

Results The analysis showed that there was an ICER (Incremental Cost-Effectiveness Ratio) of 32 000 GBP/QALY (Quality Adjusted Life Years) associated with high dose dry powder FP/S 1000/100 µg vs extrafine BDP/F 400/24 µg and an ICER of approximately 36 800 GBP/QALY associated with medium dose dry powder FP/S 500/100 µg vs BDP/F 400/24 µg. Additional analysis showed that there was an ICER of 85 200 GBP/QALY associated with high dose suspension formulation FP/S 1000/100 µg vs extrafine BDP/F 400/24 µg.

Conclusions BTS/SIGN guideline recommend that when asthma control is achieved, treatment can be stepped down to the lowest dose that maintains control. It was found that maintaining controlled patients on high dose FP/S is not cost-effective. Extrafine BDP/F 400/24 µg daily can be considered to be a cost-effective option in the UK to maintain control of asthmatic patients stepped down from high dose FP/S 1000/100 µg daily dry powder or suspension formulations and the magnitude of cost effectiveness is estimated to be highest when stepping down from the suspension formulation.

P114 DIFFICULT ASTHMA: THE PLYMOUTH EXPERIENCE

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B Castell, D Pike, M Masoli. *Plymouth Hospitals NHS Trust, Plymouth, Devon*

Introduction Difficult asthma represents a significant unmet clinical need and burden on healthcare resources. We recently set up a difficult asthma clinic (DAC) in Plymouth and conducted an observational study of our experience to date.

Methods The DAC started in April 2010 evaluating patients using a systematic multidisciplinary approach. Patients were symptomatic at = Step 4 BTS guidelines and arose from a combination of cross referrals, inherited patients and asthmatics under regular chest clinic follow-up.

Results 113 patients were evaluated within the DAC. 74 women. Mean age 48 yrs. 15 patients were felt either not to have asthma or asthma was not the primary diagnosis. Diagnoses included bronchiectasis (3), Goitre (1), obliterative bronchiolitis (1), tracheal involvement from ulcerative colitis (1), chronic pulmonary emboli (1), Churg-Strauss syndrome (1). 98 patients had difficult asthma. 14 patients had an occupational element, three with reactive airways dysfunction syndrome. 72 had comorbidities which included: vocal cord dysfunction/dysfunctional breathing (19), bronchiectasis (20), Class II Obesity (19), COPD/emphysema (9), GORD (31), immune deficiency (5), OSA (5), psychological (11), allergic bronchopulmonary aspergillosis (2). Medication at baseline: 46 patients were on long term oral corticosteroids (OCS) (mean 22 mg/d). Most patients were able to significantly reduce their OCS dose, mean reduction 53%. 12 were able to discontinue OCS entirely. Mean inhaled corticosteroid dose 2287 mcg/d (BDP equivalent). Subcutaneous terbutaline (3), cyclosporin (2), Anti-IgE therapy (1). Currently seven on anti-IgE therapy. 58 had severe refractory asthma by American Thoracic Society criteria. Mean IgE 531 kU/l, mean FeNO 40.5 ppb. 15/58 had fungal sensitivity. Adherence: 1 of 12 patients tested was identified as non-adherent with undetectable prednisolone level and normal cortisol. Healthcare utilisation: 68 patients with 12 months follow-up data demonstrated a significant reduction in hospitalisations compared to the previous 12 months, 1.00 vs 0.53.

Conclusion This study highlights the importance of alternative diagnoses and comorbidities in the work up of difficult asthma. IgE and FeNO were higher than expected as was adherence to OCS compared to published studies. The implementation of a DAC has reduced hospital admissions, reduced OCS requirement and enhanced access to treatments such as Anti-IgE therapy.

Cellular responses in the aetiology of COPD

P115 CHRONIC DIESEL EXHAUST PARTICLE (DEP) EXPOSURE DIFFERENTIALLY ALTERS MONOCYTE DIFFERENTIATION AND FUNCTION IN HEALTHY CONTROLS COMPARED TO COPD

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¹N Chaudhuri, ²H Jary, ³S Lea, ³N Khan, ¹L C Parker, ³D Singh, ¹I Sabroe. ¹Academic Unit of Respiratory Medicine, University of Sheffield, Sheffield, UK; ²Academic Unit of Respiratory Medicine, The University of Newcastle, Newcastle, UK; ³Respiratory Medicine Research Group, University of Manchester, Manchester, UK

Introduction and Objectives Alveolar macrophages are heavily implicated in the pathogenesis COPD. During chronic inflammation, macrophages mature continuously from infiltrating monocytes that are continually recruited to the airways. We have previously found DEP modulate life span and function of monocytes from healthy donors, but their effects on monocytes of people with COPD are unknown, and were therefore the subject of this study.

Methods Monocytes were purified from the blood of patients with GOLD II/III COPD and healthy age matched controls Monocyte-derived macrophages (MDMs) were generated in the presence or absence of DEP and their lifespan studied. Cytokine generation in response to TLR agonists and heat killed bacteria was assessed by ELISA and expression of CD14 was measured by FACS.

Results Chronic exposure of monocytes from patients with COPD to DEP concentrations above 10 µg/ml caused a significant reduction in cell survival. Lower concentration of chronic DEP exposure, as low as 1 µg/ml, caused impairment of cytokine responses to LPS and heat killed *Escherichia Coli*, and this phenotype was associated with a reduction in CD14 surface marker expression. However, COPD monocytes were generally more resistant to the effects of DEP compared to healthy control cells.

Conclusions In this study monocytes from healthy volunteers appeared to be more susceptible to the harmful effects of chronic DEP exposure compared to those from individuals with COPD. These findings reinforce the evidence that circulating leukocytes in COPD patients have altered phenotypes.

P116 TESTING ANTIOXIDANT AND ANTI-INFLAMMATORY THERAPIES IN A COMPLEX LUNG TISSUE MODEL

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T S Singh, F R Razali, M N North, T W Wilkinson, B L N Nicholas. *University of Southampton, School of medicine, Southampton, UK*

COPD is a disease of global importance and its primary cause airway inflammation as a consequence of cigarette smoking is well described. However, there remains a lack of effective therapies for this important condition. Animal models of disease are limited in their predictive utility and therefore creation of a complex, human disease model is an important step for testing new therapeutic interventions. We therefore established a tissue model of oxidative and inflammatory responses to relevant triggers—cigarette smoke and LPS and determined the impact of interventions in the optimised system.

Methods Human lung tissue explants from the resected lobes of six consented patients undergoing lobectomy were used. Uniform tissue explants were established on a novel culture system and then treated with CSE and LPS before the supernatants were collected optimal dosing was determined. Treatments and control experiments were performed with the anti-oxidant Vitamin C and fluticasone. Inflammatory readouts were measured by ELISA; TNF α , IL-8 and MMP-9.