Reviewer’s report

Title: Reference values of fractional excretion of exhaled nitric oxide among non-smokers and current smokers.

Version: 0 Date: 05 Jan 2017

Reviewer: Carlo Caffarelli

Reviewer’s report:

This manuscript studies FeNO levels in smokers and non-smokers. Authors may more accurately describe background data. The methods are appropriate and well defined. In the discussion section, the pathophysiological effect of smoking on FeNO should not be disregarded. The following comments are for consideration of the authors.

-In the Introduction, relevant studies showing that smokers have higher FeNO levels than controls should be quoted.

-Page 4, line 59. Please, say something more on how smoking may alter FeNO concentrations.

Methods

- The design of the study is described, but I would like to know more exactly when it was performed.

-What about comorbidities? Several diseases and drug may affect FeNO and they have not been considered. Did patients suffer from chronic lung diseases (eg. sarcoidosis) (Manna et al Italian Journal of Pediatrics 2012, 38:74) that can influence FeNO? Subjects with atopic eczema, also without asthma, have higher levels of FeNO (Zinelli C, et al Clin Exp Dermatol 2009, 34:607-612). Furthermore, it is well known that inhaled or systemic corticosteroids reduce FeNO levels. Would it be possible to consider these factors when reference values are calculated? If this is not the case, Authors should mention this point as a weakness of the study in the Discussion section.

- Page 4, line 21. Was spirometry performed before or after FeNO measurement?

Discussion

-Please discuss limitations of the study, also in relation to other studies. Authors may also comment differences in results with previous studies on smoking. What is the meaning of the study, especially with regard to possible mechanisms by whom smoking reduces FeNO levels.
Page 8 line 23. How do you explain that both cystic fibrosis and smoking reduce FeNO? Have patients with cystic fibrosis excluded from the study?

**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.

Yes

**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 recommend additional statistical review

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Please indicate the quality of language in the manuscript:

Acceptable

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