Background and Aim: Improved survival in adolescents with cystic fibrosis has led to complications including cystic fibrosis related diabetes. Cystic fibrosis related diabetes is associated with declining respiratory status and weight, higher morbidity, and mortality. These changes may precede abnormalities in glycaemic control detected by the oral glucose tolerance test (OGTT) by up to 4 years. The optimum screening test for cystic fibrosis related diabetes remains controversial and many argue the OGTT is the gold standard. However, there is evidence the OGTT may not detect transient hyperglycaemia and treating these patients improves clinical parameters. We therefore assessed whether continuous glucose monitoring is tolerated in adolescents with cystic fibrosis and whether it is more effective at determining abnormal glucose homeostasis or cystic fibrosis related diabetes than the OGTT.

Methods: This was a prospective pilot study. The continuous glucose monitoring subcutaneous device (Minimed Medtronic) was worn for up to 72 hours while subjects carried out normal activities. The data were compared with capillary blood glucose profiles and OGTT results that identified episodes of fasting, 2 hour post-prandial or casual hyperglycaemia. The subjects completed a questionnaire to determine tolerability of continuous glucose monitoring.

Results: Thirteen subjects completed the study. Seven fulfilled the criteria for cystic fibrosis related diabetes, three for impaired glucose tolerance (as defined by a cystic fibrosis expert committee) and three had normal continuous glucose monitoring studies. Eight subjects had at least one abnormality of OGTT, fasting, or random capillary blood glucose, but only two met the criteria for cystic fibrosis related diabetes (p = 0.05). There was an increase in occasions the 2 hour post-prandial glucose was 7.8–11.1 mmol/l (impaired glucose tolerance) in continuous glucose monitoring data compared with OGTT (p = 0.01). The mean duration of abnormal glucose levels during the study was 9.7% (range 0–44.8%). The questionnaires revealed 84% would use continuous glucose monitoring again. The average score of discomfort (out of 10) on a visual analogue scale was 2.3.

Conclusion: Despite this being a small pilot study the results suggest that the continuous glucose monitoring is well tolerated and may be useful in detecting abnormalities of glucose homeostasis in this population.

UK NORTHERN SCORE CENTILE CHARTS FOR PAEDIATRIC CHEST X RAYS IN CYSTIC FIBROSIS

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Background: How does a paediatrician know if a cystic fibrosis chest x ray is bad (or good) compared with a national benchmark? Measurable endpoints are needed as surrogate markers of lung damage in cystic fibrosis.

Objective: Here we provide an answer by creating the first national centile charts for the Northern Score.

Methods: All registered patients with submitted annual review data for 2002 from the UK cystic fibrosis database were analysed in 2 year cohorts from 0–20 years. Northern Score centile charts were constructed (see fig).

Results: There were 1806 patients with recorded Northern Score data for 2002 (927 male patients, M:F ratio 1.05). The centile chart (fig) demonstrates a quasi-linear rise throughout childhood. A Northern Score in excess of age in years equates to >95th centile in primary school aged cystic fibrosis patients.

Discussion: This centile chart provides a disease specific reference range for monitoring on an individual or clinic by clinic basis. Patients, parents, and clinicians may find these useful during the annual review process.


VASCULAR ACCESS IN CYSTIC FIBROSIS: SHORT AND SWEET?

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Aims: Vascular access is an important part of patient management in cystic fibrosis. In most instances, vascular access is straightforward. However, a single bad experience with venepuncture has a lasting impact. We encountered several patients described as needlephobic who were predominantly afraid of long line insertion rather than venepuncture. Clinical experience suggested that for some individuals a smaller, shorter catheter (Leaderflex) could successfully deliver intravenous antibiotics for up to 14 days. Between September 2002 and May 2004 we offered a free, fully informed choice between a standard 30 cm long line or a short (8 cm) Leaderflex line and audited this change in practice.

Methods: Data were collected prospectively on both types of line. These data included: date and time of insertion, type of sedation or anaesthesia used, type of line inserted, site of insertion, state of veins

EFFECTIVENESS AND SAFETY OF NITROUS OXIDE/OXYGEN MISTURE FOR ANALGESIA DURING PAINFUL PROCEDURES IN CHILDREN WITH CYSTIC FIBROSIS

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Background: Children with cystic fibrosis often require painful procedures to be carried out on repeated occasions during their childhood. Many become excessively fearful of such procedures. Oral or intranasal sedation is often ineffective and may have prolonged effects hampering physiotherapy. Inhalational analgesia using nitrous oxide/oxygen mixture (‘‘Entonox’’) has been shown to be effective in non-respiratory conditions, but concerns remain about its safety in chronic respiratory disease. We aimed to assess the effectiveness and safety of this technique in children with cystic fibrosis.

Method: We measured lung function, oxygen saturation, and rated pain (observed and perceived) and level of sedation before and 60 minutes after Entonox analgesia in nine children with cystic fibrosis undergoing painful procedures (venepuncture or cannulation). All parameters except lung function were also measured during and at 3 minutes after the procedure. Observed pain was rated using a behavioural pain assessment score (CHEOPS) and perceived pain using the Wong-Baker Faces scale. Values pre- and post-procedure were compared using paired t test.

Results: There were no significant differences in lung function before and 60 minutes after Entonox analgesia: mean (SD) values pre- and post-procedure for FVC were 1.78 (0.46) and 1.77 (0.52), and for FVC were 2.11 (0.50) and 2.11 (0.55). Mean pulse oxygen saturation remained at 98% throughout, with no significant differences. Median behavioural pain score remained at 4 before, during, and immediately after the procedure.

Conclusion: Our results suggest that Entonox analgesia is safe and effective in patients with cystic fibrosis, although further study using larger numbers would be required to confirm this finding.
GROWTH AND PULMONARY FUNCTION OF CYSTIC FIBROSIS CHILDREN PRESENTING WITH MECONIUM ILEUS

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Background: Older comparative studies have suggested that patients with cystic fibrosis who present with meconium ileus have a more severe clinical course compared with those who do not. With improved management of meconium ileus, we hypothesised that the longer term adverse effect of meconium ileus would be less apparent.

Aims: To determine if infants presenting with meconium ileus have a more severe clinical course than those who do not.

Methods: Prospective, longitudinal follow up of three groups of patients with cystic fibrosis from two tertiary respiratory units born between 1985 and 1990: group I, 41 subjects presenting at birth with meconium ileus; group II, 43 subjects with cystic fibrosis diagnosed as a result of newborn screening for cystic fibrosis; group III, 38 subjects detected through meconium ileus; group II, 43 subjects with cystic fibrosis diagnosed as a result of newborn screening for cystic fibrosis (age 6–16 years, mean 11.7 years), before and after bronchodilator (P, FVC, FEV1, and FEF25–75) at ages 5, 10, and 15 years and pulmonary function (P, FVC, FEV1, and FEF25–75) at ages 6, 10, and 15 years. Other outcomes included genotyping, number of courses of intravenous antibiotics, age at which pseudomonas was first isolated, gastrointestinal symptoms, and complications such as meconium ileus equivalent and liver disease. Analysis of variance was used to determine differences between the groups.

Results: Growth data were available at 5, 10, and 15 years in 40, 34, and 16 group I subjects respectively, 38, 37, and 18 group II subjects; and 39, 29, and 18 group III subjects. Pulmonary data were available at 6, 10, and 15 years in 31, 33, and 16 group I subjects, 28, 36, and 18 group II subjects; and 29, 26, and 18 group III subjects. Apart from a small difference in FEF 25–75 between groups at age 6 years and height at age 15 years, there were no significant differences in any other parameter between the three groups.

Conclusion: Infants who present with meconium ileus do not have a more severe clinical course during childhood compared with either those who are detected through newborn screening, or those who present clinically.

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Conclusion: Infants who present with meconium ileus do not have a more severe clinical course during childhood compared with either those who are detected through newborn screening, or those who present clinically.
Aims: To examine the influence of length, age, maternal smoking during pregnancy family history of asthma, gender, and gestational age at birth on interrupter resistance (R\text{int}) measured between 18 and 116 days of age.

Methods: Sixty one healthy term infants were recruited during pregnancy or before discharge from the postnatal ward and then studied from the age of 4 weeks (mean age 7 weeks). Thirty five infants were studied in Leicester and 26 in Bern, using identical technical and analytical methods. Measurements of interrupter resistance were made during natural sleep either in the laboratory or in the infant’s home. Evidence of smoking during pregnancy was taken from the maternal medical records. Family history of asthma was defined as at least one first-degree relative who had ever been diagnosed with asthma.

Results: Although there was no significant difference between mean R\text{int} in infants born to non-smokers (3.28 (kPa/l/s)) and smokers (3.86 kPa/l/s), a multivariate linear regression analysis (R^2 = 0.395) (see table) showed that only age and maternal smoking had a significant influence on R\text{int} after controlling for the remaining variables.

Conclusion: This study of unsedated healthy infants using a relatively simple technique provides further evidence of an independent adverse effect of prenatal smoking on lung function in early infancy.


Abstract G151

<table>
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<th>Variable</th>
<th>Standardised jcoefficient</th>
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<td>Maternal smoking</td>
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</tr>
<tr>
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<td>Family history of asthma</td>
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</tr>
</tbody>
</table>

Conclusion: This study of unsedated healthy infants using a relatively simple technique provides further evidence of an independent adverse effect of prenatal smoking on lung function in early infancy.

OR 3.5, 95% CI 1.6 to 5.2). Maternal, but not paternal cigarette smoke exposure was significantly associated with the salivary cotinine validated level in children (adjusted OR: 2.5, CI 1.8 to 3.4).

Conclusions: Maternal smoking, child’s age (<7 years), sex (male), and low socioeconomic status were significant factors associated with cigarette smoke exposure in young school children in Liverpool.

G154 ROAD TRAFFIC RELATED OUTDOOR AIR POLLUTION AND ASTHMA PREVALENCE: A CROSS-SECTIONAL STUDY

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Aim: There is continuing concern regarding the potential effects of road traffic related pollution on asthma prevalence. We investigated the association between modelled outdoor nitrogen dioxide (NO2) levels, a marker for road traffic related pollution, and asthma prevalence in an analytical cross-sectional study.

Methods: The NO2 model incorporated road network, traffic flow, land cover, and altitude data and was validated against measured NO2 levels (1997–98). We used survey data from a Schools Asthma Survey (1999) of children aged 8–9 years. The response to two questions were used to assess asthma prevalence (a) “In the last 12 months has your child wheezing or whistling from the chest?” and (b) “Does your child have asthma at present?” Survey data were linked to pollution using postcode of residence. We used logistic regression and adjusted for socioeconomic deprivation categories by quintile, using enumeration district level Townsend scores derived from the 1991 census. Boys and girls were analysed separately (total = 3789).

Results: The adjusted odds ratio for wheeze was 1.37 (0.91 to 2.08) in the highest, relative to the lowest, NO2 category by quintile for girls and 0.93 (0.65 to 1.35) for boys (see table). The corresponding odds ratios for presence of asthma were 1.88 (1.13 to 3.14) for girls and 1.01 (0.65 to 1.56) for boys. But, trends across categories were inconsistent.

Conclusions: Elevated levels of traffic-related outdoor NO2 appeared to be associated with increased prevalence of asthma in girls but there was no evidence of association in boys.

G155 HIGH RESOLUTION CT SCAN FINDINGS IN PATIENTS WITH DIFFICULT ASTHMA


Introduction: Children and adolescents with difficult asthma continue to experience frequent symptoms despite maximal conventional asthma therapy. Assessment of these patients should attempt to confirm the diagnosis of asthma and identify other conditions that may mimic or be associated with asthma. A high resolution CT (HRCT) scan of the chest may be useful to diagnose bronchiectasis, obliterator bronchiolitis, or other structural and parenchymal lung disease. The aim of this study was to investigate the usefulness of HRCT in patients with difficult asthma referred to a tertiary paediatric respiratory centre.

Methods: A retrospective review of patients referred for assessment of difficult asthma in whom HRCT of the chest was performed as part of their clinical evaluation. All patients had clinical features consistent with a diagnosis of asthma and evidence of reversible airflow limitation following treatment with β2 agonist or corticosteroids. All HRCT scans were reported by one of two consultant radiologists.

Results: HRCT was performed in 43 patients (21 males), with a mean age of 14.4 (range 6–18) years. All patients were prescribed >1.6 mg of inhaled budesonide (or equivalent) or regular oral corticosteroids. Other prescribed treatment included oral cyclosporin (n = 2) and methotrexate (n = 2). Twelve (28%) patients had a proven diagnosis of bronchiectasis. Asthmatic children (9%) patients had evidence of bronchiectasis. All other scans were reported as showing changes consistent with asthma (bronchial wall thickening, air trapping, atelectasis). Seven of the original 43 patients had a baseline FEV1 <50% predicted at the initial consultation. Bronchiectasis was present on HRCT in three of these seven patients.

Conclusion: Findings of bronchiectasis are particularly important as management strategies are different from those of asthma. These data suggest that the presence of significant airflow limitation may help to identify those patients with difficult asthma who also have radiological evidence of bronchiectasis on HRCT.

Supported by Asthma UK

G156 EVIDENCE THAT POLYMORPHISMS IN THE CHEMOKINE PATHWAY CONTRIBUTE TO THE EXPRESSION OF ASTHMA AND ATOPY

S. A. Al-Abdulhadi, G. Christie, P. J. Helms. Child Health, University of Aberdeen, Aberdeen, UK

Background: Chemokines contribute to asthmatic airway inflammation through their chemotactic effects on a variety of leucocytes including eosinophils and neutrophils. We sought to identify the likely relevance of genetic variants of the promotor gene of the chemokine RANTES (regulated on activation normal T cells expressed and secreted) and chemokine receptors 2 and 3 (CCR2, CCR3), variants of which have been implicated in immune disregulation.

Methods: In 154 families (n = 453) containing at least two children aged 7–18 years with physician diagnosed asthma, the prevalences of known SNPs in the CCR2 and CCR3 receptor coding regions, and in the RANTES promoter were identified by DNA pooling and allelic quantification. All individuals had comprehensive phenotypic assessments including baseline lung function, methacholine bronchial hyperresponsiveness, skin prick testing to common inhalent allergens (SPT), and total serum IgE. Individual assignment of relevant alleles was performed by PCR RFLP, TaqMan (ABI7700), with subsequent assessment of familial transmission by the pedigree disequilibrium test. 1 SNPs were also assessed by Matldn and Matldninder in order to identify likely functional binding sequences.

Results: Within CCR2 only SNP-64I was found to have a likely functional binding site and the mutant G → A allele within this site was preferentially transmitted to non affected children. SNPs – 17Y, – 21G, and 5’UTR in CCR3 were within a functional binding site but only SNP-17Y had a relevant frequency (11.9%) in our population. SNP-17Y was also preferentially transmitted to asthmatic children. Within the RANTES promoter region SNPs – 403A and – 28C were both within a common functional binding site but only SNP-403 had a clinically relevant frequency (38.3%). SNP-403 was preferentially transmitted with atopy (SPT – 3 mm).

Conclusion: Common SNPs in chemokine receptors 2 and 3 and in the RANTES promoter are likely to be functional and are transmitted respectively with absence of asthma, with asthma, and with atopy in Caucasian families at high risk of asthma. The chemokine pathway offers a number of potential therapeutic targets for both asthma and related allergic disease.


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<tr>
<th>Abstract G154</th>
<th>Odds ratios (95% confidence intervals) for wheeze and presence of asthma by NO2 category by quintile</th>
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<tbody>
<tr>
<td>NO2 category</td>
<td>wheeze Boys</td>
</tr>
<tr>
<td>1 (lowest)</td>
<td>1.00</td>
</tr>
<tr>
<td>2</td>
<td>1.02</td>
</tr>
<tr>
<td>3</td>
<td>0.93</td>
</tr>
<tr>
<td>4</td>
<td>0.83</td>
</tr>
<tr>
<td>5 (highest)</td>
<td>0.93</td>
</tr>
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<td></td>
<td>(0.65 to 1.35)</td>
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www.archdischild.com
DO THE PUFFS AND PILLS ADD UP IN ASTHMA?

G. Davies, D. L. Corrigan. Wishaw General Hospital, Lanarkshire, UK

Introduction: Barriers to optimal management of asthma in children are multifactorial and include poor concordance with therapy. Any discrepancy between the prescribed management and that perceived by the parent or child makes optimal concordance difficult to achieve.

Aims: We investigated whether perception of intended management agreed with that documented in case notes for children attending our paediatric outpatient clinics, and the influence of a written management plan on this.

Methods: Between May and July 2004, patients were asked to bring all medications to clinic. Children on regular inhaled therapy attending clinic with all medications were included in the study. Medications were observed directly and parents (or the child where appropriate) were asked the “number of puffs” and frequency taken for each inhaler and similarly for other medications brought. The actual resultant doses were calculated for each medication. We also asked if they had an up to date management plan. The previous clinic or discharge letter was used to determine the intended current management regimen.

Results: Fifty children were included, with a median age of five years. Fifteen patients (30%) had a discrepancy between intended and perceived dose of at least one medication. In two thirds of these cases the discrepancy related to the dose of inhaled steroids. Twenty four patients (48%) had a management plan and in 79% of cases this was up to date. Children with an up to date management plan were less likely to have a discrepancy between their prescribed and perceived therapy (2-tailed test p = 0.019).

Conclusion: Children are commonly not taking the intended therapy for their asthma, and we propose that management plans have a role to play in tackling this substantial yet largely unrecognised barrier to optimal care.

SO YOU THINK YOU KNOW WHO ADHERES?

P. C. Boit, W. D. Carroll, S. Clayton, W. Lenney, M. P. Samuels. Academic Department of Paediatrics, University Hospital of North Staffordshire, Stoke-on-Trent, UK

Aims: Although adherence with treatment in childhood asthma is poor,1 healthcare professionals often assume they know who is and who isn’t taking the medicine as prescribed. We undertook an audit of prescription collection for patients with asthma to determine whether our clinical judgement of adherence was correct and to identify factors which might predict adherence.

Methods: We used hospital and primary care databases to collect data on 40 children with asthma for the preceding 12 months (age range 6–16 years) at BTS-SIGN level 2 or above. 20 were considered by the Hospital Asthma Team to be poor compliers and the remainder were age-sex matched controls without suspected poor compliance. Data were entered into a STATA v8.0 database and factors predicting prescription collection were determined using multivariate regression models. Differences in continuous variables between suspected poor compliers and controls were determined using the Mann-Whitney U test.

Results: Almost two thirds of the prescriptions for regular prescribed asthma therapies were collected for the children in our study (Mean 62.9%, Median 65% SD 35%). There was only a small difference in prescription collection between those considered to be poorly compliant and those in whom no such concerns were raised (58% v 68% p = 0.19). Moreover, 40% of children with suspected poor compliance and 50% of the control group were collecting >75% of prescribed treatment. In multivariate models only annual salbutamol use was associated with increased adherence (p = 0.002). Age, gender, and perceived compliance were all poor predictors of patient behaviour (p > 0.2). There was no difference in prescription collection between oral (62%) and inhaled treatments (66%) (p = 0.74).

Conclusion: These data suggest that experienced healthcare professionals are not good at predicting compliance patterns. A high proportion of children whose difficulties had initially been attributed to poor adherence were requesting appropriate amounts of medication. Despite data suggesting increased compliance with oral treatments1 there was no evidence of this in our study. Communication about patient prescription collection between secondary and primary care can help inform clinicians about individual patient adherence: this should become routine practice.