Bronchiectasis

P100 SUCCESSFUL ERADICATION OF RESPIRATORY TRACT MRSA IN CYSTIC FIBROSIS: A RETROSPECTIVE STUDY

H Green, R Gadhok, K Alshafi, D Bilton, NJ Simmonds; *Royal Brompton Hospital, London, UK*

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Introduction The prevalence of pulmonary MRSA infection in cystic fibrosis (CF) has been increasing and is associated with accelerated pulmonary function decline and higher mortality rates. Eradication is generally recommended but there is no consensus of the optimal regimen. The current prevalence at our centre is low (3%, n = 20).

Method Retrospective review of adult patients with newly acquired MRSA infection (2007–2012) confirmed by ≥1 positive sputum culture. Data were retrieved from clinical records. "New" infection was confirmed by ≥3 consecutive preceding negative MRSA cultures over ≥12 months. Reflective of changing practice towards MRSA eradication at our centre, antibiotic therapy was categorised as either "conventional" (pre-2008) - a single oral agent, or "contemporary" (2008 +) using dual oral therapy (based on sputum susceptibilities). Our primary outcome was successful MRSA eradication from sputum at 3 months.

Results 32 infection episodes (n = 25) were identified. 19 patients had a single episode of infection, 5 had 2 and 1 patient had 3, each separated by an MRSA-free period of ≥12 months. 13 episodes were treated by conventional approaches (n = 13), and 13 by contemporary means (n = 12). Eradication was not attempted for 6 episodes. Eradication at 3 months was confirmed by negative sputum cultures after treatment by conventional or contemporary regimens in 45% and 80% episodes, respectively (p = NS).

Combined Rifampicin/Fusidic acid (Rif/Fus) and single agent tetracyclines were the most widely used regimens (treatment duration, median 2 weeks (range 1.4–4)). Rif/Fus was used for 8 infection episodes (n = 8), achieving eradication rates at 3 months of 100% (6/6 patients). Negative MRSA sputum cultures were maintained in 75% (6/8) patients at 6 months and 37.5% (3/8) at 12 months. Tetracyclines were used for 9 infection episodes (n = 9), achieving eradication rates of 42.9% at 3 months (3/7), 33.3% at 6 months (3/9) and 33.3% at 12 months (3/9). Rif/Fus was more likely to achieve eradication at 3 months compared with tetracyclines (p = 0.03), but this did not maintain statistical significance at 6 or 12 months.

Conclusion Our findings demonstrate contemporary treatment with an antibiotic combination, particularly Rif/Fus, to be an effective MRSA eradication strategy. This requires validation with a prospective controlled trial.

P101 DOES IVACAFTOR IMPROVE OBJECTIVE MEASUREMENTS OF HEALTH IN PATIENTS WITH THE G551D CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR (CFTR) PROTEIN MUTATION? THE EXPERIENCE OF A UK CYSTIC FIBROSIS CENTRE

AE Ewence, CN Eruchie, AM Higton, TBL Ho; *Frimley Park Hospital NHS Foundation Trust, Frimley, United Kingdom*

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Introduction and Objectives The CFTR potentiator, Ivacaftor, has recently been launched in England for use in adult cystic fibrosis patients with at least one copy of the G551D mutation. Formal clinical trials have demonstrated significant improvements in spirometry, weight and quality of life symptom scores in patients taking this new drug. We wish to report our experience of Ivacaftor in a standard clinic setting through longitudinal follow-up of our patients over a six month period.

Methods 11 patients were started on Ivacaftor between December 2012 and February 2013. Before starting Ivacaftor we measured spirometry (FEV1 and FVC), weight, liver function tests, quality of life symptom scores and the number of antibiotic courses for infective exacerbations in the preceding 3 months. Repeat measurements were taken at 3 months after starting Ivacaftor and compared to baseline. Liver function tests were monitored as per manufacturer's advice, with the intention to stop Ivacaftor if there was a significant rise in liver function tests.

Results 10 patients remained on Ivacaftor at 3 months (one patient was lost to follow-up). Baseline spirometry in these patients demonstrated an average percentage predicted FEV1 of 58.2% (SD ± 19.8) and average percentage predicted FVC of 77.9% (SD ± 22.2). Spirometry improved in all patients at 3 months compared to baseline; average increase in predicted FEV1 12.2% (p = 0.010) and average increase in predicted FVC 15.8% (p = 0.006). All but one patient gained weight with an average weight increase of 2.1 kg (p = 0.013). The use of antibiotics to treat exacerbations significantly improved; only 1 patient required antibiotics in the 3 months after starting Ivacaftor. One patient, whilst taking concomitant anabolic steroids, had to stop Ivacaftor after a six-time rise in alanine transaminase. After stopping steroids, he subsequently restarted Ivacaftor without deterioration in liver function.

Conclusions At 3 months our patients demonstrated statistically significant improvements in spirometry and weight after starting Ivacaftor. Importantly, Ivacaftor has been well tolerated with reported improvements in symptom burden and reduced exacerbation rates; 3 patients have returned to work/changed jobs and one has starting full-time education. Further results from six month follow-up, including quality of life symptom scores, are awaited.

P102 SWEAT CHLORIDE IS NOT A USEFUL MARKER OF CLINICAL RESPONSE TO IVACAFTOR

PJ Barry, WG Flight, J Biesty, D Clough, I Small, S Johnson, AL Brennan, RJ Bright-Thomas, AK Webb, AM Jones, AR Horsley; *Manchester Adult Cystic Fibrosis Centre, Wythenshawe, United Kingdom*

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Introduction and Objectives The development of the targeted CFTR potentiator Ivacaftor has significantly altered the landscape for cystic fibrosis (CF) therapeutics, and heralds the arrival of personalised medicine in this condition. Data from Phase III clinical trials have been encouraging and suggested that the use of Ivacaftor results in a normalisation of sweat chloride and significant increases in pulmonary function and weight in suitable patients. As part of the commissioning requirements for Ivacaftor in the UK, sweat chloride changes represent the major criteria for continuing prescription, with a reduction of 30% or reduction below 60 mmol/L proposed as cut-offs for continuation of therapy. We aimed to assess the relationship of sweat chloride to clinical outcomes in patients receiving Ivacaftor treatment.

Methods All Ivacaftor naïve patients who carried the G551D mutation were contacted to enable the commencement of the

medication. Baseline sweat chloride was recorded, and repeated at 2 months. Baseline pulmonary function, height and weight were recorded and repeated at monthly visits for 3 months.

Results To date 24 of 27 suitable subjects have commenced Ivacaftor. Mean FEV_1% predicted was 64.3% predicted at Ivacaftor commencement and mean BMI was 22.1 kg/m^2. Mean FEV_1 percent predicted increased in absolute terms by 8.9% at 1 month and 8.7% at 3 months ($p < 0.001$ at both time points). Mean BMI improved to 22.7 kg/m^2 at 1 month and 23.0 kg/m^2 at 3 months ($p = 0.002$, 0.003 respectively). There was a significant fall in sweat chloride at 2 months (median 114 to 51 mmol/L, $p < 0.001$). Improvement in sweat chloride was not correlated in absolute or relative terms with improvements in pulmonary function or BMI. Four subjects with a mean absolute FEV_1 improvement of 14.5% had sweat chloride responses not meeting pre-specified criteria at 2 months. Two of these subjects had a subsequent repeat test meeting continuation criteria. In one subject a suboptimal response was attributed to the omission of a single dose.

Conclusions The use of sweat chloride as a surrogate for clinical efficacy and a criterion for drug continuation is not supported by this data. Sweat chloride may be a marker of 100% adherence to therapy.

P103 CULTURE AND CULTURE INDEPENDANT IDENTIFICATION OF BACTERIAL COMMUNITIES IN THE CYSTIC FIBROSIS RESPIRATORY TRACT

[1]GG Einarsson, [2]J McCaughan, [3]AA Fodor, [3]MC Wolfgang, [4]MM Tunney, [5]JS Elborn; *[1]CF and Airways Microbiology Research Group, Queen's University Belfast, Belfast, United Kingdom; [2]Department of Medical Microbiology, Royal Group of Hospitals, Belfast, United Kingdom; [3]University of North Carolina at Chapel Hill, Chapel Hill, United States of America; [4]School of Pharmacy, Queen's University Belfast, Belfast, United Kingdom; [5]Centre for Infection and Immunity, Queen's University Belfast, Belfast, United Kingdom*

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Introduction and Aims The identification of complex chronic polymicrobial infections, such as those observed in the cystic fibrosis (CF) airways, are often a diagnostic challenge. Few studies have compared culture-dependent methods with molecular identification making it hard to describe bacterial communities in a comprehensive manner. The aim of the study is to compare four different methods with respect to their similarities and differences in detection of bacteria.

Methods We compared41 sputum samples fromroutine clinical-culture, extended-culture (aerobic and anaerobic), and molecular identification such as Roche 454-FLX Titanium and T-RFLP to assess concurrence between methodologies in detecting bacteria. The agreement between methodologies in detecting either absence or presence of bacterial taxa was assessed by Kappa ( ) statistics.

Results The majority of bacterial taxa identified by culture were also identified with molecular analysis. In total 2, 60, 25, and 179 different bacterial taxa were identified with clinical-culture, extended-culture, T-RFLP and 454-FLX respectively. Clinical-culture, extended-culture and T-RFLP were poor predictors of species richness when compared to 454-FLX ($p < 0.0001$). Agreement between methods for detecting *Pseudomonas* sp. and *Burkholderia* sp. was good with ≥ 0.7 [$p < 0.0001$] and ≥ 0.9 [$p < 0.0001$] respectively. Detection of anaerobic bacteria, such as *Prevotella* sp. and *Veillonella* sp., was moderate between extended-culture and 454-FLX with = 0.461 [$p < 0.0001$] and = 0.311 [$p = 0.032$] respectively, and good between T-RFLP and 454-FLX with = 0.577 [$p < 0.0001$] and = 0.808 [$p < 0.0001$] respectively. Agreement between methods for other main bacterial taxa, such as *Staphylcoccus* sp. and *Streptococcus* sp., was poor with only a moderate agreement for detection of *Streptococcus* sp. observed between T-RFLP and 454-FLX (= 0.221 [$p = 0.024$]).

Conclusions This study demonstrates the increased sensitivity culture-independent microbial identification such as the 454-FLX have over clinical-culture, extended-culture and T-RFLP methodologies. The extended-culture detected majority of the most prevalent bacterial taxa associated with chronic colonisation of the CF airways which were also detected by culture-independent methodologies. However, agreement between methods in detecting number of potentially relevant bacteria is largely lacking.

P104 NEBULISED HYPERTONIC SALINE IMPROVES QUALITY OF LIFE IN ADULT PATIENTS WITH NON-CYSTIC FIBROSIS BRONCHIECTASIS

K Bentley, ZL Borrill; *North Manchester General Hospital, Manchester, UK*

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Background Nebulised hypertonic saline (HTS) improved lung function, quality of life and exacerbation frequency in a study of patients with non-cystic fibrosis (CF) bronchiectasis[1]. It may improve chest clearance by increasing water content of airway surface liquid, enhancing mucociliary clearance. A protocol was developed for the use of HTS in a district hospital setting. Safety, tolerability, lung function and quality of life data are presented.

Methods Patients with non-CF bronchiectasis were assessed on a locally developed chest clearance pathway consisting of active cycle breathing technique, postural drainage, flutter device and mucolytic. Patients with ongoing symptoms were given a trial dose of 4 mls HTS 7% with spirometry measured pre and post. Patients continued on 4 mls HTS od/bd for 12 months if tolerated. Adverse effects, quality of life and spirometry was collected at 4 weeks and 6 months. Data were compared using paired t tests.

Results 34 patients (mean age 62, 25 female, mean FEV_1 66% predicted) were assessed. 2 (6%) patients did not proceed with treatment due to (a. FEV_1 decline >15% and b. severe nausea).

Abstract P104 Table 1. Changes in LCQ and SGRQ scores.

Leicester Cough Questionnaire	Pre HTS Mean (SD)	4/52 Mean (SD)	p value	6/12 Mean (SD)	p value
Physical	3.7 (1.4)	4.1 (1.4)	0.002*	4.0 (1.5)	0.28
Psychological	4.2 (1.7)	4.8 (1.4)	0.001*	4.7 (1.6)	0.28
Social	4.1 (1.9)	4.7 (1.6)	0.001*	4.6 (1.7)	0.20
TOTAL	11.8 (4.6)	13.7 (4.3)	0.0003*	13.3 (4.5)	0.15
St Georges Respiratory Questionnaire	**Pre HTS Mean (SD)**			**6/12 Mean (SD)**	**p value**
Symptoms	83.2 (14.2)			74.6 (19.0)	0.02*
Activity	78.0 (22.5)			68.7 (27.0)	0.14
Impact	57.2 (18.7)			43.7 (22.9)	0.07*
TOTAL	67.8 (18.7)			56.1 (20.7)	0.01*