S64 USE OF PATHOLOGICAL PHENOTYPE TO DETERMINE OPTIMAL MANAGEMENT FOR MODERATE TO SEVERE PRESCHOOL WHEEZE

[1]Y Bingham, [2]J Moreiras, [3]S Goldring, [4]J Cook, [1]L Selby, [5]L Baynton, [4]A Gupta, [1]L Fleming, [5]I Balfour-Lynn, [1]A Bush, [5]W Banya, [5]M Rosenthal, [1]S Saglani. *[1]Imperial College London, London, UK; [2]Whittington Health NHS Trust, London, UK; [3]The Hillingdon Hospitals NHS Foundation Trust, London, UK; [4]King's College Hospital NHS Foundation Trust, London, UK; [5]Royal Brompton and Harefield NHS Foundation Trust, London, UK*

10.1136/thorax-2019-BTSabstracts2019.70

Introduction Persistent episodes of wheezing are common in preschool children, however we have few effective therapies. We hypothesised that objective biomarker based management of preschool wheeze would be superior to current clinical guidelines.

Methods A single-centre randomised, controlled trial in children aged 1–5 years with moderate to severe recurrent wheeze, requiring at least 2 admissions ± short courses of oral steroids in the last 12 months, with at least one in the last 6 months. Children were recruited from September-April over a 3 year period. Clinical (episodic viral wheeze [EVW], or multiple trigger wheeze [MTW][1]) and pathological phenotypes based on blood eosinophilia ≥3%, or bacterial infection in sputum or cough swab were determined at recruitment. Children were randomised to pathological phenotype based management (beclomethasone 400 mcg/day if blood eosinophils ≥3%, or targeted antibiotics if positive culture on sputum/cough swab) or clinician directed care (control arm) for 4 months. Primary outcome was number of unscheduled healthcare visits (UHCVs). Daily symptoms were reported via a text message system. Patients treated with inhaled corticosteroids (ICS) had adherence assessed using an electronic monitoring device.

Results 60 children were randomised, 30 in each group. Baseline blood eosinophils were similar in the two groups (5.18% control, 5.15% intervention). 6 children had positive sputum cultures. 38/60 had EVW and 22/60 had MTW. Prevalence of clinical phenotypes was similar in both groups (control-EVW 18/30, MTW 12/30; intervention- EVW 20/30, MTW 10/30). In both groups 20/30 (67%) were prescribed ICS, with median adherence 67% (range 0–91%). There was no significant difference in the rate of UHCVs or symptoms between the two groups (p=0.46).

Conclusions Phenotype based management of children with moderate to severe preschool wheeze did not result in a significant reduction in UHCVs compared to clinical guideline based management. However, 56% of children in the control group with EVW were prescribed ICS by their clinician even though this is not recommended in clinical guidelines and 80% of those with EVW in the pathological phenotype had blood eosinophilia, suggesting little relationship between clinical phenotype and objective biomarkers to guide ICS prescription.

REFERENCE

1. Brand PJ, *et al*. *Eur Respir J* 2008

S65 CAPILLARY CARBON DIOXIDE AS A MEASURE OF DISEASE SEVERITY IN ACUTE BRONCHIOLITIS

[1]SA Unger, [1]C Halliday, [1]A Ziaie, [2]S Cunningham. *[1]Royal Hospital for Sick Children Edinburgh, Edinburgh, UK; [2]University of Edinburgh, Edinburgh, UK*

10.1136/thorax-2019-BTSabstracts2019.71

Carbon dioxide (CO_2) using capillary blood gas (CBG) analysis is commonly used children with acute bronchiolitis. Evidence to support its use is limited.

A retrospective observational study was conducted over two bronchiolitis seasons (2014 -2016) of infants admitted to a tertiary teaching hospital using patient electronic medical records. Using logistical regression models (STATA/IC 12.1) the association between CBG pCO_2 and markers of disease severity (length of stay (LOS) and high dependency admission (HDU)) was examined.

332 children were assessed with 526 CBG performed in 158 infants (mean age 0.31 years, 54% male, 27% premature, 77% RSV positive). The initial CBG pCO_2 was a mean 5.9kPa (SD1.1) and a maximum mean of 6.4kPa (SD1.5). Median LOS was 3 days (range 0–35). A CBG pCO_2 >7.0kPa during the admission (in 23% infants (36/158)) was significantly associated with younger age (OR 0.005 (95%CI 0.0007, 0.03); p<0.0001), the use of supplemental oxygen (OR 1.9 (95%CI 1.1, 3.3); p=0.033) (adjusted for age) and inspired fraction of oxygen (FiO_2) (slope coefficient 2.01 (95%CI 1.08, 2.94), p<0.0001) (adjusted for age). In 62% (98/158) a CBG was performed in ED and a pCO_2 >7kPa (N=26/98) in ED was significantly associated with LOS (IRR 1.4 (95%CI 1.1,1.8); p=0.008) and HDU admission (OR 3.5 (95%CI 1.7,7.8); p=0.001).

CBG pCO_2 >7 kPa identifies children in ED with more severe disease with longer length of stay and risk of admission to HDU. Our results suggest that CBG pCO_2 may be a possible marker of severity in future intervention trials for bronchiolitis.

ILD and rare respiratory diseases: cracking the code

S66 DELIVERING THE 100,000 GENOMES PROJECT TO ESTABLISH THE FUNCTIONAL ROLE OF DNA SEQUENCE VARIANTS IN RESPIRATORY RARE DISEASES

[1]CL Shovlin, [2]DJ Morris-Rosendahl, [3]F Copeland, [4]A De Soyza, [2]C Hogg, [5]G Jenkins, [6]SJ Marciniak, [1]M Lovett, [1]MF Moffatt, [1]WOC Cookson, [7]M Alikian, [2]S Hasan, [1]R Slade, [1]S Xiao, [8]F Boardman-Pretty, [8]D Brown, [8]M Caulfield, [8]A Devereau, [8]T Fowler, [8]E McDonagh, [8]R Scott, [8]ERA Thomas, [8]Genomics England Research Consortium, [1]EWFW Alton. *[1]Imperial College, London, UK; [2]Royal Brompton NHS Foundation Trust, London, UK; [3]PCD Family Support Group, Milton Keynes, UK; [4]Newcastle University, Newcastle, UK; [5]University of Nottingham, Nottingham, UK; [6]University of Cambridge, Cambridge, UK; [7]Imperial College Healthcare NHS Trust, London, UK; [8]Genomics England, London, UK*

10.1136/thorax-2019-BTSabstracts2019.72

Background and aims Between July 2016 and September 2018, NHS Genomic Medicine Centres (GMCs) recruited families with specified rare diseases to the 100,000 Genomes Project for whole genome sequencing (WGS), and linkage to phenotypic information from NHS Health Records.

Methods Genomics England protocols were followed for disease nominations, data model generation based on human phenotype ontology (HPO) terms,[1] and development/review of PanelApp gene panels.[2] Genomics England performed all WGS, data alignments, and initial variant tiering. This incorporated appropriate familial segregation patterns for variants in genes known to cause the patient's disease (Tier 1: clear loss of function variants, Tier[2]: other variants), and

Thorax: first published as 10.1136/thorax-2019-BTSabstracts2019.70 on 12 November 2019. Downloaded from http://thorax.bmj.com/ on April 9, 2024 by guest. Protected by copyright.