Mode plus settings cm H_2O and use on day 1, when stated
Bott *et al*. [5]	COPD (60)	Ward	7.35	0/30 *versus* 5/30	3/30 *versus* 9/30	Volume cycled ventilators Use 7.63 h on day 1
Brochard *et al*. [1]	COPD (85)	ICU	7.28 *versus* 7.27	25 *versus* 74%#	9 *versus* 29%#	PSV 20 Use at least 6 h per day
Kramer *et al*. [2]	Mixed (31) COPD (23)	ICU	7.28 *versus* 7.27 7.29 *versus* 7.27	31 *versus* 73%# 9 *versus* 67%#	1/16 *versus* 2/15	IPAP 11.3 EPAP 2.6 Use 20.1 h on day 1
Barbe *et al*. [6]	COPD (24)	ER Ward	7.33	0/12 *versus* 0/12	0/12 *versus* 0/12	IPAP 14.8 EPAP 5 Use 2×3 h sessions per day
Angus *et al*. [8]	COPD (17)	Ward	7.31 *versus* 7.30	0/9 *versus* 5/8	0/9 *versus* 3/8	IPAP 14–18 cm H_2O
Wood *et al*. [7]	Mixed (27) COPD (6)	ER	7.35 *versus* 7.34	7/16 *versus* 5/11	4/16 *versus* 0/11	
Avdeev *et al*. [11]	COPD (58)	RICU	7.28	12 *versus* 28%	8 versus 31%#	Bilevel 29±25 h
Celikel *et al*. [3]	COPD (30)	ICU	7.27 *versus* 7.28	1/16 *versus* 6/15#	0/15 *versus* 1/15	PSV 15.4 for mean of 26.7 h
Bardi *et al*. [9]	COPD (30)	Ward	7.36 *versus* 7.39	1/15 *versus* 2/15	0/15 *versus* 1/15	IPAP 13 EPAP 3
Martin *et al*. [4]	COPD (23) Others (38)	ICU	7.27 *versus* 7.28 103 *versus* 110	6.4 *versus* 21.3#/ 100 ICU days	2.4 *versus* 4.27/ 100 ICU days	IPAP 11 EPAP 5.7
Plant *et al*. [10]	COPD (236)	Ward	7.32 *versus* 7.31	15% *versus* 27%#	10% *versus* 20%#	IPAP 10–20 EPAP 5 h Use median 8 h on day 1
Thys *et al*. [15]	COPD (12)	ER CPO (8)	7.28 *versus* 7.24	0% *versus* 100%#	2/10 *versus* 1/10	Bilevel *versus* sham
Dikensoy *et al*. [14]	COPD (34)	Ward		4/19 *versus* 7/17	1/17 *versus* 2/17	IPAP 9 EPAP 3
Conti *et al*. [16]	COPD (49)	ICU	7.20	48% avoided ETI	26% *versus* 46%	PSV 16+2 continuously first 12 h

Data presented as n or n±SD, unless otherwise stated. ETI: endotracheal intubation; ICU: intensive care unit; PSV: pressure support ventilation; IPAP: inspiratory positive airway pressure; EPAP: expiratory positive airway pressure; ER: emergency room; RICU: respiratory intermediate care unit; CPO: cardiographic pulmonary oedema. #: $p<0.05$.

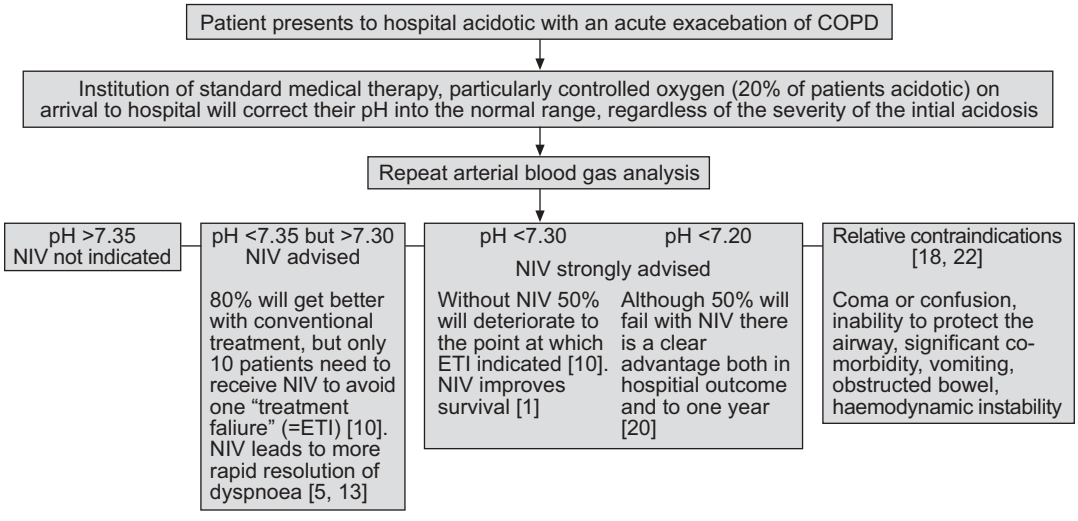

FIGURE 1. Suggested algorithm for the management of ventilatory failure in acute exacerbations of chronic obstructive pulmonary disease (COPD). NIV: noninvasive ventilation; ETI: endotracheal intubation.

WOOD *et al*. [7] suggested that failure to move to ETI in a timely fashion may have explained a trend towards a worse survival in the NIV group. The concern has been voiced therefore, that, particularly in the more severely ill, NIV may be harmful by delaying the institution of ETI and MV. However CONTI *et al*. [16] recently reported a prospective RCT of NIV *versus* immediate ETI and MV in patients with an exacerbation of COPD. The intubation rate of 52% in the NIV group was higher than in other RCTs, which is not surprising given that these were a sicker group of patients, as evidenced by the mean pH of 7.2, compared with 7.27 in the study of BROCHARD *et al*. [1] and 7.32 in the study of PLANT *et al*. [10]. It reinforces the view that NIV is best instituted early [21]. However, in these sicker patients NIV was no worse than ETI and MV. In those who could be managed successfully with NIV there were important advantages both in the short term, but also in the year after hospital discharge. Some patients were still excluded and NIV remains a complimentary technique to invasive ventilation. An algorithm for the management of ventilatory failure in acute exacerbations of COPD is suggested in figure 1.

There are no absolute contraindications to NIV although a number have been suggested [19, 22]. In part, these contraindications have been determined by the fact that they were exclusion criteria for the controlled trials. It is therefore more correct to state that NIV is not proven in these circumstances rather than that it is contraindicated.

When noninvasive ventilation can be successfully applied there are clear advantages, particularly a reduction in infectious complications [23–25] and length of intensive care unit and hospital stay [1], with an attendant reduction in costs [26, 27]. There is no convincing evidence to date that a failed trial of noninvasive ventilation is harmful. However, there is always the danger that, as confidence grows, noninvasive ventilation may be continued for too long in an individual patient to the point of cardiorespiratory arrest. Further data are needed as to when noninvasive ventilation should be abandoned in favour of invasive ventilation. A trial of noninvasive ventilation is appropriate in the majority of patients acidotic because of an acute exacerbation of chronic obstructive pulmonary disease. Early intervention is more likely to be successful [10, 20, 28], but even when patients present later in the natural history of their exacerbation there is still a significant role for noninvasive ventilation [16].

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