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Effect of intrapulmonary percussive ventilation on expiratory flow limitation in chronic obstructive pulmonary disease patients

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Negative expiratory pressure;
Airway occlusion pressure;
Expiratory flow limitation;
Intrapulmonary percussive ventilation

Abstract

Purpose: The aims of this prospective study were (1) to select, after weaning and extubation, chronic obstructive pulmonary disease (COPD) patients with expiratory flow limitation (EFL) measured by the negative expiratory pressure method and (2) to assess, in these patients, the short-term (30 minutes) physiologic effect of a session of intrapulmonary percussive ventilation (IPV).

Materials and Methods: All COPD patients who were intubated and needed weaning from mechanical ventilation were screened after extubation. The patients were placed in half-sitting position and breathed spontaneously. The EFL and the airway occlusion pressure after 0.1 second (P0.1) were measured at the first hour after extubation. In COPD patients with EFL, an IPV session of 30 minutes was promptly performed by a physiotherapist accustomed to the technique. Expiratory flow limitation, gas exchange, and P0.1 were recorded at the end of the IPV session.

Results: Among 35 patients studied after extubation, 25 patients presented an EFL and were included in the study. Intrapulmonary percussive ventilation led to a significant improvement in EFL, respectively, before and 30 minutes after IPV (65.4 ± 18.2 vs 35.6 ± 22.8; $P < .05$). Three patients were not expiratory flow limited after IPV. Intrapulmonary percussive ventilation led to a significant decrease in P0.1 (3.9 ± 1.6 vs 2.8 ± 1.1; $P < .05$). Thirty minutes of IPV led to a significant increase in Pa_{O_2} and pH and a decrease in Pa_{CO_2} and respiratory rate ($P < .05$).

Conclusion: In COPD patients, a session of IPV allowed a significant reduction of EFL and of P01 and a significant improvement of gas exchange.

1. Introduction

Intrapulmonary percussive ventilation (IPV) is a ventilatory technique that delivers small bursts of high-flow respiratory gas into the lung at high rates, intended for mobilization of secretions that has been used in several pathologies, characterized by excessive secretion [1-9]. In a

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study performed in chronic obstructive pulmonary disease (COPD) patients with initial mild respiratory acidosis, IPV has been shown to prevent the deterioration of acute exacerbation, avoiding therefore the use of mechanical ventilation [10]. Potential mechanisms of action include enhanced alveolar recruitment, improved mucus clearance, and/or direct high-frequency oscillatory ventilation-like effect [1]. Nava et al [11], in stable COPD patients, have demonstrated that the application of IPV is associated with a significant reduction of the diaphragm energy expenditure probably mediated by a true ventilatory effect. To our knowledge, the effects of IPV have not been studied in more acute COPD patients and in particular after extubation. Although the need for reintubation may be a marker of increased severity of illness, this is an independent risk factor for nosocomial pneumonia and mortality and increased hospital stay [12,13]. Patients with COPD exhibit increased inspiratory work and dyspnea due to dynamic hyperinflation caused by expiratory flow limitation (EFL). In COPD patients, it has been shown that EFL can be present over most of the tidal expiration and that it is associated with intrinsic positive end-expiratory pressure (PEEPi) [14]. The airway occlusion pressure after 0.1 second (P0.1) provides a numerical expression of the balance between load and capacity. This parameter parallels the change in work of breathing (WOB) [15]. In a recent study, we demonstrated that P0.1 and EFL, recorded 1 hour after the discontinuation of mechanical ventilation, are higher in patients in whom respiratory failure will occur compared with those who will remain stable [16]. Our hypothesis was that IPV could benefit selected COPD patients with EFL after extubation. The aims of our study were to select COPD patients with EFL in postextubation (measured by the negative expiratory pressure [NEP] method) and to evaluate in these patients the benefit of a session of IPV in terms of improvement of EFL, P0.1, and gas exchange.

2. Materials and methods

2.1. Patients

The experimental protocol was approved by the institutional review board of the hospital, and all patients or their next of kin provided written informed consent. During a 13-month period, all COPD patients who were intubated and needed weaning from mechanical ventilation were screened after extubation. The diagnosis of COPD was defined on the basis of clinical history, chest x-ray, and/or previous pulmonary function tests [17].

2.1.1. Inclusion criteria

Patients with COPD were studied 1 hour after extubation, during a phase of clinical stability defined by a respiratory frequency below 30/min and lack of hypercapnic respiratory acidosis with a pH of more than 7.35.

2.1.2. Exclusion criteria

Exclusion criteria were as follows: requirement for emergency intubation for cardiopulmonary resuscitation, respiratory arrest, Glasgow coma scale [18] ≤8, hemodynamic instability defined as a systolic blood pressure of less than 80 mm Hg or evidence on electrocardiography of ischemia or clinically significant ventricular arrhythmias, failure of more than 2 additional organs, tracheotomy, pneumothorax, facial deformity, recent history of oral, and oesophageal or gastric surgery.

2.1.3. Data collection

The following variables were recorded from patients: age, new simplified acute physiology score [19], body mass index, time with mechanical ventilation, forced expiratory volume in 1 second, and reason for initiating mechanical ventilation.

2.2. Monitoring

Throughout the study, the arterial oxygen saturation was monitored continuously, with bedside pulse oximeter (Oxisensor; Nellcor, Hayward, Calif), heart rate, arrhythmias, and respiratory rate (RR) being displayed on the screen of the monitor.

2.3. Measurements

Respiratory rate, P0.1, EFL evaluated by the NEP method, and gas exchange including Pa_{O_2}, Pa_{CO_2}, and pH were measured at the first hour after extubation. In case of EFL measured by the NEP method, the patient was included in the study and a session of IPV was performed. Gas exchange, RR, EFL, and P0.1 were recorded immediately at the end of the IPV session. P0.1 and NEP were measured according to following methodology:

2.4. NEP method

2.4.1. Procedure

A specially devised system (Micro 5000; Medisoft, Dinan, Belgium) was used to measure the EFL [20]. A flanged plastic mouthpiece was connected in series with a Fleisch no. 2 pneumotachoraph and a Venturi device capable of generating a negative pressure during expiration (Micro 5000; Medisoft). The devised system was calibrated before each new patient. The patient was placed in half-sitting position (45°) and breathed spontaneously through a standard rubber mouthpiece connected to a low dead-space (45 mL) low-resistance circuit while wearing a nose clip. After stabilization of the patient, judged on a respiratory frequency equivalent to that measured in pretest, an NEP of −5 cm H_2O was applied at the beginning of expiration and maintained throughout the ensuing expiration. The opening of the valve was accomplished without the subject's

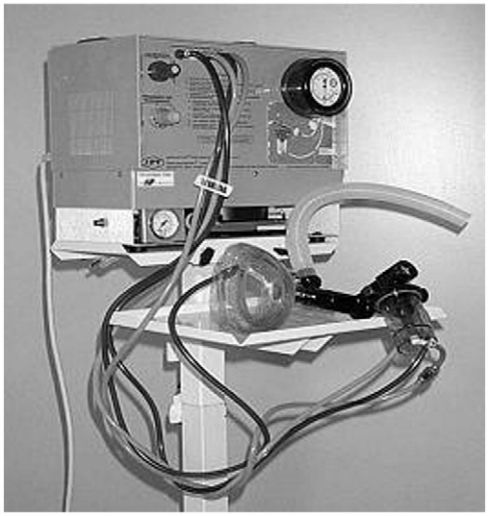

Fig. 1 The IPV device (Percussionaire Corp) and the full-face mask used in the study.

anticipation. The test breath was the breath during which the NEP was applied during expiration, and the preceding expiration served as control. A series of 5 breath tests separated by periods of quiet breathing were made in half-sitting position.

2.4.2. Detection of flow limitation

The expiratory flow-volume loops generated with NEP were compared by superimposition with those obtained during the immediately preceding breaths. Flow limitation was deemed to be present when the NEP-induced expiratory flow did not exceed the corresponding spontaneous expiratory flow, whether present throughout expiration or during any part of it. When present, the degree of flow limitation was expressed as the percentage of tidal expiration over which NEP did not induce any appreciable change in flow with respect to the control expired tidal volume (%VT) [21,22]. The value of this index was, by definition, zero when flow limitation was absent.

2.4.3. Airway occlusion pressure after 0.1 second (P0.1)

The module of NEP is replaced on the devised system (Micro 5000; Medisoft) by that which allows us to measure the P0.1. The patient, in half-sitting position, ventilates spontaneously through the system. After stabilization of the patient, judged on a respiratory frequency equivalent to that measured in pretest, the inspiratory circuit is closed without the knowledge of the patient by inflating the small balloon of occlusion to the compressed air at the functional residual capacity. After 300 milliseconds of occlusion, the small balloon is deflated automatically authorizing the continuation of the inspiration. The pressure of the air routes measured automatically after 100 milliseconds of occlusion represents P0.1. Five measurements of P0.1 will be obtained, spaced at least 15 seconds.

2.5. Intrapulmonary percussive ventilation

The method was similar to the procedure previously described [10]. Intrapulmonary percussive ventilation session was performed by the specialized and trained respiratory therapist and delivered to the patient through a full-face mask (La Cigogne, Pessac, France). The mask was adjusted and connected to the intrapulmonary percussive ventilator, IPV1 device (Percussionaire Corp, Sandpoint, Idaho; Fig. 1). After the mask has been secured, the percussions were delivered to the patient into the lungs. The frequency of the percussion was initially set at 250/min, and the peak pressure was initially set at 20 cm H_2O. Frequency and peak pressure were adjusted for each patient to improve comfort and to be certain that the entire thorax was being percussed by visualization of external thoracic movements. The *I*/*E* ratio was adjusted to 1:2.5. The duration of IPV session was 30 minutes. During IPV sessions, the nebulizer delivered only NaCl 0.9%. Oxygen was fed into the mask to maintain oxygen saturation between 88% and 92%. Before and after the IPV session, patients breathed oxygen spontaneously, whereas arterial oxygen saturation was continuously monitored. Oxygen flow was not changed between both periods.

2.6. Mucus clearance

After the session of IPV, the total mucus secretions (saliva included) were collected in a sterile mucus aspirator of 40 mL. The quantification of secretions was therefore assessed in mL.

2.7. Data analysis

Comparisons of data obtained before and after IPV were made with Wilcoxon test for paired measures. Data are

Table 1 Characteristics of the 25 patients included in the study

Male/Female	15:10
Age (y) *	63 ± 8
FEV_1 (%predicted) *	33.4 ± 6.7
Body mass index	26 ± 3
SAPS II *	35.6 ± 4.9
Ventilation time (d) *	8.0 ± 3.0
Reason for initiating mechanical ventilation (n, numbers)	
Acute-on-chronic COPD, n	19
Pneumonia, n	1
Heart failure, n	1
Postoperative respiratory failure, n	2
Miscellaneous, n	2

FEV_1 indicates forced expiratory volume in 1 second; SAPS II, new acute physiologic score [19].
* Values are means ± SD.

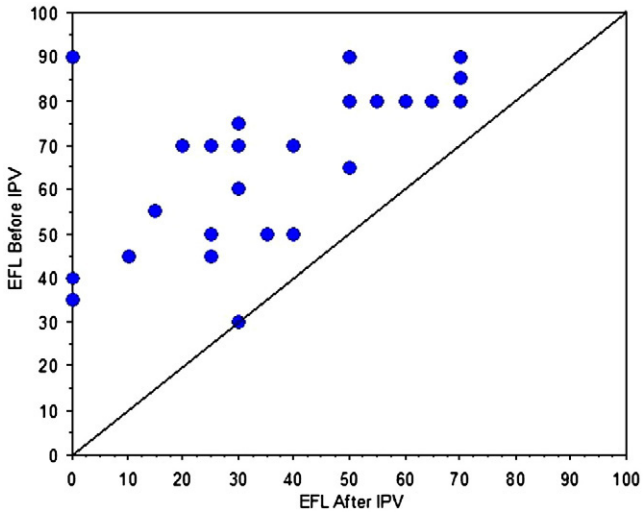

Fig. 2 Relationships of expiratory flow limitation (%VT) before and after intrapulmonary ventilation in 25 semirecumbent COPD patients. Thick line indicates identity line. A session of IPV decrease the expiratory flow limitation measured by the NEP method in COPD patients.

reported in mean (±SD) where indicated. A value of $P \leq 0.05$ was accepted as statistically significant. The coefficient of variation (SD/mean) has been evaluated for each patient for EFL and P0.1 before and after IPV. Analyses were done by statistical software, version 10 (SPSS, Chicago, Ill).

3. Results

3.1. Patients

Between September 2004 and October 2005, 35 COPD patients were screened after weaning and extubation. Ten patients were not flow limited 1 hour after extubation. Finally, 25 patients with EFL after extubation were prospectively included. The characteristics at inclusion of these patients are given in Table 1.

Table 2 Effect of IPV on the expiratory flow limitation, the airway occlusion pressure, the gas exchange, the RR, and heart rate in COPD patients *

	Before IPV	After IPV	*P*
EFL (%)	65.4 ± 18.2	34.4 ± 24.2	<.05
P0.1 (cm H_2O)	3.9 ± 1.6	2.8 ± 1.1	<.05
pH	7.39 ± 0.01	7.40 ± 0.01	<.05
$Paco_2$ (kPa)	7.35 ± 0.5	7.0 ± 0.3	<.05
Pao_2 (kPa)	8.3 ± 0.4	8.8 ± 0.4	<.05
HCO3- (mmol/L)	33 ± 3	33 ± 3	NS
RR (breaths/min)	22.6 ± 2.3	21.4 ± 1.7	<.05
HR (beats/min)	83 ± 15	85 ± 14	NS
Spo_2 (%)	90 ± 2	93 ± 3	<.05

HR indicates heart rate; Spo_2, pulse oximetry.
* Values are mean ± SD.

3.2. Expiratory flow limitation

Fig. 2 presents the relationship of EFL before and after IPV. Intrapulmonary percussive ventilation has decreased the EFL in 24 of 25 patients and has no effect in 1 patient. However, this COPD patient had presented initially an EFL of only 30%. Table 2 shows the values for the EFL data before and after IPV session. Intrapulmonary percussive led to a statistical significant improvement in EFL, respectively, 65.4% ± 18.2% vs 35.6% ± 22.8 %; $P < .05$. Three patients

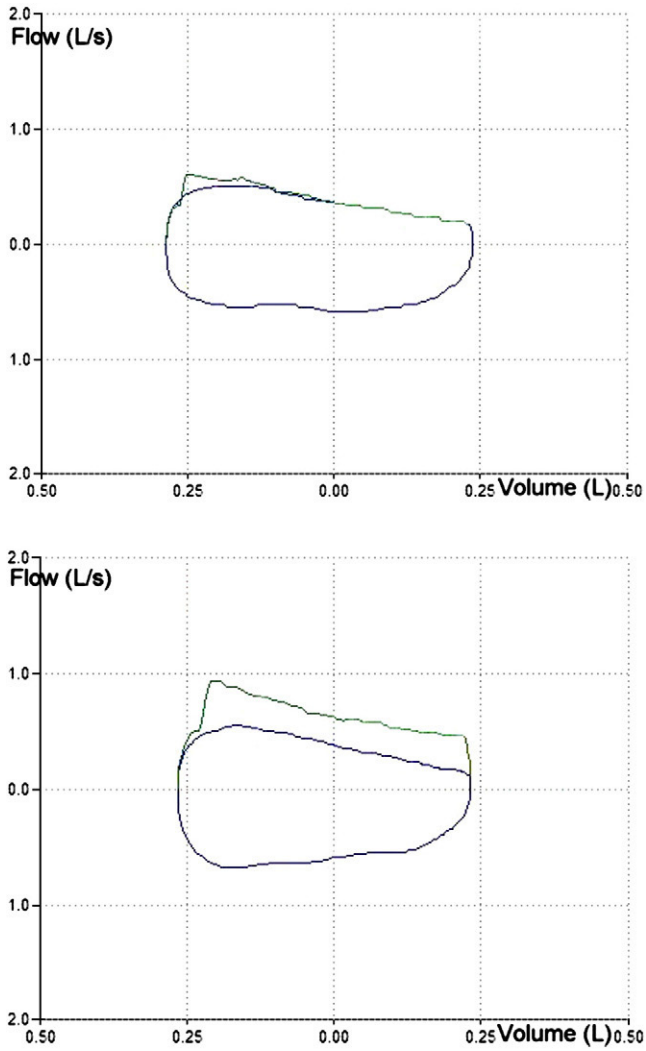

Fig. 3 Effects of IPV on expiratory flow limitation. Top panel: the NEP elicits a transient increase of flow, followed by a rapid return to control values, which indicates presence flow limitation during the control expiration. Bottom panel: in the same patients, compared with the control breath, NEP is associated with a sustained increase in flow, indicating absence of flow limitation after IPV session.

were not flow limited after a 30-minutes session of IPV as shown in Fig. 3.

3.3. Airway occlusion pressure

Fig. 4 presents the relationship of P0.1 before and after IPV. A session of IPV decreased the P0.1 in 22 of 25 patients. For 3 patients, no change was observed. However, for all these 3 patients, the P0.1 was below 3 cm H_2O. Table 2 shows the values for the P0.1 data before and at the end of the IPV session. Intrapulmonary percussive ventilation led to a statistical significant improvement in P0.1, respectively, 3.9 ± 1.6 cm H_2O vs 2.8 ± 1.1 cm H_2O; $P < .05$.

3.4. Gas exchange and RR

As shown in Table 2, IPV led to an improvement in pH, RR, Pa_{O_2}, Pa_{CO_2}, and Sp_{O_2}. Patients received oxygen with nasal cannulae to maintain a target oxygen saturation (recorded by pulse oximetry) of 88% to 92%. Mean oxygen flow was 2.0 ± 0.5 and 2.0 ± 0.5 L/min, respectively, before and during the IPV session (P = NS).

3.5. Sputum production

The results of sputum recovery (mL) assessed during the session of IPV was 20 ± 5 mL.

3.6. Coefficient of variation

In Table 3, mean intrasubject coefficients of variation (±SD) for the EFL and P0.1 are shown before and after IPV.

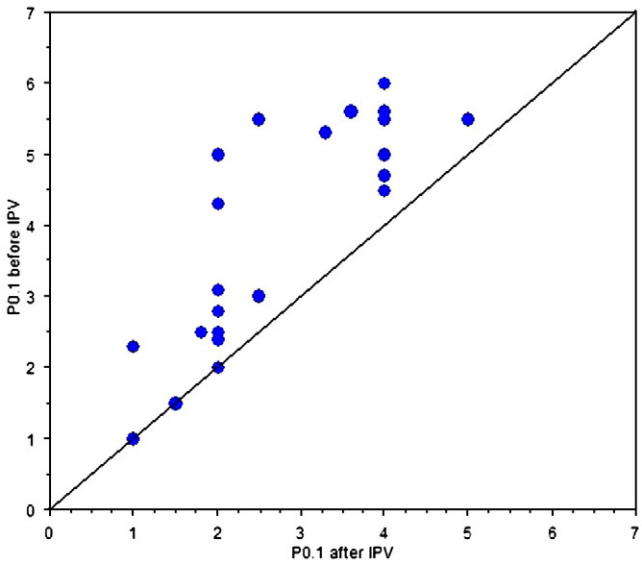

Fig. 4 Relationships of airway occlusion pressure (P0.1; cm H_2O) before and after IPV in 25 semirecumbent COPD patients. Thick line indicates identity line. A session of IPV decreases the P0.1 in COPD patients.

Table 3 Intrasubject coefficients of variation for expiratory flow limitation and airway occlusion pressure before and after IPV *

	Before IPV	After IPV
EFL (%)	0.10 ± 0.05	0.15 ± 0.09
P0.1 (cm H_2O)	0.11 ± 0.09	0.14 ± 0.09

* Values are mean ± SD.

Mean coefficients of variation did not differ for any of the measurements.

4. Discussion

Our results indicate that IPV applied during the spontaneous breathing in COPD patients with EFL brings about a change in the pattern of breathing, a beneficial effect on inspiratory muscle function, and improves gas exchange.

To date, few studies have been published on the IPV use in adult patients with pulmonary disease. However, IPV has been used essentially for the treatment of atelectasis and retained secretions in patient in a stable state, settings for a wide variety of conditions including cystic fibrosis and neuromuscular disease [2-9]. We have recently demonstrated in COPD patients with acute exacerbation and mild acidosis that IPV may prevent further deterioration, avoiding therefore the need for mechanical ventilation [10]. An interesting result of the study was that IPV led to an improvement of both Pa_{O_2} and Pa_{CO_2} [10]. However, we have only hypothesis about the mechanisms of improvement with IPV in COPD patients. Nava et al have demonstrated, in stable COPD, a marked and significant decrease in pressure time product of the diaphragm both per breath and per minute during IPV, due to a direct ventilatory effect [11]. However, it seems difficult to extrapolate these results to more acute COPD patients.

We have showed in the present study that IPV led to a significant decrease in EFL measured by the NEP method. Expiratory flow limitation is associated with abnormally low expiratory flows, which promote dynamic pulmonary hyperinflation phenomenon. This results in an end-expiratory lung volume higher than the relaxation volume and a positive static end-expiratory elastic recoil pressure called intrinsic PEEP (PEEPi). If present in stable COPD patients, PEEPi further increases during acute exacerbation [23]. The presence of dynamic hyperinflation with PEEPi has several clinical implications. Intrinsic PEEP represents a significant inspiratory threshold load, resulting in a marked negative swing in intrathoracic pressure during inspiration and an increased WOB [24]. It can flatten the diaphragm and alter its performance and can cause hemodynamic disturbances [25-29]. In COPD, it has been shown that expiratory flow limitation can be present over most of the tidal expiration and that it is associated with PEEPi [14]. In the study of Valta et al [14], patients with a PEEPi higher than 5 cm H_2O were

flow limited during most of expiration, patients with PEEPi below 5 cm H_2O but above 2.5 cm H_2O were flow limited over the range of 16% to 59% of tidal expiration, and patients with PEEPi below 2.5 cm H_2O were not flow limited. Appendini et al [30] showed that low levels of PEEP significantly unloaded the inspiratory muscles during noninvasive mechanical ventilation in patients with COPD at any level of pressure support ventilation. Any high-frequency ventilation is a positive pressure ventilation, which would increase the airway pressure and induce a "PEEP effect." During the percussive sessions, IPV maintains an intrapulmonary pressure, which serves to stabilize airway patency [1]. To our knowledge, no study supports the contention that IPV provides PEEP therapy. However, we performed a bench study concerning the effect of IPV (added to a conventional ventilator) on pressures and volumes generated [31]. One of these study's results was that IPV generated PEEP. Improvement may occur via the beneficial effects of this intrapulmonary pressure, including the reduction of PEEPi and the amount of work required to breathe, which may allow respiratory muscles to regain efficiency.

In the present study, we showed that IPV reduced significantly the P0.1 in patients with COPD. The data of the literature showed that P0.1 parallels the change in WOB [15,32]. Murciano et al [15] have showed that P0.1 provides a valid and simple index to assess the likelihood of respiratory muscle fatigue in COPD patients with acute respiratory failure. Mancebo et al [32] have showed a significant correlation between individual changes in P0.1 and in WOB when external PEEP was increased. Moreover, no patient exhibited a decrease in P0.1 and a simultaneous increase in WOB. The decrease in P0.1 was concomitant with the decrease in patient's inspiratory WOB. Berger et al [33] found a good correlation between P0.1 and WOB in patients recovering from acute respiratory failure. Partitioning of the transpulmonary WOB into its 3 components (elastic work due to PEEPi, elastic work not due to PEEPi, and resistive wok) showed that only the work related to PEEPi [34] was significantly decreased. We have demonstrated, in the present study, by an indirect way, that IPV could reduce the WOB.

During IPV, we observed a change in the pattern of breathing with a decrease of the RR. It has long been recognized that high-frequency ventilation may have an effect on the control of breathing. Using high-frequency ventilation, Bohn et al [35] reported an apnea, and in anesthetized dogs, Banzett et al [36] observed a lengthening of expiration in place of apnea. It was postulated that the rhythmic change in airway pressure induced a reflex originating from mechanoreceptors. On the other hand, rhythmic vibrations of the intercostals muscles could be a major factor influencing the control of breathing. Afferent activity from intercostal muscle spindles is known to alter the pattern of phrenic nerve activity in anesthetized cats, and rib cage vibration changes the pattern of breathing both in cats and in humans [37,38].

After the session of IPV, the mean sputum production was 20 mL. Airway plugging, which causes bronchial obstruction, impairs lung mechanics and gas exchange. There is a rationale for the use of mucus clearance therapies because even small decreases in airway resistance may be important to achieve recompensation [39]. During high-frequency oscillation, several mechanisms to improve mucus clearance have been studied. An increased mucus/flow interaction could lead to a decrease in the mucus viscoelasticity [40]. Moreover, the changes in airflow with each high-frequency cycle could produce shearing at the air-mucus interface and provide a coughlike force to the mucus layer [40]. For a clinical point of view, improve mucus clearance could be the main objective when IPV is used in COPD patients. To improve ventilation noninvasively and reduce WOB in COPD patients during acute respiratory failure, noninvasive ventilation (NIV) is the "gold standard." However, a number of failures of the technique have been reported, and patients with a frequent need to remove secretions may be difficult to treat with NIV, although this does not constitute an absolute contraindication [41]. In a recent study, Dr Antonaglia and colleagues gave us an important clinical message [42]. A bimodal therapy combining noninvasive pressure support ventilation and noninvasive high-frequency percussive ventilation could be useful to manage successfully COPD patients in acute respiratory failure, especially COPD patients with a frequent need to remove secretions [42,43].

This study has several limits. One possible criticism is the controversial use of P0.1 to measure central drive in patients with COPD. Indeed, P0.1 is influenced by hyperinflation and by resistive and elastic loads. All 3 factors work to underestimate P0.1 in these patients [44]. However, Conti et al [45] have demonstrated that the measurement of P0.1 was not influenced by the presence of PEEPi. Moreover, each patient included in our study was their own control. We used the same method, with the same limitations, to measure the P0.1 before and after IPV. Neither CPAP nor PEEP treats pulmonary hyperinflation, and levels higher than 5 to 7 cm H_2O must be used with caution not to cause a further increase in lung volume. Furthermore, it should be taken into account that application of PEEP does not increase lung volume only in patients with expiratory flow limitation. This makes the assessment of expiratory flow limitation mandatory before PEEP are applied. A falsely positive picture of non-EFL could be due to the presence of leaks. However, the presence of leaks would have been seen in the time-course analysis of the airflow and VT tracings as a sustained decrease in end-expiratory lung volume after NEP application [46]. Inspection of our records excluded this pattern. This study only assessed pre-post data from one 30-min IPV session postextubation with lack of knowledge regarding how long the effects last, how frequently IPV should be applied, and if the effects are significant enough to have an impact on reintubation rates.

Therefore, this study could be a rational for future research in patients after extubation. Successful extubation in

patients receiving mechanical ventilation is dependent on the resolution of the primary process, presence of intact airway reflexes and ability to clear secretions, an intact respiratory drive, ability to exchange gases efficiently, and respiratory muscle strength to meet the work associated with respiratory demand. In COPD patients with EFL, increased airway resistance to airflow and air trapping results in hyperinflation of the chest and inspiratory loading of the respiratory muscles, leading to fatigue. We could hypothesize that the use of IPV could be effective in avoiding further deterioration in expiratory flow-limited COPD in postextubation. A study could be interesting to test this hypothesis. Ferrer et al [47] demonstrated that the early use of NIV averted respiratory failure after extubation in patients at increased risk for this complication. It could be interesting to perform a randomized study with 3 arms: early applications of NIV, early application of IPV, and a combined therapy with early application of both NIV and IPV.

5. Conclusions

In summary, we found that in expiratory flow-limited COPD patients, IPV superimposed on spontaneous breathing improved gas exchange and relieved the load of the inspiratory muscles. This technique can have a possible impact on physiotherapy and care of patients with chronic airflow obstruction.

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