Reviewer's report

Title: Comparison of the Effects of Moderate and Severe Hypercapnic Acidosis on Ventilation-Induced Lung Injury

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Reviewer: John Laffey

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Yang et al present data from an in vivo animal experiment in which they elucidate the dose response characteristics of acute hypercapnic acidosis in the setting of VILI in the rat. The authors have addressed most of my comments, and overall the paper is significantly improved, with figure 1 in particular constituting a welcome addition. A couple of issues remain to be clarified.

Major compulsory Revisions

1. I am still unclear as to whether this was a randomized study. The authors state that ‘animals were randomly assigned to one group, then randomly assigned to another group etc. Can they provide further detail on this, as I don’t understand how the animals can have been randomly assigned if they were only assigned to one group, then subsequently to a different group. The key question is: did each animal have an equal chance of being allocated to any of the 5 groups studied? If the answer is ‘no’ then this was not a random allocation method. I don’t see this as a critical issue, but it is important for the reader to understand how exactly the animal allocation was performed. Given this, please detail the randomization method in the manuscript.

2. I also do not understand why the authors do not have the data available for the lung injury score determination for the NV group in figure 2. Contrary to their response to my point, they have presented the physiologic data for these animals in Figure 1. Also, they have stained tissue from these lungs for ICAM-1 and P65 expression. Therefore, it should just be a matter of H+E staining these slides for determination of the LIS and presenting the data and representative figures.

3. It is also a good idea to put the sample size calculations into the methods, given that the authors went to the trouble of performing this calculation and using it to guide their experimental design.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests