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REVIEW

NONINVASIVE MECHANICAL VENTILATION IN THE TREATMENT OF ACUTE CARDIOGENIC PULMONARY EDEMA

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Current literature was searched by using the MEDLINE database to find consistent evidence regarding the use of noninvasive mechanical ventilation in patients with acute cardiogenic pulmonary edema. 18 studies demonstrating that noninvasive ventilation applied by continuous positive airway pressure (CPAP) or bilevel positive airway pressure (bilevel-PAP) is safe, and that the two approaches have similar effects and are effective in preventing endotracheal intubation in patients with respiratory distress of cardiac origin, were found. The results support the concept that positive intrathoracic positive pressure must be seen as a nonpharmacological form of treatment of acute pulmonary edema rather than only a supportive measure.

KEYWORDS: Pulmonary edema. Respiratory failure. Artificial respiration. Mechanical ventilator. Respiratory therapy.

INTRODUCTION

Acute cardiogenic pulmonary edema is a common cause of acute respiratory distress among patients presenting to the emergency departments and intensive care units. Hypoxemia, sometimes associated with hypercapnia, is a common feature in the clinical presentation of acute cardiogenic pulmonary edema. Standard medical therapy includes diuretics, vasodilators, and inotropics, and it results in rapid improvement of the respiratory symptoms. In this context, oxygen delivered through a face mask is the basic respiratory support. Although many patients respond rapidly to standard treatment, a significant number progress to severe respiratory distress leading to endotracheal intubation with its associated complications.[1–9]

Positive pressure applied in the airway can relieve the respiratory failure and also improve the cardiovascular function, especially in severe cardiac-dysfunction patients.[10,11] These multiple actions of positive pressure can act synergically in the treatment of patients with respiratory distress and impaired cardiac function.[1–9,12] Noninvasive use of positive pressure delivered through a face mask reduces the need for endotracheal intubation in patients with acute cardiogenic pulmonary edema.[1–9]

There are 2 modes for applying noninvasive positive pressure: continuous positive airway pressure (CPAP) (ie, constant pressure during the whole respiratory cycle) and bilevel positive airway pressure (bilevel-PAP) (ie, adding to a continuous expiratory pressure an inspiratory support pressure above the expiratory pressure to reduce the inspirational respiratory work). In this report, we review the main physiological characteristics of CPAP and bilevel-PAP on respiratory and cardiovascular function as well as the evidences to their use in the clinical setting.

CARDIOVASCULAR AND RESPIRATORY PHYSIOLOGY

Cardiovascular effects of positive pressure ventilation are primarily modulated by the effects on preload and

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afterload. Venous return can be reduced when positive pressure ventilation is applied in hypovolemic patients, resulting in reduced cardiac output. In normovolemic patients, the pulmonary insufflation raises the abdominal pressure, and thus it raises the mean circulatory pressure, keeping the venous flow stable.[13] Pleural pressure augmentation raises the pericardial pressure and reduces the myocardial transmural pressure as well as the ventricle diameter,[14] resulting in low ventricle surface tension and afterload, mainly in patients with a dilated ventricle.[10,11,15] This anatomo-physiological alteration is associated with a reduction in regurgitant flow through the mitral valve.[11]

Airway positive pressure has well-known effects on respiratory function in patients with cardiogenic pulmonary edema. The improvement in pulmonary compliance and shunt are associated with alveolar recruitment.[10,15] Reduction of inspiratory load is associated with the improvement of pulmonary compliance and the inspiratory pressure support when bilevel-PAP is applied.[10,15] A CPAP of 10 cm H_2O reduces the pleural pressure swing and improves tidal volume and PaO_2/FiO_2 ratio during the spontaneous ventilation in patients with heart failure; these effects are more striking when using bilevel-PAP ventilation with an expiratory pressure (EPAP) of 10 cm H_2O and inspiratory pressure (IPAP) of 15 cm H_2O.[10,15]

CLINICAL USE OF NONINVASIVE POSITIVE PRESSURE VENTILATION IN ACUTE CARDIOGENIC PULMONARY EDEMA

Continuous possitive airway pressure (CPAP)

Two randomized studies have shown an improvement in hypoxemia, hypercapnia, and endotracheal intubation rate in patients with acute cardiogenic pulmonary edema using CPAP as compared to treatment with standard respiratory support (ie, oxygen delivered by mask).[1,2,9] These results have been reproduced in small physiological trials[5–7,9,16] as well as in other clinical trials.[5,6,9] The impact of CPAP on mortality in patients with acute cardiogenic pulmonary, was reduced in some trials[5,7,9] but not in others.[1,2]

The different results obtained may be related to methodology, including patient selection and levels of CPAP. One interesting point is that in the first randomized trial,[1] the patients enrolled were severely hypercapnic. In addition, the improvement in $PaCO_2$ after 30 minutes was significantly greater in the CPAP group (58 ± 8 to 46 ± 4 mm Hg) than in the oxygen group (64 ± 17 to 62 ± 14 mm Hg).

The levels of CPAP used in the trials varied, but most of them used 10 cm H_2O.[1,5,7] Alternatively, in one trial, the level of CPAP was titrated from 2.5 cm H_2O to 12.5 cm H_2O over 2.5 hours.[2] Park et al[6] showed that 5 cm H_2O of CPAP was not superior to conventional therapy in terms of tracheal intubation. Taken together, the target CPAP pressure for patients with acute pulmonary edema should be 10 cm H_2O for most patients.

Bilevel positive airway pressure (bilevel-PAP)

The effectiveness of the use of bilevel-PAP in the treatment of acute cardiogenic pulmonary edema has been tested in 6 clinical trials, with different results.[3–8] These differences may be related to different methodologies. Comparing bilevel-PAP with oxygen, Masip et al,[4] Nava et al,[8] Park et al,[5,6] and Crane et al[7] have shown physiological improvement and reduction in endotracheal intubation rates. On the other hand, comparing bilevel-PAP and CPAP, Park et al[5] and Crane et al[7] did not find physiological or clinical improvement. Mehta et al[3] found physiological improvement but with a rise in myocardial infarction rate. In a pilot study comparing bilevel-PAP and CPAP, Park et al[6] found that 5 cm H_2O of CPAP was not associated with avoidance of endotracheal intubations, but bilevel-PAP with an expiratory pressure (EPAP) of 3 cm H_2O and inspiratory pressure (IPAP) of 8 cm H_2O was.

The various levels of airway pressure used in those trials might explain some result differences among them. Nava et al,[8] in a multicenter European trial, enrolled 130 patients, 65 to oxygen support treatment and 65 to bilevel-PAP with a mean EPAP of 6.1 ± 3.2 cm H_2O and a mean IPAP of 14.5 ± 21.1 cm H_2O over 11.4 ± 3.6 hours. In this trial, normocapnic ($PaCO_2$ d•45 mm Hg) patients using bilevel-PAP showed no improvement in endotracheal intubation and mortality rates, whereas, hypercapnic ($PaCO_2$ > 45 mm Hg) patients had a reduction in endotracheal intubation rates (oxygen, 29% vs bilevel-PAP, 6%. P = 0.015). This finding was similar to that of Masip et al,[4] where hypercapnic patients had a substantial physiological and probably clinical improvement when compared to normocapnic patients using similar airway pressures to those used by Nava et al.[8] The incidence of hypercapnic patients was 49% in the study by Nava et al[8] study, and it was 50% in the study by Masip et al.[4] In contrast, Park et al [5] found that even normo- or hypocapnic patients can experience beneficial effects in physiological and clinical terms from bilevel-PAP ventilation in an acute cardiogenic pulmonary edema setting, when compared to oxygen-alone treated patients. In the last study, 80 patients were enrolled, 26 to receive oxygen only, 27 to receive CPAP (10 cm H_2O), and 27 to receive bilevel-PAP (EPAP = 10 cm H_2O and IPAP = 15 cm H_2O); 19% of these patients were hypercapnic. The endotracheal intubation rate was 42% in the

oxygen-alone group and 7% in bilevel-PAP group. There are some differences in the populations enrolled to the studies of Nava et al[8] and Park et al,[5] but the most striking difference was the EPAP level used (5 cm H_2O vs 10 cm H_2O). The real importance of the effect of EPAP on the respiratory and cardiovascular function is not yet clear in this setting, but it should be considered that 10 cm H_2O of EPAP can be safe and maybe more useful for supporting and treating acute cardiogenic pulmonary edema patients.[5] An inspiratory support pressure of 5 cm H_2O seems to be sufficient to relieve the respiratory distress and improve hemodynamic and respiratory variables.[5,10,15]

In a study comparing bilevel-PAP and high-dose nitrate therapy, Sharon et al[17] found an increased myocardial infarction rate in the bilevel-PAP group. However, this study did not have an adequate control group, the rate of myocardial infarction was much higher than the other cited studies,[4–8,16,18,19] and the diagnostic criteria of myocardial infarction was poor.

There is no conclusion about the mortality rate in acute cardiogenic pulmonary edema patients treated with bilevel-PAP when compared to conventional treatment. In fact, only 1 study, performed by Park et al,[5] has shown a reduction of mortality associated with bilevel-PAP at the 15-day follow-up. Other studies, such as those of Masip et al,[4] Nava et al,[8] and Crane et al[7] did not find a reduction in mortality rates, although there were different strategies in the respiratory support of patients.

CPAP VS BILEVEL-PAP

The use of CPAP or bilevel-PAP as a choice to treat and support acute pulmonary edema patients has recently been explored and reported. Mehta et al[3] studied 27 patients, with 13 enrolled to receive CPAP at 10 cm H_2O, and 14 enrolled to receive nasal bilevel-PAP with an EPAP of 5 cm H_2O and an IPAP of 15 cm H_2O; they found an improvement in 30 minutes in the bilevel-PAP–treated group that was more accentuated in physiological outcomes such as heart rate, respiratory rate, PaO_2, and $PaCO_2$. In clinical terms, there was an improvement in the dyspnea score, but the study had to be prematurely stopped due to a high incidence of myocardial infarctions in the bilevel-PAP group. The causes of this unexpected event were not clarified. The authors suggested that the excessive intrathoracic pressure associated with bilevel-PAP was responsible for the adverse cardiovascular effects. However, when taking into account that the patients had presented with chest pain in the emergency room, it seems that in the 71% patients who were randomized to be treated with bilevel-PAP and presented CK-MB elevations, the myocardial infarction may have actually been the cause of the pulmonary edema and not the result of bilevel-PAP ventilation. More recently Park et al,[5,6] Cross et al,[18] and Crane et al[7] have found that CPAP was similar to bilevel-PAP in physiological and clinical outcomes, including a similar incidence of acute myocardial infarction rate. However, in the last study, CPAP was associated with an improvement in in-hospital survival.[7]

Facing hypercapnic acute cardiogenic pulmonary edema patients, the rationale to use bilevel-PAP is strong.[3,1015] However, in contrast to the studies of Masip et al[4] and Nava et al,[8] where the hypercapnic patients seemed to be better supported by bilevel-PAP, the study performed by Bersten et al,[1] a CPAP of 10 cm H_2O was also effective in reducing the need for endotracheal intubation. Accordingly, Bellone et al,[19] in a randomized, prospective study, found with high statistical power (0.8) that 18 hypercapnic acute cardiogenic pulmonary edema patients ventilated with a CPAP of 10 cm H_2O had a similar endotracheal intubation requirement to that of 36 patients ventilated with bilevel-PAP with an EPAP = 5 cm H_2O and pressure support sufficient to achieve 400 mL of tidal volume (CPAP = 5.5% vs bilevel-PAP = 11.1%, $P = 0.5$). The odds ratio graph of endotracheal intubation requirements of all studies comparing CPAP and bilevel-PAP are shown in Figure 1.

The issue of acute myocardial infarction was better studied in the trial of Bellone et al,[16] where with a statistical power of 0.8, the incidence of acute myocardial infarct was similar in both groups studied: 13.6% of 22 patients treated with CPAP of 10 cm H_2O and 8.4% of 24 patients treated with bilevel-PAP with an EPAP of 5 cm H_2O and IPAP of 15 cm H_2O ($P = 0.46$). The odds ratio graph of acute myocardial infarction after admission of all studies comparing CPAP and bilevel-PAP is shown in Figure 2.

SEVERITY AND TIMING FOR APPLICATION OF NONINVASIVE VENTILATION

Pulmonary edema has a wide spectrum of severity, and few patients have severe respiratory distress at entry into a study. In the study of Parket al,[5] as in others,[4] only 20% of the patients evaluated were enrolled with severe pulmonary edema. Therefore, it is likely that the effects of noninvasive ventilation are not uniform across the whole spectrum of cardiogenic pulmonary edema.[20] In studies such as those of Nava et al,[8] Park et al,[5,6] Masip et al,[4] and Crane et al,[7] the presence of a control group treated with oxygen allowed us to estimate the expected outcome for the particular population selected.

A delay in applying noninvasive ventilation is a possible explanation for hypercapnia in some patients.[4] In contrast, when applying positive airway pressure early, low lev-

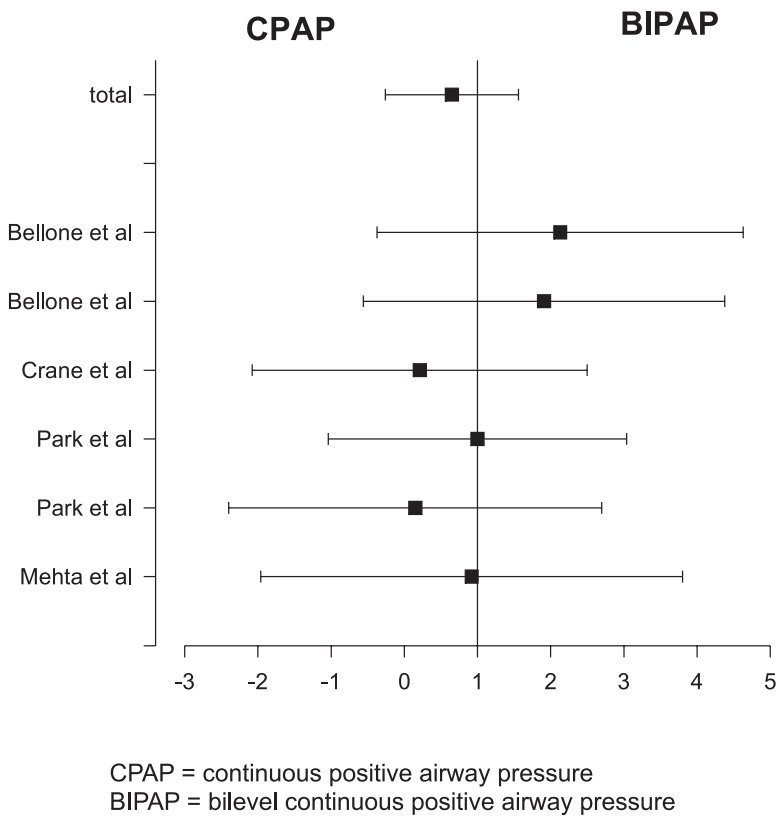

Figure 1 - ODDS ratio of endotracheal intubation requirement in the studies comparing CPAP and bilevel-PAP

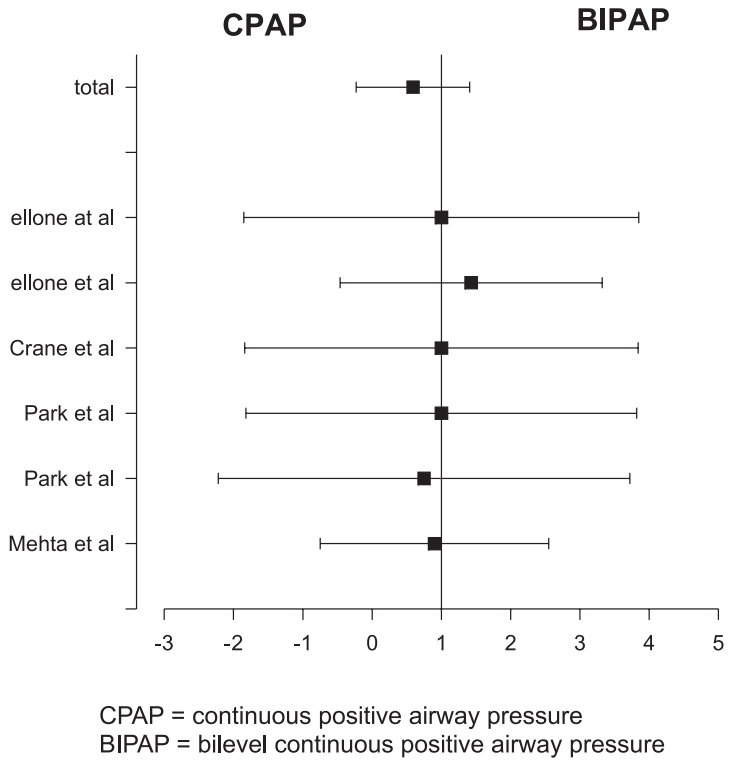

Figure 2 - ODDS ratio of acute myocardial infarction in the studies comparing CPAP and bilevel-PAP

els of pressure may not be useful,[8] but higher expiratory pressure levels can reduce the requirement for endotracheal intubation.[5]

CONCLUSION

In conclusion, the analysis of the current literature shows that noninvasive ventilation applied by CPAP or bilevel-PAP is safe, and the two approaches have similar effects and are effective in preventing the need for endotracheal intubation in patients with respiratory distress of cardiac origin. The results support the concept that positive intrathoracic positive pressure must be seen as a nonpharmacological form of treatment of acute pulmonary edema, rather than only as a supportive measure.

RESUMO

Park M, Lorenzi-Filho G. Uso da ventilação não invasiva no tratamento de pacientes com edema agudo de pulmão cardiogênico. Clinics. 2006;61(3):247-52.

Pesquisamos a literatura atual usando a base de dados MEDLINE para encontrar evidências consistentes sobre o uso da ventilação não invasiva em pacientes com edema agudo de pulmão cardiogênico. Foram encontrados 18 estudos demonstrando que a ventilação não invasiva aplicada por CPAP ou bilevel-PAP é segura, tem efeitos similares e é efetiva em reduzir a necessidade de intubação traqueal em pacientes com desconforto respiratório de origem cardíaca. Os resultados reforçam o conceito que a pressão positiva intratorácica deve ser considerada um forma não farmacológica de tratamento do edema agudo de pulmão cardiogênico e não simplesmente uma medida de suporte.

UNITERMOS: Edema pulmonar. Insuficiência respiratória. Respiração artificial. Ventilação mecânica. Terapia respiratória.

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