The intra-pulmonary percussive ventilation (IPV) device, designed to improve mucus clearance, was developed by Forrest M Bird in 1979. IPV is a form of high-frequency ventilation that delivers small bursts of high-flow respiratory gas with frequency higher than 1 Hz (usually 4–10 Hz). This causes airway pressure to oscillate between 5 and 35 cm H2O, and the airway walls vibrate in synchrony with these oscillations. Unique to IPV is the Phasitron®, which employs a sliding flow regulator based on the Venturi effect. As found with other high-frequency ventilatory modes (high-frequency oscillation [HFO], high-frequency jet ventilation, etc.), inspiration during IPV is active using small tidal volumes. In contrast to HFO, expiration is passive. This technique may be associated with nebulisation and has the potential to improve secretion clearance. This device is positioned at the patient’s proximal airway. During the percussive bursts of air into the lungs, a continued pressure is maintained, while a high-velocity percussive inflow opens airways and enhances intra-bronchial secretion mobilisation. We will briefly present the clinical and physiological studies concerning IPV in order to demonstrate its usefulness in successfully managing intensive care unit (ICU) patients.

Clinical Studies

Mucus Clearance Device

To date, few studies have been published on the use of IPV in adult patients with pulmonary disease. IPV has been used primarily for the treatment of atelectasis and retained secretions in patients in a stable state, as occurs in a wide variety of conditions, including cystic fibrosis and neuromuscular disease. Ravez et al. studied the use of IPV in a small group of adults with chronic bronchitis. They found that total lung clearance of radioaerosol was enhanced with IPV therapy, but it was unclear to what extent IPV-stimulated cough contributed to the observed benefit. In addition, small pilot studies with the IPV device have shown it to be useful for the relief of lobar atelectasis and increased sputum production in patients with chronic obstructive pulmonary disease (COPD).

Patients with Chronic Obstructive Pulmonary Disease

Rationale

Patients hospitalised for acute exacerbations of COPD with rapid clinical deterioration should be considered for non-invasive positive-pressure ventilation (NPPV) to prevent further deterioration in gas exchange and respiratory workload as well as the need for endotracheal intubation. The addition of NPPV to standard therapy in patients with acute exacerbations of COPD significantly decreases the rate of endotracheal intubation, leads to a shorter hospital stay and decreases inpatient mortality rates. However, subgroup analysis performed in a recent review showed that these beneficial effects occurred only in patients with severe exacerbations, not in those with milder ones. Enhancing ventilation by unloading fatigued ventilatory muscles is an important treatment goal in the case of acute exacerbation of COPD that is complicated by respiratory failure, and this objective can be achieved by NPPV. On the other hand, airway inflammation, bronchospasm and the increase in sputum volume are constant in these patients and are responsible for an increase in airway resistance and air trapping.

Let us recall that patients unlikely to benefit from NPPV include those with excessive secretions. In addition, excessive secretions can lead to NPPV failure and the need for intubation and invasive mechanical ventilation. In such situations, methods of treatment directed against the onset of decompensation are attractive in theory, although the benefits of mucus clearance therapies have been regularly challenged. Two studies have shown that chest physiotherapy based on a mucus clearance strategy could represent a useful therapeutic option in COPD patients. It was demonstrated in the first study that chest physiotherapy using a positive expiratory pressure mask in patients with mild acidosis requiring NPPV with pressure support could produce benefits in sputum clearance and could reduce the amount of time for which the patient requires NPPV. Wolkove et al. reported significant improvement in lung function after inhaled bronchodilator therapy. The prior use of a mucus clearance device, compared with a sham mucus clearance device, improved the subsequent bronchodilator response in patients with stable COPD.

Acute Exacerbations with Mild Respiratory Acidosis

In a randomised, controlled study, it was hypothesised that the use of IPV could prove effective in avoiding further deterioration in patients...
with acute exacerbations of COPD with mild respiratory acidosis.\textsuperscript{18} Thirty-three patients with exacerbations of COPD with a respiratory frequency of ≥25/min, a partial pressure of carbon dioxide (PaCO\textsubscript{2}) >45 Torr and 7.35 ≤ pH ≤ 7.38 were included in the study. Patients were randomly assigned to receive either standard treatment (control group) or standard treatment plus IPV (IPV group). The IPV group underwent two 30-minute sessions through a full face-mask that were performed by a chest physiotherapist. The therapy was considered successful when both worsening of exacerbation and a decrease in pH to under 7.35 (which requires non-invasive ventilation) were avoided. The session of IPV was well tolerated. Thirty minutes of IPV led to a significant decrease in respiratory rate, an increase in PaO\textsubscript{2} and a decrease in PaCO\textsubscript{2} (p<0.05). Exacerbation worsened in six out of 17 patients in the control group versus zero out of 16 in the IPV group (p<0.05). The hospital stay was significantly shorter in the IPV group than in the control group (6.8±1.0 versus 7.9±1.3 days; p<0.05).

**Bi-modal Therapy in Patients with Acute Exacerbation**
Dr Antonaglia and colleagues\textsuperscript{19} evaluated the effect of IPV by mouthpiece during NPPV with helmet in patients with acute exacerbation of COPD. The authors conducted a randomised clinical trial comparing three groups of patients with exacerbation of COPD. Two groups were prospectively studied: 20 patients treated with NPPV with helmet and ‘conventional’ respiratory physiotherapy, and 20 patients treated with NPPV with helmet and two daily sessions of IPV. In addition, 20 patients non-invasively ventilated with face-mask were included retrospectively. The rates of intubation and complications, such as sepsis and pneumonia, were comparable between groups. A benefit in favour of the NPPV-helmet plus IPV group was found in terms of a reduction in the duration of ventilatory treatment and ICU stay and improvements in gas exchange at ICU discharge. Improvement in gas exchange and other physiological variables was found after the first IPV session. To strengthen the value of these data, because two daily sessions of IPV were used in one group in place of the conventional respiratory physiotherapy used in the other group, it should have been relevant to measure the selected physiological variables not only after IPV in this group but also after conventional respiratory physiotherapy in the other group prospectively studied. The original and the most important clinical message of the study by Dr Antonaglia and colleagues is that bi-modal therapy combining NPPV and non-invasive IPV can be useful in successfully managing patients with acute exacerbation of COPD.

**Tracheostomised Patients**
In a randomised, multicentre trial, Dr Clini and colleagues evaluated the addition of IPV to standard chest physiotherapy to improve gas exchange and lung mechanics in tracheostomised patients.\textsuperscript{20} Forty-six tracheostomised patients were assigned to two treatment groups performing chest physiotherapy (control) or percussive ventilation for 10 minutes twice a day in addition to chest physiotherapy (intervention). Arterial blood gases, PaO\textsubscript{2}/PaCO\textsubscript{2} ratio and maximal expiratory pressure were assessed every fifth day for 15 days. Treatment complications that showed up in one month of follow-up were recorded. At 15 days the intervention group had a significantly better PaO\textsubscript{2}/PaCO\textsubscript{2} ratio and higher maximal expiratory pressure; after follow-up this group also had a lower incidence of pneumonia. The addition of percussive ventilation to the usual chest physiotherapy regimen in tracheostomised patients could improve gas exchange and expiratory muscle performance, and also reduces the incidence of pneumonia.

**How Does Intra-pulmonary Ventilation Improve the Clinical Status of Patients?**

**Hypothesis**
It seems that IPV can improve gas exchange in selected patients.\textsuperscript{18–20} The mechanisms of improvement with IPV do not seem to be clearly elucidated. Potential mechanisms of action include improved mucus clearance, enhanced alveolar recruitment and direct high-frequency oscillatory ventilation-like effect.

**Mucus Clearance**
During HFO, several mechanisms to improve mucus clearance have been studied.\textsuperscript{21,22} An increased mucus/flow interaction could lead to a decrease in the mucus viscoelasticity. Moreover, the changes in air flow with each high-frequency cycle could produce shearing at the air–mucus interface and provide a cough-like force to the mucus layer.\textsuperscript{21,22}

**High-frequency Oscillatory-like Effect**
Considering the effect of HFO ventilation on gas exchange and breathing pattern, one can hypothesise similar effects with IPV. Indeed, any high-frequency ventilation is a positive-pressure ventilation that would increase the airway pressure, induce a positive end expiratory pressure (PEEP) effect and thus improve oxygenation.\textsuperscript{23} Two mechanisms explain gas transport with respect to the clearance of CO\textsubscript{2} during HFO: convection and molecular diffusion. HFO maximises CO\textsubscript{2} removal primarily through facilitated diffusion.\textsuperscript{23} The theoretical increase in mean airway pressure observed with IPV, however, is less important than the increase in mean airway pressure observed with HFO. Similarly, the frequency used in HFO, generally set at 5Hz, is more important than in IPV.

**Positive End Expiratory Pressure Effect**
Any high-frequency ventilation induces a PEEP effect that can increase lung volume. However, according to the ‘waterfall theory’, if intrinsic PEEP (PEEPi) is the result of expiratory flow limitation (EFL), application of extrinsic PEEP should decrease the pressure gradient between the mouth and alveoli at the end of expiration. This should be achieved without further hyperinflation. However, O’Donoghue et al.\textsuperscript{24} found that only high levels of continuous positive airway pressure reduced PEEPi and indices of muscle effort in patients with severe but stable COPD, but only at the expense of a substantial increase in lung volume.

**Physiological Studies**

**Intra-pulmonary Ventilation and Inspiratory Effort**
Dr Nava and colleagues performed a study aimed at assessing the physiological response to IPV on the breathing patterns of patients, inspiratory effort, lung mechanics and tolerance to ventilation.\textsuperscript{25} Ten COPD patients underwent randomised trials of IPV through a face-mask at different pressure/frequency combinations (1.2bar/250cycles/min; 1.8/250; 1.2/350; 1.8/350), separated by return to baseline. In five patients they also compared the physiological changes of IPV with those obtained during NPPV. Minute ventilation did not vary among the trials, but tidal volumes were significantly greater during 1.2/250, 1.2/350 and 1.8/350 compared with spontaneous breathing (SB). The pressure time product of the diaphragm per minute (PTPdi/min) estimate of the diaphragm oxygen
expedition was also significantly reduced during 1.2/250 and 1.8/250 (209cmH2O.s/min for SB versus 143 and 125 for 1.2/250 and 1.8/250, respectively; p<0.05), as well as dynamic intrinsic end expiratory pressure. A similar reduction in PTPdi/min was also obtained during NPPV. Tolerance to ventilation and oxygen saturation was satisfactory and did not change during the different trials. IPV was able to guarantee adequate ventilation while inducing a significant unloading of the diaphragm during the ‘low-frequency’ trials.25

Intra-pulmonary and Expiratory Flow Limitation

In a study, published only in abstract form, we evaluated the effect of IPV on EFL in COPD patients.24 The aim of this prospective study was to select, after weaning and extubation, COPD patients with measured by the negative expiratory pressure (NEP) method and to assess, in these patients, the short-term (30-minute) physiological effects of a session of IPV. All COPD patients who were intubated and needed weaning from mechanical ventilation were screened after extubation. The patients were placed in a half-sitting position and breathed spontaneously. The EFL and the airway occlusion pressure after 0.1s (p=0.1) were measured at the first hour after extubation. In COPD patients with EFL, an IPV session of 30 minutes was performed by a physiotherapist accustomed to the technique. EFL, gas exchange and PO.1 were recorded at the end of the IPV session. Among 35 patients studied after extubation, 25 patients presented an EFL and were included in the study. IPV led to a significant improvement in EFL (p<0.05). Three patients were not expiratory-flow-limited after IPV. IPV led to a significant decrease in PO.1 (p<0.05). We found that in EFL COPD patients, IPV superimposed on SB improved gas exchange and relieved the load of the inspiratory muscles.

Bench Study

IPV has been used during SB, but is also proposed for use in addition to conventional ventilation. We designed a bench study with three resistances and compliances to assess the effect of IPV on tidal volume generated by conventional ventilation, PEEP and maximal alveolar pressure during volume-controlled ventilation.21 IPV was connected on the inspiratory line of a ventilator using a heater humidifier. Maximal alveolar pressure and PEEP were recorded inside the test lung. Tidal volume was inferred using flow integration at Y-piece. Resistances of 5, 20 and 50cm of H2O/l/s and compliance of 20, 50 and 100ml/cm of H2O were tested on a Michigan test lung. Three pauses (0, 0.2 and 0.4s) were used with two driving pressures of 12 and 18cm H2O. No PEEP was set on conventional ventilation. Results are different between patients treated with and without IPV. PEEP, tidal volume and maximal alveolar pressure all increased with IPV. Pressures (maximal alveolar pressure and PEEP) and volumes increased due to IPV are strongly dependent on resistance and compliance. This bench study, published in abstract form and presented in the European Society of Intensive Care Medicine of Berlin, may confirm a IPV effect and real ventilatory effect of IPV.

Conclusion

It can be said that IPV will in particular benefit patients with excessive secretions and a frequent need to remove them. Indeed, patients with a repeated need to remove secretions may be difficult to treat with NPPV. However, IPV is not exclusively suitable for patients presenting with acute exacerbation of COPD. The technique should be evaluated in other types of acute respiratory failure, including respiratory distress after extubation, where the interest of NPPV is challenged and where an excess of secretions is a frequent cause of extubation failure.

Further studies are needed to confirm the advantage of adding IPV sessions to the strongly recommended practice of NPPV and to improve the selection of those patients likely to benefit from IPV, before being able to adopt strength through unity for the non-invasive challenges.

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