Reviewer's report

Title: Determination of inflammatory biomarkers in patients with COPD: comparison of different assays

Version: 1 Date: 3 December 2011

Reviewer: Alicia Lacoma

Reviewer's report:

In the manuscript entitled: “Determination of inflammatory biomarkers in patients with COPD: comparison of different assays”, the authors describe and compare the performance of two assays (ELISA and nephelometric technique) for the detection of systemic CRP and SAA.

The manuscript is well written. However, the manuscript is rather a methodological/technical note rather than an original. In fact, the objective of the study is to compare two different assays for the measurement of CRP and SAA. So, no discussion is possible regarding cut off accuracy as no outcome is measured in these COPD patients. I agree with the authors that it is important to standardize biomarkers commercial kits. Authors should mention that the standardization of technical assays is necessary for all biomarkers studies in general, not only for COPD so cut offs values are comparable between studies. In fact, the usefulness of systemic biomarkers has been evaluated in several clinical settings (emergency room, hospitalized, intensive care unit) and different diseases, so authors should emphasize that this standardization is not only for stable COPD patients.

Introduction
Page 3. Please check reference 14, as it is not related to COPD.

Material and Methods.
Page 6. Were biomarkers measured at the time of blood collection or were samples stored until measurement? If yes, how samples were stored?
Page 6. Authors refer to sensitivity and limit of detection values for the 4 assays, but which are the values of specificity? In addition, considering for example CRP, do the authors know if both assays detect the same fragment of the protein? Are the antibodies the same? Same questions apply for SAA.

Discussion.
Page 12. Line 2. Please include “…both CRP and SAA levels in comparison to healthy controls, suggesting…”
Page 12. Please remove “recent work” when referring to a study published in 1983 (reference 26).
Page 13. Please, could authors update bibliography referring to nephelometry and its correlation with other techniques? The only reference is from 1981. Has
the agreement of nephelometry with ELISA been investigated in diseases different than COPD? Which were the results obtained?

Page 13. If authors state that “…the agreement between the two assays is remarkably low”, it is not possible that later in the discussion they state “Although the two assays correlate well, they may provide different information in COPD…”. I do not understand how both assays might provide different information, if they measure the same biomarker. Please explain and discuss.

Page 14. Line 5. In relation with the previous comment, how this difference is likely to be clinical significant?


A “Limitations” section is missing.

Considering both biomarkers and referring only to the technical information, ELISA tests are more sensitive than nephelometric assays. So, it is reasonable to expect that levels measured with ELISA will be lower, regardless of patient group. In addition, it has already been demonstrated that COPD is characterized by an increase of systemic inflammation, in comparison to healthy controls. So, I cannot really see which were the results authors expected.

Although no statistical differences were found, authors should discuss the possible influence of corticosteroids on CRP levels, as different published studies have found controversial results on this issue.

Authors should discuss the relationship between CRP and SAA synthesis, as both of them are acute phase reactants.

Tables/ Figures
I recommend keeping only Figure1, Table 1, Table 2 and Table 3
Authors should remove Figure 1 to Figure 7 (foot figures) and instead include Panel a, b, c and d respectively, as necessary. Please correct also in the text.
Table 3. Check value for SAA in controls.

Level of interest: An article of limited interest

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.