Reviewer’s report

Title: EFFECT OF PEEP AND I:E RATIO ON CEREBRAL OXYGENATION IN ARDS: AN EXPERIMENTAL STUDY IN ANESTHETIZED RABBIT

Version: 1 Date: 23 Dec 2018

Reviewer: Stefan Kreyer

Reviewer's report:

Dr. Lovisari and Co-workers present in this work their data about the effects PEEP-Level and Inspiration : Expiration ratio on cerebral oxygenation in healthy lungs and in an experimental ARDS. Their work focuses on different parameters to measure cerebral oxygenation. The authors chose an experimental ARDS in rabbits by intravenous LPS injection and saline lavage. The authors could show that IRV decreased cerebral oxygenation, while in ARDS IRV did not improve cerebral oxygenation, despite improving gas exchange. The increase in PEEP did improve cerebral oxygenation despite lower CF. Data presented here are interesting, although some questions arise.

Major concerns:
1. Animals in PEEP6 are extremely hypoxic. This level of hypoxy may influence cerebral autoregulation and cardiac function, which may create a major bias. How do you exclude this bias.
2. Without measuring cardiac output it is difficult to exclude systemic changes in cardiac output on cerebral blood flow. Did the authors measure cardiac output?
3. Research about cerebral blood flow in ARDS is always complex as changes in CO2-levels and different ventilator settings have separate influence on cerebral blood flow. The authors already stated this in the limitations section. CO2-levels are different between the PEEP-levels. In my opinion this has a significant influence on brain perfusion and subsequently brain oxygenation. Please discuss.
4. Did you randomize in ARDS levels of PEEP, like the I:E setting? If not do you think that this may have an influence on results as PEEP6 was always subsequent to PEEP9?
5. Page 14 Line 46: Do you think that reduced CVP suggest a reduced venous return? Using CVP as preload parameter is not meaningfull. Kumar et al., Crit Care Med 2004;32: 691-699

Minor recommendations:
1. I would recommend to state that this study was done in animals and transferring the results to humans is not without issues.
2. The legend of figure 2 is incorrect as there are no triangles and inverted triangles in figure 2. I would recommend to delete the box in figure 2 muscleΔHb and include symbol explanation in legend. This is also valid for figure4.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

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