Fiberoptic Bronchoscopy in Ventilated Patients*

Evaluation of Cardiopulmonary Risk under Midazolam Sedation

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One hundred seven acutely ill ventilated patients were prospectively studied to ascertain the severity and frequency of alterations in gas exchange and hemodynamic parameters during brief bronchoscopy. Sedation was performed using midazolam (0.1 mg/kg IV) without topical anesthesia. An average decline in PaO₂ of 26 percent was observed at the end of the procedure, compared to the baseline value, and this was associated with a mild increase in PaCO₂ in spite of the use of a special adapter. Alterations in mean systolic blood pressure appeared to be modest, consisting of a 10 percent decrease from the control level, related to sedation, and a 10 percent rise from baseline during the procedure, associated with a concomitant mild tachycardia. At that time, central hemodynamic measurements performed in a subset of 31 patients showed a significant increase in cardiac output associated with higher pulmonary wedge pressure. Fourteen patients developed hypoxemia of less than 60 mm Hg on FIO₂ adjusted to 0.8. Of the ten risk factors univariately associated with hypoxemia, only the presence of ARDS (p<0.001) and “fighting” the ventilator during the procedure (p<0.05) remained significant after stepwise logistic regression. Attempts to prevent hypoxemia in critically ill patients should focus on inducing complete sedation, with careful attention to hemodynamic status, or providing maximal levels of oxygen to the ventilator (or both). (Chest 1990; 97:927-33)

cfu = colony-forming units

The approach to the diagnosis of diseases of the chest increasingly involves the use of flexible fiberoptic bronchoscopy. The risk inherent in such an examination appears slight in alert, spontaneously breathing patients, although the associated occurrence of cardiac arrhythmias, hypoxemia, or laryngospasm is not unusual. In intubated patients in the ICU, the flexible fiberoptic bronchoscope has gained restricted use for the diagnosis and treatment of airway problems that occur during mechanical ventilation. The generally accepted indications for bronchoscopy in nonimmunocompromised ventilated patients are removal of retained secretions, resolution of atelectasis, and evaluation of hemoptysis.

Patients with endotracheal tubes are at a particularly high risk of nosocomial pneumonia, and the clinical distinction between bacterial colonization and true infection is often difficult. One of the most important aids to the definitive diagnosis of bacterial infection, and, specifically, of bacterial pneumonia, lies in the proper collection of specimens. Therefore, recent efforts have been made to sample the lower respiratory tract without contamination. For this purpose a catheter brush that is protected by a telescoping double sheath with a polyethylene glycol plug and passed through the suction channel of a flexible fiberoptic bronchoscope has been developed by Wimberley and associates. This brush has been documented to have reasonable precision in diagnosing nosocomial pneumonia when associated with quantitative culture techniques. Following these observations, the use of brief fiberoptic bronchoscopy has increased dramatically in ICUs; however, the morbidity associated with this procedure has been minimally investigated in large cohorts of critically ill patients.

Thus, the purpose of this prospective study was to determine the alterations in blood gas levels and hemodynamic status induced by brief fiberoptic bronchoscopy in 107 critically ill patients undergoing mechanical ventilation. It was also our aim to establish, if possible, the main risk factors for the development of hypoxemia and hemodynamic disturbances.

Materials and Methods

Population

Patients eligible for participation were those older than 15 years of age who were hospitalized in the ICU of Bichat Hospital during a 14-month period and who were being ventilated at the time of suspicion of bacterial pneumonia. The diagnosis of pneumonia was

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considered if any of three of the following clinical variables were present: new infiltrates on chest x-ray films; fever (temperature >38.3°C [100.9°F]); leukocytosis (>10,000/μl mm) or leukopenia (<5,000/μl mm); and purulent tracheal aspirations.

Criteria for exclusion of patients were: (1) severe hypoxemia (Pao, <80 mm Hg on Fio, of 0.8), (2) systolic blood pressure less than 85 mm Hg, (3) definite acidemia (pH <7.20), or (4) narrow endotracheal prosthesis (internal diameter <7 mm). Three patients were excluded according to the protocol and two others because of technical problems during blood gas sampling (discussed subsequently). Informed consent was obtained from each subject or from the nearest relative. A total of 107 consecutive ventilated patients were included.

Initial Evaluation

Patients were evaluated before the procedure using a special chart containing the following items: age; sex; indication for ventilator support divided into six classes;24 presence or absence of chronic obstructive pulmonary disease; presence or absence of underlying cardiac disease (symptomatic or recently operated); ongoing ARDS; acute physiologic score (APACHE);25 Glasgow coma score; requirement for inotropic agents (epinephrine; dopamine; dobutamine); size of endotracheal prosthesis; duration of mechanical ventilation at time of examination (days); presence of major hemostatic abnormalities; presence of major metabolic disorders; severity of pulmonary infiltrates evaluated by a radiologic score;26 use of PEEP (>5 cm H2O); inspiratory minute volume (L/min); peak inspiratory airway pressure (cm H2O); and dynamic compliance (calculated as tidal volume divided by peak inspiratory pressure minus end-expiratory pressure).

Procedure

All patients were ventilated through a volume-preset ventilator (Servo 900 C; Siemens-Elema). The Fio2 was adjusted to 0.8 at 20 minutes before premedication and was maintained unchanged during the period of study. Systemic arterial pressure and arterial blood samples were obtained through an intravascular catheter inserted into a radial artery as part of routine care of the patient. The patients were sedated with midazolam (0.1 mg/kg IV) five minutes before the examination, which was performed without topical anesthesia. A flexible fiberoptic bronchoscope (Olympus BF B3; OD, 6 mm) was introduced through an indwelling endotracheal tube using a special adapter (Bodai suction-safe Y; Sontek Medical Inc). Fiberoptic bronchoscopy was performed by one of two experienced bronchoscopists and included only the bacteriologic sampling using a telescoping cannula brush catheter (Meditech model BWF 1070/90), followed by direct suction through the inner channel of the endoscope. Samples of arterial blood were immersed in ice and measured within 30 minutes using a blood gas analyzer (Radiometer ABL 30) at 37°C. Minute ventilation, airway pressure, respiratory rate, and dynamic compliance were evaluated using the pneumotachograph of the ventilator. When a three-lumen thermistor Swan-Ganz catheter had been inserted, pulmonary artery and capillary wedge pressures were measured through the monitoring system (Hewlett-Packard 78042A). In such cases, cardiac output was measured using a cardiac output computer (Edwards Laboratories 9520 A).

Protocol

Arterial blood gases, heart rate, blood pressure, and central hemodynamic data were measured in the following order: (1) prior to preoperative medication; (2) five minutes after IV premedication; (3) at the end of the procedure, with the fiberoptic bronchoscope still in place; (4) 15 minutes after removing the endoscope; and (5) two hours after examination. Ventilator settings were maintained constant throughout the protocol. During bronchoscopy, changes in ventilation were noticed as follows: maximal decrease of minute ventilation recorded using the expiratory pneumotachograph of the ventilator; and number of incoordinate movements using variations of ventilator pressure cycle during assisted ventilation. For this latter purpose, two estimates were made: (1) the number of cycles partially aborting using a pop-off pressure set at 70 cm H2O; and (2) the number of cycles with pressure trough level lower than −10 cm H2O (triggered cycles).

Statistical Analysis

Comparisons of quantitative sequential variables were performed using a two-way analysis of variance and a Newman-Keuls test. Regression analyses were performed with the least-squares method and subjected to stepwise linear analysis. Univariate analysis of dichotomous risk factors and hypoxemia defined as PaO2 less than 60 mm Hg at any time, or hypotension defined as systolic blood pressure less than 80 mm Hg or a fall of more than 30 percent from the initial value, was accomplished by computing odds ratio and 95 percent confidence intervals. Finally, risk factors and adjusted relative odds were obtained by using multiple logistic regression analysis. The calculations were performed with BMDP software (University of California, Los Angeles).

RESULTS

Clinical characteristics of the 107 patients are summarized in Table 1. The patients had been admitted to the ICU for a variety of problems, including postoperative respiratory failure (31 cases; 29 percent), respiratory insufficiency associated with chronic obstructive pulmonary disease (24 cases; 22 percent), acute pulmonary disease (16 cases; 15 percent), neurologic emergencies (14 cases; 13 percent), drug overdose (6 cases; 6 percent), and other miscellaneous disorders (16 cases; 15 percent). Patients were intubated for an average of 4.6 ± 6.7 days (range, 0 to 45 days). Thirty-eight patients (36 percent) had bacterial pneumonia as defined by quantitative protected spec.

<table>
<thead>
<tr>
<th>Table 1—Characteristics of 107 Patients</th>
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<tr>
<td>Characteristic</td>
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</tr>
<tr>
<td>Age, yr</td>
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<tr>
<td>Sex ratio (M/F)</td>
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<tr>
<td>History of chronic pulmonary disease, percent</td>
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<tr>
<td>Presence of underlying cardiac disease, percent</td>
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<tr>
<td>Presence of ARDS, percent</td>
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<tr>
<td>APACHE score</td>
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<td>Glasgow coma score</td>
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<td>Treatment with inotropic agents, percent</td>
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<td>Presence of hydroelectrolytic disturbances, percent</td>
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<tr>
<td>Radiologic score</td>
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<tr>
<td>Use of PEEP, percent</td>
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<tr>
<td>Minute ventilation, L/min†</td>
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<tr>
<td>Peak inspiratory airway pressure, cm H2O†</td>
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<td>Dynamic compliance, mL/cm H2O†</td>
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*For quantitative variables.
†Measured at control time.
imen brush culture using a threshold of 10⁵ cfu/ml. The mean duration of the fiberoptic bronchoscopy was 120 ± 41 seconds.

Arterial Blood Gas Monitoring

Changes in PaO₂ are shown in Figure 1. The PaO₂ was not affected by sedation but had decreased significantly by the end of the procedure, with a mean decrease of 26 percent from the baseline value (p<0.01). There was a mild but significant diminution of PaO₂ that persisted for up to two hours after the investigation. In 35 patients the PaO₂ fell by more than 30 percent. Such an event was more frequent in patients with ARDS (p<0.02). For this subgroup of patients, the mean value at the end of the procedure was 63±23 mm Hg (mean ± SD) vs 175±85 mm Hg for the 93 others (p<0.001).

The magnitude of alterations in pH and PaCO₂ was relatively slight. Only three patients had a PaCO₂ greater than 60 mm Hg at the end of bronchoscopy. Development of ARDS was not associated with a higher PaCO₂ at the end of the procedure. When patients were analyzed according to their PEEP level, the mean PaCO₂ was found to be 39.8±7.6 mm Hg among those 23 patients with PEEP and was 41.8±8.5 mm Hg for the 84 others (NS). Changes in pH could be mostly explained by acute respiratory acidosis (Fig 2), and a linear relationship was evidenced between the relative variations of [H⁺] and PaCO₂ (r = 0.87). At the end of fiberoptic bronchoscopy, the pH lay within the 95 percent confidence limits of acute respiratory acidosis in 86 patients, while combined metabolic acidosis was apparent in the 21 others.

In an attempt to study the relationships between the degree of induced hypoxemia and clinical variables, including the bronchoscopic procedure, we used a linear regression analysis. The following tabulation shows the main relations between changes in PaO₂ and clinical variables, listing the F value for each factor:

<table>
<thead>
<tr>
<th>Factor</th>
<th>F</th>
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<tbody>
<tr>
<td>Baseline PaO₂</td>
<td>39.3</td>
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<tr>
<td>Use of PEEP</td>
<td>25.9</td>
</tr>
<tr>
<td>Change in PaCO₂</td>
<td>35.8</td>
</tr>
<tr>
<td>Radiologic score</td>
<td>1.6</td>
</tr>
<tr>
<td>Peak inspiratory airway pressure at control time, cm H₂O</td>
<td>1.6</td>
</tr>
<tr>
<td>Baseline pH</td>
<td>1.6</td>
</tr>
<tr>
<td>Absence of chronic pulmonary disease</td>
<td>1.3</td>
</tr>
<tr>
<td>Presence of ARDS</td>
<td>1.3</td>
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</tbody>
</table>

No relation could be established (F<0.5) for the size of the tracheal tube, baseline minute ventilation, baseline PaCO₂, decrease in minute ventilation, number of pop-off cycles, and number of triggered cycles. The baseline PaO₂, use of PEEP, and change in PaCO₂

![Figure 1](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21610/)

![Figure 2](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21610/)
were factors independently related to the degree of relative hypoxemia as determined by using the multiple regression model. As shown in the tabulation, the decrease in PaO₂ was related to the severity of pulmonary injury as identified by the level of initial PaO₂ on FiO₂ adjusted to 0.8 and use of PEEP. Alteration of alveolar ventilation was the other contributing factor. The relative weight of ARDS was obviated by the linked variable, PEEP.

The increase in PaCO₂, which was used as an indicator of alteration of alveolar ventilation, was independently related to the number of pop-off cycles (F=25.2), the decrease in minute ventilation (F=10.8), the number of triggered cycles (F=8.4), changes in PaO₂ (F=7.8), and radiologic score (F=5.1).

Hemodynamic Monitoring

Variations of heart rate and systolic blood pressure are indicated in Figure 3. The heart rate increased slightly at the end of the procedure, with an average of 103 beats per minute, but wide interindividual variations were observed (range, 30 to 170 beats per minute). Major arrhythmias were observed in six patients (tachyarrhythmia in four; bradycardia less than 50 beats per minute in one; multiform ventricular arrhythmia in one). The mean systolic blood pressure fell after sedation by approximately 10 percent, increased during bronchoscopy (136±29 mm Hg to 150±45 mm Hg; p<0.01), and returned to control levels following the removal of the bronchoscope. Substantial hypertension (systolic blood pressure >250 mm Hg) was recorded in three cases.

Central hemodynamic data were obtained through a Swan-Ganz catheter in 31 patients (Fig 4). An increase in cardiac output was observed at the end of bronchoscopy, concomitant with a rise in pulmonary wedge pressure, but without significant variations in systemic resistances. In fact, cardiac output did increase in 13 patients without underlying cardiopathy by a mean value of 24 percent, but not in the other 18 patients. Group data from 30 patients demonstrated a significant decrease in FiO₂ from 37.5±8.5 mm Hg before the procedure to 33.7±6.7 mm Hg at the end of bronchoscopy (p<0.001 by Wilcoxon test).

Risk Factors

Fourteen patients developed clinical hypoxemia as defined by PaO₂ lower than 60 mm Hg on FiO₂ adjusted to 0.8. Distribution of the variables associated
with such hypoxemia is shown in Tables 2 and 3. Using univariate analysis, ten factors could be identified. After stepwise logistic regression analysis, two independent variables were significantly associated with hypoxemia. Eight of the 14 patients with ARDS and 12 of 54 who had frequent pop-off cycles during fiberoptic bronchoscopy had a PaO₂ lower than 60 mm Hg.

When considering the risk of hypotension, defined as systolic blood pressure lower than 80 mm Hg or a decrease of more than 30 percent from the initial value, only two variables were linked using univariate calculations. The APACHE score, with a cutoff of 18 points, was the main predictor (p<0.005). Systolic blood pressure lower than 120 mm Hg during the control period was also associated with an increased risk of developing hypotension (p<0.01). Including both of these variables, as well as 25 others used as independent predictors of hypotension in multivariate analysis, gave odds ratios (95 percent confidence intervals) of 3.7 (1.1 to 12.2), and 4.3 (1.3 to 14.2), respectively.

**DISCUSSION**

Fiberoptic bronchoscopy is generally regarded as safe, based on surveys of endoscopists. Such studies provide important data for alert patients undergoing diagnostic investigation but fail to adequately identify factors that may increase the risk of endoscopy in ventilated patients. As we approach an era where bronchoscopy may supersede bronchial aspiration as a sampling procedure for diagnosing pneumonia in intubated patients, the number of endoscopic procedures will undoubtedly increase, and even small rates of complications will become magnified. Therefore, recognition of factors that may enhance the safety of fiberoptic endoscopy is crucial.

This study indicates that a decline in PaO₂ is consistently associated with fiberoptic bronchoscopy in ventilated patients and that this decline can be substantial, at least when using midazolam as the unique sedative drug. The mean change in PaO₂ from baseline during bronchoscopy was 26 percent by the end of the procedure; however, large interindividual variations in PaO₂ changes were noticed. With regard to our results, the degree of hypoxemia induced by fiberoptic bronchoscopy was linked to the severity of pulmonary dysfunction and the decrease in alveolar ventilation. This decrease in minute
ventilation was observed despite the use of a special adapter.25-26 Contrary to the results of Lindholm et al.,21 we were unable to find a relation between the size of the tracheal tube and the degree of hypoxemia (F<0.5). Because of the short duration (120 seconds) of the procedure in our study, detailed information concerning the respective implication of each time of examination could not be obtained; however, suctioning through the fiberoptic bronchoscope may be a critical factor.21,20 This point needs further study using intraarterial oxygen electrodes,20 transcutaneous oxygen monitoring,31,32 or mixed SvO2 monitoring.33

Clinical hypoxemia, as defined by PaO2 lower than 60 mm Hg, was more frequent in patients with ARDS and in those who "fought" the ventilator during the procedure, as shown by multivariate analysis. In our opinion, these results do not indicate that sampling through the fiberoptic bronchoscope should not be used to diagnose bacterial infections in patients with ARDS, because nosocomial pneumonia is particularly frequent and severe in this setting.20 The results simply imply that these patients are at higher risk of definite hypoxemia and should be monitored with particular care. Moreover, incoordinate respiratory movements could be abolished using a better anesthetic protocol. Although different groups have recommended that lidocaine not be instilled through the bronchoscope,17 the rationale for this approach has recently been challenged.34,35 Therefore, the use of a high dose of nebulized anesthesia using preservative-free lidocaine might be advocated. An alternative approach, which is our current policy, is the addition of a short-acting neuromuscular blocking agent such as vecuronium. Increasing tidal volume might also be considered,21,36 according to the basal level of maximal peak inspiratory pressure.37

As a group, ventilated patients did not demonstrate major blood pressure variations or tachycardia. The mean decrease in systolic blood pressure below baseline values was 10 percent, which was related to sedation, and not to the bronchoscopic procedure. In normal humans, midazolam at a dose of 0.15 mg/kg IV produces a similar response, associated with an increase in heart rate and a decrease in systemic vascular resistance.38 In our study, definite hypotension was linked to premedication and to the severity of illness. The APACHE score, which is a classification system representing the degree of acute illness, and the relative hypotension before the procedure were the more appropriate of the 27 items included in the multivariate analysis. The use of PEEP or the requirement for isotropic agents was not a significant risk factor. During endoscopy, a significant rise in arterial pressure was observed (10 percent above control values), associated with an increase in pulse rate of 5 percent. Such observations have been observed in routine fiberoptic bronchoscopy using an intravenous anesthetic technique of intermittent thiopental (thiopentone) and succinylcholine (suxamethonium), but not in patients receiving either Fentanyl or alfentanil.29 It is unlikely that using higher doses of midazolam would have prevented such modifications in the rate-pressure product, which are consistent with those observed by Boralessa et al.10 in intubated patients after a bolus of 0.3 mg/kg IV for induction of anesthesia. Therefore, alternative anesthetic protocols should be built up in order to minimize risks of cardiovascular impairment.

Major arrhythmias were noticed in 5 percent of the patients, which agrees with a number of studies in spontaneously breathing patients,10,12,15 but is lower than the 40 percent rate observed by Katz et al.15 In the latter report, arrhythmias were frequently associated with a period of major oxygen desaturation of up to 44 percent. Such hypoxemia was not present in our patients; the mean SaO2 was 97 percent (range, 93 to 100 percent) in the six patients suffering arrhythmias.

In conclusion, this study has shown that fiberoptic bronchoscopy is practicable in critically ill intubated patients. In the present series of 107 ventilated patients, no death or cardiac arrest occurred during or within the two hours immediately following the procedure; however, patients in the ICU are at risk of relative hypoxemia during fiberoptic bronchoscopy even when high levels of oxygen are provided to the ventilator and gas leaks around the endoscope are minimized by a special adapter. Patients with ARDS are obviously at higher risk of definite hypoxemia. Careful methodic attention to the anesthetic protocol, ventilator settings, and monitoring of patients during bronchoscopy should permit rapid correction and more frequent prevention of hypoxemia and should further decrease morbidity.

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