109 Aerosol characteristics of hypertonic saline (HS) nebulised by the eFlow® rapid

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Introduction: Inhaled hypertonic saline (HS) has been proven to be tolerable and effective for sputum induction and mucociliary clearance in CF patients (Donaldson et al., NEJM 2006, 354(3):241–50; Elkins et al., Pediatric Pulmonology, 2006, suppl. 28: 292).
This in-vitro study was conducted to assess the aerosol characteristics of eFlow® rapid upon nebulisation of 4 ml HS 6% available as a preservative single unit dose vial (MucoClear® 6%).
Methods: Aerosol delivery performance was assessed by breath simulation tests using a standardised adult breathing manoeuvre (500 ml TV, 15 bpm, inh.:exh. ratio = 1:1). NaCl collected on inspiratory filters was quantified by potentiometric titration and represents the delivered dose (DD). The respirable dose (RD) corresponding to NaCl in droplets <5 µm was calculated based on droplet size assessment obtained from laser diffraction tests at a continuous flow of 15 L/min. Results represent the data from 3 devices tested in duplicate, each (n = 6).
Results: The respirable fraction was 64.3%±2.6% for droplets <5 µm and 30.4%±4.1% for droplets <3.3 µm characterised by a mass median diameter (MMD) of 4.2±0.2 µm. 3.6±0.7 min were needed to deliver a dose of 38.9±5.7% (= 91.8±13.4 mg NaCl) corresponding to a respirable dose of 25.0±3.7% (= 59.0±8.6 mg) NaCl in droplets <5µm. The high output efficacy of eFlow® rapid is apparent from a total output rate of 821±187 mg/min.
Conclusions: The clinical effects of HS 6% reported by Elkins et al. are supported by these in-vitro data indicating good lung deposition of MucoClear® 6% when nebulised by the eFlow® rapid.

110 Aerosol characteristics of eFlow® using different control units

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Introduction: A new model of the eFlow® Electronic Nebulizer has been developed with a handset that can be customized for use with specific drugs. Customizing the handset allows optimization of the aerosol characteristics to maximize drug delivery and minimize treatment duration. The electronic control unit (CU) can be modified to include features like a display, which make the device more user friendly. It would be advantageous if handsets were compatible with existing base units such as the eFlow® rapid.
This study characterizes the aerosol output of a handset customized for aztreonam lysine for inhalation (AZLI) in combination with the control units type 178 (for eFlow rapid), type 678 (new CU with display) and type 078 (used in the AZLI clinical trials).
Method: Five handsets for use with AZLI were combined with five control units each of type 178, 678 and 078 and characterized (n = 10). Isotonic saline was used as test substance. The characterization was conducted by laser diffractometry using a Malvern Mastersizer X. Test conditions were controlled at 23±1 °C, 50±5% relative humidity and 20±1 L/min continuous flow through the nebulizer.
Results: Average values for the Mass Median Diameter (MMD) were 4.34±0.15 µm, 4.41±0.14 µm and 4.42±0.20 µm for control unit type 078, 678 and 178, respectively. Average Respirable Fractions (RF, mass % in droplets <5µm) were 62.12±3.37%, 60.64±3.38% and 60.29±4.70% for CU type 078, 678 and 178, respectively. Considering the error of the experiment, there was no difference between the results obtained from the different types of CU.
Conclusion: Three different types of control unit were investigated for use with a handset customized for delivering AZLI. Aerosol characteristics of the eFlow® Electronic Nebulizer handset for AZLI were unchanged with the use of different types of control unit.

111 Changing features of patients with cystic fibrosis (CF) referred for lung transplantation assessment

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Prognosis for patients with CF is improving though advanced lung disease remains the cause of premature mortality. Lung transplantation offers patients with CF a 10-year survival of over 50% at this centre.
Hypothesis: Intensive CF therapy has led to a change in demographics of patients referred for transplantation.
Method: Retrospective comparison of two cohorts in 1999 (n = 48) and 2007 (n = 38).
Results: The mean age in the 2007 cohort was greater at 30.3 years (range 16–57 years), vs. 1999 grp; mean age 26.3 years (16–51); though not significant p = 0.055. No significant differences in lung function were noted; mean FEV1 in 1999, 25.2% pred; range 11–47% vs. mean FEV1% pred 2007 24.9%; 10–42%; (p = 0.85). No difference in oxygenation (1999 grp. mean pa02 9.2 kPa (range 6.7–14 kPa) vs. 2007 grp 8.2 kPa (5.7–11.1 kPa); p = 0.10). Similar levels of osteoporosis were seen with 58.3% vs 55.2% (p = 0.94) and CF related diabetes (CFRD) rates of 35.4% vs 28.9%; p = 0.68. The 2007 grp. had better nutritional status; mean BMI was 20.7 kg/m^2 (range16–30) vs. 18.8 (13–24); p = 0.002. The EDTA-GFR was lower in the 2007 grp (mean 104 mls/min; range 39–154 vs 1999 grp. 137 mls/min; 82–188; p < 0.0001). Six minute walk test distance (6MWT) was 370m compared to 470m in 1999; p = 0.003.
Conclusions: The later cohort was older and had better nutritional status. The number of patients with osteoporosis was unchanged. Spirometry was equivalent but exercise tolerance as assessed by 6MWT was less. Renal function was worse, a possible effect of repeated exposure to aminoglycosides.

112 Fenretinide corrects fatty acid imbalance in CF mice: a possible therapy for CF patients?

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Cystic fibrosis (CF) patients and CF mice display increased arachidonic acid (AA) and decreased docosahexaenoic acid (DHA). Increased AA contributes to the inflammatory state of CF patients. DHA is an anti-inflammatory which could limit the effects of AA. Recently we published that CF patients and CF mice have defects in ceramide, another phospholipid. Fenretinide (a semi-synthetic retinoid) was able to correct ceramide in CF mice leading to an improved clearance of lung infection. Here, we report the effects of fenretinide on AA and DHA in CF mice.
We investigate the relationship between ceramide, AA, DHA and the severity of disease in CF patients based on the age at diagnosis. Following 28-day treatment with fenretinide (5 mg/kg/day), levels of ceramide, AA and DHA were analyzed in CF mice (n = 19 to 22) and WT controls (n = 18 to 22) from plasma, lungs, ileum, pancreas and liver. The same analysis was performed in plasma from 58 adult CF patients and 72 healthy controls. Ceramide was analyzed by TLC/ELISA, and AA and DHA by TLC and GC/MS. Treatment of CF mice with fenretinide normalized AA and DHA in plasma and in CF affected organs. Low ceramide correlated with elevated AA and reduced DHA in CF patients.
Analysis of late vs. early (<18) diagnosed patients demonstrate significant differences in AA, FEV1% and pancreatic status. We propose that fenretinide treatment could improve the biological imbalances seen in CF patients leading to clinical improvements in CF.