Reviewer's report

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

Version: 3  Date: 16 September 2014

Reviewer: Maria JC Carmona

Reviewer's report:

The authors compare the effects of moderate and severe hypercapnic acidosis on high pressure ventilation-induced inflammatory injury and evaluate the role of the NF-KB pathway in this process. The topic is original and important, considering the potential protective effects of hypercapnic acidosis on lung injury and the uncertainty regarding appropriate PaCO2.

Throughout the text, all abbreviations should be carefully described (e.g. BALF and BAL for bronchoalveolar lavage fluid). The English should be revised.

ABSTRACT: the sample size, summary of the statistical analysis and main numerical results could be presented in the abstract.

INTRODUCTION: - I suggest the authors present evidences that PIP of 30 cm of H2O promotes VILI (stretch induced injury), as well as the other causes of VILI. The aim of the study is well defined. Additionally to the main objectives, I suggest the inclusion of secondary objectives such as markers of lung inflammation and histology.

METHODS: The method is appropriate and adequately described, but some points should be considered: 1) The sample size should be justified. 2) How long the animals were ventilated in the experimental group. This information is clear in the discussion, but not in the method section. 3) Page 7, lines 118-122: specify that the anesthesia technique (pentobarbital and pancuronium bromide) is related only with NC, MHA and SHA groups (not all rats). 4) Concerning to BALF, the aspiration technique alters the cellularity and could be better explained (manual or vacuum suction?). 5) The authors mentioned that a gas mixture of carbon dioxide with oxygen was administered to maintain the target PaCO2 in the NC, MHA and SHA groups. How the FiO2 was evaluated during this period? Was the previously mentioned FiO2 (0.7) constant?

RESULTS: 1) It could be interesting the inclusion of a flowchart with the distribution of the animals between groups, as well as the exclusion data and final analysis. 2) Do the authors have data concerning the respiratory mechanics in NC, MHA and SHA groups?

DISCUSSION: I suggest the authors discuss the PIP of 30 cm of H2O as the cause of VILI (stretch-induced injury). What are the evidences that VILI is related to PIP? Could it be due to FiO2, PEEP, or a combination of these factors?
Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

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.