

## Review

# Noninvasive positive pressure ventilation as treatment for acute respiratory failure in critically ill patients

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## Abstract

Our current state of knowledge on noninvasive positive pressure ventilation (NPPV) and technical aspects are discussed in the present review. In patients with chronic obstructive pulmonary disease, NPPV can be considered a valid therapeutic option to prevent endotracheal intubation. Evidence suggests that, before eventual endotracheal intubation, NPPV should be considered as first-line intervention in the early phases of acute exacerbation of chronic obstructive pulmonary disease. Small randomized and non-randomized studies on the application of NPPV in patients with acute hypoxaemic respiratory failure showed promising results, with reduction in complications such as sinusitis and ventilator-associated pneumonia, and in the duration of intensive care unit stay. The conventional use of NPPV in hypoxaemic acute respiratory failure still remains controversial, however. Large randomized studies are still needed before extensive clinical application in this condition.

**Keywords:** acute respiratory failure, bronchoscopy, chronic obstructive pulmonary disease, facial mask, hypercapnia, hypoxaemia, noninvasive ventilation, nasal mask

## Introduction

Mechanical ventilation through an endotracheal tube is a well established, accepted and life-saving procedure for patients with acute respiratory failure (ARF). In mechanically ventilated patients, however, endotracheal intubation is the single most important predisposing factor for developing nosocomial bacterial pneumonia and infections [1,2] and increases the risk for sinusitis. Placement and maintenance of endotracheal tube increases patient's discomfort and stress, and often necessitates administration of sedative agents. Endotracheal intubation may also cause injuries and ulcerations of the tracheal mucosa that is in contact with tube's cuff, inducing inflammation,

oedema and submucosal haemorrhage. These conditions represent the pathological basis of other complications, such as airway stenosis [3,4].

Noninvasive positive pressure ventilation (NPPV) is the delivery of assisted mechanical ventilation without the need for an invasive artificial airway [1]. It is a safe and effective means of improving gas exchange in patients with many forms of ARF [5]. For example, in patients with acute exacerbation of chronic obstructive pulmonary disease (COPD) and hypercapnic respiratory failure, adding noninvasive ventilation to standard therapy decreased the need for endotracheal intubation [6–13],

and could reduced mortality [12]. Similarly, noninvasive continuous positive airway pressure was effective in patients with cardiogenic pulmonary oedema, particularly in those with hypercapnia [14–16]. This therapy also decreased the rates of intubation and complications [5] and improved survival in patients with various forms of acute hypoxaemic respiratory failure (pneumonia, congestive hearth failure, chest wall impairment, etc) [17,18].

In patients with acute hypoxaemic respiratory failure, NPPV is as effective as conventional ventilation, delivered through an endotracheal tube, in improving gas exchange [5]. The technique of NPPV is flexible and can be applied both continuously and intermittently, allows speech and swallowing, and is accepted well by patients.

### Materials and techniques

An alert and cooperative patient is essential for initiating NPPV or mask continuous positive airway pressure. Table 1 summarizes the characteristics of appropriate patients. During NPPV, patients must be able to synchronize respiratory efforts voluntarily with those of the ventilator. COPD hypercapnic patients with narcosis may represent an exception. Alertness in the majority of these patients is improved within 15–30 min. During NPPV, patients can achieve a level of control and independence that is totally different from when they are intubated, and sedation is infrequently required. However, it should be avoided in patients with severe hypotension or life-threatening arrhythmia, and in those who require an endotracheal tube to protect the airways (coma, impaired swallowing, etc; Table 1). Patients who have refractory hypoxaemia [arterial partial oxygen tension (PaO<sub>2</sub>)/fractional inspired oxygen (FiO<sub>2</sub>) ≤ 60], morbid obesity (>200% of ideal body weight) or with unstable angina or acute myocardial infarction should be closely managed by experienced personnel [5,19]. Criteria for NPPV discontinuation and endotracheal intubation must be thoroughly taken into account in order to avoid dangerous delays (Table 2).

### Interface

NPPV can be administered both with nasal and full-face masks. The nasal mask is usually well tolerated because it causes less claustrophobia and discomfort. It allows eating, drinking and expectorating. Conversely, a facial mask is preferable in severe respiratory failure, because dyspneic patients breath through the mouth in order to bypass resistance of the nasal passages, and mouth opening during nasal mask ventilation results in air leakage and decreased effectiveness [20,21]. Masks are firmly secured with elastic straps (Fig. 1) to the face in order to avoid air leaks and consequent malfunction. The dead space volumes of a facial and a nasal mask are 250 ml and 105 ml, respectively [22]. Dead space volume from the mask and the oropharynx may affect the effectiveness of ventilation.

**Table 1**

**Criteria for selection of patients for noninvasive positive pressure ventilation**

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Conscious and cooperative patient (chronic obstructive pulmonary disease patients may be an exception)
No need for urgent endotracheal intubation to protect the airways or remove copious secretions
No acute facial trauma
No recent gastroesophageal surgery
No active gastrointestinal bleeding
No impaired swallowing
Haemodynamic and rhythm stability
Face mask adequately fitted

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**Table 2**

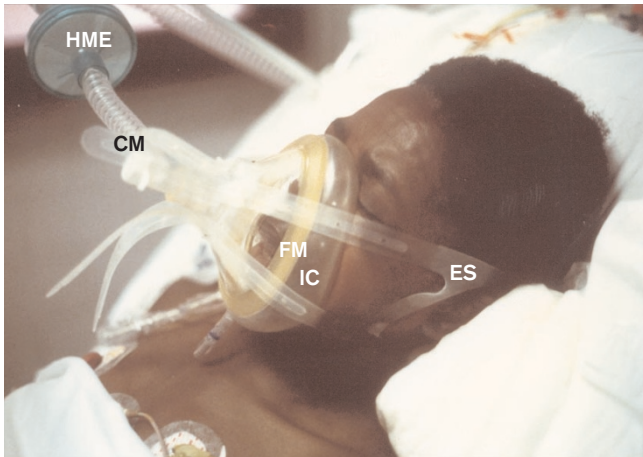
**Criteria for noninvasive positive pressure ventilation discontinuation and endotracheal intubation**

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Mask intolerance due to pain, discomfort or claustrophobia
Inability to improve gas exchanges and/or dyspnea
Haemodynamic instability or evidence of cardiac ischaemia or ventricular dysarrhythmia
Need for urgent endotracheal intubation to manage secretions or protect the airways
Inability to improve mental status, within 30 min after the application of noninvasive positive pressure ventilation, in hypercapnic, lethargic chronic obstructive pulmonary disease patients or agitated hypoxaemic patients

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In mild forms of ARF, a nasal mask could be tried first, switching to a facial mask if necessary. Among 12 patients (11 with COPD and one with pneumonia) with ARF who failed NPPV with a conventional facial or nasal mask (due to leaks or discomfort), switching to the new full-face mask improved gas exchange and avoided endotracheal intubation in 84% of the patients [23]. A mask with transparent dome is preferred because it allows visual monitoring of the oral airway for the presence of secretions (Fig. 1). The mask should be lightweight to aid in its application and have a soft, pliable, adjustable seal to reduce trauma and leaking [24]. The mask is secured with head straps (Fig. 1). In our experience, skin necrosis occurs in 7% of patients treated with NPPV for periods exceeding 72 h; after discontinuation of NPPV, however, rapid healing of the dermal lesions is observed, usually in 7–10 days. The correct approach to limit these lesions is to place adhesive dressings to the points of major pressure (usually the bridge of the nose) to increase the pressure dissipation surface and reduce the depth of skin necrosis.

**Figure 1**

Patient undergoing noninvasive positive pressure ventilation. The face mask (FM), with its soft inflatable cushion (IC), is connected to the mechanical ventilator (not shown) through a catheter mount (CM), with a heat–moisture exchanger (HME) included in the respiratory circuit. The face mask is secured with elastic straps (ES).

When a full-face mask is used and the opening pressure of the upper oesophageal sphincter (25–30 cmH<sub>2</sub>O) [25] is overcome, gastric distension may occur, but this is not a common event. Some masks allow the passage of a nasogastric tube, protecting from the risk of aerophagia, even at pressures above 25 cmH<sub>2</sub>O.

The mask is connected to the ventilator, in the same way as an endotracheal tube. To prevent drying of the nasal passages and oropharynx, a humidifier should be connected, but the heater should be turned off because the upper airways that naturally warm inspired gas are not bypassed. As an alternative to the humidifier, we prefer to add a heat–moisture exchanger to the ventilatory circuit in order to ensure 'natural' humidification and heating, and to reduce the risk of bacterial colonization (Fig. 1).

With NPPV, tidal volume, gas exchange, respiratory rate and diaphragmatic activity are improved in proportion to the amount of pressure applied [20,26]. Most NPPV studies used pressure-limited ventilation delivered by a broad range of ventilators. Pressure-limited ventilation improves the efficacy of spontaneous breathing by allowing an optimal synchrony between patient effort and delivered assistance. Inspiration is initiated by the patient's activation of the inspiratory muscles and of the inspiratory glottic abductors, with consequent widening of the glottis. During pressure support ventilation (PSV), the patient's effort determines volume and duration of inspiration. Gas flow begins after the patient's inspiratory effort reduces pressure in the inspiratory circuit of the ventilator by a predetermined value, usually 1–2 cmH<sub>2</sub>O. Pressure-control ventilation has a preset inspiratory time and respiratory

rate. It may ventilate patients with low ventilatory drive more effectively. In comparison with volume-cycled ventilation, pressure-limited ventilation minimizes peak inspiratory mask pressure and air leakage. Although tidal volume may vary as a function of the change in airway resistance and compliance, this variance has been an uncommon problem in our experience. In three comparison studies of assist-controlled ventilation and PSV in patients with hypercapnic ARF, PSV was as effective as assist-controlled ventilation in reducing the work of breathing and improving gas exchange [27], but was better tolerated [27,28] and associated with fewer complications [27]. During NPPV of stable COPD patients, flow triggering reduces the respiratory effort and intrinsic positive end-expiratory pressure (PEEP) during both PSV and assist-controlled ventilation when compared with pressure triggering [29]. No differences were found between 1 and 5 l/min flow triggers [29]. Two reports [30,31] found nasal ventilation with assist-controlled ventilation to be ineffective and time consuming in end-stage obstructive lung disease. The present trend is to favour PSV, which has the advantage of better patient comfort and fewer complications [27].

The initial ventilator settings are continuous positive airway pressure 0 cmH<sub>2</sub>O and PSV 10 cmH<sub>2</sub>O; the mask is then gently held on patient's face until the patient is comfortable and in synchrony with the ventilator. FiO<sub>2</sub> is titrated to achieve an oxygen saturation over 90%. After the mask is secured, continuous positive airway pressure is slowly increased to 3–5 cmH<sub>2</sub>O, and PSV is increased to obtain the largest (>7 ml/kg) exhaled tidal volume, a respiratory rate below 25 breaths/min and patient comfort. These objectives may not be achieved in patients with severe lung disease or with a leaky interface. It is important to recognize that excessive PSV levels can cause excessive inflation, with consequent patient–ventilator asynchrony and activation of expiratory muscles during inspiration (Table 3) [32].

During the early phase of milder respiratory failure and after an initial period of continuous administration (3–6 h in our experience) NPPV can be intermittently applied, with periods of 10–20 min interruption when it is not used. For sicker patients, NPPV application has to be continuous for at least 12–24 h [5,18]. Discontinuation is allowed for short periods only when the clinical situation improves. Aggressive physiotherapy is crucial during the periods of NPPV discontinuation. Endotracheal intubation must be rapidly available, when indicated (Table 2).

### **Applications of noninvasive positive pressure ventilation in patients with chronic obstructive pulmonary disease**

#### **Physiologic response**

NPPV is a valid method to treat COPD patients and to avoid endotracheal intubation [6,9,26,33,34]. In COPD

Table 3

**Proposed ventilator settings and monitoring for noninvasive positive pressure ventilation**

	Initial setting	Treatment setting
Continuous positive airway pressure	0 cmH <sub>2</sub> O	Slowly increased to 3–5 cmH <sub>2</sub> O, (up to 8–10 cmH <sub>2</sub> O in hypoxaemic patients)
Pressure support ventilation	10 cmH <sub>2</sub> O	Increased to obtain a TV <sub>e</sub> >7 ml/kg and respiratory rate <25 breaths/min
Fractional inspired oxygen	Titrated to achieve SAT >90%	Titrated to achieve SAT >90%
Mask application	Mask gently held on patient's face, until comfort and synchrony with the ventilator are reached	Secure the mask with head straps
Monitoring	SAT, heart rate, respiratory rate, arterial pressure, electrocardiogram	SAT, heart rate, respiratory rate, arterial pressure, electrocardiogram

TV<sub>e</sub>, expiratory tidal volume; SAT, saturation of oxygen.

patients with acute exacerbation, the increased flow resistance and the inability to complete the expiration before inspiration results in high levels of dynamic hyperinflation. Dynamic hyperinflation alters diaphragm geometry, and reduces its strength and endurance. Also, minor increases in air flow resistance (as caused by airway secretions or bronchospasm) or an augmented ventilatory demand (as in case of fever or infection) in this context can cause respiratory muscle fatigue, with rapid shallow breathing, wasted ventilation, hypercapnia and respiratory acidosis. The work of breathing is increased to overcome the inspiratory threshold load due to auto-PEEP and to drive the tidal volume against increased airway resistances.

The classical approach to management of exacerbated COPD is a combination of pharmacological interventions (bronchodilators, steroids, antibiotics and inotropes) and low-rate oxygen. When this conservative approach is not successful, patients are intubated and mechanically ventilated.

NPPV is a tool to correct the increased work of breathing and avoid intubation. The combination of PEEP and positive pressure ventilation or PSV offsets the auto-PEEP level (eliminating the additional inspiratory load) and reduces the work of breathing that the inspiratory muscles must generate to produce the tidal volume. When appropriate levels of inspiratory pressure are delivered, tidal volume increases and respiratory rate decreases. Under these conditions NPPV significantly reduces arterial partial carbon dioxide tension (PaCO<sub>2</sub>), restoring normal pH, and induces a rapid and progressive decrease in diaphragmatic activity as shown by electromyography [26].

It must be remembered that the level of applied PEEP must never exceed the amount of auto-PEEP, in order to avoid iatrogenic increases of hyperinflation. No change in end-expiratory volume has been reported if PEEP applied

by face-mask ventilation does not exceed the 80–90% of the auto-PEEP [35].

**Clinical results**

In one of the first applications of NPPV in a small sample of COPD patients [33], the improvements in gas exchanges suggested the possibility of avoiding endotracheal intubation altogether. In a case-control study, Brochard *et al* [26] showed that this approach could reduce both the need for endotracheal intubation and the duration of hospital stay, with obvious economic implications. In the first randomized, prospective study on 60 COPD patients, Bott *et al* [6] compared NPPV administered through nasal mask with conventional therapy as a treatment for ARF. Patients receiving NPPV had a significant reduction in PaCO<sub>2</sub> and dyspnea score, and improved survival (90 versus 70%;  $P < 0.01$ ).

The efficacy of NPPV in acute exacerbation of COPD was also evaluated in a European prospective randomized multicentre study [9]. In that trial, 85 COPD patients without cardiogenic pulmonary oedema, pneumonia or postoperative ARF were randomly assigned to receive conventional treatment (oxygen therapy plus drugs) or NPPV in addition to conventional treatment. After 1 h, NPPV achieved a significant improvement in gas exchange. The group of patients randomly assigned to NPPV had a significantly lower intubation rate (26 versus 74%;  $P < 0.001$ ), lower complication rate (14 versus 45%;  $P < 0.01$ ), lower duration of hospital stay ( $23 \pm 17$  versus  $35 \pm 33$  days;  $P < 0.02$ ) and lower mortality rate (9 versus 29%;  $P < 0.02$ ).

In another randomized study on 26 COPD patients that compared NPPV delivered through nasal mask with conventional treatment [11], the authors reported a reduction in intubation rate, with a significant improvement in PaO<sub>2</sub>, heart rate and respiratory rate in the NPPV group, even though PaCO<sub>2</sub> did not significantly decrease. A further

randomized study on hypercapnic and hypoxaemic ARF [36] suggested that early application of NPPV facilitates improvement, decreases the need for invasive mechanical ventilation, and decreases the duration of hospitalization. Thirty patients were randomized to receive standard treatment, or NPPV in addition to standard treatment. With standard treatment, there was significant improvement only in respiratory rate ( $P < 0.05$ ). With NPPV,  $\text{PaO}_2$  ( $P < 0.001$ ),  $\text{PaCO}_2$  ( $P < 0.001$ ), pH ( $P < 0.001$ ) and respiratory rate ( $P < 0.001$ ) improved significantly compared with baseline. Duration of hospital stay for the NPPV group was shorter ( $P < 0.05$ ) than that in the standard treatment group. One patient in the NPPV group required invasive mechanical ventilation.

Lofaso *et al* [37] recently reported the risk of carbon dioxide rebreathing with bilevel positive airway pressure (BiPAP) ventilators when PEEP was not applied or when the expiratory time was too short; this might partly explain the limited  $\text{PaCO}_2$  modification noted by Kramer *et al* [11]

In a randomized trial in 50 patients with acute exacerbation of COPD, noninvasive PSV during weaning reduced weaning time ( $P = 0.021$ ), shortened the duration of stay in the intensive care unit ( $P = 0.005$ ), decreased the incidence of nosocomial pneumonia, and improved 60-day survival rates ( $P = 0.009$ ) [34].

## **Noninvasive positive pressure ventilation in patients with acute respiratory failure**

### **Physiologic response**

Following the good results obtained in patients with acute exacerbations of COPD and the promising data from a few pilot studies (retrospective or nonrandomized) [33,38,39] in patients with ARF, NPPV is now currently under clinical evaluation as a possible alternative to conventional ventilation with endotracheal intubation and as a means to reduce the intubation rate during ARF. NPPV is adopted in ARF that is not related to COPD, with the aim of decreasing the amount of spontaneous work of breathing and correcting the rapid shallow breathing that is always present in acute conditions. NPPV can prevent respiratory muscle fatigue and endotracheal intubation.

NPPV can be administered via a nasal or a full-face mask. Selection criteria and criteria for NPPV discontinuation and endotracheal intubation are similar to those described for COPD patients (Tables 1 and 2). In our experience and that of others [5,25], face masks seem more appropriate for patients affected by severe hypoxaemia, who are usually tachypneic and breathe through the mouth.

### **Clinical results**

#### *Nonrandomized, noncontrolled studies*

Meduri *et al* [33] in 1989 reported one of the first clinical applications of NPPV in patients with ARF. In that study

PSV and pressure control ventilation were used through face masks in four patients affected by cardiogenic and noncardiogenic pulmonary oedema, with good results in three. Subsequently, Pennock *et al* [39] reported successful treatment in 50% of a large group of patients with ARF of different aetiologies; promising results were obtained in the subgroup of patients affected by postoperative ARF. Similar results were achieved using noninvasive ventilation (always through a nasal mask) in a second study [40]. Wysocki *et al* [41] reported a 47% success rate in the treatment of ARF patients.

In a study conducted on 64 patients admitted to the emergency department for ARF due to cardiogenic pulmonary oedema and pneumonia [42] there was a significant improvement in arterial blood gases after 1 h of continuous positive airway pressure ventilation. In the cardiogenic pulmonary oedema group,  $\text{PaO}_2$  surpassed 100 mmHg with a clear-cut improvement in  $\text{PaCO}_2$  and pH ( $P < 0.0001$ , for both parameters). In the pneumonia group, oxygenation was also improved, but with the persistence of a significant shunt. Fifty-four patients (84%) were successfully ventilated under continuous positive airway pressure, avoided intubation and had a favourable prognosis, mainly in the cardiogenic pulmonary oedema group, without side effects.

In a pilot study conducted in patients with haematological malignancies complicated by ARF [43] 15 out of 16 individuals were successfully treated with NPPV delivered via nasal mask by means of a BiPAP ventilator (Respironics, Pittsburgh, USA).  $\text{PaO}_2/\text{FiO}_2$  and arterial oxygen saturation significantly improved after 1 h of treatment ( $P < 0.01$ ).

NPPV delivered by simplified ventilators via facial or nasal mask can be effective for routine care, after adequate personnel training [44]. In 40 patients with hypercapnic ARF compared with 30 matched historical patients under conventional treatment, NPPV was associated with a reduction in negative events, such as endotracheal intubation, and mortality together (17 versus 60%;  $P = 0.0002$ ), but not mortality alone (5 versus 13.5%; not significant). Significant and rapid improvements in  $\text{PaCO}_2$  and pH between baseline and subsequent evaluations ( $P = 0.066$ ) were obtained.

The utility of NPPV to prevent nosocomial pneumonia in patients who need assisted ventilation was recently reported in a prospective epidemiological survey on a cohort of 320 consecutive patients, 75% of whom had ARF not related to COPD [45]. Twenty-seven patients had 28 episodes of ventilator-associated pneumonia, but the incidence of ventilator-associated pneumonia was 0.85/100 days of tracheal intubation and 0.16/100 days of NPPV ( $P = 0.004$ ).

In a recent meta-analysis [46], Keenan and Brake analyzed more than 200 published and unpublished studies and concluded that the addition of NPPV to standard therapy in patients with ARF improves survival and decreases the need for endotracheal intubation. This effect was more evident in patients whose cause of ARF was an exacerbation of COPD, however.

To assess the efficacy of NPPV in routine use, 80 patients (aged  $71 \pm 1.3$  years and Acute Physiology and Chronic Health Evaluation II score of  $17.2 \pm 0.6$ ) received BiPAP for ARF [47]. Thirty-one of them (39%) had hypoxaemic ARF and 25 (31%) had hypercapnic ARF; the other 24 patients (30%) suffered from ARF of varied origin. BiPAP was successful in 80% of the patients with hypercapnic respiratory failure, but only in 15 of the 31 (48%) patients with hypoxaemic ARF. BiPAP success was marked, with increased  $\text{PaO}_2/\text{FiO}_2$  in the hypoxaemic group, but the risk failure was significantly greater (risk ratio 2.6, 95% confidence interval 1.1–6.1) for patients with hypoxaemic ARF than for those with hypercapnic respiratory failure.

#### Randomized studies

The first prospective randomized study dedicated to this topic was reported by Wysocki *et al* [18], who randomized 41 non COPD patients with ARF to receive face-mask mechanical ventilation versus conventional medical therapy. NPPV reduced the need for endotracheal intubation (36 versus 100%,  $P=0.02$ ), the duration of intensive care unit stay ( $13 \pm 15$  days versus  $32 \pm 30$  days;  $P=0.04$ ) and mortality rate (9 versus 66%;  $P=0.06$ ), but only in those patients with hypercapnia ( $\text{PaCO}_2 > 45$  mmHg). No significant differences in the hypoxaemic group without hypercapnia were seen. On the basis of these results, the authors concluded that NPPV was not beneficial when used systematically in all forms of ARF not related to COPD. Kramer *et al* [11] randomized 31 patients to receive nasal BiPAP or conventional therapy for the treatment of ARF. This study showed significant improvement in vital signs as well as reduction in endotracheal intubation rates in the group treated with NPPV compared with the conventionally treated group (31 versus 73% endotracheal intubation rates, respectively;  $P < 0.05$ ). Evidence from this study supported the use of NPPV in order to avoid intubation and possibly reduce mortality, but this conclusion again applied mainly to the subgroup of 23 (74%) patients with acute exacerbation of COPD. Only eight patients (36%) had ARF due to pneumonia (four patients), congestive heart failure (two patients), asthma (one patient) or pulmonary embolism (one patient). These studies were specifically dedicated to evaluate NPPV as a preventive tool against endotracheal intubation, and not as an alternative treatment for ARF.

We randomized 64 patients with hypoxaemic ARF who had not improved with aggressive medical therapy to face-mask NPPV or endotracheal intubation with conventional

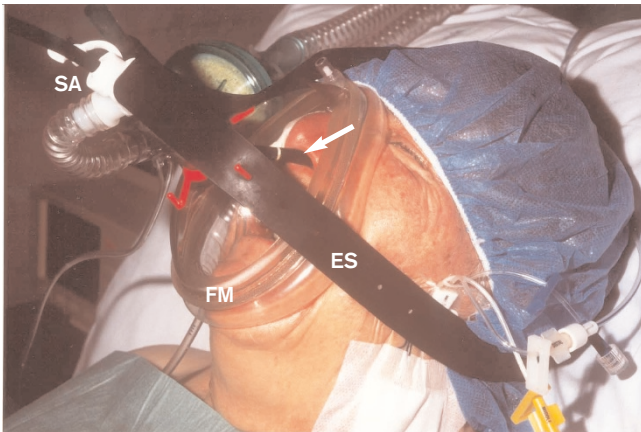
mechanical ventilation [5]. Both groups had improvement in the  $\text{PaO}_2:\text{FiO}_2$  ratio after 1 h of ventilatory support. Ten out of the 32 patients in the NPPV group required endotracheal intubation. The 32 patients in the conventional ventilation group had more frequent and serious complications (38 versus 66%;  $P=0.02$ ), and pneumonia and sinusitis related to the endotracheal tube (3 versus 31%;  $P=0.003$ ). Among the survivors, the patients in the NPPV group had a shorter duration of mechanical ventilation ( $3 \pm 3$  versus  $6 \pm 5$ ;  $P=0.006$ ) and a shorter duration of intensive care unit stay ( $6.6 \pm 5$  versus  $14 \pm 13$  days;  $P=0.002$ ). Our trial suggested that, for patients with severe respiratory distress, NPPV may lead to more favourable outcomes than conventional ventilation, in the hands of experienced staff and in a setting in which this technology can be rapidly and safely administered. Furthermore a *post hoc* subgroup analysis was performed for patients with a simplified acute physiologic score lower than 16, or 16 or greater. The 19 patients with a simplified acute physiologic score of 16 or greater, irrespective of group, had similar outcomes, whereas in the 45 patients with a simplified acute physiologic score lower than 16 NPPV was superior to conventional ventilation.

Conversely, Wood *et al* [48] had a substantially negative evaluation of the use of NPPV when applied in patients with hypoxaemic ARF. These authors randomized 27 patients in the emergency department to receive conventional medical therapy or NPPV for the treatment of acute hypoxaemic respiratory failure. The 16 patients who were randomized to the noninvasive ventilation group had a intubation rate (44%) and duration of intensive care unit stay similar to those of the 11 patients who received medical treatment alone, but there was a trend toward a greater rate of hospital mortality among the patients in the NPPV group compared with patients in the conventional medical therapy group [four patients (25%) versus none;  $P=0.123$ ]. Several factors may have influenced these negative results and may have represented biases in patient selection. First, case mix showed an unbalanced distribution of patients with pneumonia (44% in the NPPV group versus 12% in the conventional medical therapy group). Second, 14% of patients had COPD. Finally, patients in the NPPV group had a baseline  $\text{PaO}_2$  that was significantly lower than that in the conventional medical treatment group (59.8 versus 71.3 mmHg, respectively). Moreover, even though the  $\text{PaCO}_2$  levels were similar in the two groups, the range was clearly hypercapnic (around 56 mmHg in the two groups). These differences may represent increased severity of ARF in the NPPV group, and objective conclusions are therefore difficult to make.

#### Noninvasive positive pressure ventilation-assisted bronchoscopy in severely hypoxaemic patients

Pneumonia with severe hypoxaemia is a common complication in immunocompromised patients, such as those

**Figure 2**



Fiberoptic bronchoscopy during noninvasive positive pressure ventilation. The patient is connected to the ventilator via a face mask (FM) secured with elastic straps (ES). The bronchoscope is passed through a seal adapter (SA), in order to allow mechanical ventilation. The arrow indicates the optical instruments advanced into the nose.

affected by haematological malignancies, transplantations or other conditions [49]. In these individuals, early diagnosis of the aetiological agent is paramount. Unfortunately, severe hypoxaemia in nonintubated patients represents a major contraindication to fiberoptic bronchoscopy and/or bronchoalveolar lavage [50], often meaning that treatment must be initiated on an empirical basis.

We proposed a new technique to perform fiberoptic bronchoscopy and/or bronchoalveolar lavage in severely hypoxaemic, nonintubated patients by means of PSV administered through a face mask (Fig. 2) [51]. All patients were administered NPPV for 10 min before starting bronchoscopic manoeuvres and NPPV was maintained for at least 90 min after the procedure. In all patients it was possible to identify the agent that caused pneumonia, and to start an early and specific treatment. None of the patients needed endotracheal intubation.  $\text{PaO}_2:\text{FiO}_2$  ratio and oxygen saturation increased significantly after the application of NPPV and remained high throughout the study.

In a recently concluded randomized study (unpublished data) on the use of bronchoalveolar lavage with or without NPPV for the diagnosis of nosocomial pneumonia in 26 hypoxaemic patients ( $\text{PaO}_2:\text{FiO}_2 < 200$ ), we were able to demonstrate that NPPV is more efficient than Venturi mask in correcting hypoxaemia during bronchoalveolar lavage, but 1 h after treatment  $\text{PaO}_2:\text{FiO}_2$  was not different in the two groups.

Bronchoscopy with NPPV seems to be a feasible, safe and effective technique to allow an early and accurate diagnosis of pneumonia in nonintubated, severely hypox-

aemic patients. Even though good cooperation of the patient and thorough monitoring of vital functions are essential, the technique appears very promising for application on a large scale in immunocompromized patients.

## Conclusion

In COPD patients, NPPV can be considered as a therapeutic option to prevent endotracheal intubation (reducing the additive morbidity and mortality) and to deliver artificial ventilatory support [6,9]. When no contraindication exists, a trial of NPPV should be always considered if a COPD patient is observed to be in the early phase of respiratory failure.

Some evidence suggests the utility of NPPV as a first-line intervention in hypoxaemic ARF and for NPPV-assisted bronchoscopy in severely hypoxaemic patients. The application of NPPV in patients suffering from ARF not related to COPD, despite some interesting and very promising preliminary results [5,11], still remains controversial. Large, prospective, randomized, multicentre studies are therefore needed.

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