Noninvasive Positive-Pressure Ventilation vs Conventional Oxygen Supplementation in Hypoxemic Patients Undergoing Diagnostic Bronchoscopy*

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Objective: We have reported previously on the use of noninvasive positive-pressure ventilation (NPPV) to assist spontaneous breathing in high-risk hypoxemic patients (ie, PaO₂/fraction of inspired oxygen [FIO₂] ratio, ≤ 100) who are undergoing diagnostic fiberoptic bronchoscopy (FOB). The efficacy of this intervention in patients with less severe forms of hypoxemia (ie, PaO₂/FIO₂ ratio, < 200) is unknown.

Patients and methods: Twenty-six patients with PaO₂/FIO₂ ratios ≤ 200 who required broncho -scopic BAL for suspected nosocomial pneumonia were entered into the study. Thirteen patients were randomized during FOB to receive NPPV, and 13 patients were randomized to receive conventional oxygen supplementation by Venturi mask. The primary end points were changes in the PaO₂/FIO₂ ratio during FOB and within 60 min of terminating the procedure.

Results and outcome: At study entry, the two groups were similar in terms of age, simplified acute physiologic score II values, and cardiorespiratory parameters. During FOB, the mean (± SD) PaO₂/FIO₂ ratio increased by 82% in the NPPV group (261 ± 100 vs 139 ± 38; p < 0.001) and decreased by 10% in the conventional oxygen supplementation group (155 ± 24 to 139 ± 38; p = 0.23). Thirty minutes after undergoing FOB, the NPPV group had a higher mean PaO₂/FIO₂ ratio (176 ± 62 vs 140 ± 38; p = 0.09), a lower mean heart rate (91 ± 18 vs 108 ± 15 beats/min; p = 0.02), and no reduction in mean arterial pressure in comparison to a 15% decrease from the baseline in the control group. One patient in the NPPV group and two patients in the control group required nonemergent intubation. Major bacterial isolates included Staphylococcus aureus (7 of 30 isolates; 23%) and Pseudomonas aeruginosa (12 of 30 isolates; 40%).

Conclusion: In patients with severe hypoxemia, NPPV is superior to conventional oxygen supplementation in preventing gas-exchange deterioration during FOB with better hemodynamic tolerance.

(CHEST 2002; 121:1149–1154)

Key words: acute respiratory failure; bronchoscopy; hypoxemia; noninvasive positive pressure ventilation; pneumonia

Abbreviations: CPAP = continuous positive airway pressure; FIO₂ = fraction of inspired oxygen; FOB = fiberoptic bronchoscopy; MAP = mean arterial pressure; MV = mechanical ventilation; NPPV = noninvasive positive-pressure ventilation; SAPS = simplified acute physiology score; SpO₂ = arterial oxygen saturation by pulse oximetry

Early and accurate diagnosis of nosocomial pneumonia simplifies the selection of appropriate antibiotic therapy and may improve outcome.1–4 Fiberoptic bronchoscopy (FOB) with BAL is an important tool for determining the etiologic diagnosis of pneumonia. Because arterial oxygen tension routinely decreases by 10 to 20 mm Hg in patients after they undergo uncomplicated FOB, hypoxemic patients are at high risk for developing respiratory failure or serious cardiac arrhythmias.5,6 In nonintubated patients, severe hypoxemia (defined as requiring continuous positive airway pressure [CPAP] or an inspired oxygen concentration of > 50% to maintain arterial oxygen tension of at least 75 mm Hg) is an accepted contraindication to bronchoscopy.5 In these high-risk patients, the options are to intubate...
and to apply mechanical ventilation (MV) to ensure adequate gas exchange during FOB or to avoid FOB and to institute empirical treatment.

Noninvasive positive-pressure ventilation (NPPV) refers to the delivery of assisted MV without the need for an invasive artificial airway. In cases of acute respiratory failure when NPPV is effective in avoiding endotracheal intubation, the morbidity and mortality associated with MV are reduced. Three randomized studies have provided supporting evidence for the selected application of NPPV in patients experiencing hypoxemic respiratory failure of varied etiologies, including patients with pneumonia. We originally reported on the use of NPPV to assist spontaneous breathing through a facial mask during FOB with BAL in severely hypoxemic, non-intubated patients. The study included eight consecutive immunosuppressed patients with suspected pneumonia and a PaO/FIO\textsubscript{2} fraction of inspired oxygen (FIO\textsubscript{2}) ratio of < 100. We found that NPPV during FOB was well-tolerated, significantly improved the PaO/FIO\textsubscript{2} ratio, and successfully avoided the need for endotracheal intubation. The testing of BAL specimens identified a causative agent of pneumonia in all studied patients.

Whether NPPV-assisted bronchoscopy may benefit immunocompetent patients with less severe hypoxemia (ie, PaO/FIO\textsubscript{2} ratio, < 200) is not known. For this reason, patients who required bronchoscopic BAL for the confirmation of suspected nosocomial pneumonia and had a PaO/FIO\textsubscript{2} ratio of ≤ 200 were compared in a randomized study by comparing NPPV vs conventional oxygen supplementation during FOB. The primary end points were changes in the PaO/FIO\textsubscript{2} ratio during FOB and within 60 min of terminating the procedure.

**Materials and Methods**

Between May 1998 and January 1999, all consecutive patients with acute hypoxemic respiratory failure and suspected nosocomial pneumonia who were admitted to a 14-bed general ICU at La Sapienza University Hospital (Rome, Italy) were screened for enrollment into the randomized study. An ad hoc ethics committee approved the protocol, and all patients gave informed consent. Computer-generated random assignments were put into sealed envelopes. The criteria for hypoxemic respiratory failure included acute respiratory distress with severe dyspnea at rest, a respiratory rate of > 35 breaths/min, and a PaO/FIO\textsubscript{2} ratio of < 200 while breathing oxygen through a Venturi mask. The criteria for suspecting nosocomial pneumonia included a body temperature of > 38°C or < 36°C, the presence of new and persistent pulmonary infiltrates, purulent secretions, and leukocytosis (ie, WBC, > 12,000 cells/μL) or leukopenia (ie, WBC < 4,000 cells/μL). The criteria for excluding patients from the study included a requirement for emergent intubation (ie, cardiopulmonary resuscitation, respiratory arrest, severe hemodynamic instability, or encephalopathy), respiratory failure caused by neurologic disease or status asthmaticus, the presence of more than two new organ failures (eg, the simultaneous presence of renal and cardiovascular failures), the presence of facial deformities, and recent oral, esophageal, or gastric surgery. The severity of illness was assessed by the simplified acute physiology score (SAPS) II.

Before undergoing bronchoscopy, all patients were placed on a Venturi mask with adjustable FIO\textsubscript{2} (Baxter; Mirandola, Italy) starting with an FIO\textsubscript{2} ≥ 0.5 and adjusted to achieve a level of arterial oxygen saturation by pulse oximetry (SpO\textsubscript{2}) of > 92%.

Patients then were randomly assigned to receive standard oxygen supplementation or NPPV through a face mask during bronchoscopy. During the procedure, patients had continuous ECG, arterial BP, and SpO\textsubscript{2} monitoring (Biox 3700; Ohmeda; Boulder, CO).

**Standard Treatment Group**

Patients assigned to the standard treatment received oxygen supplementation via a Venturi mask, and the FIO\textsubscript{2} was kept at 0.9 for all the bronchoscopic procedures. In order to obtain a stable and reliable value for the FIO\textsubscript{2} in this group, we used a modified high-flow Venturi mask that was equipped with two unidirectional valves and a seal port for the introduction of the bronchoscope (Fig 1). The FIO\textsubscript{2} was confirmed by a portable O\textsubscript{2} analyzer (miniOX; Mine Safety Appliances Co; Pittsburgh, PA).

**NPPV Group**

Patients assigned to NPPV were connected to the ventilator through a clear full-face mask (Vitalsigns Inc; Towota, NJ) that was secured to the patient’s face with elastic straps. Two types of mechanical ventilators were used (model 7200; Puritan Bennett Co; Overland Park, KS; and Servo 900 C; Siemens Elema; Uppsala, Sweden). Ventilator parameters were set at a CPAP of 5 cm H\textsubscript{2}O and pressure support ventilation at 15 to 17 cm H\textsubscript{2}O, with a trigger of −1 cm H\textsubscript{2}O. The FIO\textsubscript{2} was kept at 0.9 while the patients adjusted to the system (at least 10 min) and during the procedure. A T-adapter was attached to the face mask for insertion of the fiberoptic bronchoscope (model IT20; Olympus; Tokyo, Japan) through the nose.

**Bronchoscopic BAL Technique**

Topical anesthesia of the nose and pharynx was obtained by spraying a 10% lidocaine solution. Topical anesthesia of the larynx and vocal cords was performed (2% lidocaine hydrochloride, not exceeding 200 mg) before advancing the bronchoscope into the tracheobronchial tree. The tip of the FOB then was wedged into the orifice of the bronchial subsegment that showed increased densities on the chest radiograph. BAL was performed by sequential instillation of five aliquots 25 mL nonbacteriostatic saline solution at room temperature. The retrieved effluent was analyzed and culturing. The methods and laboratory procedures followed consensus guidelines. Bacterial pneumonia was diagnosed when at least 100,000 cfu/mL of bacteria were measured in the BAL fluid.

During the procedure, the FIO\textsubscript{2} was reduced to 0.7, and serial arterial blood gas values were obtained every 10 min. After the bronchoscopy procedure, the FIO\textsubscript{2} was decreased to 0.7, and serial arterial blood gas values were obtained every 20 to 30 min. After 60 min, the applied FIO\textsubscript{2} was reduced to the prebronchoscopy requirements if the patient was able to maintain SpO\textsubscript{2} at > 92%. The NPPV group had ventilation continued for at least 30 min after termination of bronchoscopy, after which NPPV was discontinued if SpO\textsubscript{2} was > 92% and the patient was not experiencing respiratory difficulties.
**End Points**

The end points were changes occurring in the \( \text{PaO}_2/\text{FiO}_2 \) ratio during FOB and within 60 min of terminating the procedure, the maintenance of hemodynamic stability, and the avoidance of endotracheal intubation within 24 h of study entry.

**Criteria for Endotracheal Intubation**

The predetermined criteria for endotracheal intubation included failure to maintain a \( \text{PaO}_2 \) of \( >65 \text{ mm Hg} \) with an \( \text{FiO}_2 \) that was \( \geq 0.6 \), the development of conditions necessitating endotracheal intubation to protect the airways (eg, coma or seizure disorders) or to manage copious tracheal secretions, hemodynamic or ECG instability, the inability to correct dyspnea, or difficulty in tolerating the face mask by those randomized to noninvasive ventilation.

**Statistical Analysis**

Results are reported as the mean \( \pm \) SD. Demographic and physiologic characteristics for the two groups were compared using the \( t \) test for continuous data (separate estimates of variance were used when variance differed significantly) and with the Mantel-Haenszel extended \( \chi^2 \) test for categoric data. Fisher’s Exact Test (two-tailed) was used when the expected number of cases per cell was below five. A software package (SPSS; SPSS, Inc; Chicago, IL) was used for all analyses.15

**RESULTS**

Over a period of 9 months, 365 patients were admitted to the ICU. Of the 81 patients who met the study entry criteria, 30 were already intubated, 10 had a tracheostomy, 6 had mental status alterations or hemodynamic instability, and 9 refused to participate. Thus, 26 patients (16 men and 10 women) were enrolled into the study. Thirteen patients were assigned to each group. At study entry, the baseline characteristics of the two groups were similar, including severity of disease as calculated by SAPS II (Table 1) and hemodynamic and blood gas parameters (Table 2).

**Table 1—Baseline Characteristics of Patients and Outcome**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Noninvasive ventilation ( n = 13 )</th>
<th>Standard treatment ( n = 13 )</th>
<th>( p ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>( 52 \pm 20 )</td>
<td>( 57 \pm 15 )</td>
<td>0.5</td>
</tr>
<tr>
<td>Male gender</td>
<td>8 (61)</td>
<td>8 (61)</td>
<td>0.5</td>
</tr>
<tr>
<td>SAPS II</td>
<td>26 ( \pm 11 )</td>
<td>27 ( \pm 7 )</td>
<td>0.5</td>
</tr>
<tr>
<td>Underlying diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>COPD</td>
<td>5 (38)</td>
<td>2 (15)</td>
<td>0.18</td>
</tr>
<tr>
<td>Trauma</td>
<td>2 (15)</td>
<td>1 (7)</td>
<td>0.5</td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>2 (15)</td>
<td>2 (15)</td>
<td>0.7</td>
</tr>
<tr>
<td>Sepsis</td>
<td>2 (15)</td>
<td>2 (15)</td>
<td>0.7</td>
</tr>
<tr>
<td>Rhabdomyolysis</td>
<td>0</td>
<td>2 (15)</td>
<td>0.2</td>
</tr>
<tr>
<td>Sequential lung transplant</td>
<td>0</td>
<td>1 (7)</td>
<td>0.5</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>1 (7)</td>
<td>0</td>
<td>0.5</td>
</tr>
<tr>
<td>Severe acute hepatitis</td>
<td>1 (7)</td>
<td>0</td>
<td>0.5</td>
</tr>
<tr>
<td>Diabetic ketoacidosis</td>
<td>1 (7)</td>
<td>0</td>
<td>0.5</td>
</tr>
<tr>
<td>Pemphigus</td>
<td>0</td>
<td>1 (7)</td>
<td>0.5</td>
</tr>
</tbody>
</table>

*Values given as mean \( \pm \) SD or No. (%), unless otherwise indicated.
The procedure was well-tolerated by all patients. The mean duration of bronchoscopy was 8 ± 1 min in the NPPV group and 7 ± 2 min in the conventional oxygen supplementation group (p = 0.40). After undergoing bronchoscopy, three patients required intubation, one patient in the NPPV group (7 h after the procedure) and two patients in the conventional oxygen supplementation group (9 and 5 h after the procedure). The decision to intubate was made by a physician who was not involved in the study. In all three cases, the intubation was not related to a sudden deterioration of gas exchanges after the bronchoscopy and was apparently dictated by the progression of the underlying disease. None of the intubations occurred under emergency conditions.

During bronchoscopy, the PaO₂/FIO₂ ratio increased by 82% in the NPPV group (from 143 ± 32 to 261 ± 100; p = 0.002) and decreased by 10% in the conventional oxygen supplementation group (from 155 ± 24 to 139 ± 38; p = 0.23). The PaO₂/FIO₂ ratio recorded during bronchoscopy was significantly higher in the NPPV group than in the conventional oxygen supplementation group (p < 0.001) [Table 2]. One hour following the termination of bronchoscopy, the PaO₂/FIO₂ ratio was 176 ± 62 in the NPPV group (33% increase from baseline) and 140 ± 38 in the conventional oxygen supplementation group (10% reduction from baseline; p = 0.09). The PaCO₂ response was similar for both groups (Table 2).

During and after bronchoscopy, heart rate varied little from baseline in both groups (Table 2). During and after bronchoscopy, the mean arterial pressure (MAP) did not change in the NPPV group, and there was a 16% reduction from baseline values in the conventional oxygen supplementation group (81 ± 13 vs 96 ± 13, respectively; p = 0.013). After bronchoscopy, the NPPV group had no reduction in MAP and the conventional oxygen supplementation group had a 15% decrease from baseline (from 96 ± 13 to 78 ± 18, respectively; p = 0.02). In the conventional oxygen supplementation group, the reduction in MAP following bronchoscopy was more pronounced among the five patients with a baseline PaO₂/FIO₂ ratios of < 160 (baseline, 87 ± 10; during FOB, 75 ± 10; after FOB, 64 ± 9). One patient with cystic fibrosis who was randomized to NPPV had a baseline PaCO₂ of 103 mm Hg without alteration in mental status. The combination of noninvasive ventilation and bronchoscopic suctioning of secretions after BAL reduced the PaCO₂ to 80 mm Hg. After the patient underwent bronchoscopy, NPPV was applied intermittently as a bridge to successful lung transplantation. The patient was discharged from the hospital 55 days after admission to the study (47 days after transplantation).

A definitive etiologic diagnosis of pneumonia was established in 20 patients. Eighteen patients had significant growth of a pathogen found in BAL fluid, and 2 patients (1 in each group) had bacteremia, with a pathogen recovered in the BAL fluid at a concentration below the diagnostic threshold of 10⁵ cfu/mL. In nine patients (four in the NPPV group and five in the conventional oxygen supplementation group), the testing of BAL fluid showed the presence of more than one microorganism that was growing at a concentration ≥ 10⁵ cfu/mL. The microbiological etiology of pneumonia is shown in Table 3. The most frequently isolated microorganisms were Pseudomonas aeruginosa (40%) and Staphylococcus aureus (23%). Four patients in the NPPV group and seven patients in the conventional oxygen supplementation group died from complications of their underlying disease 5 to 7 days after study entry.

**Discussion**

In this randomized study, we found that, in patients with severe hypoxemia (ie, PaO₂/FIO₂ ratio,
Table 3—Bacterial Isolates in the Two Groups*  

<table>
<thead>
<tr>
<th>Isolates</th>
<th>Standard Treatment Group (n = 13)</th>
<th>NPPV Group (n = 13)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. aureus</td>
<td>2 (18)</td>
<td>19</td>
<td>0.50</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>3 (27)</td>
<td>9 (47)</td>
<td>0.20</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>1 (9)</td>
<td>2 (10)</td>
<td>0.70</td>
</tr>
<tr>
<td>Serratia</td>
<td>1 (9)</td>
<td>0</td>
<td>0.40</td>
</tr>
<tr>
<td>Enterococcus</td>
<td>1 (9)</td>
<td>0</td>
<td>0.40</td>
</tr>
<tr>
<td>Acinetobacter sp</td>
<td>0</td>
<td>1 (9)</td>
<td>0.40</td>
</tr>
</tbody>
</table>

*Values given as No. (%), unless otherwise indicated.

< 200, NPPV that was delivered through a full-face mask was superior to oxygen supplementation alone in improving gas exchange during and after diagnostic bronchoscopy. The procedure was well-tolerated and was not associated with complications. Following bronchoscopy, patients who were randomized to NPPV had less of a reduction in MAP and a lower heart rate. The rates for intubation within 10 h of terminating the procedure were similar in the two groups.

The potential advantages of NPPV during FOB in hypoxicemic patients are several. Bronchoscopy is associated with an alteration of the respiratory mechanics and gas exchange causing transient hypoxemia and hypercapnia. In nonintubated patients, the bronchoscope occupies about 10% of the total cross-sectional area of the trachea, thereby decreasing tidal volume and increasing the work of breathing. When suction is applied during FOB, end-expiratory volume and positive end-expiratory pressure are reduced, facilitating alveolar closure and venous admixture. These changes slowly subside following FOB, however, the time to normalization may take several hours in patients with severe parenchymal diseases. In one uncontrolled study on the cardiopulmonary risk of FOB in 107 patients who were receiving MV, significant hypoxemia (i.e., PaO2 ≤ 60 mm Hg on FiO2 of 0.8) was seen in 13% of patients and was linked to the severity of pulmonary dysfunction and to decreased alveolar ventilation. The mean drop in PaO2 was 26%, which persisted for as long as 2 h. In 1990, the American Thoracic Society guidelines recommended avoiding BAL in spontaneously breathing patients with hypercapnia and/or hypoxemia and in patients whose PaO2 levels cannot be corrected to at least 75 mm Hg or to an SpO2 level of > 90% with supplemental oxygen.

This randomized study expands on prior reports of applying NPPV or mask CPAP during bronchoscopy in patients either with hypoxemia or hypercapnia. Our group originally described the application of NPPV during bronchoscopy in eight immunocompromised hypoxemic (i.e., PaO2/FiO2 ratio, < 100) patients with suspected pneumonia. In that study, NPPV was administered in a fashion similar to the one described in this report and was associated with a significant improvement in PaO2/FiO2 ratio during bronchoscopy. The successful application of NPPV during FOB also was reported in patients with COPD. Da Conceicao et al investigated 10 consecutive COPD patients with pneumonia who were admitted to the ICU with hypercapnia (i.e., Pco2, 67 ± 11 mm Hg) and hypoxemia (i.e., PaO2, 53 ± 13 mm Hg). During FOB with NPPV, the SpO2 increased from 91 ± 4.7% at baseline to 97 ± 1.7%. In both studies, FOB with NPPV was well-tolerated by patients, no complications related to the procedure were observed, and none of the patients required intubation in the postbronchoscopy period.

In the present study, we used pressure support during bronchoscopy. Maitre et al recently reported the results of a randomized double-blind study evaluating the application of a new CPAP device during FOB in 30 patients with a mean PaO2/FiO2 ratio of < 300. The open system was based on generating positive airway pressure by four funnel-shaped microchannels that generate microjets, and thus positive pressure, for use with a face mask. The use of CPAP allowed minimal alterations in gas exchange and prevented subsequent respiratory failure. During FOB and 30 min thereafter, SpO2 was significantly higher in the CPAP group. Arterial blood gas measurements 15 min after termination of FOB showed that the PaO2 had increased by 10.5 ± 16.9% in the CPAP group and decreased by 15 ± 16.6% in the oxygen group (p = 0.01). Five patients in the oxygen group, but none in the CPAP group, developed respiratory failure and required intubation in the 6 h following the FOB procedure. No study compared CPAP with NPPV support ventilation.

In conclusion, we found that the application of NPPV was superior to oxygen supplementation alone in improving gas exchange during and after diagnostic bronchoscopy, with better hemodynamic tolerance. The findings of this randomized study agree with those of prior uncontrolled studies and provide support for the use of NPPV during bronchoscopy in patients with severe and moderate hypoxemia (i.e., PaO2/FiO2 ratio, < 200).

ACKNOWLEDGMENTS: We wish to acknowledge the expert review of the manuscript by Dr. David Arnhuber and Mrs. Gail Spake. Also, we thank participating investigators Maurizio Buﬁ (collected data), Mariano Alberto Pennisi (collected data), Riccardo Maviglia (provided and cared for study patients), and Paolo Pietropaoli (critically revised the study proposal).
REFERENCES