Reviewer's report

Title: High tidal volume mechanical ventilation-induced lung injury in rats is greater after acid instillation than after sepsis-induced acute lung injury, but does not increase systemic inflammation: an experimental study.

Version: 3 Date: 20 June 2011

Reviewer: enrique piacentini

Reviewer's report:

I have read with interest the paper: “High tidal volume mechanical ventilation-induced lung injury in rats is greater after acid instillation than after sepsis-induced acute lung injury, but does not increase systemic inflammation: an experimental study”.

I think it’s a good paper that deserves to be published.

I have one comment in the “Major Compulsory Revisions” category:

In the discussion, the paragraph:

“The systemic inflammatory response, in contrast to the pulmonary inflammatory response after different MV strategies following indirect and direct lung injury has not been studied to our knowledge.”


Shows that the level of TNF-alpha in blood is higher after injurious MV in two models of lung injury: direct and indirect.

Other studies on the subject:


I have two other comments, which fall into the category of "Discretionary Revisions".

First, I think the study has “a priori” problem; the choice of models of lung injury.

While both models (intra-tracheal acid instillation and cecal ligation and puncture) are well established, is no less true that they are little used by most lung injury researchers and that, in part, due to the variability in the degree of lung damage.

Therefore, I believe that while the findings are consistent with the hypothesis and the paper is solid, it would be good to incorporate a paragraph in Discussion, discussing the choice of models and their inherent limitations.

Second, the choice of the inflammatory mediators studied. It is known that the timing of the different cytokines involved in the immune response is variable. Moreover, the pattern of secretion also varies with the type of injury model, the intensity of the stimulus, duration, and so on. (See, for example: Orman MA, Nguyen TT, Ierapetritou MG, Berthiaume F, Androulakis IP. Comparison of the cytokine and chemokine dynamics of the early inflammatory response in models of burn injury and infection. Cytokine. 2011 Jun 6.)

It is therefore possible that the identification of other mediators different from those described in the paper have yielded different results. In fact, it is remarkable that, before the VILI model of sepsis has produced less systemic response to the primary lung injury model. It suggests that the stimulus has been mild. I think this point should also be included in the Discussion.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests