Author’s response to reviews

Title: Regulating Autonomic Nervous System Homeostasis improves Pulmonary Function in rabbits with Acute Lung Injury

Authors:

YAN LIU (liuyan8586@sina.com)
TAO TAO (22225598@qq.com)
WENZHI LI (wenzhili321@163.com)
YULONG BO (boyulong163@163.com)

Version: 2 Date: 12 Apr 2017

Author’s response to reviews:

Manuscript ID: PULM-D-16-00357R1

Regulating Autonomic Nervous System Homeostasis improves Pulmonary Function in rabbits with Acute Lung Injury

Dear editor and reviewers,

Thank you very much for your letter and comments concerning our manuscript entitled “Regulating Autonomic Nervous System Homeostasis improves Pulmonary Function in rabbits with Acute Lung Injury” (Manuscript ID: PULM-D-16-00357R1). Those comments are all valuable and helpful to improve our research.

We have studied the comments carefully and have made corrections which we are hope meet with approval. Revised portions are highlighted by track changes mode in MS word in the paper. The point-by-point response to comments are listed below.

We are looking forward to getting your approval for its publication. If you have any additional questions, please contact us without hesitation.

Sincerely yours,

Responses to comments

Editor comments:
1. There are some additional major revisions that are necessary, as highlighted by Reviewer 3’s comments below, in the "Reviewer reports" section.

Response: Thank you very much for your advice. We have carefully study the comments pointed by Reviewer 3 and answered them with point-by-point manner.

2. As reviewer 3 points out, we require a completed ARRIVE checklist so that your methodology can be fully assessed. In accordance with BioMed Central editorial policies (http://www.biomedcentral.com/submissions/editorial-policies#standards+of+reporting), could you please ensure your manuscript reporting adheres to ARRIVE guidelines (https://www.nc3rs.org.uk/arrive-guidelines) for reporting in-vivo animal research? This is so your methodology can be fully evaluated and utilized. Can you please include a completed ARRIVE checklist as an additional file when submitting your revised manuscript.

Response: Thank you very much for your comment. We have completed the ARRIVE checklist and affiliated it this time. Moreover, we have also a statement that the animal research in this manuscript performed according to the ARRIVE guidelines.

3. Please make sure that your revised manuscript contains both a tracked-changes version and a clean version, so that the reviewers are able to assess the amendments.

Response: Thank you very much for your comment. We have provided both a tracked-changes version and a clean version for this modification.

Reviewer 1:

1. Please correct the typo on page 11, write (Figure 5d) instead of Figure 4d).

Response: Thank you very much for your comment. We have changed the Figure 4d to Figure 5d.

Reviewer 3:

1. The editor suggested adding a completed ARRIVE checklist in order to adhere to journal and internationally accepted policies regarding animal welfare and research. The checklist and also several important points mentioned in these guidelines have still not been provided by the authors.

Response: Thank you very much for your comment. We have completed the ARRIVE checklist and affiliated it.

2. Unfortunately, I cannot fully appreciate the authors‘ changes in the manuscript, as they haven‘t been marked (neither in the pdf provided by the journal, nor in the downloadable Word-doc).
Response: Thank you very much for your comment. We have highlighted the first modification by yellow color in the revised manuscript and the second modifications are highlighted by track changes mode in MS word.

3. The Methods section has improved by the revision, however I still have some questions regarding the model and the treatment:

a. Why did the authors choose a FiO2 of 1.0?

b. A bolus of 5 ml bupivacaine 0.25% seems rather high to me, due the fact that the maximum dose for humans should not exceed 2 mg/kg and the rabbits in the current study received doses of 4.6 - 3.9 mg/kg. What’s the rationale for this high dose? How do the doses in rabbits compare with humans? Have any adverse events been noted (see also ARRIVE checklist)?

Response: Thank you very much for your comments.

a. A FiO2 = 1.0 indicates that the concentration of oxygen is 100%. For the ventilation of rabbit, when inspiratory PaO2 more than 400 mmHg is consider regular and less than 200 mmHg is considered ALI. During the preliminary experiment, if the FiO2 = 1.0, the rabbits can survival after 6h of ALI; whereas if the FiO2 lower than 1.0, the survival of rabbits will obviously decreased after 6h of ALI. Therefore, the FiO2 = 1.0 was selected in this study.

b. Although the clinical dose can provide a reference for the pentobarbital usage in animals, but there is still some difference between human and animals. In the preliminary experiments, a series of pentobarbital dosage were applied, including 25 mg/kg, 30 mg/kg, 35 mg/kg and 40 mg/kg. After compared, the 30 mg/kg was selected. With this concentration, pentobarbital not only can inhibits the corneal reflex and surgical pain during model induced, but also performed no obvious effect on breathing and hear rate. Meanwhile, combined with 0.1 mg/kg pipecuronium also can significantly inhibit the occurrence of bucking response.


a. I completely disagree with the authors that "SEM and SD can be mutual converted" as they state in their response to the reviewers’ comments. SD is a measure of variability and allows the reader to appreciate the data better. The concern raised by the authors that the figures would be "very disordered" is inappropriate for a scientific publication. Please see also BMJ. 2005 Oct 15; 331(7521): 903. or Br J Anaesth (2003) 90 (4): 514-516 for further information regarding this important issue.

b. The information about how normal distribution has been assessed is still missing.

Response: Thank you very much for your comments and recommendations.

a. We have carefully studied these two study to improve our knowledge on statistic. Actually, in the first revised version, the statistical results had been revised to present with mean ± standard deviation. But due to our poor statistical knowledge, the effective communication and
understanding of this results have been limited. In this revised version, we have corrected this statement as "All data were expressed as mean ± standard deviation (SD)" in the manuscript.

b. The normality of the data distributions was assessed using PROC UNIVARIATE. We have added this statement in the manuscript.

5. Results, overall: In my initial comment I suggested to report "the exact p-values for ALL reported results, also the non-significant ones". The authors now have incorporated the t statistics for all comparisons, but still do not report any exact p-value, although they say otherwise in the response to the reviewers' comments.

Response: Thank you very much for your comments. We have provided all the t and P values of the comparisons of significant difference. Because there are many comparisons included in this study, we have only provided the significant ones to avoid adding more redundant description.