Med Intensiva. 2014;38(5):311–314

medicina intensiva

www.elsevier.es/medintensiva

POINT OF VIEW

High or conventional positive end-expiratory pressure in acute respiratory distress syndrome☆

R. Díaz-Alersi*, C. Navarro-Ramírez

Servicio de Cuidados Críticos y Urgencias, Hospital Universitario Puerto Real, Puerto Real, Cádiz, Spain

KEYWORDS
Acute respiratory distress syndrome;
Positive end-expiratory pressure;
Protective ventilation

Abstract Patients with acute respiratory distress syndrome may require high positive end-expiratory pressure (PEEP) levels, though the optimum level remains to be established. Several clinical trials have compared high PEEP levels versus conventional PEEP. Overall, although high PEEP levels improve oxygenation and are safe, they do not result in a significant reduction of the mortality rates. Nevertheless, some metaanalyses have revealed 2 situations in which high PEEP may decrease mortality: when used in severe distress and when PEEP is set following the characteristics of lung mechanics. Five studies have explored this latter scenario. Unfortunately, all of them have small sample sizes and have used different means to determine optimum PEEP. It is therefore necessary to conduct studies of sufficient sample size to compare the treatment of patients with severe acute respiratory distress syndrome, using a protective ventilation strategy with high PEEP guided by the characteristics of lung mechanics and ventilation with the protocol proposed by the ARDS Network.

PALABRAS CLAVE
Síndrome de distrés respiratorio agudo;
Presión positiva teleespiratoria;
Ventilación protectora

Presión positiva teleespiratoria alta o convencional en el síndrome de distrés respiratorio agudo

Resumen En el síndrome de distrés respiratorio agudo se puede necesitar una presión positiva teleespiratoria (PEEP) elevada, sin embargo, no se ha llegado a determinar cuánto. Varios ensayos clínicos han comparado esos niveles con los convencionales en este síndrome. Globalmente, aunque la PEEP elevada mejora la oxigenación y es segura, no mejora la mortalidad. No obstante, los metaanálisis han puesto de manifiesto 2 situaciones en las que una PEEP elevada puede disminuir la mortalidad: en el síndrome de distrés respiratorio agudo grave y cuando se titula mediante las características de la mecánica pulmonar. Cinco estudios han explorado esto último, todos de pequeño tamaño muestral, usando diferentes maneras de determinar la

☆ Please cite this article as: Díaz-Alersi R, Navarro-Ramírez C. Presión positiva teleespiratoria alta o convencional en el síndrome de distrés respiratorio agudo. Med Intensiva. 2014;38:311–314.

* Corresponding author.
E-mail address: rda@uninet.edu (R. Díaz-Alersi).

2173-5727/$ – see front matter

PEEP óptima. Resulta necesario, por tanto, realizar un estudio con el suficiente tamaño muestral que compare el tratamiento de pacientes con síndrome de distrés respiratorio agudo grave mediante una estrategia de ventilación protectora, con PEEP elevada, guiada por las características de la mecánica pulmonar y la ventilación según el protocolo de la ARDS Network.

Mechanical ventilation can cause lung damage or worsen pre-existing lung damage. This may be a result of excessive lung distension, with stretching and even rupture of tissues, and the cyclic opening and closing of collapsed alveolar units. The underlying causes are excessive transpulmonary pressure, generally related to high circulating volumes (volutrauma), and inadequate positive end-expiratory pressure (PEEP) levels that do not avoid repetitive alveolar collapse and reopening (atelectrauma).[1] In order to avoid both effects, protective ventilation strategies, low circulating volumes and elevated PEEP levels have been introduced in recent years and have been evaluated in different clinical studies. Two clinical trials have shown ventilation with low circulating volumes to reduce mortality among patients with acute respiratory distress syndrome (ARDS).[2,3] As a result, this strategy has become a standard of treatment for such patients. However, the appropriate PEEP level for ventilating such individuals has not been established.

Clinical trials involving critically ill patients in general, and patients with distress in particular, are difficult to carry out, due to the complexity of both the patients and the therapeutic measures used. It is common for screening to be complicated, requiring years to complete, and such studies are often unable to recruit a sufficient number of individuals to secure statistically significant outcome results with value for patients, such as mortality. Metaanalyses are therefore regularly performed.

The Cochrane Collaboration has recently conducted a systematic review of the usefulness of elevated PEEP in the management of distress.[4] The study included 7 randomized clinical trials with a total of 2565 patients comparing high versus conventional PEEP levels in patients who met criteria of distress/acute lung injury (ALI). In 5 of these studies (2427 patients), comparison was made with the same circulating volume in both groups: patients and controls. In the remaining two publications (148 patients), the circulating volume was lower in the high PEEP group. In the analysis of mortality prior to hospital discharge, comprising only the studies that used the same circulating volumes in both groups, the metaanalysis detected no significant differences between ventilation with high versus low PEEP (relative risk 0.90, 95% confidence interval 0.81–1.01). Regarding the rest of the studied outcomes, and although high PEEP improved oxygenation, no significant differences were recorded regarding the days without mechanical ventilation, and the data were insufficient to draw conclusions referred to the duration of stay in the Intensive Care Unit (ICU). In contrast, in the study of the subgroup of patients with ARDS, i.e., excluding those with only acute lung injury, according to the definition of the North American-European Consensus Conference (NAECC) of 1994,[5] a decrease in mortality in the ICU was observed. However, it is difficult to know whether this was attributable only to the PEEP level, since two of the three studies included in the mentioned analysis combined a protective ventilation strategy with high PEEP. The authors concluded that the existing evidence suggests that high PEEP levels do not reduce mortality at hospital discharge compared with low levels—though they do not increase the risk of barotrauma, and are seen to improve oxygenation.

At least three additional metaanalyses have been published on this subject in the last few years—one of them in this journal—and the conclusions are similar in all of them; high PEEP levels do not reduce mortality at hospital discharge in patients with distress.[6–8] On considering only the abstracts of the publications, we probably would draw the conclusion that it is not useful to use such PEEP levels in the management of our patients. However, the true situation is much more complicated, and a number of aspects must be taken into account.

The main effect of high PEEP is the sustained reopening (recruitment) of collapsed alveolar units. This improves gas exchange and total compliance (by distributing the circulating volume among more units, and thereby lowering the insufflation pressure). Imaging (conventional tomography) and electrical impedance studies have shown that in order to achieve such recruitment we may need PEEP levels of 18–26 cmH_2O.[9] However, the pressure needed to recruit alveoli may cause the overdistension of less affected units, collapsing vessels and thereby elevating the pulmonary vascular resistances and dead space. Some studies have found elevated PEEP to be more beneficial in patients with a low pO_2/FiO_2 ratio and a high percentage of potentially recruitable lung volume.[10] In less diseased lungs, such levels might not be so adequate, since there is not so much recruitable volume. In these cases the risks of high PEEP (overdistension, hemodynamic instability) outweigh its benefits. Consequently, the application of elevated PEEP perhaps should be reserved for patients with severe distress. Nevertheless, in most clinical trials the patients were selected according to the definition of ARDS and acute lung injury of the NAECC, with the inclusion of patients presenting $pO_2/FiO_2 \leq 300$ and in whom the PEEP level to which they were subjected at the time of evaluation was not taken into account. It is relatively common for a patient meeting the criteria of ARDS and acute lung injury of the NAECC at first evaluation to no longer meet such criteria once they have been ventilated with an adequate (and not necessarily elevated) PEEP level. These patients, who tend to have a better outcome, are included in the trials along with individuals presenting persistently lower pO_2/FiO_2. In this context, if we only consider patients with $pO_2/FiO_2 \leq 200$, elevated PEEP is indeed seen to be associated with improved survival.[8]

As has been mentioned, clinical trials in critical patients are difficult to carry out, and such studies are therefore few and prolonged in time. This means that they are affected by changes in other types of treatments different from the treatment subject to study. In this regard, over the years in which these clinical trials have been carried out, the benefit of low-volume ventilation (protective ventilation) has been demonstrated, and our knowledge of rescue maneuvering or of prone decubitus has changed. Protective ventilation is closely related to PEEP; in this respect, the use of a low circulating volume requires us to apply a higher PEEP in order to avoid end-expiration alveolar collapse, and the use of high PEEP levels in turn obliges us to use a low circulating volume in order to avoid lung overdistension. Three trials have jointly compared both interventions,[2,11,12] selecting a high PEEP according to the lung mechanics. Overall, the studies describe global improvements in mortality in the protective ventilation group, though the results are difficult to attribute to one or the other treatment component. Perhaps as a consequence of this evolution, and due to the use of PEEP/FiO_2 tables in several studies, such as ALVEOLI[13] and LOVS,[14] the low PEEP levels used are higher than those employed in routine clinical practice—causing the difference between high and low PEEP to be less evident.

Since very high PEEP levels may be needed to keep as much lung tissue recruited as possible, and since these same PEEP levels can be harmful for the healthy alveoli, it would be logical to individualize the prescribed PEEP level, considering the mechanical characteristics of the lungs in each patient. The three aforementioned studies determined the PEEP level by analyzing the pressure–volume curves, adjusting the level to above the lower inflexion point. Overall, and apart from improvement in terms of mortality, the studies also reported a lesser risk of barotrauma. Another trial, designed to determine optimum PEEP by measuring the end-expiratory transpulmonary pressure, likewise reported a significant decrease in mortality in the multivariate analysis among those patients treated with high PEEP levels. A fifth study has recently been published that is not included in any of the reviews.[15] This was a single-center Spanish study including patients that met the NAECC criteria of ARDS 24 h after ventilation with pre-established parameters of low circulating volumes and combinations of PEEP/FiO_2, according to the tables of the ARDS Network. Optimum PEEP was defined as the level associated to the greatest static compliance, according to the method described by Suter et al.[16] This study likewise found no significant differences in terms of mortality after 28 days between the patients in the experimental group and the controls—though there was a tendency toward lower mortality. Significant improvement was also recorded in relation to the days without multiorgan failure. Curiously, no differences were observed between the mean PEEP of the group in which compliance was determined and that of the controls. Another study, the PEEP-HUPA,[17] uses a different method to determine optimum PEEP (after recruitment maneuvering), and is presently in course.

In sum, this new review contributes nothing new to what we have already published in this journal.[6] A quick examination of the abstracts of some of the reviews available to date regarding the use of high PEEP levels may lead us to conclude that such levels are not useful in application to distress patients. However, failure to go beyond the conventional PEEP levels may leave some patients without the best treatment possible. It is very likely that patients with more severe distress, with a significant proportion of recruitable lung tissue, will require high PEEP levels. Such levels should be determined on an individualized basis according to the lung mechanics of each patient, based on the pressure–volume curves or other methods, to secure maximum recruitment while avoiding overdistension. Although set within a protective ventilation strategy, those studies that have used this approach have reported a tendency toward improved survival, fewer days on mechanical ventilation, and more days without multiorgan failure. Nevertheless, the best method for defining optimum PEEP remains to be established. The plotting of pressure–volume curves is not available in many Intensive Care Units, and the reliable determination of plateau pressure may be complicated. Perhaps in some cases the measurement of esophageal pressure, and even the use of imaging studies such as impedance tomography, might be of help—provided the costs are not too high. Further well-designed clinical trials are therefore needed to explore the results of applying high (or perhaps we should say ''adequate'') PEEP levels, guided by the characteristics of the lung mechanics of distress patients. Such trials will likely be unable to recruit enough patients to secure statistically significant results referred to outcomes such as mortality. It therefore would be advisable to standardize the protocols, at least in terms of inclusion criteria, ventilation modes, rescue maneuvers and the way of determining optimum PEEP.

Conflicts of interest

The authors declare that they have no conflicts of interest.

References

1. Gordo Vidal F, Delgado Arnaiz C, Calvo Herranz E. Mechanical ventilation induced lung injury. Med Intensiva. 2007;31:18–26.
2. Amato MB, Barbas CS, Medeiros DM, Magaldi RB, Schettino GP, Lorenzi-Filho G, et al. Effect of a protective-ventilation strategy on mortality in the acute respiratory distress syndrome. N Engl J Med. 1998;338:347–54.
3. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. N Engl J Med. 2000;342:1301–8.
4. Santa Cruz R, Rojas JI, Nervi R, Heredia R, Ciapponi A. High versus low positive end-expiratory pressure (PEEP) levels for mechanically ventilated adult patients with acute lung injury and acute respiratory distress syndrome. Cochrane Database Syst Rev. 2013;6:CD009098.
5. Bernard GR, Artigas A, Brigham KL, Carlet J, Falke K, Hudson L, et al. Report of the American–European consensus conference on ARDS: definitions, mechanisms, relevant outcomes and clinical trial coordination. The Consensus Committee. Intensive Care Med. 1994;20:225–32.
6. Gordo-Vidal F, Gómez-Tello V, Palencia-Herrejón E, Latour-Pérez J, Sánchez-Artola B, Díaz-Alersi R. High PEEP vs. conventional PEEP in the acute respiratory distress syndrome: a systematic review and meta-analysis. Med Intensiva. 2007;31:491–501.
7. Oba Y, Thameem DM, Zaza T. High levels of PEEP may improve survival in acute respiratory distress syndrome: a meta-analysis. Respir Med. 2009;103:1174–81.
8. Briel M, Meade M, Mercat A, Brower RG, Talmor D, Walter SD, et al. Higher vs lower positive end-expiratory pressure in patients with acute lung injury and acute respiratory distress syndrome: systematic review and meta-analysis. JAMA. 2010;303:865–73.

9. Barbas CS, de Matos GF, Pincelli MP, da Rosa Borges E, Antunes T, de Barros JM, et al. Mechanical ventilation in acute respiratory failure: recruitment and high positive end-expiratory pressure are necessary. Curr Opin Crit Care. 2005;11:18–28.
10. Gattinoni L, Caironi P, Cressoni M, Chiumello D, Ranieri VM, Quintel M, et al. Lung recruitment in patients with the acute respiratory distress syndrome. N Engl J Med. 2006;354:1775–86.
11. Ranieri VM, Suter PM, Tortorella C, de Tullio R, Dayer JM, Brienza A, et al. Effect of mechanical ventilation on inflammatory mediators in patients with acute respiratory distress syndrome: a randomized controlled trial. JAMA. 1999;282:54–61.
12. Villar J, Kacmarek RM, Pérez-Méndez L, Aguirre-Jaime A. A high positive end-expiratory pressure, low tidal volume ventilatory strategy improves outcome in persistent acute respiratory distress syndrome: a randomized, controlled trial. Crit Care Med. 2006;34:1311–8.
13. Pintado MC, de Pablo R, Trascasa M, Milicua JM, Rogero S, Daguerre M, et al. Individualized PEEP setting in patients with ARDS: a randomized controlled pilot study. Respir Care. 2013;58:1416–23.
14. Brower RG, Lanken PN, MacIntyre N, Matthay MA, Morris A, Ancukiewicz M, et al., National Heart, Lung, and Blood Institute ARDS Clinical Trials Network. Higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome. N Engl J Med. 2004;351:327–36.
15. Meade MO, Cook DJ, Guyatt GH, Slutsky AS, Arabi YM, Cooper DJ, et al., Lung Open Ventilation Study Investigators. Ventilation strategy using low tidal volumes, recruitment maneuvers, and high positive end-expiratory pressure for acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. JAMA. 2008;299:637–45, http://dx.doi.org/10.1001/jama.299.6.637.
16. Suter PM, Fairley HB, Isenberg MD. Effect of tidal volume and positive end-expiratory pressure on compliance during mechanical ventilation. Chest. 1978;73:158–62.
17. Kacmarek R. Pilot study of positive-end expiratory pressure in acute respiratory distress syndrome (PEEP-HUPA). ClinicalTrials.gov. Available at: http://clinicaltrials.gov/show/NCT01119872 [accessed 06.09.13].