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REVIEW

Mechanical ventilation in acute respiratory distress syndrome: The open lung revisited

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Abstract Acute respiratory distress syndrome (ARDS) is still related to high mortality and morbidity rates. Most patients with ARDS will require ventilatory support. This treatment has a direct impact upon patient outcome and is associated to major side effects. In this regard, ventilator-associated lung injury (VALI) is the main concern when this technique is used. The ultimate mechanisms of VALI and its management are under constant evolution. The present review describes the classical mechanisms of VALI and how they have evolved with recent findings from physiopathological and clinical studies, with the aim of analyzing the clinical implications derived from them. Lastly, a series of knowledge-based recommendations are proposed that can be helpful for the ventilator assisted management of ARDS at the patient bedside.

PALABRAS CLAVE
Ventilación mecánica;
Síndrome de dificultad respiratoria aguda;
Lesión pulmonar asociada a ventilador

Ventilación mecánica en el síndrome de dificultad respiratoria aguda: el pulmón abierto revisitado

Resumen El síndrome de dificultad respiratoria aguda (SDRA) sigue asociándose a unas elevadas tasas de morbimortalidad. La mayoría de los pacientes con SDRA requieren apoyo ventilatorio. Esta terapia tiene un impacto directo sobre los resultados de los pacientes y se asocia con importantes efectos secundarios. De ellos, la principal preocupación cuando se aplica esta terapia es la lesión pulmonar asociada a ventilador (LPAV). Los mecanismos fundamentales de la LPAV y su tratamiento se encuentran en constante evolución. En esta revisión,

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describiremos los mecanismos clásicos de la LPAV y cómo han evolucionado con los recientes hallazgos de estudios patofisiológicos y clínicos para analizar las implicaciones clínicas que se derivan de ellos. Al final de esta revisión, extraeremos una serie de recomendaciones basadas en los conocimientos, las cuales pueden resultar útiles para la terapia con ventilador a pie de cama en pacientes con SDRA.

The acute respiratory distress syndrome (ARDS) is still related to high mortality and morbidity rates.[1] In spite of all the knowledge on its pathophysiology, there are no treatments aimed to modify the natural history of the disease. Instead, the treatment of ARDS is based on a delicate equilibrium between restoration of the most basic physiology and avoidance of side effects.

The single strategy with a major impact in ARDS is mechanical ventilation. Most of the patients with ARDS will require ventilatory support, which may restore gas exchange and decrease work of breathing, thus improving the probability of survival. But mechanical ventilation is not exempt from side effects. Among these, the potential of positive pressure ventilation to damage the lungs, included in the concept of ventilator-induced or ventilator-associated lung injury (VILI/VALI, referred to experimental models and patients, respectively), is currently considered one of the key mechanisms related to the outcome.[2] The application of strategies aimed to minimize VALI, mainly by using low tidal volumes, has decreased the mortality of the syndrome.[3] Even the benefits of other treatments such as prone position[4] or neuromuscular blocking agents[5] are attributed to its potential to minimize the secondary damage caused by the ventilator.

The impact of ventilator settings on the induction of VALI has been present in the history of ARDS since its first description. Ashbaugh et al. describe in the original report of the syndrome that those patients who were ventilated with PEEP showed a better outcome.[6] A large body of evidence since then has demonstrated that the lung damage caused by ventilation is highly dependent on some ventilator variables.[7] In other words, different strategies may yield different effects. The ultimate mechanisms behind these differences have evolved over time, and the framework of VALI is under constant evolution.

In this review, we will describe the classical mechanisms of VALI and how they have evolved with the recent findings from pathophysiological and clinical studies, in order to analyze the clinical implications derived from them. Our objective is to extract a series of knowledge-based recommendations that can be helpful for the ventilatory management of ARDS patients at the bedside.

Mechanisms of ventilator-induced lung injury

The contemporary management of mechanical ventilation is intimately linked to the concept of VALI. Ultimately, VALI is a molecular response to the application of abnormal forces within the lungs that may lead to inflammation, oedema and extracellular matrix remodelling.[8] The spread of this mechanism beyond the lungs has been linked to the development of multiple organ failure. Collectively, VALI has been related to the clinical outcome, so its avoidance is a key objective in the ventilated patient.

A large number of molecular pathways are modified during mechanical ventilation and almost any process related to cell homeostasis has been implicated.[9] Inflammatory responses, changes in cell survival signalling and processing of the components of the extracellular matrix have been described after mechanical ventilation. The description of these mechanisms at a cellular and chemical level is outside the scope of this article. Instead, we will focus on the pathophysiological mechanisms that trigger VALI.

Classical mechanisms of VALI

Mechanical ventilation is the cornerstone of the critically-ill patients support, providing better gas exchange conditions while respiratory muscles rest. In 1967, the term ''respirator lung'' was coined to describe the diffuse alveolar damage and hyaline membranes found in post-mortem studies of patients submitted to positive pressure ventilation.[10] During the following decades, studies with experimental models showed the deleterious effects of high positive pressure ventilation and the benefit obtained by the application of positive end-expiratory pressure (PEEP). These pioneering studies allowed to introduce the experimental concept of Ventilator-induced lung injury (VILI) and, later on, its clinical counterpart, Ventilator-associated lung injury (VALI).[11,12]

Three classical mechanisms responsible for VALI have been described: biotrauma, barotrauma/volutrauma and atelectrauma:

Biotrauma: The mechanical stimulus that involves the application of positive pressure during mechanical ventilation triggers, through a process of mechanotransduction, a biological response characterized by the secretion of proinflammatory cytokines and the emergence of a neutrophilic infiltrate. As a result, there is a release of inflammatory mediators from the ventilated lung that can lead to a systemic dissemination, contributing to the development of the multiple organ dysfunction syndrome.[13] The establishment of protective ventilatory strategies and the application of PEEP can attenuate this phenomenon.
The biotrauma contributes to the persistence of the inflammatory process and it is associated with worse prognosis

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