Noninvasive Nasal Mask Ventilation Beyond the ICU for an Exacerbation of Chronic Respiratory Insufficiency*

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Study objective: To assess the usefulness of noninvasive nasal mask ventilation (NMV) in the treatment of an exacerbation of chronic respiratory insufficiency in patients stable enough to be admitted to a non-ICU ward.

Design: A prospective study in which the beneficial effect of NMV was compared with conservative treatment.

Setting: A ward of respiratory medicine of a tertiary-referral teaching hospital.

Patients: The study group included 15 patients with acute respiratory acidosis. These patients had pH less than 7.35 and PaCO₂ more than 60 mm Hg, respiratory rate of 30 breaths or less per minute, hemodynamic stability, and alertness and willingness of cooperation with the NMV treatment. The control group consisted of 16 patients who fulfilled the same arterial blood gas requirements, retrospectively selected from the discharge forms of the ward of respiratory medicine for the year 1993.

Interventions: Patients underwent NMV for two sessions per day (one in the morning and one in the afternoon), each session lasting 4 h. A volumetric respirator (Monnal D; Taema; Paris, France) was used in four patients with restrictive disease. A positive-pressure ventilator (DF90; Taema; Paris, France) was used in 11 patients with obstructive disease. Control patients received standard medical, oxygen, and chest physical therapy.

Results: As compared with pre-NMV values, mean pH was significantly higher at 4 h of NMV after the patient’s ventilatory adaptation (t=8.814, p<0.001) and at the end of NMV (t=12.06, p<0.001). Ventilatory support also produced a significant improvement in hypercapnia (pre-NMV vs NMV after the patient's ventilatory adaptation, t=6.675, p<0.001; pre-NMV vs post-NMV, t=6.976, p<0.001). Posttreatment pH and PaCO₂ values were significantly higher and lower, respectively, in NMV-treated patients than in controls. At the end of treatment, a significantly higher PaO₂/FIO₂ ratio was documented in the study group than in controls (post-NMV vs posttreatment, t=2.846, p<0.01).

Conclusions: NMV associated with standard treatment may be more beneficial than conservative treatment alone for improving blood gas exchange in patients with chronic respiratory insufficiency admitted to the hospital (but not the ICU) for an episode of acute decompensation and respiratory acidosis.

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Key words: blood gas analysis; chronic obstructive pulmonary disease; chronic restrictive pulmonary disease; intermittent positive-pressure; respiratory acidosis; respiratory failure; ventilation

Over recent years, intermittent positive-pressure ventilation through a tightly fitted nasal mask has been used successfully in patients with severe chronic restrictive disorders requiring domiciliary ventilatory support.1–6 Long-term nasal mask ventilation (NMV) has been shown to prolong the life expectancy in patients with Duchenne’s muscular dystrophy.7 In the ICU, NMV has also been used to treat selected patients with chronic respiratory insufficiency and acute exacerbation as an alternative to intubation and mechanical ventilation.8–10 The purpose of this study was to extend the use of NMV to the usual care setting of a ward of respiratory medicine. This is the first report, to our knowledge, that evaluates noninvasive NMV for treating acute exacerbations of chronic respiratory insufficiency beyond the ICU.

Materials and Methods

The study protocol was approved by the ethical research committee of our hospital, and informed consent of participants was obtained.

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Patients

Patients affected with chronic respiratory insufficiency referred to the ward of respiratory medicine from the emergency department of our hospital for treatment of an acute exacerbation episode were eligible to enter in a prospective study. The following inclusion criteria were required: acute respiratory acidosis (pH less than 7.35 and PaCO₂ more than 60 mm Hg), respiratory rate less than 30 breaths or less per minute, hemodynamic stability, and alertness and willingness of cooperation with the NMV treatment. Patients with status asthmaticus and acute respiratory acidosis, respiratory rate of 30 breaths or more per minute, potentially severe arrhythmia, evidence of mental disorder or alteration of the nasal permeability, history of recent (3 months) myocardial infarction or surgical operation in the upper abdomen, or other relevant diseases were excluded.11

Measurement of Ventilatory Muscle Function and Respiratory Drive

In six patients selected at random, respiratory muscle strength was assessed by measuring maximum inspiratory pressure (MIP), maximum expiratory pressure, and pressure-time index (PTI) using an electromanometer (Siebelmed 163; Siebel; Barcelona, Spain) (range, ±300 cm H₂O; resolution, 1 cm H₂O) connected to a recorder (x-y Servogor 731; Goertz Metrawatt; Nuremberg, Germany). Airway occlusion pressure at 100 ms (P0.1) was measured in a module (Masterlab; E. Jaeger; Wurzburg, Germany). PTI was derived from the following equation:12,13

\[
PTI = \frac{(Pawo/MIP) \times (T_{i}/T_{tot}) \times 100}
\]

where Pawo is the airway pressure measured in the circuit open during spontaneous breathing, Ti is inspiratory time, and T_{tot} is total breathing cycle length. Pawo was recorded during 15 min at a rate of 6 cm/min; it was calculated as the mean value of the average value for each minute for at least 10 min. Ti/T_{tot} was calculated as the mean value of 20 to 30 cycles at a rate of 30 cm/ min and expressed as a percentage. MIP (near residual volume) was obtained as the best of three maximum inspiratory maneuvers in which intratrace differences were less than 10%. Respiratory drive monitoring was carried out before NMV and between 2 and 3 days after the patient's ventilatory adaptation.

Ventilatory Support System

Patients with restrictive disorders were ventilated by means of a volumetric respirator (Monnal D; Taema; Paris, France). In patients with obstructive disease, the ventilatory support system we used (DP90; Taema; Paris, France) is also used in the application of continuous positive airway pressure for the treatment of sleep apnea. With this ventilator it is not possible to set respiratory rate. Positive end expiratory pressure (PEEP) and inspiratory positive airway pressure (IPAP) increments should be adjusted to ensure that a maximum target of 20 cm H₂O is not exceeded (a technical limitation of this ventilatory mode is the inability to provide IPAP greater than 13 cm H₂O when the patient's respiratory rate is greater than 25 breaths/min). Patients were fitted with a commercial nasal mask (Sullivan) with "air cushion" to which a cannula for supplemental oxygen was inserted in patients ventilated with DP90. In patients ventilated with Monnal D, expiratory grooves of the Sullivan mask were occluded.

Administration of NMV

Blood gases were measured (Radiometer ABL 520; Radiometer, Copenhagen, Denmark). Blood oxygenation was continuously monitored by pulse oximetry (Oxipulse; Radiometer). The initial setting of 7 cm H₂O IPAP in the DP90 system was then adjusted to improve the PaCO₂ taking into account the optimal comfort for the patient and the technical limitations of this ventilatory mode (IPAP needed varied between 9 and 15 cm H₂O). PEEP was set at 4 cm H₂O in all patients. Oxygen delivery was adjusted to obtain arterial saturation (SaO₂) between 91 and 93%. When NMV was provided by a volume-cycled ventilator, initial settings included a tidal volume of about 15 mL/kg of body weight with an inspiratory/expiratory ratio of 1, a respiratory rate near spontaneous breathing that was usually reduced after trial-and-error assays, and trigger sensitivity ~3 cm H₂O. Fractional concentration of inspired oxygen (FiO₂) was adjusted by pulse oximetry to maintain SaO₂ greater than 90%.

Ventilation was performed during the day. Patients underwent NMV for two sessions per day (one in the morning and one in the afternoon), each session lasting 4 h, with constant control during the first 4 h and under close supervision of medical and nursing staff during the period of the patient's ventilatory adaptation. The adaptation of patients to NMV usually required 1 to 2 days. Arterial blood gas values were obtained preceding initiation of ventilatory support (pre-NMV), at 4 h of the afternoon NMV session after the patient's ventilatory adaptation, and at the end of NMV, ie, after 3 h of discontinuation of treatment (post-NMV). Supplemental oxygen was provided during NMV and time off. Vital signs, tolerance and duration of NMV, causes of exit from the study, and possible complications were also recorded.

Controls

Patients in the control group were retrospectively selected from the discharge forms of the ward of respiratory medicine for the year 1993. Eligible patients had to fulfill the same clinical criteria, blood gas requirements, an absence of associated conditions than patients in the study group, ie, candidates to receive NMV if this modality of therapy would have been available when these patients were admitted to hospital. It was found that 16 patients (13 patients with COPD, 3 patients with restrictive disorders) fulfilled the above-mentioned requirements. Patients received standard medical, oxygen, and chest physical therapy. Clinical, functional, and laboratory data were obtained from the patient's medical history. In every case, blood gas measurements on admission to the ward of respiratory medicine (baseline) and the most favorable measurement obtained on the following 3 to 4 hospitalization days (posttreatment) were recorded.

Data Analysis

All data are presented as mean±SD. Paired and unpaired t tests were carried out for intragroup and intergroup comparisons, respectively. The Welch's test was applied when homogeneity of variances was rejected. A p value of less than 0.05 was considered significant.

RESULTS

Seventeen consecutive qualified patients were entered into the study. Thirteen patients had COPD and 4 had kyphoscoliosis resulting in chronic restrictive respiratory disease. Of the 17 patients who met the entrance criteria, one patient with obstructive disease was not able to sustain NMV for longer than 20 min (IPAP at 7 cm H₂O) due to an apparent and unexplained inability to keep his mouth closed. A further patient with COPD was not able to cope with the DP90 ventilator because tachypnea (33 breaths/min) prevented the unit to cycle from IPAP to expiratory positive airway pressure.

Fifteen patients with a mean age of 55.6±18.4 years (range, 48 to 70 years) completed the program of NMV.
and were included in the study group. Cumulative hours of NMV ranged from 24 to 32 (mean, 28.2±3.9 h). Patients in the control group had a mean age of 64.3±5.7 years (range, 52 to 75 years). No significant differences were seen in baseline values for the flow/volume curve between NMV-treated patients and controls (0.85±0.31 vs 0.85±0.26 L). Arterial blood gas values for patients in the study group and patients in the control group are shown in Tables 1 and 2. Two patients in the control group (cases 8 and 11 in Table 2) had to admitted to the ICU because of deterioration of clinical condition and lack of improvement of arterial blood gas values after standard medical therapy.

Changes in pH, PaCO₂, and PaO₂/FIO₂ over time in controls and in patients receiving NMV are shown in Table 3. As compared with pre-NMV values, mean pH was significantly higher at 4 h of NMV after the patient's ventilatory adaptation (t=8.814, p<0.001) and at the end of NMV (t=12.06, p<0.001). Posttreatment pH values were significantly higher in NMV-treated patients than in controls (Welch's test, t=5.013, p<0.001).

Ventricular support also produced a significant improvement in hypercapnia (pre-NMV vs NMV after the patient's ventilatory adaptation, t=6.675, p<0.001; pre-NMV vs post-NMV, t=6.976, p<0.001). Posttreatment PaCO₂ values were significantly lower in NMV-treated patients than in controls (Welch's test, t=5.59, p<0.001). In NMV-treated patients, mean PaCO₂ values at discharge from the hospital were significantly lower as compared with post-NMV (53±6 mm Hg vs 46±2 mm Hg, t=6.44, p<0.001).

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>FVC* FEV₁</th>
<th>pH</th>
<th>PaO₂/FIO₂</th>
<th>PaCO₂</th>
<th>pH</th>
<th>PaO₂</th>
<th>PaCO₂</th>
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<th>PaO₂/FIO₂</th>
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<td>69</td>
<td>58</td>
<td>7.38</td>
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</table>

*FVC (liters) in patients 1 to 4 with restrictive disease; FEV₁ (liters) in patients 5 to 15 with obstructive disease; PaO₂ and PaCO₂ in mm Hg.
Table 3—Comparison of Mean Blood Gas Values Between Patients Treated With NMV and Controls

<table>
<thead>
<tr>
<th>Group</th>
<th>pH</th>
<th>PaCO2, mm Hg</th>
<th>PaO2/FIO2</th>
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<tr>
<td>Pre-NMV</td>
<td>7.30±0.03</td>
<td>75±14</td>
<td>216±73</td>
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<tr>
<td>During NMV</td>
<td>7.40±0.02</td>
<td>52±9</td>
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<tr>
<td>Post-NMV</td>
<td>7.39±0.01</td>
<td>53±6</td>
<td>276±38</td>
</tr>
<tr>
<td>Controls</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>7.31±0.02</td>
<td>70±9</td>
<td>224±42</td>
</tr>
<tr>
<td>Posttherapy</td>
<td>7.33±0.05</td>
<td>73±13</td>
<td>241±29</td>
</tr>
</tbody>
</table>

A significant improvement in the PaO2/FIO2 ratio was found in both NMV-treated patients (pre-NMV vs post-NMV, t=3.338, p<0.01) and controls (baseline vs posttreatment, t=2.011, p<0.05). At the end of treatment, however, a significantly higher PaO2/FIO2 ratio was documented in the study group than in controls (post-NMV vs posttreatment, t=2.846, p<0.01).

In the subgroup of six NMV-treated patients (patients 2, 3, 7, 11, 13, and 15; Table 1) in whom parameters of ventilatory muscle function and respiratory drive were monitored, statistically significant changes in MIP (55±11 vs 66±8 cm H2O, p<0.01), PTI (0.208±0.009 vs 0.138±0.020, p<0.05), and P0.1 (5.63±0.24 vs 3.87±1.50 cm H2O, p<0.05) were found when values obtained before NMV and after the patient’s ventilatory adaptation were compared.

The mask was well tolerated and in all cases NMV was completed successfully.

The length of hospital stay was significantly shorter in NMV-treated patients as compared with controls (6±0.7 vs 10±2 days, t=9.74, p<0.001). Restrictive patients were discharged from the hospital with the ventilator and were able to substitute continuous oxygen therapy for nocturnal noninvasive ventilation at home.

**DISCUSSION**

Our results demonstrate that NMV can achieve a significant improvement in gas exchange in patients with chronic respiratory insufficiency and acute respiratory acidosis hospitalized beyond the ICU. In the series reported by Leger and colleagues in which most subjects had restrictive chest wall disorders and neuromuscular diseases, nasal intermittent positive-pressure ventilation was provided by a volume-cycled ventilator. In the present study, volumetric respirators (Monnal D) were also used in patients with kyphoscoliosis, whereas positive-pressure ventilators (DP90) in current use were applied in decompensated patients with obstructive airway disease. This easily handled apparatus, simpler than Monnal D, delivers pressure support with PEEP that minimizes a possible auto-PEEP effect from dynamic hyperinflation. Given that intrinsic PEEP may present a marked variability, between zero and 12 cm H2O in the study of Brochard et al., and measurement of auto-PEEP was not possible with the DP90 equipment, extrinsic PEEP was set at 4 cm H2O (minimum level available in the DP90) which, in turn, prevented PEEP-induced unfavorable hemodynamic effects.

In different studies published in the literature, the duration of intermittent positive-pressure ventilation in patients with acute respiratory failure ranged from 6 to 20 h/d (cumulative hours between 6 and 192). In our study, NMV was performed early in the morning and early in the afternoon, each session lasting 4 h, not only to facilitate cooperation on the part of patients, but also to establish assumable periods of amount of time spent with these patients for health-care professionals in a ward of respiratory medicine, particularly during the patient’s ventilatory adaptation. In the six patients described by Chevrolet et al., nasal positive pressure ventilation was considered a difficult and time-consuming procedure for nurses. In four of these patients, however, the ICU team judged that criteria for immediate intubation and mechanical ventilation were present. It is therefore possible that a more severe clinical condition of these patients may be responsible for a greater amount of work imposed on the nurses as compared with our study.

Changes in mean pH and PaCO2 levels achieved with NMV in the present study are similar to data reported in the literature, with the exception of patients in the first series of Meduri et al.—clearly more hypcapnic and acidotic—and patients in the first series of Pennock et al. who presented with a more favorable clinical condition (pH, 7.38; PaCO2, 49.2). It should be noted that in patients with obstructive disease and in contrast to other studies, a respiratory rate of 30 breaths or greater per minute was considered an exclusion criteria on the basis of its clinical significance and the technical characteristics of the DP90 ventilator.

It has been shown that noninvasive positive pressure ventilation results in improvements in the tidal volume dead space ratio and reduction of respiratory-muscle work. Brochard et al. have demonstrated that the efficacy of face mask ventilation involved an improvement in the inspiratory activity of the diaphragm. Our findings of decreased PTI and slightly increased MIP are compatible with an improvement in ventilation and a more efficient respiratory muscle contraction. A decrease in P0.1 together with an improvement in blood gas values may be an expression of a probable improvement in respiratory performance.

Although in the present study patients were not randomized to NMV ventilation or conservative treatment when qualified health-care staff can provide adequate clinical monitoring of patients, NMV associated
with standard treatment may be more beneficial than
conservative treatment alone for improving blood gas
exchange in patients with chronic respiratory insuffi-
ciency admitted beyond the ICU for an episode of
acute decompensation and respiratory acidosis.

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