Reviewer’s report

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

Version: 1 Date: 07 Jun 2019

Reviewer: James Dilger

Reviewer's report:

The authors note that Dex is often administered with local anesthetics, so it is important to investigate whether Dex may have side effects, such as on the circulatory system. They chose to study its effect on pulmonary arteries. Following the lead of a similar study on gastroepiploic arteries (Ref 7), they perform a logical series of experiments and come to similar conclusions.

General Comments.

1. Manuscript organization. The Methods section should contain a general description of the experimental approach rather than a figure-by-figure description. Moving some of the text in the Methods to the appropriate place in the Results section, would make the manuscript easier to read. In addition, in the Results section, the authors could add a sentence explaining the rationale for each experiment. This is, indeed, found in the Discussion, but the paper would flow more clearly with some commentary in the Results. The Discussion could then be shortened somewhat.

2. Dex concentrations. I could not find any mention of clinical concentrations that are used with Dex. This should be provided to allow the reader to assess the clinical importance of the findings.

3. Choice of pulmonary artery. The authors do not provide any motivation for this choice. When Dex is given with a local anesthetic, is there a possibility of sufficiently high Dex concentrations in the lung?

4. Statistics. Please provide the statistical test used in each figure legend. For example, in Fig 2D, this should be analyzed with ANOVA and then a post-hoc test. Was the post-hoc test performed for each concentration vs control?
Specific Comments. I use the line numbers at the far left side of the page.

1. p 3, line 33. Please include Dex concentrations in the abstract.

2. p. 5, line 12. This would be a good place to include the concentration of Dex used in local anesthesia.

3. p. 6, line 56. What is the "incubator"? At what temperature were the experiments performed?


5. p. 10, line 33. Are the "untreated samples" the control muscles?

6. p. 10, line 30-35. It is contradictory to say "no significant changes" in one sentence then "slight increases" in the next sentence. It looks as if the changes seen at high [Dex] in Fig 1 are significant. Please clarify.

7. p. 10, line 56. I don't normally think of having only 1 or 2 points different from control as evidence for a "concentration dependent" effect.

8. p. 11, line 51. It would be better to write "a transient increase" rather than "transient increases".

9. p. 13, lines 7-12. This is not a complete sentence.

10. p. 14, line 51. You are not measuring effects on "cell membrane depolarization".

11. p. 16, line 48. Define "high doses".

12. p. 17, line 20. Here we have a definition of "high doses" as (>10−8 mol/L). That would suggest that most of your significant results are with high doses. Please comment.

13. p. 17, line 40. You used multiple concentrations of Dex, so this sentence does not make sense.

14. p. 24, lines 20-25. Are these changes significant? If not, do not give the numbers.

15. Fig 1. Are the tensions measured relative to the adjacent baseline (before adding KCl + drug) or the KCl baseline? This also applies to other figures.

16. Fig 2 B, D. The y-axis label should be "Relative tension (%)" only.

17. Fig 3. Here, I refer to panels such that the upper part has panels 1, 2, and 3 and the lower has 4, 5, and 6. The effect of Dex shown in panel 4 is much smaller than that reported in Fig 2. Please comment.
18. Fig 3. Panels 5 and 6 contradict panels 2 and 3. Or, are the bars mislabeled such that R should be D and P should be D?

19. Fig 4. IC50 values should be calculated for the various ligands.

20. Fig 5. My question about baselines (question 15) is relevant here.

**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

**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

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