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Negative-pressure ventilation: is there still a role?

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Negative-pressure ventilation: is there still a role? A. Corrado, M. Gorini. ©ERS Journals Ltd 2002.
ABSTRACT: Negative-pressure ventilation (NPV) was the primary mode of assisted ventilation for patients with acute respiratory failure until the Copenhagen polio epidemic in the 1950s, when, because there was insufficient equipment, it was necessary to ventilate patients continually by hand *via* an endotracheal tube. Thereafter, positive-pressure ventilation was used routinely. Since it was also observed that patients with obstructive sleep apnoea could be treated noninvasively with positive pressure *via* a nasal mask, noninvasive positive-pressure ventilation (NPPV) has become the most widely used noninvasive mode of ventilation.

However, NPV still has a role in the treatment of certain patients. In particular, it has been used to good effect in patients with severe respiratory acidosis or an impaired level of consciousness, patients that to date have been excluded from all prospective controlled trials of NPPV. NPV may be used in those who cannot tolerate a facial mask because of facial deformity, claustrophobia or excessive airway secretion.

NPV has also been used successfully in small children, and beneficial effects on the cardiopulmonary circulation maybe a particular advantage in children undergoing complex cardiac reconstructive surgery.

This review is divided into two parts: the first is concerned with the use of negative-pressure ventilation in the short term, and the second with its use in the long term.
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To accomplish ventilation, a pressure difference must be developed phasically across the lung. This difference can be generated by negative pressure in the pleural space, by positive pressure applied to the airway opening, or by a combination of both. Negative-pressure ventilation (NPV) can be defined as a type of ventilation in which the surface of the thorax is exposed to subatmospheric pressure (*i.e.* negative pressure) during inspiration (fig. 1). This subatmospheric pressure causes thoracic expansion and an attendant decrease in pleural and alveolar pressures, thereby creating a pressure gradient for air to move from the airway opening into the alveoli. When the pressure surrounding the thorax increases and becomes atmospheric (or greater than atmospheric), expiration occurs passively owing to the elastic recoil of the lung and chest wall.

It is pertinent to remember that NPV has played a pivotal role in the history of ventilatory support for patients with respiratory failure. With the introduction of noninvasive positive-pressure ventilation (NPPV) and its widespread success, the role of NPV has been questioned. In 1996, a comprehensive review examining the literature on this topic was published [1]. NPV does not have the same body of randomised controlled trial data to support its use in acute-on-chronic respiratory failure, but there have been seven uncontrolled studies [2–8] and two case controlled studies [9, 10]. The studies have often been of large numbers of patients, and recently, the preliminary results of two randomised controlled trials comparing NPV with both invasive mechanical ventilation and mask ventilation have been reported in abstract form [11, 12].

This review will focus on the clinical applications of NPV in patients with acute and chronic respiratory failure. The indications, contraindications and side-effects of NPV, nursing of patients during NPV, and external high frequency ventilation are also reported.

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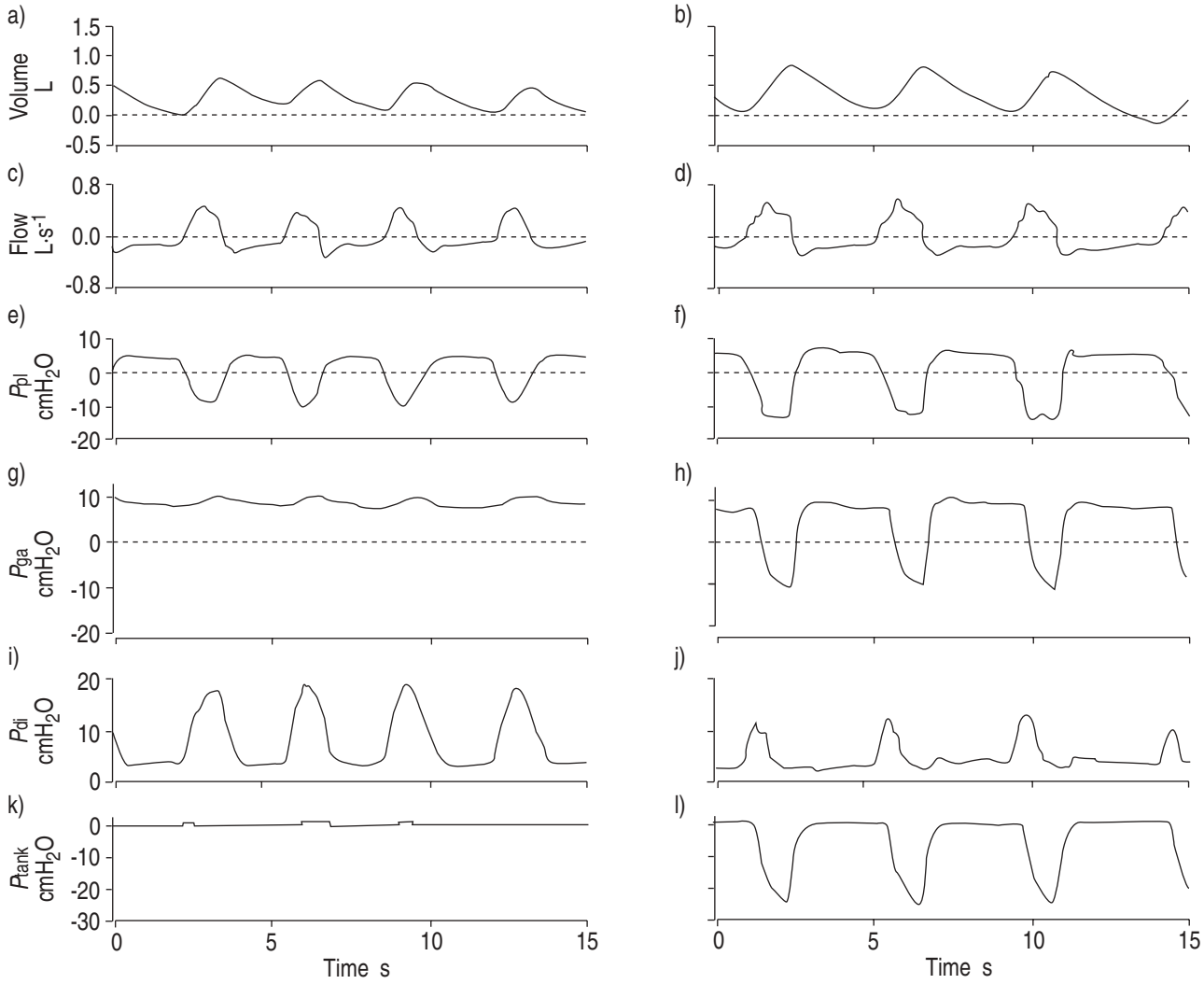

Fig. 1. – Tidal volume, flow, pleural pressure (P_{pl}), gastric pressure (P_{ga}), transdiaphragmatic pressure (P_{di}), and tank pressure (P_{tank}) in a patient with acute exacerbation of chronic obstructive pulmonary disease during spontaneous breathing (a, c, e, g, i and k) and assist negative-pressure ventilation (b, d, f, h, j and l) provided by iron lung.

Acute respiratory failure

Chronic obstructive pulmonary disease

MONTSERRAT *et al.* [4] evaluated the acute effects of NPV by a poncho wrap in 20 consecutive patients with chronic obstructive pulmonary disease (COPD) in acute respiratory failure (ARF) due to bronchial infection. Arterial blood gas tensions and maximal inspiratory pressure (MIP) were measured before and after 6 h of NPV or conventional medical treatment, given in random order on 2 consecutive days. MONTSERRAT *et al.* [4] reported that NPV increased MIP and decreased carbon dioxide tension in arterial blood (P_{a,CO_2}). There was no effect on oxygen tension in arterial blood (P_{a,O_2}). No change in these parameters was observed with conventional medical treatment. Although all patients completed the study, six were not compliant with NPV and these patients did not show the improvement in MIP and P_{a,CO_2} that was seen in those who were successfully treated [4].

SAURET *et al.* [5] studied 17 patients with severe COPD (forced expiratory volume in one second 0.60±0.15 L) in acute hypercapnic respiratory failure due to intercurrent bronchial infection. All patients underwent NPV with oxygen therapy for 6 h for 1 day only. Oxygen was administered using a Venturi mask (Trident Medical International, Denmark), with inspiratory oxygen fractions (F_{I,O_2}) of 24% at the beginning of treatment, 28% during the first hour, and 30% thereafter until the 6-h period of NPV was completed. A significant improvement in arterial blood gases and pH was seen during NPV. The same F_{I,O_2} of 24% during spontaneous breathing 1 h after the end of NPV, produced a better degree of oxygenation compared to that observed at baseline (P_{a,O_2} 7.09±0.8 *versus* 6.28±0.4 kPa (53.3±6 *versus* 47.2±3 mmHg)), whereas the improvement of P_{a,CO_2} and pH obtained during NPV remained unchanged. All patients reported a marked improvement in their dyspnoea and all were compliant with the ventilator; none experienced musculoskeletal pain or any other complications. SAURET *et al.* [5] concluded that NPV

allowed an increased oxygen flow in patients with severe hypercapnic respiratory failure due to advanced COPD, and, in some cases, prevented the need for more aggressive ventilatory support. However, in the absence of control data, little can be done with this observation, as it may simply reflect the natural history of recovery from an acute exacerbation.

Recently, it has been shown that assist NPV, provided by a microprocessor-based iron lung capable of thermistor triggering, is able to improve ventilatory patterns and arterial blood gases and to unload inspiratory muscles in patients with acute exacerbation of COPD (fig. 1) [13, 14]. While short-term changes in physiological variables may be important, it is not uncommon for such changes to be associated with no change in patient outcome. However, in a number of large uncontrolled studies the use of NPV has been shown to cause a similar outcome to the use of invasive ventilation.

In a study of 560 patients, 475 of whom had an exacerbation of COPD, NPV using an iron lung was applied successfully during an episode of ARF [2]. There was a significant improvement in gas exchange and pH. The overall mortality rate of 10.5% in the COPD patients was comparable to that reported in a more recent study [3], which retrospectively analysed 16 yrs of activity in a respiratory intensive care unit (RICU). During the period 1975–1991, 2,564 patients with ARF (2,011 with COPD and 553 with restrictive thoracic disorders) were treated with NPV provided by an iron lung. The in-hospital mortality rate was 9.9% for the group as a whole and 10% and 8.9% for patients with COPD and restrictive thoracic disorders, respectively. The average length of stay in the RICU was 10.5±9.5 days [3].

NPV, used as first-line treatment in severe COPD patients with ARF, has also been shown to be associated with a good long-term prognosis [6]. The outcome of 105 COPD patients with chronic respiratory insufficiency, admitted to an RICU from 1976–1980 because of ARF, was evaluated retrospectively. All subjects underwent NPV by means of iron lung. ARF was defined as an acute exacerbation of chronic disease, characterised by an increase in dyspnoea at rest, signs of right heart failure (ankle oedema), severe hypoxaemia (P_{a,O_2}<6.65 kPa (50 mmHg)), hypercapnia (P_{a,CO_2}>6.65 kPa (50 mmHg)), and pH<7.3. The main causes of ARF were exacerbations of chronic disease (55%) and bronchopneumonia (40%). Twelve patients died during hospitalisation, while 93 were successfully weaned and included in a follow-up lasting 5 yrs. Six patients were lost after discharge. All relapses of ARF during follow-up were treated by NPV. The survival rates after 1 and 5 yrs were 82% and 37%, respectively [6]. The observed survival in this study was better than that reported previously in COPD patients with ARF submitted to conventional mechanical ventilation [15].

Although comparisons with previous studies can be subjected to a number of biases (differences in the selection of patients, medical therapy and degree of monitoring applied), these data suggest that the treatment of ARF in COPD patients by NPV might improve survival. In recent years, NPPV has been successfully employed in the treatment of COPD patients with ARF. However, it has been suggested that careful selection of patients is mandatory and coma may be a contraindication [16, 17]. A retrospective and uncontrolled study [8] aimed to evaluate whether NPV provided by an iron lung could be successfully used in patients with hypoxic hypercapnic coma (HHC). Of a total of 1,430 patients with ARF admitted to an RICU, a series of 150 consecutive patients with HHC on admission were evaluated retrospectively. COPD was the most common underlying disease (79%). On admission severe hypoxaemia (P_{a,O_2} 5.8±3.0 kPa) and hypercapnia (P_{a,CO_2} 14.9±2.8 kPa) with acidosis (pH 7.13±0.13) were present, Glasgow coma score ranged 3–8 and the mean Acute Physiology and Chronic Health Evaluation (APACHE) II score was 31.6±5.3. All patients underwent intermittent NPV by means of an iron lung. The study end point was based on a dichotomic classification of treatment failure (defined as death or need for endotracheal intubation) *versus* therapeutic success. The treatment-failure rate was 45 of 150 (30%) and the observed mortality rate was 24 *versus* 67.5% predicted mortality, according to the APACHE II score. Nine patients (6%) required intubation because of a lack of control of the airway. The total duration of ventilation was a median of 27 h per patient (range 2–274). The group of 105 (70%) successful cases recovered consciousness after a median of 4 h (range 1–90) of continuous ventilation and were discharged after 12.1±9.0 days [8]. The study's data [8] show that, in a patient population with acute-on-chronic respiratory failure and hypoxic-hypercapnic coma, ventilation with an iron lung resulted in a high success rate. However, the study has the typical limitations of all retrospective and uncontrolled studies, and the results need to be formally confirmed by controlled prospective studies.

In 1998, CORRADO *et al.* [9] published the first controlled study that formally compared NPV and conventional invasive mechanical ventilation (IMV) for the treatment of ARF in COPD patients. The aim of this retrospective case-controlled study was to evaluate the effectiveness of NPV *versus* IMV for the treatment of ARF in COPD patients admitted to an RICU and four general intensive care units (ICUs). Seventy-six consecutive patients in ARF, admitted in 1994, underwent NPV (Group A) or IMV (Group B). Patients were matched according to age, sex, causes triggering ARF, APACHE II score, pH and P_{a,CO_2} on admission. The primary end points of the study were in-hospital death for both groups and the need for endotracheal intubation in patients in Group A. The secondary end points were length and complications of mechanical ventilation and duration of hospital stay [9]. A total of 26 pairs were submitted for analysis. The effectiveness of matching was 95.5%. Mortality rate was 23.1% in Group A and 26.9% in Group B (p=nonsignificant); two patients in Group A needed endotracheal intubation and one subsequently died. The duration of ventilation in survivors was significantly lower in Group A than in Group B with a median of 22.5 h (range 2–114) *versus* 96 h

(range 12–336) (p=0.0009), whereas the length of hospital stay was similar in the two groups with a median of 12 days (range 2–47) for Group A *versus* 12 days (range 3–43) (p=nonsignificant) for Group B. No complications were observed in Group A whereas four patients in Group B developed infective complications. These results suggest that NPV is as efficacious as IMV in the treatment of ARF in COPD patients and that it is associated with a shorter duration of ventilation and a similar length of hospital stay compared with IMV [9].

To date there has been no comparison of NPPV and IMV as patients deemed to need intubation were excluded from randomised control trials. However, the study by CORRADO *et al.* [9] indicates that NPV, provided by iron lung, can be effective in patients with severe acute hypercapnic exacerbation, widening the field for noninvasive ventilatory techniques. This has been recently confirmed by the preliminary results of a prospective randomised controlled study reported in abstract form [11]. The effectiveness of NPV and IMV in COPD patients with severe ARF was evaluated in 44 patients (22 randomised to NPV and 22 to IMV). Treatment failure was defined as need for endotracheal intubation and mortality for NPV, and mortality alone for IMV. The rate of treatment failure was similar in the two groups, whereas duration of mechanical ventilation and length of hospital stay were significantly lower in the NPV than IMV group.

A direct comparison between the two noninvasive ventilatory techniques in the treatment of COPD patients with ARF has recently been reported in a retrospective case-controlled study involving four respiratory intermediate ICUs [10]. The aim of this study was to investigate whether there were differences in outcome and complications that could be related to the different ventilatory treatments employed. Out of a total of 393 COPD patients admitted to hospital in 1996, 53 pairs were treated with the iron lung (NPV group) and NPPV (NPPV group). The two groups were matched according to age (70.3±7.1 *versus* 70.3±6.9 yrs), sex, causes of ARF, APACHE II score (22.4±5.3 *versus* 22.1±4.6), pH (7.26±0.05 *versus* 7.27±0.04) and P_{a,CO_2} (88.1±11.5 *versus* 85.1±13.5 mmHg) on admission. The effectiveness of matching was 98.4%. Five patients in the NPV group (9.4%) and seven of the NPPV group (13.2%) needed endotracheal intubation. Treatment failure (death and/or need for endotracheal intubation) was 20.7% in the NPV group and 24.5% in the NPPV group (p=NS). The duration of mechanical ventilation (29.6±28.6 *versus* 62.3±35.7 h) and the length of hospital stay (10.4±4.3 *versus* 15±5.2) among the 35 concordant surviving pairs were significantly lower in the NPV group than the NPPV group (p=0.001 and p=0.001, respectively). These data suggest that both ventilatory techniques are equally effective in avoiding endotracheal intubation and death in COPD patients with ARF. These findings have recently been confirmed by preliminary results of a prospective randomised controlled study reported in abstract form [12]. In order to compare the effectiveness of NPV and NPPV used as first-line treatment in COPD patients with ARF, and to evaluate the rescue power in preventing endotracheal intubation of NPV and NPPV used as second-line treatment in case of failure of NPPV or NPV, a randomised multicentre prospective trial was carried out in 73 patients (39 assigned to NPV and 34 to NPPV). The rate of success was similar for the two techniques. Among the failures of the first ventilatory treatment, endotracheal intubation was avoided in 64.3% of cases when one of the two techniques was used as rescue of the other. Hospital mortality rate and hospital stay were similar for NPV and NPPV groups. The data from this study show that NPV is as effective as NPPV for the treatment of COPD patients in ARF and that endotracheal intubation can be avoided in a high percentage of cases if the two techniques are combined.

Neuromuscular disorders

Only a few uncontrolled studies have investigated the effect of NPV in the treatment of neuromuscular patients with ARF in the last two decades. In these studies, NPV provided by iron lung [18–21] or pneumowrap [22] was successful in avoiding endotracheal intubation and in facilitating the weaning process from IMV in a small group of patients. SHNEERSON [18] suggested that for neuromuscular disorders, the chest shell or wrap style ventilator may be sufficient to overcome ARF for some patients, but for many the more effective tank ventilator may be needed.

In a retrospective study, the present authors reported the effects of NPV in the treatment of 15 neuromuscular patients with ARF admitted to an RICU from 1980–1985 [23]. Their diagnoses were as follows: Amyotrophic lateral sclerosis (46.7%), muscular dystrophy (33.3%), myasthenia gravis (13.3%) and multiple sclerosis (6.7%). The most common causes of ARF in these patients were infection of upper or lower respiratory tract and heart failure. On admission all patients exhibited severe hypoxaemia (P_{a,O_2} 5±1.6 kPa (37.6±12.4 mmHg)) and hypercapnia (P_{a,CO_2} 11.7±2.7 kPa (88.2+20.4 mmHg)), with uncompensated respiratory acidosis (pH 7.25±0.08). The mean Glasgow coma score was 10.7±3.6 with a range of 3–15. Five patients (33.3%) were in hypoxic-hypercapnic coma (Glasgow score 6.4±2.1), and another five (33.3%) were obtunded (Glasgow score: 11.8+0.4). All patients were managed by NPV provided by means of an iron lung. Nasogastric tubes were placed for the obtunded and comatose patients to minimise the risk of bronchial aspiration. To prevent obstruction of the upper airways due to tongue retraction, an oropharyngeal airway was inserted until consciousness was regained. The treatment was successful in 12 of 15 patients (80%). There were three treatment failures: one patient died and two required intubation. One of the intubated patients subsequently died while using invasive ventilatory support [23].

To assess the efficacy of NPV and NPPV in the treatment of ARF in patients with neuromuscular diseases, the outcome of 65 patients consecutively

admitted to two RICUs from 1995–1998 were analysed retrospectively [24]. Thirty patients were treated with NPV (NPV group) and 35 with NPPV (NPPV group). There was no significant difference in mortality rate (37 and 23% in the NPV and NPPV groups, respectively) and need for endotracheal intubation (17 and 14% in the NPV and NPPV groups, respectively) between the two groups, although on admission the NPV group had a lower pH, Glasgow coma score and P_{a,O_2}, and a higher APACHE II score and age than the NPPV group. These data support the use of both NPV and NPPV for the treatment of ARF in patients with neuromuscular diseases.

Although these reports suggest that NPV provided by an iron lung can be effective in the treatment of ARF in patients with neuromuscular diseases, many important questions remain unanswered. Prospective controlled studies are needed to confirm the results of uncontrolled reports [20–24] and to clarify the impact of noninvasive ventilatory support techniques on both mortality and length of hospital stay for patients with neuromuscular disorders who develop ARF.

Paediatric diseases

In the 1970s, several uncontrolled [25–27] and controlled [28, 29] studies showed that NPV was effective in the management of the neonatal respiratory distress syndrome. In 1989, SAMUELS and SOUTHALL [30] reported, in an uncontrolled clinical trial, the effects of NPV in 88 infants and young children (age range 1 day–2 yrs) with respiratory failure principally due to bronchopulmonary dysplasia and neonatal distress syndrome. After 2 h of ventilatory treatment with NPV, the F_{I,O_2} was reduced in 75 patients (85.2%) and a further decrease in F_{I,O_2} was achieved in 74 patients after 48 h. Of the 40 patients intubated at the start of treatment, 28 were successfully extubated with the aid of negative extrathoracic pressure and 24 survived. No potential complications, such as fluid retention, intrathoracic air leak, gastro-oesophageal reflux with aspiration or neck soreness, were reported. Upper-airway obstruction due to subglottic stenosis after extubation became evident during NPV in only one infant and required tracheostomy [30]. More recently, SAMUELS *et al.* [31] performed a prospective randomised controlled trial over a period of 4 yrs in 244 neonates comparing continuous negative extrathoracic pressure (-4–-6 cmH_2O) with standard therapy, which included continuous positive airway pressure (CPAP) of 4 cmH_2O. They demonstrated that the need for intubation was slightly less in the group treated with continuous negative extrathoracic pressure (CNEP) compared to the group that received standard therapy (86 *versus* 91%).

Infants with ARF who fail to respond to conventional ventilation are considered elective candidates for extra corporeal membrane oxygenation (ECMO). Although this technique can be life-saving, it is associated with significant complications [32] and high mortality rates [33]. In 1989, an uncontrolled study reported that the use of CNEP administered by a tank ventilator in conjunction with intermittent mandatory ventilation *via* an endotracheal tube was successful in five newborns suffering from respiratory failure and persistent pulmonary hypertension, thus avoiding the use of ECMO [34]. The benefit of combining intermittent mandatory ventilation and CNEP in these patients has recently been confirmed by the same group in a prospective randomised study [35]. Patients treated with CNEP showed a marked rise in P_{a,O_2} (9.2±2.3 kPa (69±17 mmHg)) 30 min after randomisation, which was statistically different to that observed in patients treated with positive end-expiratory pressure (P_{a,O_2} 6.2±3.6 kPa (48±27 mmHg); $p<0.05$). The use of CNEP did not increase morbidity and the overall survival rate was 83.3% [35]. These data suggest that CNEP is a noninvasive and safe method for the rescue of infants with severe hypoxaemia and can be successfully employed following invasive intermittent mandatory ventilation as initial therapy for infants who meet ECMO criteria.

Recently a case series reported the successful use of NPV provided by chest cuirass in critically ill children aged 4–16 months suffering from pneumonia, bronchopulmonary dysplasia, and bronchiolitis obliterans [36].

Positive-pressure ventilation (PPV) usually lowers cardiac output, primarily as a result of decreased venous return due to increased intrathoracic pressure [37]. Although the haemodynamic effects of NPV have not been studied extensively, these effects have been assumed to be opposite to those of PPV, *i.e.* more physiological and more likely to maintain a normal cardiac output. On theoretical grounds, however, the exposure of the entire body (except the airway opening) to NPV would result in the same haemodynamic effects as occurs with PPV [38]. This is because intrathoracic pressure is actually raised relative to body surface pressure, thereby reducing the gradient for venous return. It has been shown that this is not the case when the application of NPV is confined to the chest wall by using cuirass or jacket [39, 40]. Unlike tank ventilators, these machines selectively decrease intrathoracic pressure so that right atrial pressure becomes more negative relative to the rest of the body, enhancing the gradient for venous return [40]. In 1997 SHEKERDEMIAN *et al.* [41] studied the haemodynamic effects of conversion from conventional PPV to cuirass NPV in nine acute patients after Fontan operation. NPV resulted in an increase in pulmonary blood flow (54% mean increase) due to an improvement in stroke volume from 25–37 $mL \cdot m^{-2}$. SHEKERDEMIAN *et al.* [41] concluded that the improvement in cardiac output of this order and by this mechanism is currently unmatched by any therapeutic alternatives.

The effects of cuirass NPV were also studied in 23 intubated children who were initially ventilated using intermittent PPV in the early postoperative period after complete correction of tetralogy of Fallot [42]. SHEKERDEMIAN *et al.* [42] found that, after 45 min of NPV application, there was an increase in pulmonary blood flow of 67%. These results have recently been confirmed by the same authors [43].

Advantages, contraindications and side-effects

As with other modalities of noninvasive mechanical ventilation, the major advantage of NPV is the avoidance of endotracheal intubation and its related complications, while preserving physiological functions, such as speech, cough, swallowing and feeding. Moreover, therapeutic and diagnostic manoeuvres by fibreoptic bronchoscopy are easily performed during NPV [44]. Nevertheless, when treating patients with NPV, the following limitations should be considered. 1) The lack of upper airway protection, especially in unconscious and/or neurological patients may result in aspiration, given the reported effect of NPV on the lower oesophageal sphincter [45]. This can be reduced by premedication with metoclopramide. Secretions can be reduced using atropinic drugs. 2) Upper airway obstruction may occur [46] or be enhanced in unconscious patients, in patients with neurological disorders with bulbar dysfunction and in those with sleep apnoea syndrome. This can be avoided by the use of nasal CPAP, although in this situation, it may be more appropriate to move to NPPV. It has also been reported [1] that in unconscious patients with normal bulbar function, the placement of a nasogastric tube and the positioning of an oropharyngeal airway can minimise the risk of aspiration and/or airway collapse. The indications, contraindications and side-effects of NPV are reported in table 1. Most of the reports of side-effects of NPV come from stable, chronically-ventilated patients. In these studies the most common side-effects were poor compliance, upper airway obstruction and musculoskeletal pain. All negative-pressure ventilators restrict motion and back pain is a common problem. NPV has been associated with rib fractures and pneumothorax [47]. In the study by CORRADO *et al.* [9], two of 26 (8%) patients reported uneasiness and back pain and two others experienced vomiting during NPV. These percentages are similar to those reported for NPPV [48].

Negative-pressure ventilation and noninvasive positive-pressure ventilation

Several prospective, randomised clinical studies have clearly shown that NPPV is more effective than medical treatment in preventing endotracheal intubation in patients with acute exacerbation of COPD. The likelihood of success with NPPV is influenced by several factors, including early application [49], the severity of respiratory acidosis [49] and illness [16, 50], the degree of airway secretion [50], and the possibility of preventing excessive air leaks from the mask [50]. To date, all the randomised controlled trials have excluded patients deemed to need intubation. Studies of NPV [8, 9, 11, 12] have shown that COPD patients with severe respiratory acidosis, severe illness and hypercapnic encephalopathy may be successfully treated with this technique. These findings indicate that NPV may be more effective than NPPV in more severe disease, such as those requiring endotracheal intubation. Furthermore, NPV can be successfully used in patients in whom excessive airway secretion or difficulty in wearing a mask prevent the application of NPPV. It should be stressed, however, that there are some difficulties in introducing this modality in the vast majority of ICUs or RICUs, where NPPV is preferred as a noninvasive modality of mechanical ventilation [51]. This may be due mainly to the fact that the iron lung is cumbersome and needs a large amount of space rather than problems associated with NPV *per se*.

Nursing

The effectiveness of NPV depends on strict supervision by well-trained nurses and physiotherapists with considerable expertise with NPV. The major problems related to the assistance of patients with NPV by an iron lung are: 1) transfer from the bed to inside the chamber of the tank ventilator; and 2) access to patients for nursing procedures during mechanical ventilation. However, well-trained nurses can easily manage both transfer by using aids (a roll mattress and a mechanical elevator) and nursing procedures (insertion of urinary catheter and venous lines, placement of electrocardiogram electrodes and arterial oxygen saturation (S_{a,O_2}) probe for monitoring the level of oxygenation, *etc.*) by using the portholes in the tank ventilator. Other tasks for nurses or physiotherapists during NPV include the periodic measurements of tidal volume and minute ventilation, easily performed using a Wright's ventilograph, and the promotion of secretion clearance by means of assisted cough and suction. There are no published data about nursing workload during NPV. However, in the current authors' unit the time spent by nurses on the second day after admission on COPD patients with ARF treated with the iron lung has been measured. The procedures considered and findings were as follows: 1) transfer of patients from the bed to inside the tank ventilator (three times per day), 105 min (this time also includes the placement of

Table 1. – Indications, contraindications, and side-effects of negative-pressure ventilation

Indications	Contraindications	Side-effects
Severe respiratory acidosis	Sleep-apnoea syndrome	Upper airway collapse
Severe hypercapnic encephalopathy	Severe obesity	Back pain
Excessive airway secretions	Severe kyphoscoliosis	Tiredness or depression
Facial deformity	Claustrophobia	Oesophagitis
Inability to fit mask	Rib factures	Rib fractures
Mask intolerance	Recent abdominal surgery	Poor compliance

electrodes and monitor probes); 2) measurement of tidal volume and minute ventilation by means of Wright's ventilograph, 30 min; 3) tracheobronchial suction, 35 min; 4) arterial blood gas samples, 30 min; and 5) drug administration, 20 min; 6) other procedures, 30 min. The total time spent by nurses on these procedures was 250 min. Although there have been no studies comparing nursing workload in patients submitted to NPV and IMV, NAVA *et al.* [52] have reported that nursing workload in patients treated with IMV was 527.5±51.1 min during the first 48 h after admission.

Long-term application of negative pressure in stable conditions

Chronic obstructive pulmonary disease

On the basis of the hypothesis that chronic hypercapnia in severe COPD patients may be caused by an excessive load on the inspiratory muscles, several studies have evaluated the effects of NPV in terms of improvement in arterial blood gases, muscle function, and exercise performance [47, 53–56]. CROPP and DIMARCO [53] performed a short-term controlled study on patients with severe COPD. When eight patients were treated with a cuirass for 3–6 h daily on 3 consecutive days, maximal inspiratory and expiratory pressures increased 14 and 12%, respectively, mean P_{a,CO_2} decreased 1.06 kPa (8 mmHg), and the duration of maximal voluntary ventilation increased compared to baseline measures. All these parameters remained unchanged in seven patients who served as the control group. In an uncontrolled study, GUTIERREZ *et al.* [54] reported improvement in blood gases, inspiratory muscle strength, and clinical condition in five hypercapnic patients (P_{a,CO_2}=7.7±1.3 kPa (59±10 mmHg)) ventilated with a cuirass for 8 h once a week.

In contrast with the two previous studies, ZIBRAK *et al.* [47] showed no improvement in pulmonary-function test, blood gases and exercise endurance in a group of 20 stable patients with severe COPD (P_{a,CO_2}=6.4±1.3 kPa (48±10 mmHg)) treated with poncho-wrap ventilator for 2–6 h a day for 6 months. However, 11 of the 20 patients dropped out the study because of intolerance of the ventilator, and all but one of the nine patients who completed the study expressed dissatisfaction with it. Musculoskeletal pain and inconvenience when putting on the wrap were the most frequent complaints of patients. CELLI *et al.* [55] studied the effects of NPV provided by pneumowrap on exercise endurance, maximal transdiaphragmatic pressure, and tension-time index of the diaphragm in 16 patients with severe COPD (P_{a,CO_2}=5.9±2.0 kPa (44±9 mmHg)). After enrolment in the study and baseline measurements, patients were randomly assigned to one of two groups. One group (seven patients) underwent a 3 week in-hospital rehabilitation programme, and the other group (nine patients) received rehabilitation plus NPV. NPV was provided by pneumowrap ventilator for 3–11 h a day. After treatment, pulmonary function and maximal transdiaphragmatic pressure ($P_{di,max}$) remained unchanged, but the patients in both groups exhibited improvement in tension-time index of diaphragm and leg exercise endurance with no difference between groups. This study shows that NPV provided by pneumowrap, as a means of resting respiratory muscles in patients with COPD, does not have an added effect to that achieved by a pulmonary rehabilitation programme alone. The significant improvement in P_{a,CO_2} and $P_{di,max}$ observed in the patient with the highest degree of hypercapnia suggested that NPV may be helpful in COPD patients with severe hypercapnia.

In 1992, SHAPIRO *et al.* [57] published the results of the largest trial on the effects of NPV in patients with COPD. The hypothesis that patients with COPD have chronic inspiratory muscle fatigue was tested in a randomised controlled trial in 184 patients allocated active (92 cases, P_{a,CO_2}=5.8±0.9 kPa (43.8±6.7 mmHg)) or sham (92 cases, P_{a,CO_2}=5.9±1.0 kPa (44.4±7.3 mmHg)) NPV treatment for a 12-week period of home use. The distance walked in a 6-min walk test was the primary outcome variable with severity of dyspnoea, quality of life, arterial blood gases, and respiratory muscle strength as secondary outcomes. There was no evidence of significant differences in any outcome measurements between the two groups. The compliance of the patients was poor: of the 184 patients randomised, 10 (two sham NPV and eight active NPV) did not use the ventilator at all, and 53 others (27 sham and 26 active) stopped before completing 12 weeks' treatment. Difficulty with carrying out NPV, tiredness, depression and chest pain were the reasons for stopping NPV. The mean duration use of the ventilator was 2.4 h in the active group and 3.0 h in the sham group.

In summary, there is no evidence that long-term treatment with NPV is able to improve respiratory-muscle function, exercise endurance, quality of life and survival in patients with severe COPD. It also appears that NPV provided in control mode by cuirass or pneumowrap is poorly tolerated by stable COPD patients in a typical outpatient setting. However, it is important to stress that up to now, no other ventilatory techniques, including mask ventilation with the most technologically advanced ventilators, have been show to be effective for the long-term treatment of stable COPD patients.

Neuromuscular disorders

Considering data from the literature in the last 40–50 yrs, there is no doubt that patients with restrictive ventilatory impairment due to neuromuscular and chest wall diseases can derive benefits from NPV [20, 58–61]. In 1981, GARAY *et al.* [20] described the long-term effect of the application of NPV at home in a pivotal study carried out on eight patients with alveolar hypoventilation syndromes due to poliomyelitis and scoliosis,. After reversal of severe hypercapnia, all patients were discharged and maintained at home for an average period of 10 yrs, utilising NPV provided by a tank ventilator or

pneumowrap. The 5-yr survival was 100% and all patients continued their previously productive lives. SPLAINGARD *et al.* [60] reported 20 yrs of experience using NPV at home to ventilate 40 patients with neuromuscular disease. The purpose of the study was to determine the costs, complications and clinical outcome of this form of respiratory support. Emerson tank respirators, used mainly during sleep, and intermittent positive-pressure breathing machines were used by 98% of patients, with an average equipment cost of $2,700 annually. Patients in whom NPV was initiated on an elective rather than emergency basis saved an average of $12,000 during their initial hospitalisation. Life-table analysis showed a 5-yr survival of 76% and a 10-yr survival of 61%. Complications were minor and occurred at an average rate of less than one per year per patient at home on NPV. Failure to achieve satisfactory NPV in nine patients was associated with age (six patients were <3 yrs of age) or severe thoracocervical scoliosis, which prevented proper fitting of the NPV. The ventilator-management protocol followed over 12 yrs in 23 patients with Duchenne muscular dystrophy (DMD) and six polio survivors with chronic respiratory failure (CRF) secondary to the late effects of poliomyelitis or post-polio syndrome has been reported by CURRAN and COLBERT [58]. After the onset of respiratory failure, patients with DMD continued to show a classic course of progressive, generalised muscle weakness and a steadily declining vital capacity from an average of 0. 48–0.34 L. The DMD group required an average increase of 0.95 h in their daily use of assisted ventilation, provided by a tank ventilator, per year. Their overall average length of survival was increased from 19 yrs 9 months to 25 yrs 9 months. The 5-yr survival was 76%. SCHIAVINA and FABIANI [61] reported the clinical course in 31 patients with chronic respiratory failure due to neuromuscular or chest-wall disorders treated at home for 6 months with NPV. The ventilatory assistance during the night was provided by poncho wrap or pneumowrap. The average duration of mechanical ventilation was 8 h per day at the beginning of the follow-up period. Some patients needed to increase the number of hours of ventilation because of a significant decrease in vital capacity and an increase of the level of dyspnoea. Five patients underwent polysomnographic studies before and during NPV. The recording during NPV showed a general improvement in all but one patient in the quality and the structure of sleep with an increase in sleep efficiency and in the percentage of the rapid eye movement phase. This happened despite an increase in the number of arousals associated with the appearance of obstructive apnoeas. However, the level of desaturation caused by obstructive events was lower than that caused by central events in the baseline recording. At the end of the 6-month follow-up period the survival was 87%.

The effect of 5 yrs of nocturnal cuirass-assisted ventilation in 25 patients with neuromuscular and chest-wall disorders complicated by CRF were reported by JACKSON *et al.* [59]. Individual cuirass shells were made for each patient, which were used with a Cape cuirass pump or Newmarket pump. NPV was performed during the night and additionally during the day when necessary. The ability of cuirass-assisted ventilation to produce adequate ventilation and to rest the respiratory muscles was assessed by measuring tidal volume, arterial blood gases and the electromyographic activity on the respiratory muscles. Before the commencement of home mechanical ventilation, upper airway obstruction during NPV was excluded by clinical observation and monitoring of oxygen saturation and carbon dioxide levels during sleep. Fifteen patients (60%) were alive after 5 yrs of follow-up. Two patients refused to continue NPV and both died within 1 yr. Three patients were shifted to intermittent PPV *via* nasal mask or tracheostomy (one patient) due to increasing difficulty fitting the cuirass. Mortality during follow-up was not predicted from age, lung volumes or the arterial blood gases at presentation. The median amount of time spent in hospital declined from 15 days per patient in the first year after discharge with NPV to 3–5.5 days per patient in subsequent years.

A recent study by BAYDUR *et al.* [62] on long-term effects of noninvasive mechanical ventilation in patients with musculoskeletal disorders has been published. This retrospective study described 46 yrs of experience in 79 patients submitted to home ventilatory assistance with NPV (tank respirator or cuirass in 31 cases) or mask positive-pressure ventilation (mPPV) (in 48 patients). The proportion of patients that reported a positive outcome, in terms of improved sense of well being and independence, was greater with mPPV than NPV (67 *versus* 29%), and in the subgroup of patients with poliomyelitis, the number of tracheostomies was greater with NPV than mPPV. It is important to stress, however, that the population treated with NPV and mPPV was not homogeneous in terms of age, diagnosis and pulmonary function. Furthermore, the duration of home mechanical ventilation in patients treated with NPV was much greater than in those with mPPV (24 *versus* 3.2 yrs).

From these studies, although uncontrolled, it appears that NPV has been used successfully for long-term home mechanical ventilation in patients with neuromuscular and chest-wall disorders. NPV devices, however, are more cumbersome and difficult to use than recent home PPV devices. Although direct comparisons between the efficiency of NPV and mPPV are rare, in patients with muscular dystrophy and bulbar weakness NPV tends to predispose patients to obstructive apnoeas during sleep [63]. This is probably due to the absence of coordination between upper airway muscle activity and the ventilator cycle [46, 64]. For these reasons, NPV has been largely supplanted by mPPV in the last decade. In experienced hands, NPV remains a second choice to be used in patients who, for technical or other reasons, can not be offered mPPV. It has been reported that brief discontinuation of mPPV in some patients who were affected by chronic hypercapnic respiratory failure, due to intolerable nasal irritation or upper airway congestion, is associated with significant worsening of the arterial blood gas tensions

[65]. In these cases and other clinical conditions, such as facial deformity or lack of teeth, NPV should be used as an alternative to mPPV.

External high-frequency oscillation

High-frequency ventilation using a jet system can be applied *via* a tracheal tube or a tracheostomy. An alternative approach, not requiring intubation, is to apply high-frequency oscillation externally by using a cuirass [66]. The Hayek oscillator consists of a cuirass, a power unit, and a control unit. The cuirass is designed to fit over the front of the chest and upper abdomen. The power unit consists of two pumps: a diaphragmatic pump which can operate over a wide range of frequencies to generate an oscillating pressure wave and a vacuum pump that enables this oscillation to be superimposed on a negative pressure baseline. Peak inspiratory ($\leqslant$-70 cmH_2O) and peak expiratory ($\leqslant$70 cmH_2O) pressures, frequency (8–999 cycles·min^{-1}) and inspiratory:expiratory ratio (1:6 to 6:1) can be set on the control unit.

It has been shown that external high-frequency oscillation (EHFO) can provide effective ventilation in healthy adults [66]. SPITZER *et al.* [67] studied 20 patients with severe COPD in a stable condition. They found that by using frequencies of 60–140 cycles·min^{-1} end tidal carbon dioxide tension (P_{a,CO_2} in three patients) decreased and S_{a,O_2} increased both in eucapnic and hypercapnic patients [67]. In five patients with ARF (two with acute respiratory distress syndrome), EHFO, applied for a 30-min period, improved oxygenation by 16% and reduced P_{a,CO_2} by 6% compared to conventional PPV [66]. Several studies have investigated the haemodynamic effects of EHFO in patients after cardiac surgery. In a randomised controlled study, SIDENO and VAAGE [68] found that EHFO, applied for a 4-h period, improved cardiac index and tissue perfusion in adult patients after coronary artery bypass grafting compared to conventional PPV.

NPV delivered with the Hayek oscillator improved cardiac output in 11 children after total cavopulmonary connection and tetralogy of Fallot repair compared to conventional mechanical ventilation [69]. However, there are no studies comparing EHFO to conventional mechanical ventilation in terms of mortality, complication of mechanical ventilation, and length of stay in the ICU.

Conclusion

There is evidence from case-controlled studies and preliminary data from prospective randomised controlled trials suggesting that: 1) NPV provided by the iron lung is as effective as mask ventilation in the treatment of patients with acute exacerbation of COPD; and 2) NPV is as effective as IMV in the treatment of COPD patients with severe ARF. However, this evidence is mainly based on results reported by a single group of clinicians. Further studies are needed that particularly address the relative role and the integration of NPV and mask ventilation.

There is long-term data supporting the use of negative-pressure ventilation in patients with chronic respiratory failure, but its place has largely been taken by noninvasive positive-pressure ventilation, which is easier to apply and less cumbersome for patients. There is still a role for negative-pressure ventilation in patients with chronic respiratory failure who are unable to tolerate noninvasive positive-pressure ventilation.

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