Arch Bronconeumol. 2010;**46(8)**:399-401

ARCHIVOS DE BRONCONEUMOLOGIA

www.archbronconeumol.org

Editorial

Non-Invasive Mechanical Ventilation and the Prognosis in Chronic Obstructive Pulmonary Disease☆

Ventilación mecánica no invasiva y pronóstico de la enfermedad pulmonar obstructiva crónica

Miquel Ferrer[a,b,*]

[a]*Servei de Pneumologia, Institut Clínic del Tórax, Hospital Clínic, Institut d'Investigacions Biomèdiques Agust Pi i Sunyer (IDIBAPS), Universitat de Barcelona, Barcelona, Spain*
[b]*Centro de Investigación Biomédica En Red-Enfermedades Respiratorias (CibeRes, CB06/06/0028)-Instituto de Salud Carlos III-Ministerio de Ciencia e Innovación, Madrid, Spain*

Non-invasive ventilation (NIV) is a first-line treatment for severe exacerbation of chronic obstructive pulmonary disease (COPD), especially when presented with hypercapnic respiratory failure and respiratory acidosis and the patient does not improve with conventional treatment of the exacerbation. This indication is reflected in the current standards for diagnosis and treatment of this disease developed by the Spanish Society of Pneumology and Thoracic Surgery and the Latin American Thoracic Association.[1] In these patients, clinical studies show a 50-60% reduction in the risk of treatment failure, the need for tracheal intubation and mortality during exacerbation when treated with NIV.[2]

The alterations in ventilatory mechanics, muscle function and gas exchange that occur during severe exacerbation of COPD have been extensively investigated.[3-5] Critical airflow limitation, the subsequent dynamic pulmonary hyperinflation and decreased inspiratory capacity seem to be the most immediate deleterious events. This leads to an increase in respiratory rate and central ventilatory stimulus, deterioration in gas exchange with increased dead space, neuromechanical uncoupling and deterioration of the cardiovascular function with an increase in pulmonary arterial pressure, decreased right ventricular preload and increased left ventricular afterload.

The increase in pulmonary volume due to dynamic pulmonary hyperinflation and the trapping of air leads to flattening of the diaphragm, with shortening of the respiratory muscle fibres and decreased lung compliance. In addition, intrinsic positive end-expiratory pressure (PEEPi) appears. All this results in an increased respiratory effort and a decreased effective muscle power in the ventilatory pump. In response to this imbalance between the load and the respiratory muscle capacity, patients develop a rapid and shallow breathing pattern as a protection mechanism against respiratory muscle fatigue, leading to a deterioration in the hypercapnia and the appearance of respiratory acidosis. Acidosis compromises respiratory musculature even further.[6]

In COPD exacerbations, arterial pH is the best indicator of severity and translates into an acute deterioration in alveolar hypoventilation compared with the stable phase situation.[5,7] Regardless of the chronic $PaCO_2$ values, an acute increase in $PaCO_2$ due to worsening alveolar hypoventilation is associated with a decrease in arterial pH. In patients hospitalised for COPD exacerbation, mortality is associated with, among other factors, a low pH (with arterial pH < 7.26 associated with a particularly poor prognosis) whereas hypoxemia and hypercapnia tend not to be very different between survivors and non-survivors.[8] Similarly, several studies on NIV have found that a low arterial pH is an important predictor of the need for intubation and of hospital mortality.[2] All this information supports the concept that it is not the absolute level of $PaCO_2$ what is important, but rather the magnitude and speed of its changes, which is reflected in arterial pH. It is estimated that respiratory acidosis may be present in approximately 20% of all hospital admissions for COPD exacerbations.[9]

NIV can partially reverse most of the previously described anomalies by unburdening the respiratory muscles and improving gas exchange. The use of external PEEP can help overcome some of the burden imposed on the respiratory muscles and thus reduce the pressure required to overcome PEEPi and initiate inspiration or trigger the ventilator.[10] Adding inspiratory pressure support further unburdens the respiratory muscles by reducing the excess in the elastic component of respiratory muscle work due to dynamic pulmonary hyperinflation, which increases the circulating volume and the minute ventilation and improves gas exchange in these patients.[10]

The use of NIV in patients with COPD exacerbations and hypercapnic respiratory failures corrects the rapid and shallow respiratory pattern, increases overall the ventilation-perfusion indexes due to the combination of increased minute ventilation and decreased pulmonary perfusion without major changes in the pulmonary ventilation perfusion ratio.[11] These mechanisms lead to an increase in PaO_2 and arterial pH and a decrease in $PaCO_2$.

☆IDIBAPS, CibeRes(CB06/06/0028)-ISCiii,2009SGR911.
*Corresponding author.
E-mail address: miferrer@clinic.ub.es

The most obvious benefits of using NIV in patients with acute respiratory failure (ARF) are seen in those with severe exacerbations of COPD.[2] A consistent finding is that patients who benefit from NIV are those with an intermediate severity of respiratory failure that is not severe enough to need life support measures such as tracheal intubation and invasive mechanical ventilation but serious enough that oxygen therapy is not sufficient. This concept has been termed the "window of opportunity". Theoretically, a patient with COPD exacerbation can progress from a less severe clinical situation to a more serious one. In a less severe situation, oxygen therapy together with the specific treatment of the exacerbation will be sufficient to overcome the episode. When the exacerbation has progressed, life support measures may be necessary such as intubation and invasive mechanical ventilation. However, when the severity is intermediate, NIV may be the best option for managing ARF. The duration of this period can be quite variable between different patients, but it seems that the development of respiratory acidosis is the most characteristic piece of clinical information and best defines the "window of opportunity" for using NIV in COPD exacerbations.

As was the conclusion of a systematic review and meta-analysis of published randomised clinical studies, NIV shows beneficial effects as first-line intervention for managing ARF along with standard medical treatment in patients with hypercapnic respiratory failure and respiratory acidosis.[2] This review also emphasises that NIV should be initiated early in the evolution of respiratory failure before patients develop severe acidosis with the goal of reducing the probability for tracheal intubation, treatment failure and mortality.

In contrast to the abundance of clinical studies and systematic reviews that document the effectiveness of NIV in severe exacerbations of COPD, studies that evaluate the subsequent evolution of these patients once the exacerbation has been overcome are scarce. In an issue of Archivos de Bronconeumología (Archives of Bronchopulmonology), Echave-Sustaeta et al. analysed the prognosis of patients following a severe exacerbation of COPD who were treated with NIV.[12] The authors established a study to determine the rates of readmissions and mortality in these patients during the year following hospital discharge and to analyse the factors associated with both outcomes. For this study, they analysed a cohort of 93 patients that survived a COPD exacerbation that required NIV and who were monitored after discharge from hospital. They measured the need for hospitalisation for respiratory reasons and the survival rate and they analysed the possible factors associated with these events by means of a multivariate analysis.

This study showed that in the year following discharge 66% of the patients required rehospitalisation. The multivariate analysis showed that a poorer functional respiratory state, as assessed by a low forced expiratory volume in the first second of the forced spirometry manoeuvre (FEV_1), and a high average length of stay in the hospital were independently associated with an increased risk of rehospitalisation. Also, the study showed a 69.5% survival rate after one year. In the multivariate analysis, age, the $PaCO_2$ level prior to initiating NIV and the number of days in hospital in the year prior to the exacerbation were the factors that were independently associated with an increased risk of mortality. The authors concluded that this group of patients with COPD presented a high mortality and need for rehospitalisation in the year following the discharge. They also suggest that the variables related to the severity of COPD and of the actual exacerbation are associated with these events and could be used to apply specific monitoring programmes in this subset of patients.

An earlier study analysed the evolution in the year following hospital discharge for a group of 15 patients with COPD exacerbation who had required NIV, comparing them with another group of 15 patients that had only received medical treatment.[13] Despite the similarity in both groups in the complications, hospital stay and mortality during the hospital stay, the patients who received NIV had a more pronounced improvement in arterial blood gases during their hospital stay, as well as a better evolution of respiratory function parameters, lower rates of readmission and a higher survival during the following year.

Another study compared a group of 24 patients who received NIV for severe exacerbation of COPD with another historical control group treated conventionally.[14] As in the previous study, despite similar mortality rates during hospital admission, arterial blood gases improved faster during the hospital stay in patients treated with NIV, coupled with a lower rate and duration of hospitalisations for exacerbation and higher survival during the following year. Both studies show a long-term protective effect from NIV beyond the short-term beneficial effects during the exacerbation.[13,14] The long-term prognosis of the patients in these studies was variable. While one study that included patients with minimum respiratory acidosis obtained a high survival rate at one year,[13] another study with patients with a higher level of respiratory acidosis showed a lower survival rate,[14] a finding similar to a study done by Echave-Sustaeta et al.[12]

This study had some limitations, as stated by the authors,[12] mainly in terms of the small number of patients studied, which limited the inclusion of certain variables that have been associated with COPD prognosis, such as the body mass index and dyspnea. Another limitation was that comorbidity was measured only by the Charlson index.

The long-term prognosis of patients admitted for severe exacerbations of COPD with hypercapnic respiratory failure was studied in a series of more than 1000 patients.[15] This study was conducted before the use of NIV in COPD exacerbations was generalised, which leads us to believe that the proportion of these patients who received NIV during their hospital admission was low. Nevertheless, the survival at one year as well as the hospital readmission rates for these patients was similar to the study by Echave-Sustaeta et al.,[12] taking into account the mortality during hospitalisation and the subsequent follow-up period. As in this study, the survival time of the patients was independently related to the severity of the disease, age, and the functional state prior to admission.[15] However, this study also identified the following factors that were independently associated with worse survival: low body mass index, low levels of albumin, increased arterial hypoxemia on admission and the presence of congestive heart failure and cor pulmonale.

Another factor that may have contributed to the long-term prognosis in the Echave-Sustaeta et al. study[12] was the use of home NIV in a significant subset of the patients. The authors indicated home NIV in the majority of cases based on the tolerance to disconnection of the NIV, the $PaCO_2$ level, the number and severity of previous admissions for COPD exacerbation, especially previous episodes of respiratory acidosis, the presence of hypoventilation induced by oxygen therapy, documentation of associated nocturnal hypoventilation, as well as symptoms associated with hypercapnia.[12] In fact, as observed in this work, patients who received home NIV had higher functional respiratory deterioration and needed NIV three times longer during hospitalisation, which suggests a subpopulation with a more evolved disease. However, the influence of home NIV in the long-term prognosis is uncertain, as indicated by clinical studies.[16]

The identification of variables related to hospital readmission observed in these studies[12-14] allows us to identify a subset of patients that deserve special attention. These patients may be the object of specific monitoring programmes for reducing the number and severity of exacerbations and thereby improve the functional prognosis and cost associated with these readmissions. Additionally, the factors associated with mortality identified in these studies[12,15] also allows us to identify subsets of patients in whom the interventions should include the improvement of the nutritional state and the avoidance or delay of developing cardiovascular complications.[17]

References

1. Peces-Barba G, Barbera JA, Agusti A, Casanova C, Casas A, Izquierdo JL, et al. Diagnosis and management of chronic obstructive pulmonary disease: joint guidelines of the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR) and the Latin American Thoracic Society (ALAT). Arch Bronconeumol. 2008;44:271-81.
2. Ram FS, Picot J, Lightowler J, Wedzicha JA. Non-invasive positive pressure ventilation for treatment of respiratory failure due to exacerbations of chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2004;CD004104.
3. Calverley PM. Respiratory failure in chronic obstructive pulmonary disease. Eur Respir J Suppl. 2003;47:26s-30s.
4. O'Donnell DE, Parker CM. COPD exacerbations. 3: Pathophysiology. Thorax. 2006; 61:354-61.
5. Barbera JA, Roca J, Ferrer A, Felez MA, Diaz O, Roger N, et al. Mechanisms of worsening gas exchange during acute exacerbations of chronic obstructive pulmonary disease. Eur Respir J. 1997;10:1285-91.
6. Yanos J, Wood LD, Davis K, Keamy M. The effect of respiratory and lactic acidosis on diaphragm function. Am Rev Respir Dis. 1993;147:616-9.
7. Juan G, Calverley P, Talamo C, Schnader J, Roussos C. Effect of carbon dioxide on diaphragmatic function in human beings. N Engl J Med. 1984;310:874-9.
8. Jeffrey AA, Warren PM, Flenley DC. Acute hypercapnic respiratory failure in patients with chronic obstructive lung disease: risk factors and use of guidelines for management. Thorax. 1992;47:34-40.
9. Plant PK, Owen JL, Elliott MW. One year period prevalence study of respiratory acidosis in acute exacerbations of COPD: implications for the provision of non-invasive ventilation and oxygen administration. Thorax. 2000;55:550-4.
10. Appendini L, Patessio A, Zanaboni S, Carone M, Gukov B, Donner C, et al. Physiologic effects of positive end-expiratory pressure and mask pressure support during exacerbations of chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 1994;149:1069-76.
11. Diaz O, Iglesia R, Ferrer M, Zavala E, Santos C, Wagner PD, et al. Effects of noninvasive ventilation on pulmonary gas exchange and hemodynamics during acute hypercapnic exacerbations of chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 1997;156:1840-5.
12. Echave-Sustaeta J, Comeche-Casanova L, Garcia-Lujan R, Sayas-Catalan J, Gomez de la Camara A, Lopez-Encuentra A. Pronóstico tras una agudización grave de la EPOC tratada con ventilación mecánica no invasiva. Arch Bronconeumol. 2010; 46:405-10.
13. Bardi G, Pierotello R, Desideri M, Valdisserri L, Bottai M, Palla A. Nasal ventilation in COPD exacerbations: early and late results of a prospective, controlled study. Eur Respir J. 2000;15:98-104.
14. Confalonieri M, Parigi P, Scartabellati A, Aiolfi S, Scorsetti S, Nava S, et al. Noninvasive mechanical ventilation improves the immediate and long-term outcome of COPD patients with acute respiratory failure. Eur Respir J. 1996;9:422-30.
15. Connors AF, Dawson NV, Thomas C, Harrell FE, Desbiens N, Fulkerson WJ, et al. Outcomes following acute exacerbation of severe chronic obstructive lung disease. The SUPPORT investigators (Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments). Am J Respir Crit Care Med. 1996;154:959-67.
16. Kolodziej MA, Jensen L, Rowe B, Sin D. Systematic review of noninvasive positive pressure ventilation in severe stable COPD. Eur Respir J. 2007;30:293-306.
17. Villar AF, Mendez BM, de Miguel DJ. Chronic obstructive pulmonary disease and heart failure. Arch Bronconeumol. 2009;45:387-93.