Noninvasive ventilation in patients with acute cardiogenic pulmonary edema

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Abstract

The term noninvasive ventilation (NIV) encompasses two different modes of delivering positive airway pressure, namely continuous positive airway pressure (CPAP) and bilevel positive airway pressure (bilevel-PAP). The two modes are different since CPAP does not actively assist inspiration whereas bilevel-PAP does. Bilevel-PAP is a type of noninvasive ventilation that helps keep the upper airways of the lungs open by providing a flow of air delivered through a face mask. The air is pressurized by a machine, which delivers it to the face mask through long, plastic hosing. With bilevel-PAP, the doctor prescribes specific alternating pressures: a higher pressure is used to breathe in (inspiratory positive airway pressure) and a lower pressure is used to breath out (expiratory positive airway pressure). Noninvasive ventilation has been shown to reduce the rate of tracheal intubation. The main indications are exacerbation of chronic obstructive pulmonary disease and acute cardiogenic pulmonary edema (ACPE). This last is a common cause of respiratory failure with high incidence and high mortality rate. Clinical findings of ACPE are related to the increased extra-vascular water in the lungs and the resulting reduced lung compliance, increased airway resistance and elevated inspiratory muscle load which generates a depression in pleural pressure. These large pleural pressure swings are responsible for hemodynamic changes by increasing left ventricular afterload, myocardial transmural pressure, and venous return. These alterations can be detrimental to patients with left ventricular systolic dysfunction. Under these circumstances, NIV, either by CPAP or bilevel-PAP, improves vital signs, gas exchange, respiratory mechanics and hemodynamics by reducing left ventricular afterload and preload. In the first randomized study which compared the effectiveness of CPAP plus medical treatment *vs* medical treatment alone, the CPAP group showed a significant decrease in its 48 h mortality rate and no patient required endotracheal intubation. This result was successively confirmed in many reviews and meta-analyses.

There are still unanswered questions regarding the role of NIV in ACPE: this review aims to support clinicians treating patients in emergency departments with various presentations of ACPE. It also covers recent developments in the treatment of ACPE and associated evidence.

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What is the role of noninvasive ventilation in diastolic acute cardiogenic pulmonary edema?

The diagnosis of diastolic heart failure can be made on the basis of clinical evidence of heart failure in a patient who has a normal left ventricular ejection fraction and no valvular abnormalities.[1-13] In patients with ACPE due to diastolic dysfunction, the role of noninvasive ventilation is poorly understood. Recently, Agarwal and colleagues[14] suggested that CPAP benefits only patients with systolic heart failure, by decreasing both preload and afterload. In patients with diastolic dysfunction, positive pressure therapy may compromise venous return and decrease left ventricular end-diastolic (LVED) volume, thus further limiting stroke volume and hence cardiac output because of the steep curve for left diastolic ventricular pressure in relation to volume. The final output is a deterioration in hemodynamics. Consequently, caution must be used because patients with diastolic heart failure are sensitive to preload reduction and may develop hypotension or prerenal azotemia.[13] Contrastively, two preliminary studies[15,16] have shown that CPAP seems to be safe and effective to treat patients with diastolic ACPE. The benefits of CPAP are probably due to the fact that positive pressure reduces not only venous return but also left ventricular transmural pressure in acute diastolic dysfunction where left ventricular afterload is increased.[17] Moreover, chronic diastolic heart failure is different from diastolic ACPE, where LVED volume is normal and not low.[18] Finally, the risk of developing hypotension or azotemia might be greater in patients with a systolic dysfunction rather than diastolic heart failure, where cardiac output is already compromised. These findings led to daily use of NIV in diastolic ACPE. When we treat patients for diastolic heart failure with NIV, it is necessary to be confident with ventilators and monitors and to have a skilled and experienced staff.

Does bilevel-positive airway pressure increase the incidence of acute myocardial infarction?

One of the main results in the study by Mehta *et al*.[19] was the possible association between the use of bilevel-PAP and increased acute myocardial infarction (AMI) in patients with ACPE. This result may have been due to the inappropriate enrollment of patients who possibly had acute coronary syndromes before treatment. Nonetheless, in the following years, clinical practice still questioned about using bilevel-PAP to treat patients with ACPE. In contrast with the previous study, Bellone *et al*.[20] used a combination of creatine phosphokinase and its isoenzyme MB plus myoglobin and a more specific marker, cardiac troponin, in order to detect AMI correctly. Furthermore, upon admission to the emergency department, the patients who presented chest pains, abnormal electrocardiograms and elevated cardiac enzymes were excluded from the study. It was concluded that there was no difference in the occurrence of AMI between the two modalities of treatment. Subsequently, two papers definitively showed that bilevel-PAP is as safe as CPAP in relation to the incidence of AMI.[9,21] Moreover, NIV was effective in patients with cardiogenic pulmonary edema of all etiologies, including AMI.[22] Therefore, we can affirm that bilevel-PAP is not a cause of acute coronary syndrome but rather acute coronary syndrome is one of the causes of ACPE. This understand-

ing has led to changes in the management of ACPE so that CPAP and bilevel-PAP represent first-line therapies.

Is bilevel-positive airway pressure better than continuous positive airway pressure in acute hypercapnic pulmonary edema?

It is well known that bilevel-PAP is more effective than CPAP in unloading respiratory muscles in ACPE.[23] Consequently, we can hypothesize that in hypercapnic patients with signs of respiratory distress, such as patients with ACPE, the addition of pressure support to CPAP might improve respiratory pumping and alveolar ventilation, thereby improving the respiratory pattern and arterial carbon dioxide tension ($PaCO_2$) more than solely using CPAP. Surprisingly, a recent paper[24] comparing CPAP and noninvasive pressure support ventilation (NIPSV) in hypercapnic ACPE patients, showed that NIPSV is as effective as CPAP regarding resolution time. The main physiological mechanism of ventilator pump failure in patients with ACPE might be related to an increase in energy demands by inspiratory muscles.[25] Increasing energy demands are due to an increase in the work required for breathing such as when the inspiratory muscles must compensate for the elastic load (alveolar congestion and consequently a decreased lung compliance) and hyperventilation (shallow breathing). Therefore, the main hypothesis is that in patients with hypercapnic ACPE, positive airway pressure produces a favorable hemodynamic effect by reducing *pre*- and afterload on the left ventricle, leading to an improvement in lung compliance by reducing pulmonary congestion.[26] The increased lung compliance eases the work of breathing and the load imposed on the respiratory muscles. The result is an improvement in gas exchange, respiratory mechanics, and alveolar ventilation, with a significant reduction in $PaCO_2$. In sum, the addition of pressure support to CPAP does not seem to offer any additional treatment advantages.

The role of noninvasive ventilation in patients with hypotensive acute cardiogenic pulmonary edema

A recent study investigated mortality in ACPE patients treated with CPAP in order to identify clinical characteristics associated with mortality.[26] Normal-to-low blood pressure was one of the predictors of increased risk of in-hospital mortality. The explanation for the increased mortality in these patients is poorly understood. A previous study by Masip *et al.*[3] showed that systolic blood pressure below 140 mmHg was an independent predictor for intubation in patients affected by ACPE. Actually, we do not know whether an increased intrathoracic pressure due to positive airway pressure might compromise venous return and cardiac output and consequently have a worse outcome, or whether low pressure is a poor prognostic index regardless of the application of NIV. In any case, considering the respiratory benefits of CPAP, the use of CPAP in ACPE hypotensive patients seems to be safe. Caution should be reserved about the application of bilevel-PAP in ACPE and arterial hypotension.

Does noninvasive ventilation have an effect on mortality?

Previous guidelines and meta-analyses have shown a beneficial effect of NIV on mortality.[10,11]

In contrast with the previous studies, a recent paper by Gray *et al.*[27] suggests that NIV in ACPE encourages more rapid improvements in patients suffering from respiratory distress and metabolic disturbances than standard oxygen therapy does, but has no effect on short-term mortality.

In this study, there was considerable cross-contamination among the treatment groups. Furthermore, the competency level with NIV use was highly variable between the centers which took part in the trial. Notably, the intubation rates were very low in this trial indicating a less severely disabled patient population. The hypothesis that NIV was not going to be better than oxygen therapy was plausible because the patients in the study were not clinically compromised.

The severity of disability in patients suffering from acute heart failure (AHF) is often unclear. It is well known that ACPE is the most frequent pathophysiologic class of AHF syndromes.[28,29] It is accompanied by severe respiratory distress, such as a respiratory rate >30 breaths/min, use of accessory respiratory muscles and a peripheral oxygen saturation (SpO_2) lower than 90% with oxygen supplementation >5l/min through a bag reservoir mask. Patients typically exhibit impairments in gas exchange characterized by hypercapnia and hypoxemia. Vice versa, patients admitted to the emergency room because of acute decompensated heart failure complain of progressive worsening of the clinical signs over several days. They may have orthopnea, diminished diuresis, edema in their legs and only mild hypoxemia with normocapnia or hypocapnia.[30] In these patients, respiratory distress is rarely present. This difference between ACPE and decompensated heart failure may have a significant impact on therapeutic management. Noninvasive ventilation might have a prominent role in the treatment of ACPE because of its effects on hemodynamics, gas exchange and respiratory mechanics. A meta-analysis of Weng *et al*. still supported the use of NIV for patients with ACPE and showed that continuous positive airway pressure reduces mortality more in patients with ACPE secondary to acute myocardial ischemia or infarction.[31]

Continuous positive airway pressure compared to bilevel positive airway pressure in patients with acute cardiogenic pulmonary edema: which is best?

Recent systematic reviews have not found bilevel-PAP to be better than CPAP in terms of avoiding intubation or lowering mortality.[10,11,32] In the majority of studies over the last 10 years, there is no evidence supporting the superiority of one modality over the other. The only discrepancy present in favor of bilevel-PAP regards the rapid improvement of gas-exchange (more rapid decrease in $PaCO_2$) in comparison to CPAP, without any significant differences in the final outcome parameters.[33] Therefore, from a clinical perspective, using CPAP or bilevel-PAP is equivalent, and the debate about the superiority of one ventilatory mode over the other is anachronistic. The choice of a ventilatory mode should rather be based on factors such as the clinical setting (*pre*-hospital, emergency room, intensive care unit or intermediate respiratory care unit) and the level of comfort and experience of the staff with the chosen mode. In emergency departments, where NIV is often initiated, the best modality of delivering NIV is not evident: CPAP is easier and cheaper than bilevel-PAP, which in turn is faster (in terms of shorter resolution time) than CPAP when timing is critical.

Helmet *versus* face-mask in acute cardiogenic pulmonary edema: which, when and where

The helmet is an interface conceived for applying CPAP.[34,35] In the last decade, the hel-

met was proposed for delivering bilevel-PAP, but three studies[36-38] have clearly shown that helmets are mechanically less effective than face-masks in delivering bilevel-PAP in healthy volunteers as well as in patients. The main reason is the high or elevated compliance of the helmet, which behaves like a damper interposed between the patient and the ventilator, thus weakening and delaying the inspiratory pressure support. In order to increase the effectiveness of helmet bilevel-PAP, some studies proposed to apply a higher positive end expiratory pressure and pressure support together with faster pressurization; however, the results were not encouraging.[39,40] Recently, preliminary data by Mojoli *et al.*[41] showed that an optimized set-up for helmet bilevel-PAP, which limits device compliance and ventilator circuit resistance as much as possible, may be highly effective in improving pressure support delivery and patient-ventilator interaction. Simultaneously, it is widely accepted that the helmet should be the best interface with a very high tolerability when prolonged and continuous assistance is needed, for instance in intensive care unit or during *pre*-hospital treatment of presumed ACPE, where it has been shown to be feasible, efficient and safe.[37,42,43] In contrast, in the fast pace of emergency departments where the ventilation time of ACPE patients is short and patients are frequently old with high comorbilities including chronic obstructive pulmonary disease, the best interface for delivering bilevel-PAP seems to be the face-mask. However, as for the comparison between CPAP and bilevel-PAP modalities of NIV, the choice of ventilatory interfaces should be based on factors such as staff experience, habit and individual patient's choice.

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