Reviewer’s report

Title: Anticholinergics aggravate the imbalance of the autonomic nervous system in stable chronic obstructive pulmonary disease

Version: 0 Date: 27 Dec 2018

Reviewer: Reviewer 2

Reviewer's report:

PEER REVIEWER ASSESSMENTS:

OBJECTIVE - Full research articles: is there a clear objective that addresses a testable research question(s) (brief or other article types: is there a clear objective)?

Yes - there is a clear objective

DESIGN - Is the current approach (including controls and analysis protocols) appropriate for the objective?

No - there are minor issues

EXECUTION - Are the experiments and analyses performed with technical rigor to allow confidence in the results?

No - there are minor issues

Statistics - Is the use of statistics in the manuscript appropriate?

No - there are issues with the statistics in the study

INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?

No - there are minor issues
OVERALL MANUSCRIPT POTENTIAL - Is the current version of this work technically sound? If not, can revisions be made to make the work technically sound?

Probably - with minor revisions

PEER REVIEWER COMMENTS:

GENERAL COMMENTS: This is a well organized and largely well written report that heart rate recovery is decreased in COPD patients on anti-colinergics. The overall implication is that decreased HRR indicates para-sympathetic imbalance predisposing these patients to cardiovascular events.

The MS is largely well written with clear goals (there are some minor grammatical issues in the Introduction and part of the Discussion). The results are of interest and may instruct on how to address this potential parasympathetic imbalance and monitor more closely the patients on anti-colinergics.

My main recommendation is to move several parts of the discussion to the Introduction, notably on summarizing the overall concept of parasympathetic imbalance, its frequency in patients on Tiotropium, and the value of HRR as an measure of this imbalance. I would suggest that the authors emphasize the importance of their findings and the potential implications on patient management.

As the study did not involve a followup, it is unclear whether these patients are/were at increased risk of adverse CV events. Though one prior study is mentioned, it may be worthwhile mentioning how a subsequent study can be organized and the hypothesis to be tested (to further expand the reported data).

REQUESTED REVISIONS:

My answers largely refer to the organization of the MS and how to best discuss the overall relevance and novelty of the reported findings.

ADDITIONAL REQUESTS/SUGGESTIONS:

None.

Note: This reviewer report can be downloaded - see attached pdf file.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

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.

No

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:

Needs some language corrections before being published

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.

This reviewer has been recruited by a partner organization, Research Square. Reviewers with declared or apparent competing interests are not utilized for these reviews. This reviewer has agreed to publication of their comments online under a Creative Commons Attribution License attributed to Research Square and was paid a small honorarium for completing the review within a specified timeframe. Honoraria for reviews such as this are paid regardless of the reviewer recommendation.

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