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Fiberoptic Bronchoscopy during Nasal Non-Invasive Ventilation in Acute Respiratory Failure

E. Chiner J.N. Sancho-Chust M. Llombart C. Senent A. Camarasa
J. Signes-Costa

Pulmonology Section, University Hospital of Sant Joan d'Alacant, Sant Joan d'Alacant, Spain

Key Words
Acute respiratory failure · Chronic obstructive pulmonary disease · Fiberoptic bronchoscopy · Intubation · Non-invasive positive pressure ventilation · Oxygen saturation

Abstract
Background: Various methods have been described for safely performing fiberoptic bronchoscopy (FB) while applying non-invasive positive pressure ventilation (NIPPV) in patients with acute respiratory failure (ARF). ***Objectives:*** To evaluate the safety of a new method to perform FB in patients with ARF. ***Methods:*** Patients with ARF in whom FB was indicated were studied. The primary end-point was a mean drop in oxygen saturation (S_aO_2) after the procedure. During nasal NIPPV, FB was performed via the mouth using a bite block sealed with an elastic glove finger allowing bronchoscope insertion. ***Results:*** Thirty-five patients were included in the final study (63 ± 17 years, 74% men, P_aO_2/F_iO_2 ratio 168 ± 63). A total of 35 bronchoaspirates, 21 protected brushings, 11 bronchoalveolar lavages and 8 bronchial biopsies were done. The cardiorespiratory variables at the start and end of FB were: S_aO_2 93 ± 3 to 94 ± 5%, heart rate 95 ± 17 to 99 ± 22 b.p.m. and respiratory rate 24 ± 11 to 25 ± 11 respirations/min. The lowest S_aO_2 value reached during the procedure was 86 ± 3% and the maximal $ETCO_2$ rise was 41 ± 4 mm Hg. Leakage was <50 ml/s in 32 patients. The clinical course was favorable in 66%. Invasive ventilation was necessary in 11%, 5 ± 4 days after FB. Twelve patients (33%) died 3 ± 2 days after FB as a result of their underlying disease. ***Conclusions:*** The system allowed to perform FB safely in patients with ARF. Although there is a relatively high rate of intubation and invasive mechanical ventilation due to illness severity, there was no worsening of oxygenation or complications attributable to the procedure.

Introduction

The effectiveness of non-invasive positive pressure ventilation (NIPPV) in acute respiratory failure (ARF) patients with chronic obstructive pulmonary disease (COPD), immunodepression, pneumonia, acute pulmonary edema, adult respiratory distress syndrome or thoracic trauma is well known. Compared with invasive mechanical ventilation, this type of ventilation achieves the same physiological benefits of reduced work of breathing and improved gas exchange. Furthermore, it avoids the complications of intubation and the increased risk of ventilator-associated pneumonia. Moreover, other physiologic effects as minimizing or counterbalancing intrinsic positive end-expiratory pressure in critically ill patients with COPD have been described [1–6].

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Eusebi Chiner
Pulmonology Section, University Hospital of Sant Joan d'Alacant
Ctra. Alacant-València s/n
ES–03550 Sant Joan d'Alacant (Spain)
Fax +34 96 565 8750, E-Mail chiner_eus@gva.es

Many of these patients have pulmonary infiltrates or retention of secretions which make it necessary to perform fiberoptic bronchoscopy (FB) [1, 2, 7] in order to reach an etiological diagnosis and thus implement the measures necessary to reduce the high mortality that exists in these patients. In cases of severe pneumonia, early microbiological diagnosis helps in selecting the right antibiotic and may improve the prognosis [8]. In addition, approximately 15% of patients with cancer develop ARF, and FB with bronchoalveolar lavage (BAL) is the basis of causal diagnosis [9].

Bronchoscopy is a widely performed procedure that is generally considered to be safe and effective. In recent years, its range of application has been greatly expanded. However, FB is not devoid of risks. Severe complications occurred in 0.637% and mortality was noted in 0.013% of patients [10]. The bronchoscope occupies approximately 10% of the normal airway and may cause the arterial oxygen pressure (P_aO_2) to drop between 10 and 20 mm Hg during the procedure [9, 11]. This may cause serious respiratory complications or cardiac arrhythmias. For this reason, FB is contraindicated in non-intubated patients with hypoxemia (inspiratory oxygen fraction (F_iO_2) >50%, necessary to maintain a P_aO_2 of 75 mm Hg) [12]. In these patients, there have traditionally been two options: intubate in order to carry out FB with invasive mechanical ventilation (IMV) or not perform the procedure and apply empirical treatment with all the risks this implies.

In recent years, FB has been done while simultaneously applying NIPPV in order to reduce the risks of FB in patients with ARF. Very few studies have been published: two methods of applying NIPPV have been described [13–16] as well as another method that makes use of continuous positive airway pressure (CPAP) [17].

We present the results of a new method whose main advantage is the simplicity of the procedure, which makes it easy to perform.

Patients and Methods

Study Subjects

From November 2004 to November 2008, adult patients admitted to the Sant Joan d'Alacant University Hospital were studied. In order to be included in the study, the patients had to fulfill the following criteria:

(a) They were admitted to the pulmonology ward or intensive care unit.
(b) They had ARF, meeting 2 or more of the following criteria:
  (1) $P_aO_2/F_iO_2 < 200$;
  (2) respiratory rate (RR) >35 respirations/min, and
  (3) dyspnea at rest.
(c) FB was indicated for diagnostic or therapeutic purposes according to any of the following criteria:
  (1) atelectasis;
  (2) infiltrates or pulmonary masses on chest X-ray;
  (3) retention of secretions, and
  (4) hemoptysis.

Exclusion criteria were:

(a) Inability to maintain $S_aO_2 \geq 90\%$ despite NIPPV via the nasal route.
(b) Intolerance to NIPPV.
(c) Clinical indication for IMV, defined as one or more of the following:
  (1) need for cardiopulmonary resuscitation;
  (2) hemodynamic instability;
  (3) encephalopathy, and
  (4) coma.

Study Design

This is a prospective observational study designed to assess the safety of FB via the oral route by means of a sealed system and applying NIPPV via a nasal mask. The primary end-point was the evaluation of the reduction in pulse oximeter oxygen saturation (S_aO_2) during FB. The secondary end-points were changes in RR, end-tidal CO_2 ($ETCO_2$) and heart rate (HR), the existence of complications and need for intubation and IMV after the procedure. The study was approved by the local ethics committee and all the patients gave their informed consent.

Methods

When FB was indicated, arterial blood gases (ABG) were obtained with the patient receiving conventional oxygen therapy via a Venturi-type mask, which gave the initial P_aO_2/F_iO_2 ratio. Once this parameter had been determined and after obtaining the patient's informed consent, NIPPV was started.

This was done using a bilevel nasal positive pressure system (BiPAP; Respironics, Murrysville, Pa., USA) in the spontaneous/cycled mode adjusting the inspiratory (IPAP) and expiratory positive airway pressure (EPAP) independently in order to achieve effective ventilation (expiratory tidal volume ≥10 ml/kg). In all cases, minimum IPAP and EPAP of 14 and 5 cm H_2O, respectively, were considered. In order to ensure that the pressures administered remained steady during NIPPV, the remote control of the apparatus was used to monitor the expiratory tidal volume, leaks, IPAP and EPAP continuously by means of a digital system. These were adjusted during the procedure whenever necessary according to S_aO_2 and $ETCO_2$.

The interface used was a nasal mask (ComfortClassic; Respironics), with a chin support connected to the head harness holding the mask in place. Supplementary oxygen therapy was delivered (between 5–15 l/min) via a cannula connected to the mask, and regulated to maintain $S_aO_2 \geq 90\%$.

Initially, the patient underwent a 15- to 20-min period of adaptation to the NIPPV. During this time, the S_aO_2 was continuously monitored using a pulse oximeter (Nonin 8600®; Nonin Medical, Minneapolis, Minn., USA) and the clinical tolerance evaluated. If the S_aO_2 was found to be ≥90% and the patient adapted well to NIPPV, FB was started. Continuous non-invasive monitoring of $ETCO_2$ levels was performed with a Microstream capnograph (Oridion, Needham, Mass., USA). $ETCO_2$ was mea-

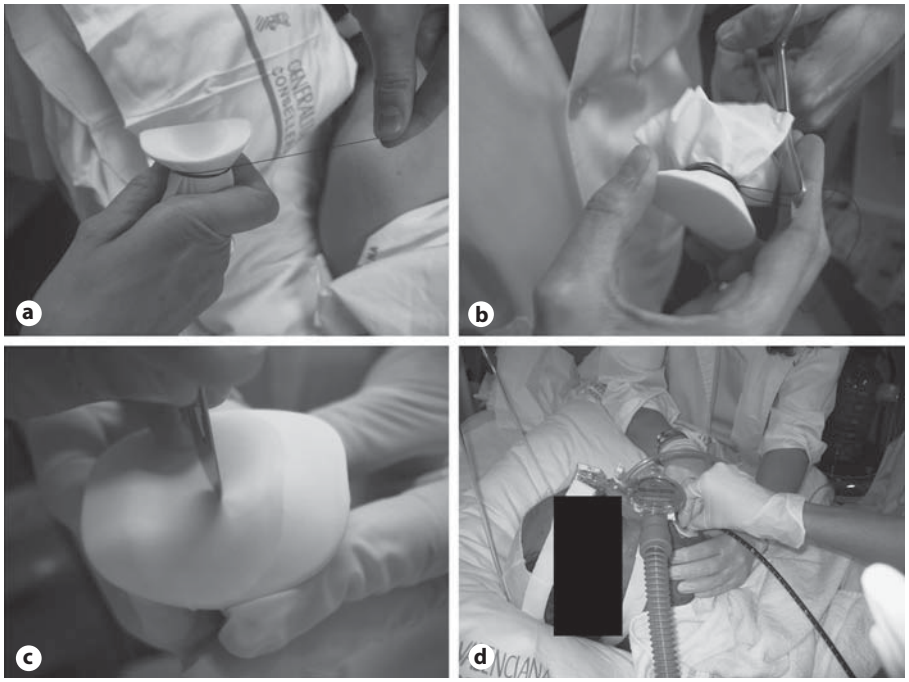

Fig. 1. Construction of the sealed mouthpiece. **a** The mouthpiece is tied inside the glove using a conventional suture via the external channel. **b** Excess material is trimmed. **c** A small incision is made in the tip of the glove finger using a scalpel. **d** The device is then placed in the patient's mouth, permitting insertion of the bronchoscope through the hole in the glove finger.

sured by a sampling line connected to the nasal mask. Microstream sampling lines blocked by secretions were replaced as needed.

FB was performed via the oral route using a mouthpiece (MB-142; Olympus, Tokyo, Japan). This was inserted in a latex glove, which was then tied with conventional suture through the external channel of the mouthpiece leaving one finger of the glove in the center. After tying the glove, excess material was cut away and with the help of a scalpel, a small incision (~1–2 mm) was made at the tip of the glove finger, through which the bronchoscope was inserted (fig. 1). The resulting device consisted of a mouthpiece, closed by an elastic membrane through which the bronchoscope was inserted and which acted as a retention valve for the pressure administered.

A flexible videobronchoscope was used (EB250S; Fujinon; Saitama, Japan). For topical anesthesia of the pharynx, a 10% lidocaine solution was sprayed. For anesthesia of the larynx and vocal cords, a 2% lidocaine solution was instilled through the lumen of the bronchoscope.

The bronchoaspirate was obtained by aspiration through the internal channel of the bronchoscope. Samples were sent for cytological and microbiological study. In patients in whom there was suspicion of an infectious etiology, a protected-specimen brush was used in the zone with the greatest radiological alteration. BAL was done in patients in whom there was a clinical indication. The tip of the bronchoscope was inserted into the orifice of a subsegmentary bronchus that showed infiltrates on chest X-ray. Three aliquots of 50 ml of non-bacteriostatic saline serum were instilled at room temperature. Quantitative cultures with a number $>10^5$, $>10^3$ and $>10^4$ colony-forming units/ml, respectively, for bronchoaspirate, protected-specimen brush and BAL were considered significant [15]. Bronchial biopsies were done when necessary if there was suspicion of bronchial neoplasia or alteration in the bronchial mucosa. Secretions were suctioned when necessary after instillation of saline or sodium-2-mercaptoethane sulfonate.

During the procedure, S_aO_2, $ETCO_2$, HR and RR were continuously monitored. After FB, patients continued with NIPPV for 15 min, while still being monitored. Subsequently, conventional oxygen therapy was continued as before the procedure. ABG were collected 2 h after the FB. Any complications attributable to the procedure were recorded: e.g. sudden appearance of: (1) deterioration of ABG, (2) decreased level of consciousness or (3) cardiac arrhythmias, need for orotracheal intubation and IMV (time after FB and cause) and cause of death.

Statistical Analysis

Statistical analysis was done using a statistical package for Windows (SPSS, version 13; SPSS, Chicago, Ill., USA). Kolmogorov-Smirnov's test was done to assess the normality of the distribution of all the quantitative variables. Respiratory parameters were compared using Student's t test for paired data or the Mann-Whitney test. $p \leq 0.05$ was considered significant.

Results

During the study period, 39 patients fulfilled the inclusion criteria. Four of these were excluded: 1 due to inability to maintain $S_aO_2 \geq 90\%$ despite NIPPV via the nasal route, 1 due to intolerance to NIPPV and 2 due to clinical indication for IMV. Finally, 35 FBs were performed in 35 patients, whose characteristics are shown in table 1. The indications for FB are shown in table 2.

Table 1. Basal characteristics of the patients included in the study

Age, years	63 ± 17
Males	26 (74)
Females	9 (26)
P_aO_2/F_iO_2	168 ± 63
P_aO_2	55 ± 18
P_aCO_2	46 ± 15
pH	7.33 ± 0.09
Prior NIPPV	14 (40)
Underlying disease	
Neuromuscular disease	9 (26)
Extrapulmonary neoplasia	9 (26)
COPD	6 (17)
Ischemic cardiopathy	3 (9)
Cerebrovascular disease	2 (6)
Tuberculosis	2 (6)
Cystic fibrosis	1 (3)
HIV	1 (3)
Systemic lupus erythematosus	1 (3)
Rheumatoid arthritis	1 (3)

Values expressed as means ± SD or numbers (%). HIV = Human immunodeficiency virus.

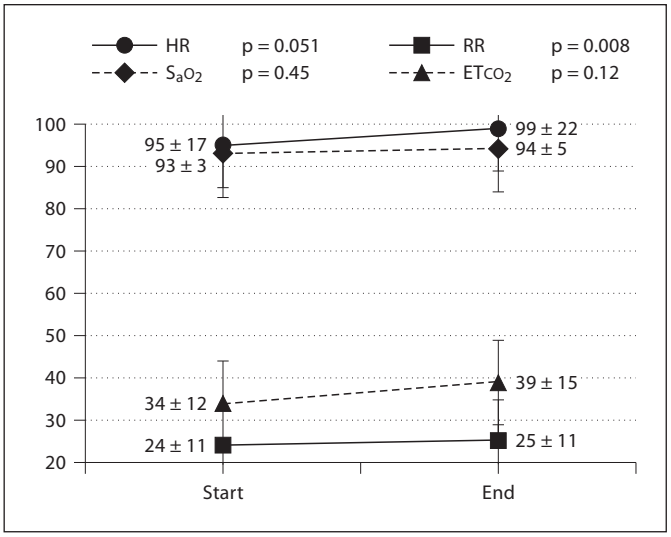

Fig. 2. Cardiorespiratory variables at the start and end of FBA. Means ± SD.

Table 2. Indications for flexible bronchoscopy

Indication	Absolute value
Pulmonary infiltrates	18 (51%)
Atelectasis	7 (20%)
Retention of secretions	7 (20%)
Pulmonary mass	2 (6%)
Hemoptysis	1 (3%)

Table 3. Final diagnosis after FB

Diagnosis	Absolute value
Pneumonia	20 (57%)
Mucous plugs	5 (14%)
Bronchogenic carcinoma	3 (9%)
Alveolar hemorrhage	2 (6%)
Pneumonitis	2 (6%)
Metastatic carcinoma	2 (6%)
Other	1 (3%)

For NIPPV an IPAP of 16 ± 1.5 cm H_2O and an EPAP of 6 ± 1 cm H_2O was used, with nasal masks in 34 patients (97%) and nasal pillows in 1 (3%). Only 1 patient (3%) did not tolerate the procedure due to air leakage.

The cardiorespiratory variables at the start and end of FB are shown in figure 2. Notably, an increase in mean S_aO_2 may be seen although it did not reach statistical significance. The lowest S_aO_2 value reached during the procedure was 86 ± 3% and the maximal value for $ETCO_2$ was 41 ± 4 mm Hg. Supplementary oxygen was increased in 8 patients with a mean of 4 ± 2 l/min. In 3 patients the leak was 85, 110 and 130 ml/s, respectively, and <50 ml/s in 32 patients. No significant differences were observed in ABG obtained before and 2 h after FB.

In total, 35 (100%) bronchoaspirates, 21 (60%) protected-specimen brush samples, 11 (31%) BAL and 8 (23%) bronchial biopsies were done. The patients' final diagnoses after FB are shown in table 3.

The main indication was the diagnosis of pulmonary infiltrates and the procedure led to a change in antibiotic treatment in 80% of patients with pneumonia. Furthermore, specific diagnoses such as bronchogenic carcinoma or alveolar hemorrhage resulted in a different therapeutic approach in these patients. On the other hand, FB was therapeutic in 14% of cases, contributing to the resolution of ARF.

There were no complications attributable to the procedure. The clinical course was favorable in 23 patients (66%). A total of 12 patients (33%) died as a result of their

Table 4. Patients in whom orotracheal intubation and IMV was necessary after the procedure

Case No.	Underlying disease	Indication for FB	Final diagnosis	Days after FB	Cause of intubation and IMV
4	systemic lupus erythematosus	pulmonary infiltrate	alveolar hemorrhage	1	progressively decreasing ABG
12	COPD	pulmonary infiltrate	pneumonia	1	hemodynamic instability
19	COPD	atelectasis	pneumonia	6	deteriorating level of consciousness
35	extrapulmonary neoplasia	pulmonary infiltrate	pneumonitis	10	progressively decreasing ABG

underlying disease with a mean survival after the procedure of 3 ± 2 days. No death was attributed to FB in any patient. Hospital stay after the procedure was 9 ± 7 days. Orotracheal intubation and IMV was done in 4 patients (11%), on average 5 ± 4 days after the procedure (table 4).

Discussion

This study shows that FB with a mouth seal system and nasal NIPPV is a safe procedure in patients with ARF in whom FB would not otherwise be done due to the high risk associated with intubation and IMV.

There are only a limited number of studies on FB with NIPPV and they include a small number of patients. Overall, the results are favorable, demonstrating the safety of the different methods used.

Antonelli et al. [13] reported the first study using pressure support concomitant with CPAP in 8 immunodepressed patients with ARF in whom conventional FB was contraindicated. They applied NIPPV via a face mask connected to the ventilator and held in place by elastic straps, with a T-shaped adaptor in the mask in which to insert the bronchoscope nasally. They used CPAP at 4 cm H_2O and a support pressure of 17 cm H_2O, with F_iO_2 of 1. During FB, the P_aO_2/F_iO_2 ratio and oxygen saturation (S_aO_2) improved significantly, resulting in good tolerance, and there was no need for intubation in any of the patients after the procedure. In 10 patients with COPD in whom FB was contraindicated in spontaneous ventilation, Da Conceiçao et al. [14] assessed the safety of FB with BAL done using NIPPV with the same method. S_aO_2 did not fall below 90%, and neither P_aO_2 nor P_aCO_2 changed following the procedure. Intubation was also not needed in any patient. In a later paper, Antonelli et al. [15] performed a randomized prospective study comparing this method with oxygen therapy using a Venturi-type mask. They recruited a total of 26 patients with a P_aO_2/F_iO_2 ratio ≤200 and suspicion of nosocomial pneumonia that required FB with BAL. In the NIPPV group, the P_aO_2/F_iO_2 ratio rose by 82% (261 vs. 139), while it fell by 10% in the oxygen therapy group (155 vs. 139). Furthermore, the P_aO_2/F_iO_2 ratio was higher 60 min after FB with NIPPV, and there was better hemodynamic stability.

NIPPV with a helmet-like interface has been shown to have similar efficacy to that of a face mask. In view of this, Antonelli et al. [16] designed another method in 4 patients with ARF and suspicion of pneumonia, who received NIPPV via a helmet and required FB with BAL. The fiberoptic bronchoscope was inserted using a specific sealed connector via the nasal route. The support pressure mode was used with good tolerance. There was no worsening of the gaseous interchange, and the only differences found were a mean increase in HR and arterial pressure of 5 and 7%, respectively. It was not necessary to intubate any patient.

The CPAP mode with Boussignac's system has also been used by Maitre et al. [17], who performed a double-blind study in patients with P_aO_2 <125 mm Hg despite a high flow mask. Using the face mask, oxygen was either given alone or combined with CPAP at 7.5 mm Hg, and 15 patients were included per group. In the group with CPAP, S_aO_2 was maintained, with a significant difference compared with the group receiving oxygen therapy alone (in which it decreased). In addition, there was less need for NIPPV and intubation, although this did not reach statistical significance.

In an earlier publication [19], our group was the first to describe another technique, which differs from the others in that FB was performed via the oral route and this constitutes the basis of our present study. Using a device consisting of a part that fits in the mouth, closed by means of an elastic membrane, FB was combined with NIPPV. Two cases were described in whom there was good tolerance, with no clinical or ABG complications or need for intubation. In the present work we used non-invasive monitoring of $ETCO_2$ during the procedure for close monitoring of NIPPV. The lack of a fall in S_aO_2 also demonstrates the safety of the procedure. Nevertheless, the patients presented borderline gaseous interchange

and mainly hypoxemic respiratory failure, with no significant hypercapnia, and the main objective of this study was to verify that oxygenation was not worsening during the procedure.

Making use of the oral route has various potential advantages: (a) FB may be done as a continuation of the ventilation process and does not require adaptors or interface changes; (b) the orotracheal route allows the fiberoptic bronchoscope to be extracted without damaging the nasal route; (c) it avoids the danger of aspiration of gastric content, as occurs in patients with a helmet or face mask; (d) it may be applied in the case of aspiration of a foreign body or mucous plugs or threatened hemoptysis, circumstances that often make it necessary to extract the bronchoscope, and (e) it is a method that is easily accessible for the different hospitalization units and does not require expensive, complex systems.

It has been shown that FB in patients with mechanical ventilation is cost effective. FB allows therapeutic maneuvers such as the aspiration of secretions to improve adaptation to the ventilator as well as microbiological sampling in order to choose the appropriate antibiotic. Furthermore, FB may be therapeutic, contributing to the resolution of ARF.

This study has a potential limitation, i.e. the lack of a control group. Due to ethical reasons, since we are dealing with patients with ARF in whom conventional FB with oxygen therapy was contraindicated due to the high risk of complications, it was not considered acceptable to carry out a randomized study in this sense.

In conclusion, NIPPV appears to be a safe, effective procedure for maintaining oxygenation in patients with ARF while FB is being performed. Given the possible problems that may arise with the interface, it may be said that the different methods of performing FB are not mutually exclusive but complementary, and thus may be used alternatively, just as the interfaces are alternated. Therefore, application of NIPPV should be considered in all patients with ARF in whom FB is indicated.

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