Reviewer's report

Title: Occupational exposures, smoking and airway inflammation in refractory asthma

Version: 2 Date: 27 October 2014

Reviewer: Rakesh Kumar

Reviewer's report:

This paper emphasises the important point that taking an occupational history may be critical in planning the management of an asthmatic patient whose clinical status has deteriorated. It also addresses some other interesting issues, although aspects of the study are somewhat unclear.

- Major Compulsory Revisions

1. The hypothesis being tested in relation to smoke exposure is not articulated explicitly. While it is certainly true that whatever the hypothesis might have been, it was not supported by the data, it would be appropriate to spell this out.

2. A key limitation of the study, in relation to assessment of inflammation largely in terms of percentage of neutrophils in sputum, is not adequately discussed. Because all of the patients were on high doses of inhaled corticosteroids, and because corticosteroids prolong the survival of neutrophils (Cox G. J Immunol. 1995;154:4719-25) this needs to be considered. The authors do mention the work by Cowan and others (cited ref #39) which points out that inhaled corticosteroids cause phenotype misclassification, but do not discuss this. The point was again emphasised recently by Arron and others (Eur Respir J. 2014;43:627-9) who noted the poor correlation between sputum neutrophil percentages and other measures of airway inflammation in asthmatics.

- Minor Essential Revisions

1. What was the randomisation procedure for the selection of macrophages for photography?

2. In the Discussion, please comment on the extent to which exposure to motor exhaust fumes may induce a neutrophilic bronchitis independent of whether or not the person has asthma.

3. Please amend the sentence in the conclusions that reads "Exposure to both environmental and occupational particulate matter may be a key contributor to the presence of neutrophilic asthma." by deleting the word "key", as this appears to be an overstatement.

4. Please correct minor typographical errors (e.g. "verses" should be "versus).
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 that I have no competing interests.