Reviewer's report

Title: Inhaled beta-agonist does not modify sympathetic activity in patients with COPD

Version: 2 Date: 12 February 2015

Reviewer: Surya Bhatt

Reviewer's report:

The authors performed a single arm partially blinded interventional study to assess the sympathetic effects of salmeterol, a beta agonist. This study is very relevant as COPD patients have heightened sympathetic activation that possibly contributed to cardiovascular comorbidity in these patients. While the medication can potentially cause sympathetic activation, it could potentially decrease this activation by effects on lung hyperinflation. The authors used muscle sympathetic nerve activity to assess systemic sympathetic activity. I have a few comments.

Major:
1. There was a significant reduction in the actual number of subjects studied, significantly decreasing the power of the study. This needs more comment.
2. It is known that an increase in resting heart rates is associated with an increase in mortality. While the authors report a 4 BPM increase in HR acutely after salmeterol administration at both visits, what was the impact on resting heart rate?
3. The administration of salmeterol for 4 weeks could potentially result in saturation of beta receptors, thus preventing further effects at visit 2. The authors should comment on this.
4. Half the patients were current smokers. Smoking is known to increase sympathetic activation. Was this controlled for?

Minor:
1. The authors state that the baseline MSNA was elevated. Please provide reference values for normal subjects.
2. Results.. Lines 194 and 195..“As an acute effect of salmeterol, low frequency power (reflecting sympathetic tone) was significantly elevated while high frequency power (reflecting parasympathetic tone) decreased”. Please clarify what measurements these results pertain to.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

I declare that I have no competing interest.