Review of: "Sputum Interleukin-32 in childhood asthma: correlation with IL-1β"

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Potential competing interests: No potential competing interests to declare.

Sabrine Louhaichi et al, have studied the relationship between interleukins 32 and IL-1beta and asthma severity in children and found that the level of IL-32 in induced sputum correlates with asthma severity.

The study presents some issues that need to be clarified.

1.Table 1 shows the IgE values in blood, but does not show eosinophils values, a biomarker that has been shown to be useful when phenotyping asthmatic patients and that in some studies has been shown to correlate with eosinophilia in induced sputum.

2. Figure 2D shows the correlation (no correlation) between IL-32 levels in sputum with BMI. The number of children who are overweight and even obese (BMI higher than 35) is not negligible. Since obesity has been associated with severe asthma with elevated levels of IL-1beta and neutrophils in sputum, it seems appropriate to further explore these relationships. The table should show the BMI values of the different studied groups in order to analyze potential differences among groups.

3. Table 1 surprisingly shows that FVC% (58.7±62) in severe asthmatics is lower than FEV1% (65.81%±62), if the data is true, and not due to an error in recording the numbers, would mean that severe asthmatic patients show a restrictive ventilatory pattern. Finding that would require an explanation.

4. Table 1 shows the values of neutrophils in the induced sputum and indicates that there is a statistically significant difference (p=0.001) between severe asthma (31.7; 30-53.4) with respect to the control group (35.6; 13.3 -41.8) and instead, surprisingly, no differences were found with mild asthmatics (19.2;18.5-20.5) with much lower values than controls with a similar n. These data should be reviewed to verify that there is no error.

5. It is striking that the group with severe asthma appears to be an isolated group extraordinarily different from the other asthma groups, which do not differ at all from the controls. In theory it would be expected that there would be differences between the groups with different severity and all of them, or at least between severe and moderate with the healthy controls in the levels of the cytokines analyzed. The question that arises is: are we studying asthma with different severity

or with different inflammatory pheno/endotype? With the data collected with induced sputum, it cannot be concluded that severe asthma is associated with any of the reported inflammatory phenotypes (eosinophilic, neutrophilic, mixed, or paucigranulocytic).

Suffer the severe asthmatics comorbidities (obesity, frequent infections, ...) that are associated with elevated IL-1beta and IL-32? These potential comorbidities are poorly analyzed in the study and therefore the question cannot be answered.

6. Due to the exceptional behavior of severe asthma patients, the authors focus their studies with multiple correlations on this group of patients. It is methodologically correct, for example, to look at the correlation between cytokine values and FEV1 only in the severe group? Or should it be done with all patients regardless of their severity. In the event that they are only observed in partial analyzes (only with the severe group), interpretation of the observations should be sought.