Severe asthma and exacerbations

S60 ASPERGILLUS POLYMERASE CHAIN REACTION TESTING IN THE SEVERE ASTHMA POPULATION

doi:10.1136/thoraxjnl-2012-202678.066

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Background Allergic Broncho-Pulmonary Aspergillosis (ABPA) is associated with known pulmonary fungal colonisation and proven response to long term anti-fungal therapy. A recent trial at our site, confirmed that anti fungal therapy was effective in a group of patients with Severe Asthma with Fungal Sensitisation (SAFS). Whether these patients have pulmonary fungal colonisation remains unknown. Previous hypotheses have indicated that bowel colonisation causes an allergic reaction leading to bronchoconstriction. Our hypothesis is that patients with SAFS, who respond to anti-fungal therapy, do have airway colonisation. Aspergillus polymerase chain reaction (APCR), represent a novel and more sensitive way to detect the presence of Aspergillus.
Methods We have performed sputum APCR tests in clinical practise over the last 2–3 years. We reviewed a retrospective cohort of patients attending a Severe Asthma Service, whose results were stored on the Mycology results system. Patient notes were reviewed to determine patient's total serum IgE's, IgE's specific to Aspergillus and anti fungal therapy status.
Results 77 results were logged on the microbiology of which 70 cases were available for notes review. Of these 44 (63%) were female with an average age of 57.5 years. 26 had ABPA, 42 SAFS and 2 had neither ABPA nor SAFS, but had severe asthma. Overall 57% of ABPA or SAFS patients were APCR positive. 55% of SAFS patients were APCR positive, this number increased to 68% for those who were not taking anti-fungal therapy at the time of the test. The equivalent numbers for ABPA were 65% and 70% respectively. Neither of the 2 control severe patients had positive APCR. The full data is presented in table 1.

Abstract S60 Table 1

	Treatment Status	Positive Aspergillus PCR	Negative Aspergillus PCR
ABPA	On treatment	8 (62%)	5 (38%)
	Off treatment	7 (70%)	3 (30%)
SAFS	On treatment	10 (43%)	13 (57%)
	Off treatment	15 (68%)	7 (32%)
Control	Off treatment	0 (0%)	2 (100%)

Conclusion This data supports the concept that patients with Severe Asthma with Fungal Sensitisation (SAFS) have pulmonary colonisation with Aspergillus. Suppression of such colonisation and reduced allergic response may then be the mechanism of action for anti-fungal therapy.

S61 CLINICAL OUTCOMES AND INFLAMMATORY BIOMARKERS IN CURRENT SMOKERS AND EX-SMOKERS WITH SEVERE ASTHMA

doi:10.1136/thoraxjnl-2012-202678.067

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Rationale Some clinical outcomes are worse in current smokers and ex-smokers with mild to moderate asthma compared to never smokers, but little is known about the influence of smoking status in severe asthma.
Objectives The objectives of the analysis were to examine the association of current or previous cigarette smoking with clinical and inflammatory variables in severe asthma.
Methods We compared patient demographics, disease characteristics and biomarkers of inflammation in never smokers (n=461, 62.3%), ex-smokers (n=210, 28.4%) and current smokers (n=69, 9.3%) with refractory asthma (n=760) recruited to the British Thoracic Society Severe Asthma Registry.
Results Current smokers had poorer asthma control, more unscheduled health care visits, more rescue courses of oral steroids and higher anxiety and depression scale scores than ex-smokers or never smokers. Compared to never smokers, current smokers had a reduced proportion of sputum eosinophils (3.75% and 1.25% respectively) and lower fraction of exhaled nitric oxide (Fe_{NO50}) values (35 ppb versus 14 ppb), whereas ex-smokers had an increased proportion of sputum neutrophils (43.8% versus 56.9%), but similar proportion of sputum eosinophils (2.8%) and Fe_{NO50} values (35 ppb). Both current and ex-smokers had reduced serum specific IgE levels to some common environmental allergens.
Conclusion Current smokers with severe asthma exhibit worse outcomes for a range of clinical and health care variables compared to ex-smokers and never smokers with severe asthma. Inflammatory profiles in sputum and blood differ between current smokers, ex-smokers and never smokers, possibly constituting separate phenotypes of severe asthma, which may influence responses to targeted therapies.

S62 A SYSTEMATIC REVIEW OF FACTORS ASSOCIATED WITH FUTURE ASTHMA ATTACKS TO INFORM A RISK ASSESSMENT QUESTIONNAIRE

doi:10.1136/thoraxjnl-2012-202678.068

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Asthma attacks occur across all subtypes and severities of disease. Accurate quantification of asthma attack risk would enable targeting of interventions with a potential reduction in morbidity, mortality, and costs. We aimed to develop a risk assessment questionnaire underpinned by a systematic literature review.

We searched major databases up to February 2012 using the terms: asthm* AND (exacerbati* OR admission) AND (risk OR predic* OR associat*) NOT review.

Included studies were those in individuals >12 years old with doctor-diagnosed asthma on treatment. Outcomes were asthma attacks defined as: deterioration of symptoms, fall in objective measures of airflow, and need for a short course of augmented asthma therapy OR admission to hospital OR attendance at emergency department. Statistical analysis was carried out using RevMan 5 and SPSS 19.

3536 unique publications were retrieved. After title screening and comparison of abstracts against a standard checklist and age criteria, data extraction was undertaken in duplicate on the remaining 143 papers (see figure).

Of 18 major research themes identified, 8 factors had a consistent and clinically important (OR>1.25) association with asthma attacks across publications free from major bias. The questionnaire derived from these factors is shown below. Simplified weighting is proportional to the effect size when expressed as an odds ratio (in brackets).

I smoke (3)

I take fewer than 8 out of 10 prescribed doses of my regular preventer medication (3)

In the last month I have used my reliever inhaler more than once per day on average (3)

I sneeze, or get a runny, or a blocked nose when I do not have a cold (2)

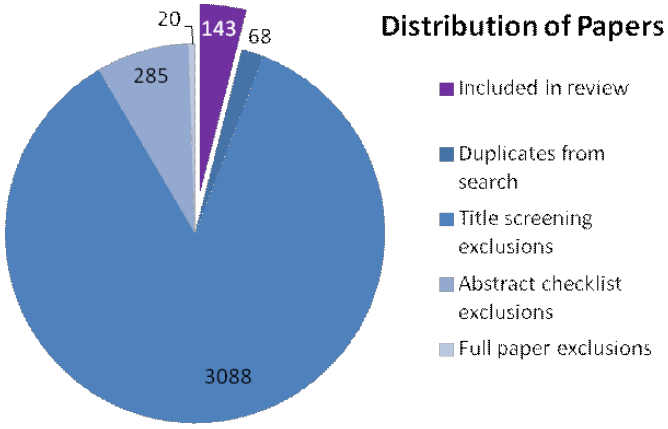
In the last 5 years, I have attended a hospital emergency department or been admitted to hospital because of asthma (2)

I have a body mass index of ≥ 30 (1)

I have not received asthma related education or a written asthma management plan (1)

I left school before sitting my A-levels/highers (1)

In summary, we systematically identified factors from the literature that are independently associated with the risk of asthma attack. These factors inform a questionnaire which will require validation and subsequent impact assessment.



Abstract S62 Figure 1

S63 BASELINE ASTHMA CONTROL AND SEVERITY INFLUENCES THE OUTCOME OF VIRUS-INDUCED ASTHMA EXACERBATIONS

doi:10.1136/thoraxjnl-2012-202678.069

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Background Rhinovirus (RV) infection is the most common cause of asthma exacerbations (AE). Mechanisms underlying this remain poorly understood. A human model of experimental RV induced AE has been developed however published studies have only recruited subjects with mild, well-controlled asthma naive to inhaled corticosteroid (ICS) therapy. The influence of asthma severity and baseline control on outcome remains unknown. For these studies to be more representative of those who experience virus-induced AE there is a need to establish the safety of using this model in subjects with moderate, poorly-controlled asthma and to investigate clinical outcomes.

Method 48 adults - 14 healthy, 14 mild asthmatic, and 18 moderate asthmatic (defined by GINA) were recruited and inoculated nasally with RV-16. Daily symptom scores and spirometry were recorded throughout the study. Asthma control at baseline was recorded using the ACQ. Nasal lavage (NL) for viral shedding was performed on days 0, 2, 3, 4, 5, 7, 10. Clinical infection was confirmed by demonstration of RV16 RNA by RT-PCR in NL and/or serum titre of RV-16 specific antibodies greater than 1:4 on d42.

Results 11/14 healthy, 11/14 mild asthmatic and 17/18 moderate asthmatic volunteers met criteria for infection. Both groups of asthmatics developed greater lower respiratory symptoms, falls in FEV1, and airway hyper-responsiveness (AHR) compared to healthy volunteers (all $P=<0.01$). These changes were significantly greater in the moderate asthmatics than in the mild asthmatics ($P=<0.05$). Poorly-controlled asthmatics experienced greater chest symptoms ($P=<0.01$) and RV-induced falls in lung function ($P=<0.05$) compared to subjects with well-controlled asthma.

Conclusion RV infection results in more severe chest symptoms and falls in lung function in moderate asthma than in mild asthma. Within the moderate group the poorly-controlled asthmatics experienced the most severe exacerbations. This occurred despite therapy with ICS. This is the first study to experimentally inoculate both moderate, poorly-controlled and milder well-controlled asthmatics. Both severity and baseline control appear to influence the outcome of virus-induced AE. Measures to improve control will significantly reduce the likelihood of a severe virus-induced AE and lessen the healthcare costs associated with them.

S64 THE COST OF REFRACTORY ASTHMA IN THE UK - A PRELIMINARY ANALYSIS

doi:10.1136/thoraxjnl-2012-202678.070

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Introduction Refractory asthma poses a potentially significant burden in terms of healthcare costs. Relatively little is known about the cost of treatment or what factors explain variations in treatment costs. This study uses data from the British Thoracic Society (BTS) Difficult Asthma Registry to estimate the healthcare costs associated with a sample of well-characterised refractory asthmatics and examines the role of a range of factors in explaining variations in healthcare.

Methods In this analysis data were extracted from the Registry on 689 patients and examined healthcare utilisation including all prescribed medicines, hospital inpatient stays, ITU stays, A&E/GP visits and CT scans over a 12 month period prior to the patient first being assessed at the specialist clinics. Patient characteristics included age, gender, lung function, clinical centre were care was provided, adherence status, BMI and whether or not the patient was on maintenance oral steroids. Unit costs were based on standard published sources. Costs were examined by category with respect to patient characteristics and total cost with respect to patient characteristics in multivariate regression analyses.

Results Mean total treatment cost among refractory asthmatics ranged between £3,402 (SD=2,680) to £4,234 (SD=£3,036). In a comparator non-refractory group mean total cost ranged from £1,944 (SD= £1,728) and £2,565 (£2,065). Drug costs comprised approximately 58% of all costs in refractory asthmatics and approximately 55% in the non-refractory group. In the refractory group significant predictors of total costs were FEV1, clinical centre in which care was provided, maintenance oral steroids and BMI. Patients who were on maintenance steroids cost 48% more than those who were not. Patients who were morbidly obese cost approximately 23% more than those who were normal weight.

Conclusion Treating individuals with refractory asthma presents a significant cost to the health service. The role of maintenance steroids in cost is dramatic and may relate to the impact of steroid induced morbidity and warrants further investigation.