Reviewer’s report

Title: Effect of low tidal volume ventilation on lung function and inflammation in mice

Version: 1 Date: 19 November 2009

Reviewer: Vincenzo Cannizzaro

Reviewer’s report:

Major compulsory revisions

General comments and major limitations of this study:

1. Mechanical ventilation for 30 min is very short. Why did the authors use such a short-term protocol? A 30 min study protocol is most likely too short to “evaluate whether lower tidal volumes could be used as protective ventilation and serve as reference ventilation” (discussion, para 2). Other research groups have shown similar results using longer ventilation protocols.

2. The fact that “all mice were ventilated with a frequency of 150/min” – irrespective of applied tidal volume (5, 7, 10, or 30 mL/kg) – can be considered a major study flaw. Differences in minute volume ventilation may have had a major impact on PaCO2, lung perfusion, and acid-base status resulting in a relevant bias. How can the authors be sure that differences found can be attributed to the selected tidal volumes?

3. Number of animals per group: why did the authors include n=3 animals per group in both 30 mL/kg groups while all other groups had at least n=6?

4. Material and methods, protocols: “Mechanical ventilation was carried out for at least 30 min until a drop in oxygen saturation of >20% or a pulse rate below 200/min”. The readers should know if certain groups were more affected than others (how many animals in which group). Did the authors experience survival issues?

5. Measurement of respiratory system mechanics: the authors present relative changes in resistance and compliance. However, the flexiVent system does provide R (Newtonian resistance), G (tissue damping), and H (tissue elastance). Why did the authors present resistance and compliance only?

Specific comments:

Did the authors transform 1/H in order to present compliance? In addition, the reviewer believes that presentation of relative changes (instead of raw data) and compliance (instead of H) can be misleading. Were there any differences at baseline (raw data)? Lastly, in para 1 of the discussion, the authors state that lower tidal volumes were associated with worse lung function. In fact, the authors only found statistically significant differences in resistance and omitted the fact that resistance does not reflect “lung function”.
6. Introduction, para 2, line 2:
What is the difference between “protective” and “quasi-protective”?
The statement “while in murine models tidal volumes of 10 mL/kg are currently used as quasi-protective ventilation” can be considered a generalization. The authors should provide more references from murine studies that support their statement. To my best knowledge, different research groups in this field use different “definitions”. There is no consensus on definitions of low, protective, high, and extreme tidal volumes during mechanical ventilation in murine models.

7. Introduction, last para, last sentence:
It is difficult to imagine that such a short period of ventilation (30 min) can allow for drawing a conclusion about protective ventilation strategies, particularly when considering that inflammatory response is time dependent.

8. Material and methods, lung function measurements:
Which perturbation signal did the authors use (frequency range, duration)?

9. Material and methods, histological measurements:
The authors should provide additional information. How and when were the lungs fixed, for how long and at which pressure level?

10. Results, Figures:
Figures 1 and 2 are unclear. It is difficult to identify different study groups. The authors might use different symbols and higher resolutions.

11. References:
Reference 11 and 21 are identical

**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