Reviewer’s report

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

Version: 0 Date: 20 Nov 2016

Reviewer: Davor Plavec

Reviewer’s report:

Abstract:

Page 2, line 7: The aim of the study is not clearly defined. The purpose of these reference values is not clear, although it seems from the manuscript that they are developed for the purpose of diagnosing allergic asthma. Please clarify! This is essential for the type of study, exclusion criteria and statistical analysis.

Line 13: Definition of atopy is not accurate and it is in contradiction with the main text.

Introduction:

Page 3: Please revise English (e.g. line 13, line 17, line 24, lines 30-33 - "judging normality", "extended population"). Also see previous comment on the clear definition of the aim of the study.

Material and methods:

Page 4, line 17: Phadiatop test is not described accurately. The test is "This test demonstrates the presence of IgE antibodies to common inhalant allergens and acts as an objective and reliable first step when testing for allergy." Also its performance should be mentioned: sensitivity, specificity, PPV, NPV, diagnostic efficacy (Tschopp JM et al. Allergy. 1998 Jun;53(6):608-13.) and discussed in the limitation section of the manuscript.

Line 46: It is not clear why you have excluded patients with asthma from the study because including them could give you the sensitivity, specificity, PPV, NPV, and diagnostic efficacy of the reference values you established. This would give additional value to the analysis and the manuscript itself. I recommend including them for the mentioned purpose. It is not clear why you have excluded patients with chronic bronchitis and asymptomatic airway obstruction. Please give the rationale.

Line 50: Statistical analysis describes only the FeNO values and regression analysis. Please describe the rest. There is no rationale to present data in Table 1 as median and 5th and 95th
percentiles for all the variables. These is no data on the distribution of subjects by age (per each decade).

Results:

Page 6, line 1: Please revise English - "basic data"???

Line 5: Correct the data either in Table or in text: in text it is 30.0 ppb and in Table 1 is 39.0 ppb!

Lines 5-13: Please cite the p-values in the text. Also include exact p-values in Table 2 for the post-hoc analysis of the ANOVA.

Lines 21-30: This paragraph would significantly benefit in clarity if you would add a graph(s) representing median and 95th percentile lines for the age, sex and atopy. Also an Excel calculator including prediction equations would be nice as an supplemental file for the online version of the manuscript.

Discussion:

Page 7, line 1: As the actual numbers are not presented anywhere in the text this statement is not clear for the reader. Please add actual numbers or add proposed graphs.

Lines 15-18: Please give the example. This is not clear for the reader from the presented data.

Lines 21-27: From your discussion it is not clear why you have decided to include subjects with atopy. Please explain! Also you have decided to include subjects with atopy based on Phadiatop results. In the methods you don't mention that they were non-symptomatic. Were symptomatic ones excluded?

Lines 48-60: It is not clear why you haven't used subjects with asthma to answer these research and clinically important questions. Using the subjects with asthma (allergic asthma based on Phadiatop results) you could clearly evaluate your reference values. I recommend that you do so and include also these data in the present manuscript.

Page 8, lines 21-29: Please be specific about the low values that you refer to from the cited publications so that the reader can compare them with the ones (5th percentiles) from your current manuscript.

Add: Please add the limitations section to the Discussion!

Table 3: Please revise the headline. Change "prevalence of atopy" to "presence of atopy". Please add 5th and 95th percentile values to presented medians.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

No

**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 am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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