Author’s response to reviews

Title: Effects of dexmedetomidine on porcine pulmonary artery vascular smooth muscle

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Version: 3 Date: 21 Aug 2019

Author’s response to reviews:

Martin Kaczocha, PhD
Editor-in-Chief
BMC Anesthesiology

BANE-D-19-00220R1

Effects of dexmedetomidine on porcine pulmonary artery vascular smooth muscle
Kenichi Sato; Mami Chikuda

20 August 2019

Dear Professor Kaczocha,

Thank you very much for your consideration of our manuscript. We fundamentally agree with all comments and have incorporated them in the revised version of our manuscript. Red font in the revised manuscript indicates the changes according to Reviewer #1. Blue font indicates the changes according to Reviewer #2.

Our responses are on the following pages. We hope that you find them sufficient and are able to view them positively.
We look forward to hearing from you at your earliest convenience.

Sincerely yours,

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Responses to Reviewers’ Comments

James P Dilger, PhD (Reviewer 1):

Most of my criticisms were adequately addressed. However, I still have questions about the statistical analysis and graphs.

1. Some of the graphs are poorly made. I didn't notice this before, but it should be clear from my attachment "Figure 1b with rulers". The spacing between the tick marks on both the x- and y-axes is not uniform. In the attached graphic, I used a software ruler, scaled in pixels to overlay on Fig 1b. I used the zoom control to have there be 50 px between 10 and 9 on the concentration axis. The spacing between the other ticks ranges from 52 to 60 px. On the y-axis, the distance between 0 and 10 is 96 px and between 10 and 20 is 108 px. There are similar discrepancies in other graphs. Please check all of them.

Response: Thank you for your careful review. Accordingly, we checked all the graphs and fixed the tick marks. We also remade Figures 1, 2, 5, 6, 7.
2. I realize that ANOVA was used to analyze Fig 1b. I would venture a guess that the result was \( p<0.05 \). Then you performed post-hoc tests with Scheffe’s multiple comparison procedure. Although the Scheffe test decreases the probability of a Type I error (false positive), it increases the probability of a Type II error (false negative). Because the Scheffe test compares all combinations of groups (dex concentrations), it makes \( 7! \) (factorial) comparisons. That may not be the ideal way to consider this data. You could consider the lowest concentration point to be your control, and just test whether each successive point is significantly different from that. You will end up with 6 comparisons, providing a more powerful test of whether there are differences. My guess is that the highest concentration point will definitely be significantly different, and perhaps the second highest as well.

Response: Thank you for your Comment. We recalculated all the statistics with new statistical software (SPSS Statistics 26, IBM Corp.) and stated so in the revised manuscript, as follows.

“Statistical analysis was performed using SPSS for Windows 10 (IBM SPSS Statistics 26; IBM Corp., Armonk, NY, USA). Differences among multiple groups were evaluated with one-way analysis of variance followed by Dunnett’s or Scheffe’s multiple comparison procedure. Differences were considered significant at \( p<0.05 \).” (Page 9, lines 14-19)

We also made the relevant corrections in the figures and added Figure 3.

Jean-Pierre Estèbe, MD, PhD (Reviewer 2)

I have carefully read the revised manuscript and the authors' responses. Clarifications have been done. I think that this experimental study has been expressed at its maximum. I would like the authors to put in the limits of their study the lack of new control at the end of each procedure (i.e. as at the beginning .. "infusion 5 microM adrenaline as control value"). This would have made possible to confirm the reproducibility the contraction tension, with or without a decrease effect of the baseline of the response.

Response: Thank you for your Comment and your kind words. We are sorry but we are not sure exactly what you mean by the lack of a new control….” If you could provide an example using our data it would be helpful. We would be more than happy to revise the manuscript further.

To the Reviewers: Thank you for your reviews and helpful suggestions. We hope that our responses have addressed your concerns. Please let us know if you require further clarification.