Mannitol inhaler device culture: no evidence of an increased microbiological contamination

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The airways of patients with cystic fibrosis (CF) are chronically infected with bacteria, which theoretically poses a risk of microbial contamination of inhaler devices. Inhaled dry powder mannitol has been investigated in patients with CF, showing improvement in FEV1, evidence of decreasing exacerbations, and no increase in qualitative or quantitative sputum microbial growth over a 6 month period. Mannitol can be used in the microbiology laboratory as a substrate for certain bacteria in vitro, and therefore we investigated the potential risk of bacterial growth on the device after 1 week of twice daily mannitol use.

Methods: Eighty-five devices from 34 CF patients (1–3 per patient returned) were analysed for microbial content after 1 week’s use. The presence of P. aeruginosa, S. aureus, MRSA, Candida, yeasts, Aspergillus, coliforms, Burkholderia and Sinosinmonus was determined. Cultures were examined daily during the first week, then weekly until the end of the incubation period for each media.

Results: There was no microbiological growth on 82/85 (96.5%) inhalers. Microbiological growth was reported in one device from each of 3 patients (S. aureus and MRSA, Aspergillus, Candida). In all 3 patients, the contaminated device was the first of 3 used, with subsequent inhalers testing negative for growth of pathogens. None of the 3 patients reported an acute pulmonary exacerbation during the 6 month trial period.

Conclusions: These data suggest that contamination with CF-specific pathogens is infrequent after 1 week of use of the inhaler, the recommended duration of use. There was no increase in acute pulmonary exacerbation in patients with a contaminated device.

Combined data from two phase III studies of Bronchitol (inhaled dry powder mannitol) in adult cystic fibrosis (CF) patients

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Most patients with CF now reach adulthood, with the median predicted survival now about 37 yrs with respiratory disease being the primary cause of mortality. Mannitol is an osmotic agent that increases water content of the airway surface liquid and improves mucociliary clearance. Two 6 month phase III studies assessing the efficacy and safety of inhaled dry powder mannitol (IDPM) or control (C), twice daily have been performed.

Methods: Efficacy and safety data from these 2 randomised, double-blind, controlled phase III studies of IDPM was combined for analysis for patients ≥18 yrs. Baseline data for the 341 adult patients included mean age 28.6 yrs; males 58.1%; baseline 5% predicted FEV1 (mean SD) 59.3±15.6%; 66.7% of pts on rhDNase. Data presented is from the 26 wk DB phase.

Results: Mean change from baseline (wk 6−26) in FEV1 for IDPM was 91.6 mL (95% CI 50.2, 133.0) compared to −7.8 mL (95% CI −52.2, 37.6) on C (A90 mL cuff; 95% CI 49.14, 149.87, p < 0.001). Increase in FEV1 was seen regardless of concomitant rhDNase, A90.0 mL cuff (95% CI 29.70, 158.42, p = 0.004) and A110.0 mL cuff (95% CI 25.93, 190.62, p = 0.007) for rhDNase users and non-users, respectively.

There was a positive trend with a 24.1% reduction of exacerbations with IDPM in the incidence of protocol defined pulmonary exacerbations. Serious AEs in the IDPM and C arms were 22.7% and 26.9%, respectively. Most common treatment related AEs were cough (IDPM 12.1%, C 6.0%), haemoptysis (IDPM 5.8%, C 3.6%) and condition aggravated (IDPM 4.8%, C 3.7%).

Conclusion: In a well treated group of adult CF patients IDPM shows significant improvements in FEV1. This further supports the efficacy of inhaled mannitol treatment in CF.

Inhaled dry powder mannitol in cystic fibrosis (CF): the microbiology demographics and results from the phase III studies (CF301 and CF302)

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Patients with CF have lungs infected early in life causing a cycle of inflammation and damage. As mannitol is a mucolytic agent, it is of interest to review the safety of inhaled mannitol bronchotherapy.[1–3] Methods: Sputum samples (if unobtainable a pharyngeal throat swab) were taken at wks 0, 6, 14 & 26 from the mannitol and control arms of the CF301 & CF302 studies. Regular standard CF clinic laboratory procedures at each site were used to define the sputum pathogens screened for. Standard laboratories were used for determining level of growth. A separate collection procedure and central laboratory processing was conducted to determine quantitative sputum microbiology for S. aureus and P. aeruginosa in the CF302 study.

Results: Qualitative sputum microbiology data at baseline from the phase III studies was similar for the mannitol and control groups. The 3 most common bacterial morphotypes isolated at screening were P. aeruginosa (mucoid and non-mucoid), and S. aureus. B. cepacia was isolated in baseline in 5.4% of subjects.

At wk 26 the % of subjects with abnormal flora was similar to baseline in both groups. Furthermore quantitative sputum microbiology results from the CF302 study for S. aureus and P. aeruginosa demonstrated no difference between the mannitol and control groups after 26 wks of therapy.

Conclusions: The combined analysis from 2 phase III trials, provide no evidence for an increase in growth of microorganisms with inhaled mannitol in CF and supports the finding of a lower exacerbation rate on mannitol.[2,3]