Reviewer's report

Title: Inflammatory cytokine response to exercise in alpha-1-antitrypsin deficient COPD patients 'on' or 'off' augmentation therapy

Version: 2 Date: 3 February 2014

Reviewer: Warren Davidson

Reviewer's report:

The MS was well written. Table 1 and the Figures were clear and well-described.

Minor Essential Revisions

METHODS section

(1) Please clarify if other systemic manifestations of AATD (i.e. liver disease/dysfunction) were evaluated prior to enrollment. Please explain if this was part of the exclusion criteria - if not, what was the rationale?

(2) Please clarify why COPD medications were not listed/provided. Please clarify whether high dose inhaled corticosteroid use (or other medications such as Roflumilast) could affect systemic cytokine levels.

(3) Exclusion criteria listed oral corticosteroids. Was recent use of parenteral corticosteroids an exclusion?

(4) "Cardiovascular disease" was listed as an exclusion. Please clarify whether this was based on history or clinical evaluation/investigations.

(5) Please clarify what metric, if any, was used to evaluate the baseline "daily physical activity" in the study subjects.

(6) Please clarify what is meant by "genetic assessment of alpha-1 antitrypsin levels".

(7) Please justify the use of the single-leg knee -extensor exercise in these patient populations.

(8) Please clarify the order of exercise testing on study day 1. Was the order randomized?

(9) The authors mention the importance of the inflammatory/anti-inflammatory balance in exercise and the COPD population. Please explain why anti-inflammatory markers (i.e. IL-10) were not measured in this study.

(10) Please clarify why the cytokine data was square root transformed rather than using a non-parametric test (i.e. Friedman test).

RESULTS

(1) Authors state that the similar KE exercise capacity suggests similar sedentary lifestyle between patient and control groups. Please justify this statement by providing background on how KE exercise capacity correlates directly with daily exercise activity.
(2) Please describe the metric used to assess baseline daily activity level for the study populations.

(3) Please comment on IL-1beta levels near the minimal detection level (AATD+AUG, AATD PFTnorm).

Discretionary Revisions

METHODS

Please change Pulmonary function to "Spirometry". Only spirometry was measured and the term "pulmonary function" suggests lung volume +/- diffusing capacity measurement.

Level of interest: An article of outstanding merit and interest 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 interests.