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Collateral sensitivity cycling of antibiotics for cystic fibrosis airway

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Methods: Epidemiological ambispective multicenter study. Health status was measured by EQ-5D-3L questionnaire [Descriptive part (DS) (5 dimensions) + EQ-VAS]. PEx were defined as the European Consensus Group proposal. Patients were included consecutively. Informed consent was collected and the study was approved by the EC of the Ramon y Cajal Hospital.

The communication corresponds to an interim analysis.

Results: Data from 145 patients were collected (49% from the theoretical number). 54% were female. 66 patients were included without PEx, 47 had mild PEx and 32 had severe PEx. 63, 47 and 35 patients had a mild, moderate or severe disease respectively. DS score in patients with severe PEx were worse than patients with mild PEx (p-values from 0.039 to <0.001 among different dimensions), the same was seen with 5Q-VAS score (52.58 ± 14.25 vs 70.98 ± 18.22 ; $p < 0.001$). DS score by state of lung disease was different between moderate and severe patients in two of five dimensions whereas 5Q-VAS score was not different (63.50 ± 19.28 vs 56.91 ± 21.52 ; $p = \text{N.S.}$).

Conclusion: Health status in patients with more severe status (either lung disease or PEx at inclusion) is worse than in the remaining patients as expected. Patients suffering a severe PEx have health status measurements (dimensions and VAS) lower than patients with a severe lung status which seems to show the important role of PEx in patient's quality of life.

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Lung function response to intravenous antibiotic treatment in a paediatric CF population in East of England

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Objectives: Our purpose was to characterize the Forced Expiratory Volume in 1 second (FEV₁) and forced expiratory flow rate between 25% and 75% of vital capacity (FEF₂₅₋₇₅) response to intravenous antibiotic therapy in our CF paediatric population between January 2015 and December 2015.

Methods: Data were obtained from a retrospective and descriptive analysis of IV treatment courses given during January to December 2015 to CF children attending the Norfolk and Norwich University Hospital with documented and valid spirometric measures of lung function forced vital capacity (FVC), FEV₁, and FEF₂₅₋₇₅.

Results were compared as differences of FEV₁ % predicted and FEF₂₅₋₇₅ % predicted at the beginning and at end of an IV antibiotic course. Results were analyzed using paired t-tests. P values <0.05 were considered statistically significant. Statistical analysis was performed and correlated with others clinical variables studied.

Results: 35 IV antibiotic courses from 18 CF patients aged between 6 and 17 years were examined. Valid lung function courses were identified. Intravenous antibiotic treatment given to CF paediatric patients resulted in a significant improvement of FEV₁ % predicted (p 0.002) and FEF₂₅₋₇₅ % predicted (p 0.024) in lung function when patients are treated. Duration of antibiotic treatment didn't have any correlation with this improvement (Pearson correlation -0.00019).

Conclusion: This study demonstrates a significant improvement in FEV₁ % predicted and FEF₂₅₋₇₅ % predicted to antibiotic IV treatment in paediatric CF patients.

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Collateral sensitivity cycling of antibiotics for cystic fibrosis airway infections

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Objectives: The main cause of morbidity and mortality in cystic fibrosis (CF) patients is bacterial airway infections, and to combat these infections the patients are treated with large amounts of antibiotics. Despite the treatments, the infections (in particular by

Pseudomonas aeruginosa) persist. *P. aeruginosa* is inherently resistant to many antibiotics and develops multi-resistance over time, resulting in major limitations of antibiotic treatment possibilities. Therefore we propose the use of antibiotic "Collateral drug cycling" for treatment of both initial persistent infections as well as chronic infections with *P. aeruginosa*.

Methods: Treatment of CF patients with the collateral drug cycling approach is a way to secure a continued treatment of the infection, with lower risks of creating resistant bacterial populations.

Results: For *P. aeruginosa* reference strain PAO1 collateral sensitivity has been found, where e.g. treatment with Ciprofloxacin and Aztreonam results in decreased resistance towards Tobramycin. This will be further tested in *P. aeruginosa* clinical isolates from multiple CF patients and should be directly applicable for the design of new treatment strategies.

Conclusion: If the collateral sensitivity can be translated directly to clinical treatment regimes, this is specifically useful for the treatment of chronically infected CF patients. This antibiotic treatment approach will also be applicable in other infection scenarios where resistance against one or multiple antibiotics has occurred.

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Antimicrobial susceptibility of *Pseudomonas aeruginosa* in Vilnius CF children centre, Lithuania

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Objectives: In this study our objective was to analyse the frequency of microorganisms and composition of antimicrobial susceptibility of isolated *Pseudomonas aeruginosa*.

Methods: 97 sputum samples or cough swab or BAL were obtained from 30 patients under 18 years old (2–17 years) during 1 year period – from January to December 2015. 81 samples were positive with 31 different species and were tested for isolation, identification and antimicrobial susceptibility.

Results: Out of all positive samples the most common pathogens were *S. aureus* – 51.85%. *Pseudomonas aeruginosa* was isolated in 50.62% of samples. 34.15% of *Pseudomonas aeruginosa* is detected as mucoid form. 100% of *Pseudomonas aeruginosa* strains were susceptible to colistin, 76.6% to ciprofloxacin, 76% to imipenem, 56% to ceftazidim, 54% to piperacillin, 50% to tobramycin, 33.3% to amikacin. *Pseudomonas aeruginosa* resistance to gentamicin is 67.3%, to amikacin 51.5%, to tobramycin 50%.

Conclusion: The most common isolated pathogens were found to be *S. aureus* and *Pseudomonas aeruginosa*. High resistance to medications used in first line *Pseudomonas aeruginosa* infection treatment suggest the need to adapt our treatment regimens to more suitable ones.

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Susceptibility of *Staphylococcus aureus* isolates from patients with and without cystic fibrosis to ceftobiprole

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Introduction: Ceftobiprole is a broad spectrum "5th generation" cephalosporin antibiotic, which has demonstrated activity against Gram-positive cocci, including Metcillin sensitive and resistant *Staphylococcus aureus* (MSSA and MRSA). This study aimed to compare the susceptibility of a range of MSSA and MRSA isolates from both CF and non-CF patients, to ceftobiprole and comparator antibiotics.

Methods: The susceptibility of MSSA (CF: n=25; non-CF: n=24) and MRSA (CF: n=24; non-CF: n=29) isolates to ceftobiprole, linezolid, rifampicin and vancomycin was determined using E-test® strips with minimum inhibitory concentrations read after 24 h of incubation at 37°C. Where possible, isolates with a diverse genetic background were selected for inclusion in this study. Isolates were classified as either susceptible, intermediate or resistant to each antibiotic in accordance with Clinical and Laboratory Standards Institute breakpoints.

Results: No MSSA isolates tested were resistant to any of the antibiotics tested. Of the MRSA isolates tested, 3/53 (5.6%), all from CF patients, were resistant or intermediately resistant to rifampicin.