The Difficult Asthma Patient

S1 BIOMARKERS IN ADULT ASTHMA: A SYSTEMATIC REVIEW OF 8-ISOPROSTANE IN EXHALED BREATH CONDENSATE

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Introduction The potential of exhaled breath condensate (EBC) as a non-invasive indicator of airways disease has been studied for three decades or more. 8-isoprostane is a product of lipid peroxidation which can be detected within EBC. Studies have reported this as a potential objective indicator of oxidative stress in asthma. We therefore aimed to assess the evidence for the use of 8-isoprostane in exhaled breath condensate (EBC) as a biomarker in adult asthma.

Design A systematic review and meta-analysis of EBC 8-isoprostane in asthma.

Methods We searched a number of online databases (including PubMed, Embase and Scopus) in January 2016. We included studies of adult non-smokers with EBC collection and asthma diagnosis conducted according to recognised guidelines. We aimed to pool data using random effects meta-analysis and assess heterogeneity using I². Study quality and risk of bias was assessed using QUADAS-2 and GRADE.

Results We included twenty studies, the findings from which were inconsistent. Seven studies (n = 329) reported 8-isoprostane concentrations in asthma to be significantly higher than that of control groups, whilst six studies (n = 403) did not. Only four studies had results appropriate for inclusion in a random effects meta-analysis of mean difference between asthma and controls (see Figure 1). This found a statistically significant between-groups difference of +22 pg/ml in asthma.

Confidence in the result is limited by the small number of studies; by substantial methodological and statistical heterogeneity (I² = 94); and by an inability to assess the risk of bias in key domains of the quality assessment tool.

Conclusion The clinical value of EBC 8-isoprostane as a quantitative assessment of oxidative stress in asthma remains unclear due to variability in results and methodological heterogeneity. It will be essential to develop accurate, reliable and standardised methods of both EBC collection and 8-isoprostane analysis if its use as a biomarker in asthma is to be evaluated.

S2 FRACTIONAL EXHALED NITRIC OXIDE (FENO) SUPPRESSION TO IDENTIFY NON-ADHERENCE IN DIFFICULT ASTHMA

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Introduction Non-adherence, both intentional and non-intentional, is prevalent in 'difficult to manage' asthma and identification of patients who should respond to inhaled corticosteroids (ICS) is essential to reduce exacerbation risk and improve asthma control, but also to prevent inappropriate escalation of treatment (oral corticosteroids or biological therapies). Composite biomarker assessments (FeNO and blood eosinophils) have been shown to predict exacerbation risk in patients with asthma and these biomarkers also predict response to steroid treatment. It has previously been demonstrated that suppression of FeNO with directly observed ICS over 7 days can identify non-adherence to ICS treatment. The aim of this work was to further validate this test across UK severe asthma centres in the RASP-UK Consortium and to examine if the test can identify patients who should achieve good asthma control with better adherence to ICS treatment.

Methods Using remote monitoring technology (Vitalograph INCA™ device and Aerocrine NIOX Vero), we developed a web-based interface to deliver FeNO suppression testing in RASP-UK Severe Asthma Centres. We examined the utility of FeNO suppression testing to predict inhaled steroid responsiveness and composite biomarker profile after 30 days of monitored optimised treatment on standard high dose ICS/LABA.

Results Forty of seventy patients had a positive suppression test. Using information from the Vitalograph INCA™ server to highlight technique and timing errors, these issues were addressed and patients proceeded to 30-day monitoring of high dose ICS/LABA. A positive FeNO suppression test (Figure A) identified a biomarker-low population when adherent with high dose ICS (≥80% of inhaled steroid) whereas a negative test (Figure B) identified a biomarker-high population when adherent with high dose ICS.

Conclusion FeNO suppression testing is an effective means of identifying non-adherence to inhaled steroids in patients with difficult to manage asthma. This test can identify patients who should be optimised on inhaled steroids prior to consideration of treatment escalation.

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Abstract S1 Figure 1 Random effects meta-analysis of mean between-group difference (asthma vs controls)