Reviewer’s report

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

Version: 2 Date: 07 Apr 2019

Reviewer: Pablo Cruces

Reviewer's report:

Dear Dr. Bayat

I agree with most of the answers and modifications made to the manuscript.

However, I have some queries

1. R5. Volume control mode was not used, because this ventilator mode is seldom used in patients with ARDS, because of the risk of ventilator-associated lung injury.

Whether pressure-controlled ventilation (PCV) can reduce ventilator-associated lung injury (VALI) compared to volume-controlled (VCV) ventilation is a matter of debate. A meta-analysis of three randomized controlled trials (RCTs) concluded that PCV was not superior to VCV [1]. Another systematic review which included 34 studies concluded that outcome is "unlikely influenced by simply using one breath type vs the other for all patients" [2]. Since flow, driving pressure, and frequency determine the power, and the factor by which ventilation injures the lungs, it seems unlikely that the manner in which this power is delivered (i.e., flow pattern) plays a major role. Despite their theoretical benefits, the clinical evidence of both techniques remains unproven and controversial for ARDS patients [3].

Undoubtedly it is much simpler to measure pulmonary mechanics (i.e. plateau pressure) in VCV mode. I understand that it is not the central theme of the manuscript in evaluation.


R9. As stated in the Methods section (page 7), the order of I:E ratios was randomized.

Q2. What method was used to randomize the rats.

12. Is it possible to affirm, using CVP, MAP and CF, that "increasing the I:E ratio decreased venous return"?
R12. The statement was revised. We take the reviewer's point that it would have been better to measure cardiac output and agree with the reviewer that CVP is an imperfect indicator of volume status, however, it does seem to vary with hypovolemia and fluid resuscitation in rabbits (see: Chen et al. J Trauma. 2009 Mar;66(3):676-82). We have added a comment on this point in the study limitations section of the Discussion.

Q2. I understand the difficulties of measuring cardiac output by pulmonary thermodilution in subjects of 3.5 kg. However, the authors state that: "Arterial, central venous and respiratory pressure, ECG and CF signals were digitized and recorded at 1 kHz using an analog/digital interface (Powerlab model 8/35, ADInstruments)".

Why not use dynamic preload markers (PPV or SPV) to estimate preload?

Q2. Table 1. Tables should be self-explanatory
Vein SO2 is Jugular bulb saturation (SjO2) or central venous saturation (ScvO2)?
When reading the manuscript I understand that the authors refer to SjO2.

ScvO2 values were recorded?
It would be interesting to have ScvO2. Parallel changes of SjO2 and ScvO2 reaffirm that hemodynamic deterioration due to inverted I:E ratio ventilation induces cerebral oxygenation deterioration. The homogeneity of venous lactate is surprising in the successive measurements.

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

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I am able to assess the statistics

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