Prediction of Asthma Exacerbation: Does Breath Acidity Perform Better than FeNO?

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The Global Initiative for Asthma (GINA) guidelines published in 2006 emphasized the importance of assessing asthma control, which is characterized by patients' symptoms, pulmonary function and quality of life. Because asthma is a highly variable disease, it is crucial to monitor the level of control on a periodic basis to decide whether therapy should be adjusted. A number of studies suggest that assessments of asthma symptoms, daily functioning, medication use, quality of life and lung function provide independent yet complementary information about asthma status. An unmet need of asthma management is for monitoring tools that may allow us to predict disease exacerbations.

The importance of asthma as an inflammatory disease has long been appreciated, and biologic markers such as the eosinophil counts in sputum and more recently exhaled nitric oxide (FeNO) have been used to judge asthma control [1, 2]. It is generally acknowledged that once control of asthma is achieved, a reduction of therapy to the lowest effective dose is in the patient's best interest. A number of studies have shown that FeNO can be used to titrate the dose of inhaled steroids (ICS) and a low FeNO value predicted successful steroid reduction [3–6]. However, more recent studies [7–10] revealed that an asthma treatment strategy based dominantly on FeNO measurement could not reduce asthma exacerbations

when compared with current asthma guidelines. Besides, the ICS dosage at the end of the study was mostly higher in the FeNO group than in the control group.

There are many determinants of FeNO levels, and these levels vary between healthy and asthmatic individuals. Cigarette smoking may decrease FeNO levels. Certain foods and drinks high in nitrates may increase FeNO levels. Atopy without asthma, viral infection, liver cirrhosis, bronchiectasis and inflammatory bowel disease are associated with increased FeNO. Decreases in FeNO levels have been reported in patients with cystic fibrosis and primary ciliary dyskinesia. Thus, care should be taken when interpreting FeNO measurement in the management of asthmatic patients to ensure that an increase in FeNO level due to factors other than airway inflammation is considered.

Exhaled breath condensate (EBC) is a non-invasive method for sampling the airways. There is some evidence that certain markers in EBC differ between patients with asthma and controls [11, 12], and some markers may correlate with asthma severity. Methodological issues have hampered the use of many EBC biomarkers. However, EBC pH is a biomarker of airway inflammation and/or oxidative stress that is reproducible and quick and easy to obtain. A reduced EBC pH has been reported in acute or stable asthma [13]. Carraro et al. [14] found negative cor-

relation between FeNO levels and exhaled ammonia concentrations with EBC in asthmatic children, supporting the hypothesis that airway acidification may have a role in the pathophysiology of asthma [15].

In this issue of *Respiration* Liu et al. [16] tested the performance of breath acidity parallel to FeNO and FEV₁ as a predictor of asthma exacerbation. In a small but homogeneous population of non-smoking, young adults with moderate persistent asthma, EBC was collected at home during ICS dose reduction. Spirometry, EBC pH and FeNO were measured monthly during study visits for a total of 6 months. As expected, there was a linearly increasing pattern for FeNO associated with step-down titration of ICS. However, in the Cox's model for the hazard of exacerbation, only a drop in EBC pH was associated with an increased hazard ratio for asthma exacerbation. It is a very interesting observation, but there are many points that will have to be clarified before acidopnea will

be included in daily asthma management. First, there are no data about EBC pH specificity and sensitivity as a diagnostic test of asthma in populations of unselected symptomatic subjects. The next step in future research should be a prospective randomised study directed towards demonstrating that the use of EBC pH is better than current asthma guidelines for controlling asthma exacerbations.

Finally, there is a lack of data on which aspects of asthmatic inflammation the low EBC pH exactly reflects.

In summary, the presented study confirms previous observations that there is not one single parameter that could be used in isolation to guide asthma therapy. This limitation of each individual test is likely to reflect the complexity of asthma physiology. And so it is possible that beside therapy fitted to specific asthma phenotypes, we will be confronted in the near future with asthma phenotype fitted asthma biomarkers.

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