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ORIGINAL

Preemptive hemodynamic intervention restricting the administration of fluids attenuates lung edema progression in oleic acid-induced lung injury

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KEYWORDS
Acute lung injury;
Oleic acid;
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Early protective lung strategy;
ARDS;
Pulmonary edema;
Respiratory mechanics;
Preemptive hemodynamic intervention

Abstract
Objective: A study is made of the influence of preemptive hemodynamic intervention restricting fluid administration upon the development of oleic acid-induced lung injury.
Design: A randomized in vivo study in rabbits was carried out.
Setting: University research laboratory.
Subjects: Sixteen anesthetized, mechanically ventilated rabbits.
Variables: Hemodynamic measurements obtained by transesophageal Doppler signal. Respiratory mechanics computed by a least square fitting method. Lung edema assessed by the ratio of wet weight to dry weight of the right lung. Histological examination of the left lung.
Interventions: Animals were randomly assigned to either the early protective lung strategy (EPLS) ($n = 8$) or the early protective hemodynamic strategy (EPHS) ($n = 8$). In both groups, lung injury was induced by the intravenous infusion of oleic acid (OA) (0.133 ml kg^{-1} h^{-1} for 2 h). At the same time, the EPLS group received 15 ml kg^{-1} h^{-1} of Ringer lactate solution, while the EPHS group received 30 ml kg^{-1} h^{-1}. Measurements were obtained at baseline and 1 and 2 h after starting OA infusion.
Results: After 2 h, the cardiac index decreased in the EPLS group ($p < 0.05$), whereas in the EPHS group it remained unchanged. Lung compliance decreased significantly only in the EPHS group ($p < 0.05$). Lung edema was greater in the EPHS group ($p < 0.05$). Histological damage proved similar in both groups ($p = 0.4$).
Conclusions: In this experimental model of early lung injury, lung edema progression was attenuated by preemptively restricting the administration of fluids.

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PALABRAS CLAVE
Lesión pulmonar aguda;
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Estrategia precoz protectora pulmonar;
SDRA;
Edema pulmonar;
Mecánica respiratoria;
Intervención hemodinámica preventiva

La restricción preventiva en la administración de fluidos disminuye la formación del edema en la lesión pulmonar inducida por ácido oleico

Resumen
Objetivo: Conocer cómo influye una intervención hemodinámica preventiva basada en la restricción de fluidos sobre el desarrollo de la lesión pulmonar inducida por la administración de ácido oleico.
Diseño: Estudio aleatorizado en animales vivos.
Lugar: Laboratorio universitario de investigación experimental.
Variables: Mecánica respiratoria (método de los mínimos cuadrados), medidas hemodinámicas (doppler esofágico), estimación del edema pulmonar (relación peso húmedo/seco del pulmón derecho) y daño histológico del pulmón izquierdo.
Intervenciones: Ocho animales fueron asignados a un grupo con una estrategia protectora pulmonar (EPP), y otros 8 a otro grupo con una estrategia protectora hemodinámica (EPH). En ambos grupos la lesión pulmonar se desencadenó mediante la administración intravenosa de ácido oleico (0,133 mL/kg^{-1}/h^{-1} durante 2 h), recibiendo simultáneamente los animales del grupo EPP 15 mL/kg^{-1}/h^{-1} de Ringer Lactato y los del grupo EPH 30 mL Kg^{-1} h^{-1}. Se obtuvieron medidas basales, a la hora y a las 2 h.
Resultados: Transcurridas las 2 h de experimento el índice cardiaco permaneció estable en el grupo EPH, pero disminuyó en el grupo EPP ($p < 0,05$). Por el contrario, la distensibilidad pulmonar disminuyó significativamente solo en el grupo EPH ($p < 0,05$), en el cual el edema pulmonar estimado mediante la relación peso húmedo/seco del pulmón derecho fue mayor ($p < 0,05$). El daño histológico fue similar en ambos grupos ($p = 0,4$).
Conclusiones: En este modelo experimental de lesión pulmonar aguda en fase inicial, la formación del edema pulmonar fue atenuada por la restricción preventiva en la administración de fluidos.

Introduction

Acute respiratory distress syndrome (ARDS) is a catastrophic form of respiratory failure that has been described in more than 30 entities or triggering conditions.[1,2] A common finding in all of them is a delay, which can range from hours to several days, between the time this initial aggression occurs and the subsequent clinical presentation of ARDS.[3] During this time gap, further attacks or impacts called ''second hits'' frequently occur that, although less intense, affect the lungs that are already damaged and sensitized, further aggravating the initial lung inflammation, and may precipitate the clinical onset of ARDS.[4,5] Most commonly, second hits are iatrogenic insults, such as transfusions, mechanical ventilations with high tidal volumes, or the inappropriate administration of fluids.[4–6] The theory of second hits implies that ARDS may have preclinical stages, offering to clinicians an opportunity to intervene earlier before devastating respiratory failure when clinical criteria of ARDS are present. In fact, a recent interdisciplinary intervention aimed at avoiding large tidal volumes and inappropriate transfusions in mechanically ventilated patients was associated with a decreased frequency of new cases of ARDS.[7]

Diffuse alveolar damage with severe inflammation and high permeability protein-rich edema in the lungs represents the most characteristic pathological finding in more than half of patients with ARDS.[8] In these patients, high permeability pulmonary edema contributes significantly to the development of the disease and represents a potential target for early preventative therapy. Pulmonary edema is determined by the Starling relationship, which predicts the net flow of liquid across a membrane. In high permeability pulmonary edema, the most common mechanism for a rise in the transcapillary filtration of fluids is an increase in capillary permeability. However, experimental studies demonstrated that, at a given increase in capillarity permeability, a modest change in pulmonary vascular pressure greatly modifies the quantity of pulmonary edema.[9] This is probably one of the reasons why a strategy of restricting the administration of fluids has demonstrated to be useful in ARDS for decreasing pulmonary edema and improving lung function.[10] However, whether this strategy restraining fluid administration may also be useful in preventing the development of ARDS is not well known.

We hypothesized that a preemptive hemodynamic intervention by restricting the administration of fluids, right at the very start of lung injury, would be successful in reducing the formation and the progression of pulmonary edema, decreasing the severity of the resulting respiratory failure. We refer to this strategy as the early protective lung strategy (EPLS) and compare it against another strategy to maintain hemodynamic stability, which we call the early protective hemodynamic strategy (EPHS). In this study, we applied from the very inception of the injury and pulmonary inflammation in a rabbit model of lung injury with the involvement

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