40 Experience with Colobreathe® in a large adult cystic fibrosis unit

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Objectives: Inhaled antibiotics are a cornerstone of treatment for many CF patients with chronic pseudomonal pulmonary infection, but the nebulised route is time-consuming and limits adherence. However, recently powder forms delivered by inhaler have become available, which are easier to administer and should improve compliance. We wished to study the acceptance of one of these, Colobreathe® (CB), which delivers colistin, by patients in our large adult CF clinic.
Methods: We looked at lung function and adherence in the 3 months before and after the introduction of CB following a test dose in 17 patients (mean age 27 years, 8 male) previously taking other forms of colistin. In 9 of these we also measured patient-related outcomes (PROMs).
Results: Sixteen patients were taking CB continuously and 1 patient month on/month off with TOBI Podhaler®. There was no change in spirometry following the introduction of CB (mean FEV1 % predicted: pre 64 versus post 61). However, 3 patients discontinued CB within 3 months (3 chest tightness, 1 fall in FEV1), and a further 3 could only tolerate it once daily.
As regards PROMs, 8 patients reported improved adherence due to a marked reduction in administration time. Although 7 patients had a significant improvement in their overall respiratory symptoms, 4 had increased cough, 1 had haemoptysis and 1 reported chest tightness.
Conclusion: We have found that Colobreathe® is effective and quick to administer, leading to improved adherence and increased patient satisfaction. Although it is a viable alternative to nebulised colistin for many patients, a significant proportion develop side-effects which limit or prevent its use.

41 Pharmacokinetics of nasally administered tobramycin, colistin sulphomethate sodium and a combination of tobramycin and colistin sulphomethate sodium

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The paranasal sinuses can constitute a niche for bacteria which can migrate to the lungs. Nasal administration of antibiotics may be effective, but safety of this treatment has to be established first.
Objectives: Investigation of the pharmacokinetics (PK) of nasally administered tobramycin (T), colistin sulphomethate sodium (CSS) and a combination of both drugs using systemic absorption, expressed as % absorbed, as surrogate for safety. In addition, tolerability of the nasal irrigations was examined.
Methods: Ten adult CF patients performed three different nasal irrigations: 300 mg of T, 2 million IU of CSS and 300 mg of T combined with 2 million IU of CSS. Serum concentrations T and CSS were analysed using a validated assay. Individual PK parameters were calculated and assimilated with T and colistin serum values using a computerized CF-based population model. Maximum serum level (C_{max}), trough serum level (C_{trough}) and bioavailability (F) were calculated. T C_{max} >30 mg/L and C_{trough} >0.5 mg/L were considered to be toxic. For colistin toxic levels are not known. Tolerability was measured using a Visual Analog Scale (VAS).
Results: Following the T and the combined irrigation only 2 patients had detectable tobramycin serum levels with a C_{max} < 0.06 mg/L and C_{trough} values < 0.015 mg/L. T bioavailability was approximately 0.76% for one patient and 0.27% for the other patient. The results on colistin pharmacokinetics are expected in February 2014. Tolerability for all irrigations was high, with the tolerability of CSS being the highest.
Conclusion: Nasal irrigations with T and a combination of T and CSS resulted in safe T serum levels and were well tolerated.

42 Tobramycin powder for inhalation is effective in advanced stage CF lung disease: the EAGER trial

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Objectives: A *post-hoc* analysis of the EAGER trial assessing the impact of tobramycin powder for inhalation (TIP™) and tobramycin inhalation solution (TIS) across different stages of cystic fibrosis (CF) lung disease categorized by baseline FEV_1% predicted.
Methods: This analysis included randomized patients from the EAGER trial categorized into less advanced lung disease (LA): FEV_1 ⩾50% predicted; and more advanced lung disease (MA): <50% predicted.
Results: Baseline demography was similar in the TIP and TIS arms, and between disease stages (LA, n = 300; MA, n = 217), with adults having more advanced disease. For MA, FEV_1% improved from baseline to Week 20 for TIP compared with TIS: TIP-TIS (95% CI) of 4.0% (−1.9, 9.8). Hospitalization rates were similar between TIP and TIS for both disease stages: OR (95% CI) 1.28 (0.70, 2.32) for MA and 1.04 (0.57, 1.88) for LA. Use of i.v. anti-*Pa* antibiotics was similar in TIP and TIS patients with MA: OR (95% CI) 1.11 (0.64, 1.92), and 1.08 (0.65, 1.80) for LA. TIP patients in both disease stages reported higher scores for convenience, effectiveness and global satisfaction, with no difference in medication side effects scores between TIP and TIS. Safety profile was similar between the subgroups of the same treatment arm irrespective of disease stage, except for lung disorder (pulmonary exacerbations) being higher for the MA patients.
Conclusion: There was a trend towards greater improvement in FEV_1 with TIP than TIS in MA patients. Safety profiles were similar between the disease stages except for lung disorder. The majority of treatment satisfaction questionnaire scores were higher for TIP, regardless of disease stage.

43 Experience with fosfomycin: clinical outcomes at an adult UK CF centre

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Objectives: To ascertain the clinical effectiveness and safety of intravenous fosfomycin in an adult UK CF centre.
Methods: Following the introduction of intravenous (iv) fosfomycin in November 2011 the medical notes were reviewed for 22 separate patients who received 63 courses of iv fosfomycin during this period. All of the patients treated were colonised with *Pseudomonas aeruginosa* and received fosfomycin in combination with one or more other antibiotics. For each course of fosfomycin: treatment dates and concurrent antibiotics were recorded as were all available peri-treatment spirometry, weight, sputum microbiology, CRP (C-reactive protein) and white cell counts to indicate efficacy. All available renal function, hepatic function and patient reported adverse effects were recorded to indicate safety.
Results: Treatment with fosfomycin containing regimens consistently reduced inflammatory markers (CRP and white cell count) in the group. Improvements in both spirometry and weight were not demonstrated during the treatment courses. Despite this 58 of 63 courses were considered clinically successful. Use of fosfomycin containing regimens was not associated with any deterioration in renal or hepatic function. Two patients reported gastrointestinal upset which caused treatment cessation. One patient accidentally self-adminstered a dose of fosfomycin by bolus injection rather than infusion with no adverse effects.
Conclusion: Fosfomycin appears to be an effective and safe addition to the range of antibiotics used to treat *Pseudomonas aeruginosa* in cystic fibrosis. It provides a useful alternative to aminoglycosides and colistimethate.