Reviewer's report

Title: Exhaled nitric oxide is related to atopy, but not asthma in adolescents with bronchiolitis in infancy

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Reviewer: christophe marguet

Reviewer's report:

This paper aimed to define persistent airway inflammation in teenagers who underwent an acute bronchiolitis during infancy. FeNo, lung function and HBR have been chosen as inflammatory outcomes. A control population has simultaneously been studied. The conclusion of the authors was that FeNO remained an atopic marker as previously described. This long term study was well and successfully conducted and the originality was supported by the specific population that the authors studied and the connection with the debate of post RSV bronchiolitis atopy. Moreover, the authors provide additional data on the weak utility of FeNO in clinical practice.

However, this paper could be improved as regards the aim of the study.

major compulsory revision:

The strenghts of this study is the post bronchiolitis population that was studied and the discussion on the persistent inflammation. Therefore, the FeNO results should be displayed accounting this feature. The figure displayed the results regarding asthma and atopy status, and those on RSV +ve and RSV -ve should be also appeared somewhere.

The results of FeNO are displayed as means and 95%CI. However, the number of patients did not exceed 5 or 9 in some groups. This is disturbing, and individual values as dots are required on the figure, and will be more informative.

Lung function and BHR were also identified as outcome markers, and should be also discussed in this paper. The authors should have a global interpretation by associating FeNO, LF and BHR, all being potent inflammation markers. In fact, the decrease in FEF25-75% was expected to be sequelae of bronchiolitis. The lack of relationship between small airways diseases and FeNo would support that this LF alteration was not related to an active disease and should be added in table 3. The same comments could be applied for BHR, and the results more detailed as regards the aim of the study (table 3)

We need to have the description of the population, which surprisingly was added as supplementary files. Conversely, p values of table 2 could be displayed on the figure, and significant data of table 1 could be switch in the text. These tables 1&2 did not provide additional information, and could be withdrawn.

The chapter page 9 "regression analyses...InFeNo( table3) remains unclear. On
which analyses did the first paragraph refer to? Table 3? The results of regression analyses in the post bronchiolitis group are confusing; i.e. FeNO was not related to DRS, but was in the above paragraph. In addition, the authors claimed in the discussion that HBR was not related with FeNO.

Because the originality of the paper was supported by this studied population, this part of the results should be improved, structured and made more readable. Univariate and multivariate should be clearly separated and the results displayed. In fact, RSV negative bronchiolitis was related to FeNO and disappeared in the multivariate analyses. Therefore, that means a link with another variable(s).

Atopy was expected, but it is not. It would be interesting to understand this part of statistics. The fully adjusted model is not defined.

Discussion: FeNO is more and more discussed in the medical literature as a potent specific marker of asthma. This part should be added, and related to the interpretation of the results. I don’t understand their opinion. The levels that they found are low, and match with our experience. Thus, the lack of RSV related atopy, controlled asthma or the absence of in progress airways disease could explain these results. This could be discussed in accordance with the other markers that they used (FEF25-75, BHR).

RSV vs. no RSV: the lack of PCR diagnosis should be somewhere mentioned, because false negative RSV might be expected.

FeNO and BHR: this paragraph did not really match with the exposed results (see above)

Conclusion is restricted to asthma. I think that the main results was to demonstrate that persistent inflammation is rare at 11y in a population who suffered from acute bronchiolitis in the infancy, did not depend of the viral aetiology (in opposition with the relationship between RV and early asthma), and FeNo mainly remains an atopy marker.

Minor essential revision:

Does really reference 15 match with the corresponding text? references 16 and 17: which one was used? one is sufficient.

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