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EDITORIAL

Markers of asthma: The quest of the Holy Grail

Asthma is a complex disease or – probably more accurately – a group of diseases which share common signs and symptoms. In the last years there has been a plethora of information in the scientific literature on types, phenotypes, endotypes and other kind of ''types'' of asthma, both in adults and in children. After several decades looking for markers which could be used to distinguish between healthy people and asthmatics; to differentiate between asthma types; to predict asthma; and to help monitoring the condition, the efforts from many researchers have yield a meagre result. We have come through eosinophils and their proteins, FeNO, periostin and, more recently the ''omics''.

In the present issue of A&I we include a very interesting paper on the use of circulating fibrocytes as a tool for monitoring asthma. Those are key cells in airway remodelling. The results show clearly that in controls and in mild, moderate and severe asthmatic patients the number of fibrocytes was significantly higher in patients with much more severe disease than in those with less severe asthma and healthy controls. Additionally, the authors found and inverse correlation between circulating fibrocytes and FVC, FEV1, and asthma control test (ACT). Furthermore, the number of fibrocytes was directly correlated with the use of short acting beta-2 agonists.[1] The question is to what extent this measurement helps to monitor asthma follow up in the real world. Maybe the future will bring a point of care or over the counter test as easy to use and as cheap as the glucometer. However, no advantage would be retrieved from such a test unless it is able to anticipate a change in asthma control even before FEV1 is reduced. Otherwise, we have pocket spirometers which do well.

To certain extent FeNO, measuring airway inflammation, could anticipate reductions in lung flows even before they are detected by spirometry and might – at least in theory – help to tailor treatment addressed to improve one of the two main components of asthma: inflammation. However, the use of FeNO measurements in the clinical setting to help the following up of asthmatic patients has not met the expectations generated by the ''FeNO-mania'' of the previous decade. In fact, a Cochrane review concludes that ''The role of utilising exhaled nitric oxide to tailor the dose of inhaled corticosteroids cannot be routinely recommended for clinical practice at this stage and remains uncertain''[2] and a very recent trial concludes something similar, specifically in children.[3]

Two different papers in this issue of A&I address two different approaches for the use of FeNO measurements. In the first one[4] FeNO values were found to be significantly higher in ill-controlled asthmatics and were associated to lowwe values of ACT, higher frequency of symptoms and, not surprisingly, to lower corticoid dose. Those are expected outcomes, albeit the main merit of the paper is to confirm previous findings in an appreciable number of patients. The authors, however, did not use FeNO as a guide to treat asthma. The comment here would be similar to the previous one: is FeNO adding something to treatment based on symptoms and lung function tests?

The second paper on FeNO[5] is a total different story and examines the role of the measurement of this inflammation marker to diagnose asthma in a general population of children. The authors use an elegant statistic method to measure FeNO variability and to what extent asthma diagnosis explain that variability. The conclusion is clear ''The proportion of FeNO inter-individual variability which can be explained by individual (including suffering from asthma or rhinoconjunctivitis), family, and environmental factors is very low (20–27%)''. In other words, there seem to be unknown factors that account for 70% of variability which are different from the presence of asthma. This render FeNO as a little useful tool to diagnose asthma and maybe explains why it does not seem to be useful to tailor treatment (unless variability among asthmatics is much lower and depends mainly upon airway inflammation).

In summary, we need to continue our search for markers of asthma, both for helping to tailor treatment, or differentiate between pheno/endotypes, or diagnose/predict the disease. Are ''omics'' (metabolomics, genomics, breathomics, etc.)[6–8] the new Holy Grail?

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