Asthma Control and Sputum Eosinophils: a Longitudinal Study in Daily Practice

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1. KEYWORDS
Asthma control, sputum eosinophils, longitudinal, daily practice

2. INTRODUCTION
Asthma is defined by the Global Initiative for Asthma (GINA) as a chronic inflammatory disorder of the airways, involving various inflammatory cells including eosinophils (GINA (2012)).

It is now well established that a relationship exists between sputum eosinophilic inflammation and the rate of asthma exacerbations (TILLIE-LEBLOND (2009)).

In contrast to what has been shown for exacerbations, the association between sputum eosinophilic inflammation and asthma control has been less firmly established. Several cross-sectional studies showed that patients with a poorly controlled asthma or a more severe disease had higher levels of sputum eosinophils (LOUIS (2000); ROMAGNOLI (2002); DUNCAN (2003); QUAEDVLIEG (2009); TILLIE-LEBLOND (2009)). Longitudinal trials have also suggested that asthma control may be influenced by fluctuations in eosinophilic inflammation (TILLIE-LEBLOND (2009)). This association has however never been confirmed in daily practice.

3. OBJECTIVES
Our first objective was to investigate the relationship between asthma control and within-individual variations in sputum eosinophil and neutrophil counts over time. Secondly, we sought to define cut-off changes in sputum eosinophils corresponding to individual important variations in asthma control assessed by the Asthma Control Questionnaire (ACQ).

4. METHODS
4.1 Study design, setting and participants
A retrospective longitudinal study was conducted in 187 asthmatics who underwent at least two successful sputum inductions at the University Asthma Clinic of Liege between 1 October 2003 and 1 January 2014. This retrospective study was conducted with the approval from the ethics committee of the University Hospital of Liege.

4.2 Variables
All variables used for the analysis were recorded during the routine visits to the Asthma Clinic. Sputum induction and processing were performed as previously described (DELVAUX (2004))

4.3 Statistical methods
Linear mixed models were performed to assess the relationship between asthma control and individual changes in sputum eosinophils. ROC curves were constructed to define cut-off variations in sputum eosinophils associated with a change of at least 0.5 in ACQ.
5. RESULTS

5.1 Association between asthma control and within-patient changes in sputum eosinophilic and neutrophilic inflammation

We first assessed the association between ACQ-6 (asthma control score excluding FEV1) and the within-individual changes in eosinophilic inflammation (percentage of sputum eosinophils and FENO). We also included in the model within-individual changes in variables known to be potentially confounding factors when considering the relationship between asthma control and eosinophilic inflammation (FEV1, FEV1/FVC, inhaled and oral corticosteroids dose). In the univariate analysis, a within-patient increase in sputum eosinophil count and FENO was associated with an increased ACQ-6 (p < 0.001 for both) whereas a decreased ACQ-6 was associated with a within-patient increase in pre-bronchodilator FEV1 (p < 0.001), FEV1/FVC (p = 0.001) and ICS dose (p = 0.04). In the multivariate analysis, only sputum eosinophils (p < 0.01) and FEV1 (p < 0.001) remained independently associated with asthma control. We constructed another multivariate linear model in which we replaced the variables sputum eosinophils and FENO by sputum neutrophils. In this model only FEV1 was significantly associated with asthma control.

5.2 Thresholds of sputum eosinophil variation corresponding to clinically significant change in ACQ

We calculated a minimal important decrease in the percentage of sputum eosinophils of 4.3% (AUC: 0.691, p=0.0001) or 3.4 folds (AUC: 0.648, p=0.003) for a significant improvement in asthma control and a minimal important increase of 3.5% (AUC: 0.675, p=0.004) or 1.9 folds (AUC: 0.634, p=0.02) for a significant worsening in asthma control.

6. CONCLUSION

At the individual level, asthma control was associated with fluctuations in sputum eosinophil count over time.

7. REFERENCES


