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Title: Exhaled air volatile organic compounds and eosinophilic airway inflammation in asthma

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Body: Rationale Eosinophilic inflammation in asthma is predictive for responses to inhaled steroids. The application of sputum analysis is somewhat limited by requirement of lab facilities and not-directly available results. Exhaled air metabolomics is associated with eosinophilic inflammation in COPD (Fens et al. ERJ 2011). We hypothesized that breath volatile organic compounds (VOCs) can be adequate surrogate markers of airway inflammation in asthma. Aim To identify VOCs in exhaled air by gas chromatography and time-of-flight mass spectrometry (GC-TOFMS) that can discriminate eosinophilic asthma from non-eosinophilic asthma. Methods Breath samples were analysed by GC-TOFMS in 40 patients (>18yr) with moderate/severe asthma (GINA-criteria). All patients were non-smokers and required inhaled corticosteroids (≥500ug FP or equivalent). Differential cell counts were measured in induced sputum. Correlation coefficients and corresponding p-values between the peaks and measured sputum eosinophils were calculated by univariate analysis (p-value<0.01). Results Sputum was successful in 36 patients, of which 21 patients had sputum eosinophils >3%. Linear regression analysis showed associations for 5 VOCs with sputum eosinophils. The correlation coefficients varied between 0.42-0.47. When excluding patients on oral corticosteroids (n=8), 8 VOCs were associated with sputum eosinophils with higher correlation coefficients varying between 0.49-0.62. Conclusion Exhaled air VOCs are modestly associated with sputum eosinophils in patients with moderate/severe asthma on (inhaled) steroids. This suggests that exhaled breath analysis requires further optimisation in the assessment and monitoring of airway inflammation in asthma.