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POINT OF VIEW

Individualized positive end-expiratory pressure application in patients with acute respiratory distress syndrome☆

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KEYWORDS
Acute respiratory distress syndrome;
Positive end-expiratory pressure;
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Abstract Current treatment of acute respiratory distress syndrome is based on ventilatory support with a lung protective strategy, avoiding the development of iatrogenic injury, including ventilator-induced lung injury. One of the mechanisms underlying such injury is atelectrauma, and positive end-expiratory pressure (PEEP) is advocated in order to avoid it. The indicated PEEP level has not been defined, and in many cases is based on the patient oxygen requirements for maintaining adequate oxygenation. However, this strategy does not consider the mechanics of the respiratory system, which varies in each patient and depends on many factors–including particularly the duration of acute respiratory distress syndrome. A review is therefore made of the different methods for adjusting PEEP, focusing on the benefits of individualized application.

PALABRAS CLAVE
Síndrome de distrés respiratorio agudo;
Presión positiva al final de la espiración;
Lesión pulmonar inducida por el respirador;
Ventilación mecánica

Aplicación individualizada de la presión positiva al final de la espiración en pacientes con síndrome de distrés respiratorio agudo

Resumen En el manejo actual del síndrome de distrés respiratorio agudo, la aplicación de ventilación mecánica se debe realizar bajo una estrategia protectora, evitando el desarrollo de iatrogenia, entre la que se incluye el daño pulmonar asociado a la misma *(ventilator-induced lung injury)*. Uno de los mecanismos implicados en este daño es el atelectrauma, abogándose por la aplicación de presión positiva al final de la espiración (PEEP) para evitarlo. El nivel de PEEP a aplicar no está definido y en muchas ocasiones se realiza dependiendo de la cantidad de oxígeno aportada al paciente en cada momento. Sin embargo, esta estrategia no tiene

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en cuenta la mecánica respiratoria que varía de un paciente a otro y que depende de múltiples factores entre los que destaca el tiempo de evolución del síndrome de distrés respiratorio agudo. Por ello, revisamos los diferentes métodos de ajuste de la PEEP, centrándonos en las ventajas derivadas de una aplicación individualizada.

Acute respiratory distress syndrome (ARDS) involves a complex pulmonary response as a consequence of direct or indirect injury resulting in the development of acute respiratory failure with bilateral lung infiltrates suggestive of lung edema in the absence of left heart failure.[1] Standard management consists of correction of the underlying cause, with the provision in most cases of protective mechanical ventilation, the adoption of safe fluid restriction measures, and the avoidance of iatrogenic complications.[2]

A number of studies have shown that mechanical ventilation can induce or worsen lung injury (a situation known as ventilator-induced lung injury), and may contribute to the appearance or persistence of multiorgan dysfunction syndrome.[3,4] One of the most important mechanisms underlying ventilator-induced lung injury is atelectrauma, which is characterized by repeated alveolar collapse and opening, mainly in areas where lung surfactant function is altered—this type of situation being very common in patients with ARDS.[4,5] A number of authors have proposed the use of positive end-expiratory pressure (PEEP) to avoid the development of atelectrauma.[4,5] The use of PEEP also offers other benefits in the ventilation of patients with ARDS, with improvement of gas exchange and lung function by increasing the residual functional capacity, the induction of alveolar recruitment, the redistribution of extravascular lung water, and especially improvement of the ventilation—perfusion ratio.[6] However, the use of PEEP also has potential adverse effects, such as alveolar overdistension and circulatory depression with a drop in cardiac output.[6]

A widely accepted practice in patients with ARDS is the use of mechanical ventilation with a lung protective strategy involving the application of tidal volumes in the order of 6 ml/kg ideal body weight and the limitation of plateau pressure to under 30 cmH_2O.[7] This strategy is fundamental on a large study of patients with ARDS in which mortality was seen to worsen when high tidal volumes of 12 ml/kg ideal body weight were used. In this study,[8] the applied PEEP level was determined according to the fraction of inspired oxygen (FiO_2) applied on the basis of pre-established tabled values—the latter not having been validated by other studies but developed by the authors of the study. The mentioned table was not even derived from observational studies of routine clinical practice, since examination of the literature reveals that the mentioned tabled PEEP values are higher than those applied in routine clinical practice, both in general and according to the FiO_2 applied to the patient.[8–10]

Therefore, it is not clear whether the application of PEEP based on a pre-established table of values, without taking into account the respiratory mechanics of the patient at each point in time, is able to serve its intended use, i.e., to keep the alveoli open throughout the respiratory cycle. In effect, different studies report that the level of alveolar recruitment varies from one patient to another. In this regard, Gattinoni et al.[11] demonstrated that the percentage recruitable lung measured by computed axial tomography (CAT) at the same pressure level varies between 5 and 60% in different patients, and moreover in 20% of the cases recruitment is either not achieved or is less than 5%. Measurement of the amount of aerated lung tissue based on CAT is regarded as the gold standard for detecting alveolar recruitment. Studies based on determining the applied PEEP level based on CAT measurements of the amount of aerated lung tissue at different PEEP levels have revealed improved oxygenation and lesser mortality among patients with a larger proportion of recruitable lung tissue.[11] However, this method for determining the PEEP level is not easy to use in the routine practice setting of the Intensive Care Unit—in part because of problems referred to the availability of the Radiodiagnostic Department, the high radiation applied to the patients, the cost in terms of time and resources, and particularly the risk of complications during patient transfer.

Many authors consider that the best method for determining the PEEP level to be applied at the patient bedside is the pressure—volume curve.[7] The ideal PEEP level would be above the lower inflexion point of the curve, which defines the appearance of alveolar derecruitment. The upper inflexion point of the curve in turn determines the appearance of alveolar overdistension.[12] This method has been correlated to the level of alveolar recruitment measured by CAT.[13] Three randomized studies[14–16] and a metaanalysis[17] have compared the application of PEEP according to the pressure—volume curve versus the application of PEEP with different criteria. All of these studies have concluded that individualized application based on the pressure—volume curve is associated to decreased mortality. The problem is that comparison was moreover made of the application of high tidal volumes (9–12 ml/kg) versus low tidal volumes (5–8 ml/kg), which have been shown to increase mortality.[8]

A criticism of the use of the pressure—volume curve is that it does not take increases in pleural or intraabdominal pressure into account. The end-expiratory transpulmonary pressure is not altered by the presence of affected chest and/or abdominal wall distensibility, in contrast to when it is established according to pressures measured in the airway.[18,19] In this regard, Talmor et al.,[20] in their study of ventilated patients with ARDS, compared the determination of PEEP based on the applied FiO_2 according to the ARDS network study[8] versus possible combinations of FiO_2 and transpulmonary pressure (which would be the result of subtracting pleural pressure estimated with a balloon-catheter inserted in the esophagus from alveolar pressure) in order to maintain an expiratory transpulmonary pressure of between

0 and 10 cmH_2O and an inspiratory pressure of <25 cmH_2O. The authors recorded improvement in oxygenation and lung compliance after 72 h of treatment, accompanied by improved survival after 28 days in the more seriously ill patients. Recently, Grasso et al.[21] found that although the plateau pressure measured in the airway was the same in all patients, the same could not be said of the transpulmonary pressure measured with an esophageal catheter. These patients presented ARDS secondary to H1N1 virus infection with refractory hypoxemia despite conventional therapy, including protective mechanical ventilation according to the criteria of the ARDS network study,[8] and with criteria for starting extracorporeal membrane oxygenation therapy. The authors described two types of patients: those with an elevated transpulmonary pressure (close to the upper limit recommended by several studies as the level of maximum alveolar recruitment: 25 cmH_2O[18,19,22]) and those with a low transpulmonary pressure. In this second group of patients the applied PEEP level was adjusted to achieve a transpulmonary pressure of 25 cmH_2O—an improvement in oxygenation sufficient to not require extracorporeal membrane oxygenation being recorded in all cases. While usable at the patient bedside and minimally invasive, this method for determining PEEP is limited by the fact that transpulmonary pressure measured with an esophageal catheter may be altered by the weight of the mediastinal organs and influenced by esophageal peristalsis, the patient position, and the presence of abdominal bloating.[23] Furthermore, this method may result in the application of higher PEEP values if the plateau pressure is not limited—with the consequent risk of hemodynamic deterioration, particularly in hypovolemic patients.[24]

In theory, the best static compliance (determined from the tidal volume divided by the difference between the plateau pressure and PEEP) would be the point minimizing the pulmonary areas with atelectasis and overdistension that heterogeneously affect the lungs of patients with ARDS. Moreover, this approach would effectively take into account alterations in chest wall compliance, which could benefit from additional PEEP in order to avoid lung collapse.[21] Our group has conducted a study[25] in patients with ARDS, comparing the application of PEEP according to ''best static compliance'' versus the application of PEEP according to FiO_2 as determined from the table of the ARDS network study.[8] The rest of the respiratory and hemodynamic parameters were identical in both patient groups. A lung protective strategy was used, involving the application of tidal volumes between 6 and 8 ml/kg ideal body weight, with limitation of the plateau pressure to 30 cmH_2O. In the ''best static compliance'' group there were almost half as many deaths as in the control group (20% versus 38%, respectively). These differences were not statistically significant, however, perhaps because of the fact that this was a pilot study with only 70 patients. Nevertheless, we observed more days without mechanical ventilation and of multiorgan failure in the intervention group. It is very important to underscore that the mean applied PEEP level did not differ between the two groups, though 80% of the patients in the treatment group had a PEEP level different from that which would have been assigned by the predetermined table. This concept is supported by CAT studies of alveolar recruitment[11] in which it has been seen to be impossible to reach the same recruitment level in each patient.

The ART study in patients with ARDS is currently being carried out. In this trial the intervention group will be treated with an optimum PEEP likewise based on ''best static compliance'' following maximum alveolar recruitment maneuvering.[26]

Different methods have also been proposed for determining the PEEP level suited to each individual in each moment and at the patient bedside: portable radiography,[27] ultrasound,[28,29] the stress index,[30] dead space measurement,[31] electrical impedance tomography,[32] PaO_2,[33] and dynamic compliance.[34] Although these methods are reported to afford improvement of the measured parameters (oxygenation, recruitment, respiratory mechanics, etc.), no randomized studies demonstrating their efficacy in terms of patient survival are available.

In conclusion, there is growing evidence that the individualized application of PEEP in patients with ARDS can improve oxygenation, limit the duration or development of multiorgan dysfunction, and thus lessen patient mortality. This displaces the concept of high or low PEEP in patients with ARDS and places greater emphasis on individualized patient treatment. Accordingly, when patient lung injury allows recruitment, the PEEP level will be high, while in very rigid lungs the PEEP value must be low in order simply to avoid airway collapse.[35] Randomized, multicenter and controlled studies with a sufficient number of patients are needed in order to demonstrate improvements in terms of survival after applying PEEP with an individualized strategy and including different groups of patients, as well as different treatment strategies that are increasingly seen as being useful, such as prone decubitus,[36] neuromuscular relaxation,[37] or the use of extracorporeal techniques.[38]

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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