Reviewer’s report

Title: Intravenous superoxide dismutase as a protective agent to prevent impairment of lung function induced by high tidal volume ventilation

Version: 0 Date: 28 May 2017

Reviewer: Robert Foronjy

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The authors conducted a rigorous study evaluating the impact of intravenous SOD1 on the development of high tidal volume induced acute lung injury. They document that SOD1 treatment attenuates the injury responses that occur in this model. These findings could potentially expand our understanding of the role of oxidative stress and antioxidant responses on the lung injury that occurs during mechanical ventilation. This manuscript is well written but there are some concerns that limit my enthusiasm in its present form. These are listed below:

1. They need to do a control for SOD1 infusion. It is conceivable that infusing a protein could induce protective responses that limit the extent of HTV mediated lung injury. As an example, low dose LPS attenuates experimental acute lung injury. The ideal control would be heat inactivated SOD1.

2. They need to restate what they say in the Introduction on page 6. It's not accurate to say that there are no recommendations for optimal ventilator management strategies. Recommendations of 5-7 cc/kg are well established and ICUs are judged by their adherence to this vent strategy.

3. Does the SOD1 they infuse reach the lungs? Perhaps they could add a fluorescent tag to SOD to see if it actually reaches the lavage fluid.

4. The high tidal volume they choose seems to be very high. Some of the literature suggests a normal tidal volume for a 300 g rat would be about 1.6 ml. The volume used here would be more than double that (5.4 ml/300 g mouse). This is more than would occur with humans so they should at least comment on this in the Discussion.

5. The image quality for Figure 1 should be improved. Some images are much darker than others and there is no scale bar for reference.

6. It is not necessary to show every immunoblot in Figure 8. They should show representative examples.

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.

No

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
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