Reviewer’s report

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

Version: 2
Date: 24 January 2014
Reviewer: Alice Turner

Reviewer’s report:

I enjoyed reading this article, which contains interesting data on the concept of systemic inflammation and comorbidity in AATD, and how this may differ from usual COPD in addition to the data on differences between augmented and non-augmented patients. Whilst the paper is well written on the whole I think it might benefit from a few modifications as described below.

Major compulsory revisions

I felt that the paper was quite long and would benefit from being made more succinct - it is currently over 5000 words in length. This is reflected by the number of references the paper has; many other journals restrict referencing to n=35 on original articles; whilst this might not be a requirement for BMC Pulm Med it is a bit unusual to need 57 references. I would favour reducing to 4000 words or less, preferably 3500. This might necessitate a data or methods supplement, but would also allow the authors to focus on the outcomes they feel are the most important messages from the study, rather than presenting all in the primary paper. Examples of information more appropriate for a supplement include the CV of ELISAs and minimum detection values for Luminex/ELISA.

Minor essential revisions

I would welcome response to the following questions

1) The authors have included a PiSZ individual alongside PiZZ and a PiMZ alongside healthy individuals. The PiSZ person in particular could well have marked differences from the others in their group; were any differences observed? Some justification for their inclusion should be provided.

2) Were there any socio-demographic factors that differed between augmented and non-augmented AATD patients? Could these have influenced results?

3) What was the proportion of never smokers and pack year smoke exposure per group?

4) Are the authors sure there was no difference in BMI between any of the groups? The data is said to be shown as mean +/- SE and BMI is in the obese category for the COPD patients (32.1) yet is pretty much healthy in the AATD+AUG group (25.2). Looking at the SE I would have thought that these groups do differ from one another? Perhaps the BMI was non-normally distributed, or this data is shown in some other format than +/- SE which might explain this discrepancy? If there were a difference in the proportion of obese
patients it could explain some of the difference in systemic inflammation, since circulating cytokines can be elevated in obese people.

5) In the discussion the authors propose that a poor CRP response might be seen in the presence of liver disease, and this could explain some of the findings in AATD. I am not convinced by this argument - can the authors provide some evidence from liver disease that this is the case? Did their AATD patients have liver disease? What were their LFTs?

6) The table and figures are not easy to read. I would suggest reformatting the table to show p values for the main comparisons (i.e. COPD v AATD, AUG- v AUG+) rather than having lots of footnotes. I’d also reformat the graphs in Fig 1 and 2 as line charts showing time on x axis and cytokine level on the y axis, with a different line for each patient group.

Discretionary revisions
None

**Level of interest:** An article whose findings are important to those with closely related research interests

**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 I have no competing interests