145 The efficacy of the inhalatory treatment with tobramycin in controlling *Pseudomonas aeruginosa* lung infection in patients with cystic fibrosis

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Background: *Pseudomonas aeruginosa* lung infection in cystic fibrosis (CF) leads to a negative impact in disease evolution and enforces therapeutic programs for controlling and eradication of this infection.
Objectives: The assessment of tobramycin inhaled therapy in patients with CF associated with *P. aeruginosa* chronic lung infection.
Methods: The study includes 15 patients with CF associated with chronic airway infection with *P. aeruginosa*. CF diagnosis was confirmed through positive sweat test and genetic testing of the CFTR mutations. The patients' average age was 14.86±5.6 years (8–25 years). Tobramycin aerosol therapy (TOBI 300 mg/5 ml) was performed in an alternating program (300 mg ×2, 28 days 4–6 cycles). Respiratory FVC and FEV1 indices were used for lung function monitoring.
Results: Before starting tobramycin treatment, all the patients showed decreased spirometric indices: FVC (63.66±1.64%) and FEV1 (59.8±1.46%). After 12 months of treatment, these indices improved to FVC 67.23±1.11%, FEV1 62.95±2.33%. Inhaled tobramycin treatment also determined a suppression of *P. aeruginosa* infection in patients with CF. *P. aeruginosa* titres were 10^3–10^8 (mean titre 6.31±0.11) before the treatment and decreased with 1–3 titres in 46.7% of cases. *P. aeruginosa* infection was completely eradicated in 13.3% of cases.
Conclusion: Tobramycin aerosol therapy helps to control and eradicate *P. aeruginosa* lung infection and improves respiratory function by increasing FVC and FEV1 spirometric indices.

146 *Pseudomonas* serology can guide aggressive *Pseudomonas* eradication programmes

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UK *Pseudomonas* serology (Ps Ab) use is sparse. The EPIC study suggests raised Ps Ab (RPsA) in 1st/new growths of *Pseudomonas aeruginosa* (PA) predict recurrent PA. Chronic PA is defined as Ps Ab >2, recent PA Ps Ab >1 and normal <1. Ps Ab levels have been used in our PA eradication protocol for 6 years. Ps Ab levels are taken annually, at 1st/new PA (post previous eradication) (1st/newPA) and at 3 months of standard eradication (3 months colistin and 3 weeks ciprofloxacin). RPsA children also receive TSI +/– iv antibiotics in the 2nd of 3 month regime. If Ps Ab remain raised at 3 months colistin is continued.
Objectives: To explore if RPsA predicted time to regrowth/development of chronic PA.
Methods: Retrospective review of 1st/newPA growths (previous Ps Ab >1.1 excluded).
Outcomes: Time to PA re-growth and Leeds Criteria PA status over mean 3.5 yr follow-up (f/u).
Results: 54 children (27 male). Median age at 1st/newPA was 4.9 yr (IQR 1.7–8.9). 19 (35%) had RPsA. 13 received TSI +/– iv antibiotics. Time to PA regrowth: 1.36 yr in RPsA vs 1.29 yr in not raised. At f/u 4/19 (21%) in RPsA had chronic PA vs 3/35 (9%) in not raised. Rates of complete eradication over 3.5 yr f/u were similar 7/19 (36%) vs 11/35 (31%) in not-raised group. Ps Ab rise was higher if developed chronic PA: 1.21 vs 0.79 if intermittent and 0.74 if eradicated ($p = 0.01$).
Conclusion: We found no difference in time to PA re-growth if RPsA, maybe due to the more aggressive attempts at eradication. Those going on to have chronic PA infection had a significantly greater initial rise in Ps Ab levels (>1.21). This may be a useful tool to direct early aggressive attempts at eradication at 1st/new PA growth.

147 Causes of failure to eradicate *Pseudomonas aeruginosa* in patients with CF

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Background: Respiratory infection with *P. aeruginosa* (PA) is a leading cause of morbi-mortality in patients with Cystic fibrosis (CF). It is associated with a more rapid decline in pulmonary function, worsening nutritional status, more hospital admissions and a shorter life expectancy. Although several protocols for eradication of PA after the first isolation are in use, the optimal antibiotic combination, dosages, modes of delivery and duration of therapy remains unresolved. Still, 10–20% of PA infections cannot be eradicated and become chronic infection; therefore, it is imperative to understand what are the factors associated with failure to eradicate PA in CF.
Aims: To analyze the rate of eradication failure of first or new PA infection and to identify clinical and laboratory factors that are associated with eradication failure.
Methods: Records of 130 CF patients treated at the Hadassah Medical Center and in other 5 CF centers in Israel were reviewed. Demographic, clinical and laboratory data collected over the last 7 years were retrospectively analyzed.
Results: Older age, pancreatic insufficiency status, less often visits to the CF center, multi/pan-resistant PA, colonization of PA in the past, later age at diagnosis, air-trapping in the CT scan, later age at CF diagnosis, and no-treatment with hypertonic saline were identified as risk factors for eradication failure. After multivariate analysis, the lasts two issues were the more strongly associated with failure to eradicate PA.
Conclusions: Early diagnosis and appropriate therapy is required in order to augment the rate of efficiently eradication of PA in patients with CF.

148 Use of whole-genome sequencing to identify transmission of *Pseudomonas aeruginosa* between cystic fibrosis patients

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Objectives: *Pseudomonas aeruginosa* is the most commonly isolated pathogen from the sputum of adults with cystic fibrosis (CF). The Midlands-1 clone is the most commonly recovered genotype in our local patient population, affecting one-third of *P. aeruginosa* positive patients. Although Midlands-1 is readily identified by conventional typing schemes, such assays lack the discriminatory power to identify potential transmission events.
Methods: We sequenced the complete genomes of >150 isolates of Midlands-1 isolates from: (i) *P. aeruginosa* positive patients attending the West Midlands Adult CF Centre in a prospective survey, (ii) all Midlands-1 isolates collected over 5 years from the Liverpool Heart and Chest Hospital and (iii) a national collection of isolates from Public Health England over 15 years.
Results: Whole-genome sequencing (WGS) and phylogenetic analysis using core genome single nucleotide polymorphisms confirmed Midlands-1 has a clonal population structure. Evidence for direct transmission of *P. aeruginosa* was suggested from phylogenetic reconstructions, with diversity seen in isolates from three patients fully contained within the diversity seen in a single other patient. Epidemiological data suggested transmission from this patient to others was possible during inpatient stays. Long branches on the tree were associated with a hypermutator phenotype and increased levels of antibiotic resistance.
Conclusions: It is likely that new acquisitions of *P. aeruginosa* may result from transmission between patients. WGS is a useful and increasingly affordable tool which may be used to enhance surveillance and infection control of *P. aeruginosa* in CF patients.