ONLINE SUPPLEMENT

Lung Clearance Index in cystic fibrosis subjects treated for Pulmonary Exacerbations

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Methods:

Study Population:

Eligible Cystic Fibrosis (CF) patients aged 6-18 years were recruited on the day of their hospital admission to the Hospital for Sick Children for treatment with 2 weeks intravenous antibiotic for a pulmonary exacerbation. The choice of antibiotic was made by the admitting physician. Study patients were determined to have a pulmonary exacerbation if their Akron Pulmonary Exacerbation Score (PES) was ≥5.[1]

Eligible patients were capable of performing acceptable and reproducible spirometry, and had a diagnosis of CF as defined by two or more clinical features of CF and a documented sweat chloride >60mEq/L by quantitative pilocarpine iontophoresis test or a genotype showing two well-characterized disease-causing mutations. Subjects were excluded from participation if they required daytime supplementary oxygen, use of oral steroids or intravenous antibiotics 14 days prior to screening, had previously received a lung transplant, had taken investigational drugs within 30 days of screening, or presented with physical findings that would compromise their safety or the quality of the study data. Patients with respiratory cultures positive for non-tuberculosis mycobacteria (NTM), methicillin-resistant *Staphylococcus aureus* (MRSA), or *Burkholderia Cepacia* complex in the year prior to or at the screening visit were also excluded from the study. This study was approved by the Research Ethics Board (REB) at the Hospital for Sick Children (REB# 1000023162). Informed written consent was obtained from the parents or legal guardians of the study participants.

Outcome Measures:

Patients who met the eligibility criteria performed multiple breath washout (MBW) tests in triplicate on each of two different devices at admission and discharge from hospital. Multiple Breath Nitrogen Washout (MBW N_2) was performed using the open circuit bias flow Exhalyzer D (EcoMedics AG, and Duernten, Switzerland) system and associated software (Spiroware 3.1 EcoMedics AG). During the test subjects breath 100% O_2 during the washout phase until the N_2 concentration is reduced to $1/40^{th}$ the starting concentration. As there is no wash-in phase, subjects re-equilibrated in room air between trials. Multiple Breath SF_6 Washout (MBW SF_6)

was peformed using a respiratory mass spectometer (AMIS 2000; Innovision A/S, Odense, Denmark) where subjects breathe a 4% SF6, 4% He, 21% O2, balance N2 gas mixture until equilibrium is reached. Once the SF_6 gas concentration stabilizes at 4%, the gas source is removed and the subject breathes room air until the tracer gas concentration reaches $1/40^{th}$ the starting concentration. For both the MBW_{SF6} and MBW_{N2} trials were performed in triplicate on each test occasion, and technical acceptability of each trial was assessed by the operator. MBW data from both systems were analyzed by trained personnel using the custom analysis software (TestPoint, Capital Equipment Corp., Billerica, MA, USA). Spirometry was performed according to ATS standards using the Vmax systems (VIASYS, Cardinal Health).[2]

1. Siracusa C, Gothard M, Spoonhower K, NC K. Does Using a Standardized Pulmonary Exacerbation Score in Patients 6 Years Old and Younger with Cystic Fibrosis Improve Outcomes? *Pediatr Pulmonol* 2011: 46(S34): A471, 383.

2. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, Crapo R, Enright P, van der Grinten CP, Gustafsson P, Jensen R, Johnson DC, Macintyre N, McKay R, Navajas D, Pedersen OF, Pellegrino R, Viegi G, Wanger J. Standardisation of spirometry. *Eur Respir J* 2005: 26(2): 319-338.