Noninvasive pressure support ventilation in COPD patients with postextubation hypercapnic respiratory insufficiency

G. Hilbert, D. Gruson, L. Portel, G. Gbikpi-Benissan, J.P. Cardinaud

ABSTRACT: Patients with chronic obstructive pulmonary disease (COPD) who have been intubated and mechanically ventilated may prove difficult to wean. Noninvasive ventilation may be used in an attempt to avoid new endotracheal intubation.

The efficacy of administration of noninvasive pressure support ventilation was evaluated in 30 COPD patients with postextubation hypercapnic respiratory insufficiency, compared with 30 historically matched control patients who were treated conventionally. Patients were included in the study if, within 72 h postextubation, they presented with respiratory distress, defined as the combination of a respiratory frequency $>25$ breaths·min$^{-1}$, an increase in the arterial carbon dioxide tension ($P_aCO_2$) of at least 20% compared with the value measured after extubation, and a pH $<7.35$.

Noninvasive pressure support ventilation was effective in correcting gas exchange abnormalities. The use of noninvasive ventilation significantly reduced the need for endotracheal intubation: 20 of the 30 patients (67%) in the control group required endotracheal intubation, compared with only six of the 30 patients (20%) in the noninvasive-ventilation group ($p<0.001$). In-hospital mortality was not significantly different between the two groups, but the mean duration of ventilatory assistance for the treatment of the postextubation distress, and the length of intensive care unit stay related to this event, were both significantly shortened by noninvasive ventilation ($p<0.01$).

In conclusion, noninvasive ventilation may be used in the management of patients with chronic obstructive pulmonary disease and postextubation hypercapnic respiratory insufficiency.

postextubation hypercapnic respiratory insufficiency was established if, within 72 h of discontinuation from mechanical ventilation, the patients presented with respiratory distress, defined as the combination of a respiratory frequency \( (f_R) >25\text{ breaths-min}^{-1} \), an increase in the arterial carbon dioxide tension \( (P_a,CO_2) \) of at least 20%, compared with the postextubation value measured during spontaneous breathing with supplemental \( O_2 \) and a \( pH <7.35 \). Five patients were excluded from the study because of either haemodynamic instability with sustained systolic arterial blood pressure <80 mmHg (n=3), or failure of more than two organs [14] (n=2). The remaining 30 patients (22 males and eight females) were studied prospectively.

The 30 control patients (22 males and eight females) were chosen from a group of 72 patients admitted to the ICU in the 4 preceding years. They had all been intubated for acute exacerbations of COPD, having presented with hypercapnic respiratory insufficiency after weaning with \( PS \) ventilation. They had also received conventional therapy, including a new intubation and mechanical ventilation if necessary.

All COPD patients were weaned using \( PS \) ventilation. The criteria for initiating weaning with \( PS \) ventilation were similar in the two groups, i.e. vital capacity >10 mL·kg\(^{-1} \), arterial oxygen saturation \( (S_a,O_2) >90% \) at the fraction of inspired oxygen \( (F_i,O_2) \) 40% and maximal inspiratory pressure >25 cmH\(_2\)O. The procedure was similar in both groups, and the decision to perform endotracheal extubation was made by the patient’s attending physician according to the usual criteria used in the ICU, i.e. the patient was able to tolerate spontaneous breathing with 6 cmH\(_2\)O of \( PS \) during a period of 6 h.

For each patient treated with NIPSV, a matching control patient was selected according to the following criteria: 1) Regarding intubation for acute exacerbation of COPD: severity of illness on admission within 4 points of that of treated patients, as assessed by the new Simplified Acute Physiologic Score (SAPS II) [15]; mean duration of intubation and ventilatory assistance within 3 days; and age within 10 yrs of that of the treated patient. 2) Regarding hypercapnic respiratory insufficiency diagnosed after weaning from mechanical ventilation: period between extubation and diagnosis of hypercapnic respiratory insufficiency within 24 h; arterial pH within 0.03 of the value for the treated patient; \( P_a,CO_2 \) within 0.7 kPa of the value for the treated patient when the value was <9.3 kPa, and within 1.3 kPa when the value was >9.3 kPa.

In matching each patient, priority was given to arterial pH, the period between extubation and diagnosis of hypercapnic respiratory insufficiency and the mean duration of intubation and ventilatory assistance. Matching was not possible on all criteria for all patients. Nevertheless, 83% of our subjects met at least the three criteria indicated on the priority list and the remaining 17% of patients met at least two of the three criteria.

**Methods**

**Mask fitting.** NIPSV was delivered to the patient through a full-face mask (La Cigogne®, Pessac, France). The proper mask size was chosen for each patient. If the patient felt pain when the mask was applied, or if redness was observed on the skin compressed by the mask, we used wound care dressing on the bridge of the nose under the mask.

**Ventilation.** The mask was adjusted and connected to an Evita ventilator (Dräger, Lübeck, Germany) set in the PS mode.

**Protocol.** After the mask was secured, the level of \( PS \) was increased progressively and adjusted for each patient to obtain an expired tidal volume, as measured by the ventilator, 57 mL·kg\(^{-1} \) and \( f_R <25\text{ breaths-min}^{-1} \). A slight level of positive end-expiratory pressure (PEEP), i.e. 4 cmH\(_2\)O, was also applied. The \( F_i,O_2 \) was adjusted to an \( S_a,O_2 >90% \), as measured by a bedside pulse oximeter (Oxisensor, Nellcor®, Hayward, CA, USA). Arterial blood gases were measured at the end of 30 min of ventilation with these first adjustments. Ventilatory support was then interrupted. \( F_i,O_2 \) was increased if arterial oxygen tension \( (P_a,O_2) <8\text{ kPa} \). PS and/or PEEP were modified if ventilatory efficiency was thought to be insufficient.

After this optimization of ventilator adjustments, a new ventilation session of 45 min was programmed, with analysis of arterial blood gases at the end of the session. Ventilatory support was interrupted after this session of 45 min. Ventilation parameters were sometimes modified during the course of the study according to clinical and blood gas analysis data collected by the physician managing the patient. The objective was to obtain the best possible compromise between tolerance and ventilatory efficiency.

NIPSV was not maintained continuously and was used for a minimum of 30 min every 4 h. The nurse and physiotherapist were asked to maintain periods of ventilation for as long as possible, mainly at the beginning of the protocol, taking into account the patient’s tolerance, and trying to encourage in all cases a minimal duration of 30 min of ventilation. Between periods of ventilation, patients received a minimal oxygen flow adjusted to blood gas analysis data, under continuous monitoring of heart rate, blood pressure, \( f_R \) and \( S_a,O_2 \). Patients were systematically returned to NIPSV when \( S_a,O_2 \) was <85% or when dyspnoea worsened, with an \( f_R \) of >30 breaths-min\(^{-1} \). After the first 24 h of the protocol, if the patient improved, ventilation sessions could be separated by longer intervals. NIPSV was withdrawn when patients reached an \( f_R \) of <25 min\(^{-1} \) and a \( pH >7.38 \) in spontaneous breathing without worsening for 24 h. Therapy was considered to be a success when intubation was avoided and the patient was transferred from the ICU.

**Criteria for reintubation.** The decision to perform endotracheal intubation was made by the patient’s attending physician, according to the usual criteria used in the ICU, i.e. severe encephalopathy, major agitation requiring sedation, increase in \( f_R \) and gas exchange deterioration, and shock.

**Analysis**

Prior to NIPSV, measurements of \( f_R \), \( P_a,CO_2 \), pH, and \( P_a,O_2 \) were compared to those obtained after 45 min of ventilatory support with optimal settings, by using the Student’s paired t-test. Baseline data, the number of patients requiring a new intubation, the mean duration of ventilatory assistance for the treatment of the postextubation distress, the length of stay in the ICU related to this event and the in-hospital mortality were compared between the group of patients treated with NIPSV and the control.
group, using an unpaired t-test and a Chi-squared test with Yates’ correction. A p-value of <0.05 was considered as the level of significance.

Results

NIPSV: optimization of ventilatory settings

The level of PS was fixed at 16±4 cmH2O and PEEP at 5±1 cmH2O. The FIO2 was adjusted to 29±5%.

Physiological effects of NIPSV

There was a significant improvement in the mean fR, pH, PaCO2, and PaO2 between measurements made before to NIPSV and those obtained after 45 min of ventilatory support with optimal settings (table 1).

Clinical study

The demographic and stable-state functional characteristics of all patients are shown in table 2. The functional characteristics of all patients at the time of inclusion are shown in table 3. The patients in the two groups were well matched with regard to the severity of their underlying respiratory disease, i.e. functional stable-state characteristics were similar in the two groups. The same was found for the severity of acute decompensation, i.e. there were no significant differences in SAPS II (27±7 versus 28±6) or the mean duration of intubation and ventilatory assist-

Table 1. – Changes in pH, arterial carbon dioxide tension (PaCO2), arterial oxygen tension (PaO2) and respiratory frequency before noninvasive pressure support ventilation (NIPSV) and after 45 min of ventilatory support with optimal settings

<table>
<thead>
<tr>
<th></th>
<th>Before NIPSV</th>
<th>p-value</th>
<th>NIPSV</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.33±0.04</td>
<td>&lt;0.01**</td>
<td>7.39±0.05</td>
</tr>
<tr>
<td>PaCO2 kPa</td>
<td>8.0±1.5</td>
<td>&lt;0.01**</td>
<td>10.2±1.3</td>
</tr>
<tr>
<td>PaO2 kPa</td>
<td>9.2±0.9</td>
<td>&lt;0.01**</td>
<td>7.7±1.1</td>
</tr>
<tr>
<td>fR breaths·min−1</td>
<td>30±4</td>
<td>&lt;0.01**</td>
<td>24±3</td>
</tr>
</tbody>
</table>

Values are presented as mean±SD. fR: respiratory frequency. **: p<0.01 significant difference between pre-NIPSV and NIPSV measurements.

Table 2. – Demographic and functional stable-state characteristics of all patients

<table>
<thead>
<tr>
<th></th>
<th>NIPSV group</th>
<th>p-value</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age yrs</td>
<td>68±10</td>
<td>ns</td>
<td>69±9</td>
</tr>
<tr>
<td>FEV1 % pred†</td>
<td>33±9</td>
<td>ns</td>
<td>35±10</td>
</tr>
<tr>
<td>FEV1/VC % pred†</td>
<td>53±11</td>
<td>ns</td>
<td>54±8</td>
</tr>
<tr>
<td>PaCO2 kPa</td>
<td>8.0±0.9</td>
<td>ns</td>
<td>7.7±1.1</td>
</tr>
<tr>
<td>PaO2 kPa</td>
<td>7.6±1.1</td>
<td>ns</td>
<td>7.8±0.8</td>
</tr>
<tr>
<td>Bicarbonate mmol·L−1</td>
<td>30±3</td>
<td>ns</td>
<td>30±4</td>
</tr>
</tbody>
</table>

Values are presented as mean±SD. NIPSV: noninvasive pressure support ventilation; FEV1: forced expiratory volume in one second; VC: vital capacity; PaO2: arterial oxygen tension; PaCO2: arterial carbon dioxide tension; ns: nonsignificant. †: Functional stable-state characteristics were obtained from previous spirometric tests in 20 of the patients in the NIPSV group, and in 21 of those in the control group. Reliable pulmonary-function data were obtained within 2 months after inclusion in nine of the patients in the NIPSV group, and in seven of those in the control group. Data recorded in air in spontaneous breathing.

Table 3. – Functional characteristics of all patients at inclusion

<table>
<thead>
<tr>
<th></th>
<th>NIPSV group</th>
<th>p-value</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.33±0.04</td>
<td>ns</td>
<td>7.32±0.04</td>
</tr>
<tr>
<td>fR breaths·min−1</td>
<td>30±4</td>
<td>ns</td>
<td>32±5</td>
</tr>
<tr>
<td>PaCO2/PaO2</td>
<td>30.4±5.4</td>
<td>ns</td>
<td>31.2±5.8</td>
</tr>
<tr>
<td>PaCO2 kPa</td>
<td>9.2±0.9</td>
<td>ns</td>
<td>9.4±1.1</td>
</tr>
<tr>
<td>fR breaths·min−1</td>
<td>96±11</td>
<td>ns</td>
<td>99±12</td>
</tr>
</tbody>
</table>

Values are presented as mean±SD. NIPSV: noninvasive pressure support ventilation; fR: respiratory frequency; PaCO2: fraction of inspired oxygen; ns: nonsignificant.

Table 4. – Outcome in all patients

<table>
<thead>
<tr>
<th></th>
<th>NIPSV group</th>
<th>p-value</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients requiring intubation %</td>
<td>6 (20)</td>
<td>&lt;0.001</td>
<td>20 (67)</td>
</tr>
<tr>
<td>Deaths %</td>
<td>2 (7)</td>
<td>ns</td>
<td>6 (20)</td>
</tr>
<tr>
<td>Outcome in survivors days</td>
<td>3±3</td>
<td>&lt;0.01</td>
<td>1±1</td>
</tr>
<tr>
<td>Duration of ventilatory assistance+</td>
<td>6±4</td>
<td>&lt;0.01</td>
<td>11±8</td>
</tr>
<tr>
<td>Length of ICU stay+</td>
<td>8±4</td>
<td>&lt;0.01</td>
<td>14±2</td>
</tr>
</tbody>
</table>

Values are presented as mean±SD. NIPSV: noninvasive pressure support ventilation; ICU: intensive care unit. +: relative to the period postextubation hyacrapnic respiraory insufficiency.

Outcome in the 30 patients treated with NIPSV and the 30 control patients are shown in table 4. In-hospital mortality was not significantly different in the treated versus the control group (7 versus 20%). Death occurred only in patients who had to be intubated, either after failure of conventional treatment in the control group or after failure of ventilation in the NIPSV group.

However, 20 of the 30 patients (67%) in the control group required endotracheal intubation compared with only six of the 30 patients (20%) in the NIPSV group (p<0.001). In the NIPSV group, the period between intubation and intubation was 16±12 h (range, 3–46 h) for the six patients. In the control group, the period between hypercapnic respiratory insufficiency and intubation was 9±7 h (range, 1–41 h) for the 20 patients. The reasons for endotracheal intubation were comparable in the two groups in the treated and control groups, respectively.
severe encephalopathy two (33%) versus eight (40%); major agitation requiring sedation one (17%) versus two (10%); increase in fR and deterioration in gas exchange three (50%) versus ten (50%).

The mean duration of noninvasive ventilatory assistance in the ICU was 5±2 days (range, 2–9) in the 24 patients treated successfully with NIPSV. The duration of invasive mechanical ventilation was 13±6 days (range, 6–20) in the 4 patients in the treatment group who required reintubation and who had favourable outcomes. In the surviving patients, the total time of ventilatory assistance for the treatment of the postextubation distress (duration of NIPSV in all patients in the treatment group, and duration of invasive mechanical ventilation performed after reintubation in patients in both groups who required reintubation) was 6±4 days (range, 2–21) in the treatment group compared with 11±8 days (range, 5–25) in the control group (p<0.01). Similarly, the length of ICU stay was 8±4 days (range, 4–24) in the treatment group, compared with 14±8 days (range, 4–31) in the control group (p<0.01). Two patients in the treatment group developed nosocomial pneumonia (leading to death in one patient); six patients in the control group had nosocomial pneumonia (leading to death in two patients). All of them were intubated. Because of weaning difficulties, a tracheostomy had to be performed on two patients in the NIPSV group and four patients in the control group.

In the first 24 h of NIPSV, the mean duration of treatment for each patient was 7±4 h. After the first day, the mean duration of NIPSV per day was 6±3 h.

NIPSV, with sequential utilization, was well tolerated. No gastric distension was observed. Five patients had nasal pain and two had moderate abrasion of the nose.

Discussion

The efficacy of noninvasive positive-pressure ventilation in avoiding endotracheal intubation and improving the immediate outcome during episodes of acute respiratory failure in COPD patients, in comparison with conventional treatment, has been reported by many authors [1, 3–5, 13, 16, 17]. The present study suggests that a sequential use of NIPSV may also be favourable in patients with acute exacerbations of COPD in order to prevent reintubation after weaning from mechanical ventilation. The mean duration of ventilatory assistance for the treatment of the postextubation distress, as well as the length of stay in the ICU related to this event, were significantly shortened by NIPSV.

The patients in the present study were comparable to those studied by MEDURI et al. [18], who had "hypercapnic respiratory insufficiency", defined as the combination of a moderate to severe dyspnoea, a fR >25·min⁻¹, a pH <7.35, and a PaCO₂ >6.0 kPa. They had not reached the objective criteria for reintubation at the time of entering the study, and NIPSV was indicated early on to prevent reintubation. The patients in the present study were not particularly acidoic (mean pH 7.33) when NIPSV was initiated. This strategy may appear to be premature in some patients, but the patient's condition may deteriorate rapidly, with the risk of increased intolerance to NIPSV. Furthermore, COPD patients who have been intubated and mechanically ventilated may prove difficult to wean [6–8]. These patients are generally confronted with another long period of weaning.

In the absence of sufficient ventilatory autonomy, weaning difficulties will then make necessary a prolonged mechanical ventilation, and possibly the resorting to tracheostomy in order to facilitate ventilation. Therefore, in the present study, a tracheostomy had to be performed on two patients of the NIPSV group and four patients of the control group. These factors can only contribute to a longer hospitalization in ICU and increase the number of severe complications that may worsen the vital prognosis of the patients. Thus, it seems to be justified to institute noninvasive methods early in order to limitate morbidity and even mortality of these COPD patients hospitalized in ICU. AMBRUSINO et al. [19] demonstrated a relationship between initial pH and outcome with NIPSV in COPD patients with acute respiratory failure, thus also supporting the idea that early use may be advantageous.

NIPSV was successfully used by other authors [18, 20] in patients who developed acute respiratory failure after extubation. However, to our knowledge, the present investigation is the first controlled study concerning NIPSV utilization to prevent reintubation after weaning from mechanical ventilation. The study confirms the possible advantage of NIPSV in this situation.

NIPSV induced a fall in mean fR and was effective in correcting abnormalities in gas exchange. These findings are in accord with the results of previous studies [1, 3, 4, 13, 18, 21]. At the beginning of the protocol, patients underwent a first session of NIPSV of 30 min, then, after blood gas analysis, a second session of 45 min of ventilation with optimization of ventilator adjustments. This can be sufficient to halt the worsening of respiratory failure. Indeed, comparison between measurements of pH before NIPSV and those obtained after 45 min of support with an optimal setting showed a significant correction of acido-sis, this being considered as one of the main determinants of persistent respiratory failure. Furthermore, several authors [4, 5, 13, 18, 22] have emphasized that rapid improvement in the blood pH is crucial for successful NIPSV.

Some authors [1, 4, 5, 20, 23] have previously proposed administering NIPSV discontinuously. One of the original aspects of the present study was the sequential use of NIPSV. Some authors [2, 12] have emphasized that NIPSV is not easily accepted by patients with acute respiratory failure. This explains, at least partly, why in many studies the objectives of either continuous ventilation or prolonging periods of ventilation have not been achieved. In the study by FOGGIU et al. [2], patients were submitted to an average of 4 h of NIPSV. The mean number of hours of treatment-day⁻¹ in the study by BROGLARD et al. [1] was 7.6.

In the study by BOTT et al. [4], patients were encouraged to use NIPSV for up to 16 h·day⁻¹, and finally received 7.6 h of ventilation-day⁻¹. Furthermore, the time needed to improve patients' conditions can be very short. Thus, in the study by FERNANDEZ et al. [24], NIPSV was performed for a period of only 8±4 h. In the first 24 h of the present protocol, the mean number of hours of mask ventilation-day⁻¹ for each patient was 7±4. Finally, these durations of ventilation on the first day of the protocol are close to those noted in other studies [1, 4, 24], whilst offering a harmonious distribution of ventilation sessions. In our experience [13, 25, present study] NIPSV with a sequential utilization is well tolerated by patients and allows use of the technique for several days until the patient's condition improves. This may diminish the risk of
the side-effects observed with mask ventilation. Between ventilation periods, the safety of patients is assured by continuous monitoring of cardiac frequency, blood pressure, \( f_{R} \) and \( S_{O_2} \), with the possibility of returning patients to NIPSV if the \( S_{O_2} \) is <0.85 or when dyspnoea worsens with an \( f_{R} \) of >30 breaths-min\(^{-1}\). During periods without the mask, patients can receive respiratory therapy and nursing, nebulized bronchodilator agents or expectorate, or talk, rest or drink. Some authors [3, 12] believe the techniques of NIPSV are time-consuming for nurses, although in a recent study [25] it was found that NIPSV was not very time-consuming for the staff. The method of sequential ventilation is appreciated by nursing staff and has contributed to the standardization of techniques of NIPSV in the ICU. It has not been necessary to modify the organization of the Unit since the introduction of these new techniques. This fits the experience of PENNOCK et al. [26] based on several years’ practice of noninvasive ventilation.

The present study, presented well-known limits, given that it used historically matched controls [27]. A common source of bias with historical controls is that the mere fact of implementing a prospective study may improve patient care. Furthermore, historical comparisons of two different patient populations are influenced by the change in treatment strategies and are considered to favour the group treated with the new method. However, with the exception of the use of NIPSV, medical strategies in the ICU at Pellegin Hospital have not changed significantly since 1990 and were similar in both groups of patients of this study.

With this limitation in mind, the study demonstrates that noninvasive ventilation performed with a sequential mode may be used in the management of patients with chronic obstructive pulmonary disease who fail extubation.

References