Reviewer’s report

Title: Associations of AMP and adenosine induced dyspnea sensation to large and small airways dysfunction in asthma

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Reviewer: Tobias Müller

Reviewer’s report:

In this manuscript Cox and coworkers compared dyspnea in 2 different bronchoprovocation tests using either adenosine or AMP. In general, the manuscript is well written and contains some new data which are of interest. However, several points should be addressed:

1. In general: The authors hypothesize that due to particle size AMP targets large airways whereas adenosine targets small airways. However, this is neither supported by the data presented in the manuscript nor by data derived from the literature. Therefore, this point remains speculative.

2. What was the asthma diagnosis of patients included into the study based on?

3. The authors suggest that adenosine induces dyspnea via a different mechanism compared to AMP. Hence, studies to reveal the underlying mechanisms should be performed. However, this point is also speculative as the effects on pulmonary function induced by adenosine and AMP were very similar.

4. Both AMP and adenosine are indirect acting agents for bronchoprovocation. Comparing either adenosine of AMP to a direct acting agent (e. g. methacholine) would be of greater interest.

5. Did the authors also perform body plethysmography? It would be of interest whether the degree of dyspnea is correlated to airway resistance or hyperinflation.

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.
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

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