Reviewer’s report

Title: Optimal dose of pretreated-dexmedetomidine in fentanyl-induced cough suppression: a prospective randomized controlled trial

Version: 0 Date: 21 Feb 2019

Reviewer: George Dumas

Reviewer's report:

This article is titled "Optimal dose of pretreated-dexmedetomidine in fentanyl-induced cough suppression: a prospective randomized controlled trial". The authors have used a prospective randomized controlled study to investigate and determine the optimal dose of pretreated-dexmedetomidine for suppression of fentanyl induced cough. Suppression of fentanyl induced cough is important in certain clinical situations. Also, dexmedetomidine has several side effects that may limit its use.

Methods: Overall methods are good; however, please define hypotension and impairment of liver and kidney function parameters/criteria.

Are the conclusions drawn adequately supported by the data shown: Yes; however, the paper needs better organization regarding MAP and HR (safety) in the results section. MAP and HR significance is stated for group 4 at various time points. It would be worth additional clarification in the Results section to state nonsignificance in the groups 1, 2, and 3 regarding HR at all time points compared to T0. You did make that point in the discussion "There were no significant changes of MAP, HR, or SpO2 occurred in the other three groups" but clarification is needed in the Results section.

Extensive Language editing will be required to make the paper flow smoothly and unambiguously.

Other Comments:

1. The word "pumped" is used often and should be changed to intravenous, bolus, etc depending on the context.

2. Background:

line 33- need to change phrase "to hinder or relieve this side effect" as it doesn't flow well.
line 37- the phrase adrenoceptor "excitatory effect" is used often throughout the paper. I would consider changing to "agonist effect"

line 47- states that another study does not exist regarding optimal dose of dexmedetomidine (Dex), this is not entirely correct- please cite and review: Liang He, Jun-Mei Xu, Ru-Ping Dai. Dexmedetomidine reduces the incidence of fentanyl-induced cough: A double-blind, randomized, and placebo-controlled study. Ups J Med Sci. 2012 Mar; 117(1):18-21. Better cough suppression was found at 1 mcg/kg bolus vs. 0.5 mcg/kg Dex bolus without an increase in side effects.

3. Study protocol:
I would consider changing dex dosing information to "mcg/kg bolus given over 10 minutes" as this is how it is typically written in similar studies. The current description: mcg/kg/min for 10 minutes is technically accurate but not the typical manner that dex bolus dosing is usually described.

4. Sample size determination:
line 3- why did you hypothesize that incidence of FIC would be reduced to 15%?

5. Effects of pretreatments on the onset time of cough:
line 13- need to add information to table 2 regarding onset time of cough

6. Safety: this paragraph needs more HR information. Please separate HR information from MAP information from adverse event information- it is a little unclear as written.

See comments above related to conclusion, need some more detail on comparisons in safety section pertaining to HR for groups 1,2, and 3.

7. Discussion:
line 15- "as compared to 'lower doses' in the previous studies" did you mean to state "slower injection"?

line 21- mechanism of FIC- need citations for mechanism (3) and (4)
line 9- need citation for suppression of FIC by penetration of blood brain barrier and inhibiting cough center directly

line 17- "Prolonging the injection time of fentanyl over the time to reach the threshold of its plasma concentration may reduce the incidence and severity of FIC further, which is our next work to be done"- it is already known that extending the time of administration of fentanyl will reduce incidence of cough

line 23- please rewrite the following sentence to make it flow better: "First, judging measures. . . and no more accurate indicators have been found till now"

8. Table 1: the Numbers row is not essential. That info is already in the table. Also the term "Figure Legends" above Table 1 needs to be deleted.

9. Table 2: please add cough onset time data as a new row, this is important data

10. Figure 1: add "refused to participate" after "5 did not meet the inclusion criteria and 7"

11. Figure 2 and 3: T3 needs to be defined below both figures. Please clarify precisely that p-values (a,b) pertain to group 4 (this seems to be the intent).

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
Quality of written English
Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal