CRITICAL CARE

COMMENTARY

Lung ventilation strategies and regional lung inflammation

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See related research by de Prost et al., http://ccforum.com/content/17/4/R175

Abstract

Protective mechanical ventilation is currently accepted as a key strategy for the management of acute lung injury (ALI) and its most severe form, acute respiratory distress syndrome. The study by de Prost and colleagues in the current issue of *Critical Care* provides new insights into the impact of ventilation strategies on pulmonary function, gas exchange, and regional cellular metabolic activity during early ALI in sheep. The group reports that a protective ventilation strategy may attenuate neutrophil activation in dependent lung regions during early experimental ALI. This is an innovative report that provides the basis for further study.

Commentary

In the current issue of *Critical Care*, de Prost and colleagues [1] evaluated the impact of protective and injurious ventilation strategies on lung neutrophil distribution and activation in sheep 2 hours after endotoxin infusion. The protective ventilation strategy consisted of 8 mL/kg tidal volume and titration of positive end-expiratory pressure (PEEP) to achieve a plateau pressure of 30 cm H_2O. PEEP was not applied in the injurious ventilation protocol, and tidal volumes of 14 to 18 mL/kg were delivered. Positron emission tomography (PET) imaging and ^{13}N-[nitrogen]-saline infusion were performed to evaluate regional lung perfusion and shunt fraction. Cellular metabolic activities were measured by using an ^{18}F-fluorodeoxyglucose (^{18}F-FDG) infusion protocol, and lung leukocyte infiltration was determined by histological analysis. Their results show that protective ventilation was associated with better gas exchange and lower shunt fraction in dependent lung regions prior to endotoxin infusion. Endotoxin infusion worsened gas exchange in both groups, but less so in sheep receiving protective ventilation. Protective ventilation also attenuated ^{18}F-FDG uptake and phosphorylation after endotoxin infusion, particularly in dependent areas of the lungs. The authors conclude that a protective ventilation strategy that optimizes alveolar recruitment and minimizes alveolar distension may mitigate neutrophil activation in the lung, particularly in dependent areas, during early experimental acute lung injury (ALI).

Use of the sheep model in this study had several advantages. With a size comparable to that of the human, the ovine model allowed an analysis of physiological endpoints that are clinically relevant and permitted the application of ventilation strategies that are similar to those used in clinical practice. The tidal volumes and PEEP applied in the protective strategy are similar to those advocated for use in the clinical setting. Alternatively, a study by Takeuchi and colleagues [2] described a method of pressure-volume curve analysis to identify the most appropriate PEEP during mechanical ventilation in an adult sheep model of ALI, which may further optimize lung protection and would be interesting to apply in the model used by de Prost and colleagues [1]. The endotoxin infusion model has the advantage of being reproducible and easily titrated and is known to induce neutrophil accumulation in the lungs [3]. However, the protocol appears to have induced minimal histological evidence of lung injury as indicated by lung injury scores of 0 to 1 (on a scale of 0 to 4) in both groups. Given the lack of demonstrable lung injury at the histological level, it is possible that differences in normal lung recruitment and hemodynamics contributed to the dissimilarities in gas exchange and shunt fraction observed between groups. However, changes in alveolar-capillary integrity that were not detectable by light microscopy may also be present early after endotoxin infusion and could have contributed to the observed gas exchange perturbations.

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Evidence indicates that dysregulated inflammation and the inappropriate accumulation and activation of leukocytes, especially neutrophils, contribute to the pathogenesis of ALI [4,5]. Furthermore, investigators have postulated that protective ventilation strategies decrease regional lung inflammation in subjects with ALI [6,7]. The assessment of cellular metabolic activity by using PET imaging and ^{18}F-FDG infusion along with the evaluation of lung perfusion and ventilation, as performed by de Prost and colleagues [1], is an informative, non-invasive approach that provides useful data regarding regional differences in cellular metabolic rate. The technique may have practical utility since studies have shown that evaluation of ^{18}F-FDG uptake may be valuable in predicting respiratory failure and evaluating therapy in clinical and experimental models of ALI [8-10]. The present study extends previous reports by documenting the impact of ventilation strategies on regional metabolic activity and neutrophil accumulation early during the course of ALI. Although differences in cellular metabolic activity were observed between groups, neutrophil accumulation in the lungs was not different when sheep receiving protective or injurious ventilation were compared. The authors interpret that finding as possibly being indicative of increased neutrophil activation in sheep receiving injurious ventilation. That conclusion is based, in part, on previous studies that showed neutrophil activation to be the primary factor contributing to increased ^{18}F-FDG uptake and phosphorylation during ALI [11,12]. However, as noted by the authors, it is unclear whether the alterations in ^{18}F-FDG uptake and phosphorylation observed in their analysis are entirely specific for neutrophils. It is possible that the metabolic rates of other leukocyte and non-leukocyte cell populations were affected. Evidence indicates that alterations in macrophage, epithelial, and endothelial cell functions occur during ALI [4,13]. Thus, cell populations other than neutrophils may be activated by the endotoxin infusion. Further studies are needed to identify the cell populations that are affected and the functional importance of the observed alterations.

Overall, the study by de Prost and colleagues provides new insights into the impact of ventilation strategies on regional cellular metabolic activity during early ALI. More investigation is needed to extrapolate their findings into the clinical setting and determine the functional importance of their findings. It is hoped that the group will perform follow-up studies to determine whether the observed changes in regional leukocyte activation are predictive of progressive respiratory failure and pulmonary injury as well as better define the specific cell populations involved.

Abbreviations

^{18}F-FDG: ^{18}F-fluorodeoxyglucose; ALI: Acute lung injury; PEEP: Positive end-expiratory pressure; PET: Positron emission tomography.

Competing interests

The authors declare that they have no competing interests.

Published: 05 Sep 2013

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10.1186/cc12881
Cite this article as: Luan *et al.*: Lung ventilation strategies and regional lung inflammation. *Critical Care* 2013, 17:184