Bronchodilator responsiveness and IgE in pediatric cystic fibrosis patients
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Bronchodilators are widely used in Cystic Fibrosis (CF), due to hyperreactive secondary to bronchial damage and/or atopy. They improve sputumotology and prevent bronchostenconstriction associated with treatments. Many show acute improvement of FEV1 following β-agonist administration, but response varies over time. A sub-group has acute airways obstruction reversible by β-agonists and atopy, often revealed by increased IgE. These patients may benefit more from bronchodilators chronic use.

Aims: To determine the prevalence of bronchodilator responsiveness and its association with IgE in CF pediatric patients.

Methods: Retrospective study of all patients over 5 years-old followed in our CF Center during 2008 that had ≥2 lung function tests (LFT) and IgE determination. Data collected included demographics, IgE and LFT with bronchodilation test using inhaled salbutamol. An increase in FEV1 ≥10% was considered significant.

Results: 35 patients fulfilled the inclusion criteria. The median age was 13 years (±4.2). Global severity of lung disease was mild (FEV1 76.2±27.7%). Positive bronchodilation test was found in 34.3% and 11.4% maintained responsiveness in ≥2 LFT. 42.9% patients had increased IgE, 40% of whom had bronchodilation. There was no association between increased IgE and responsiveness. Patients with bronchodilation responsiveness had lower FEV1 (74.9% vs 77%; p < 0.05) as did those with increased IgE (72.6% vs 78.9%; p < 0.05).

Discussion: In our study many patients had bronchodilator responsiveness, though few showed consistent response over time. Increased IgE prevalence was high. Both bronchodilation and increased IgE were associated with lower FEV1. Studies are needed to determine the real benefits of β-agonists use in the long term in patients with and without atopy.

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Rationale for a low dose liposomal Ciclosporin A for inhalation via a customised eFlow® electronic nebuliser to prevent and treat bronchiolitis obliterans (BO)
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Bronchiolitis obliterans (BO) is a major cause of death after lung and stem cell transplantation being treated today with systemic immunosuppressive drugs, e.g. Ciclosporin A (CsA). Since systemic CsA is of limited efficacy to prevent or treat BO and it also has severe nephrotoxic effects direct inalapulmonary CsA delivery may result in higher local drug exposure and better effect in association with less systemic side effects. Reports on positive therapeutic effects upon nebulisation of CsA (Iacono et al. 2006) dissolved in propyleneglycol (CsA-PG) indicated that inhaled CsA may be advantageous. Still treatment compliance to inhaled CsA was poor due to the irritating organic solvent and long nebulisation times up to 1 hour. A well tolerable inhalation formulation in a low, non toxic dose with short delivery times was the target. A novel aqueous liposomal CsA (L-CsA) formulation showed good cell tolerability in a Calu-3 epithelial cell culture model and was non toxic in rats when inhaled for 6 months. Lung deposition in 12 lung transplanted patients was about 40% after inhalation of 10 mg L-CsA via a customised eFlow® electronic nebuliser and 50% were found in the lung periphery (Behr et al. 2007). Compared to CsA-PG a sustained release could be observed for L-CsA after incubation of human lung cell homogenates (Trammer et al. 2008). In a perfusive rabbit lung model, highest drug distribution was found after 6 h in homogenates (78%), perfusate (6%) and lavage (16%) (Leuchte et al. submitted). A soon starting phase II program may prove the efficacy and safety of inhale L-CsA delivered via a customised eFlow® electronic nebuliser.

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HRCT and LFT in monitoring CF lung disease
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The severity of chronic bronchopulmonary inflammation is the limited factor for surviving of CF patients. Novel therapies (inhaled antibiotics, rhDNase, respiratory physiotherapy) and multidisciplinary approach results to rising median surviving age and better QoL as we well. Lung function testing is an important marker of lung impairment, but it seems to be less sensitive in comparison to HRCT of lung in CF. In previous study (Belfast, 2003) we concluded that HRCT was more sensitive method of evaluating pathologic changes in CF lung (mucus plugging, thickening of airway wall, bronchiectasias, inflammatory process, air-trapping, emphysema) than LFT, which could be in normal ranges in patients with advanced CF disease. According to localisation and type of changes we can start with segmental physiotherapy, more intense mucolytic therapy (rhDNA), anti-inflammatory therapy.

Aims: To evaluate the changes of lung function (LFT) and morphologic changes in HRCT in 8 years period and correlate them with genotype and clinical status of patients.

Methods: We examined 116 CF pts with more than 3 HRCT (every 2 yeras) examinations done from the year 2000.

Results: 79 pts with severe CFTR mutations (mean age: 18.8 years, FVC: 86.4%, FEV1: 83.7%, MEF50: 69.9%). Staging according Bhalla: 6.97 for right lobe, 6.71 for left lobe. 37 pts with mild CFTR mutations with normal LFT (FVC: 89.4%, FEV1: 89.3%, MEF50: 80.3%), but significantly lower HRCT score (RL: 2.97, LL: 2.53).

Conclusion: Mean HRCT score and LFT did not change in most CF patients with intensive standard therapy in this time period. HRCT score correlates with CFTR genotype and compliance with therapy.