**60** Investigation of the potential mechanisms of antibiotic resistance in the cystic fibrosis pathogen, Burkholderia cepacia complex

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The ability of the Cystic Fibrosis pathogen, Burkholderia cepacia complex (Bcc) to form biofilms plays a key role in resistance to host defence mechanisms and antibiotic therapy. The objectives of this study were to determine the antibiotic susceptibility of Bcc biofilms and the effects of efflux pump inhibitors (EPI) in combination with antibiotics, to enhance susceptibility. Confocal analysis of antibiotic treatment of B. multivorans and B. dolosa biofilms with tobramycin resulted in decreased biofilm thickness. Ciprofloxacin had no effect on B. dolosa biofilm thickness. Cefazidime treatment did not decrease Bcc biofilm biomass, but the cells within the biofilms formed “spindle” like structures. Interestingly, B. cepacia biofilms appeared to form thicker and more structured biofilms in the presence of the antibiotics. The effect of EPIs on minimum inhibitory concentrations (MIC) of Bcc strains against a panel of antibiotics was investigated and found a two fold decrease in MIC values in the presence of EPIs. We also investigated the effects of the EPIs on the formation and metabolic activity Bcc biofilms, where 1-(1-naphthylmethyl)-piperazine (NMP) was found to be most effective at decreasing the formation of Bcc biofilms. Additionally, two B. dolosa 24 hour biofilms were found to be metabolically inactive when treated with NMP at 100 μg/ml and at 50 μg/ml in combination with 100 μg/ml Thiorizadine. This work demonstrates that antibiotic susceptibility of Bcc is affected by biofilm maturity, strain and antibiotic type thus highlighting the need for a greater understanding of Bcc biofilm antibiotic resistance mechanisms.

**61** Suspected adverse drug reactions (ADRs) caused by intravenous colistin in cystic fibrosis patients may not be dose dependent

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Intravenous colistin has been associated to dose-dependent nephrotoxicity and neurotoxicity. We conducted a retrospective analysis of the electronic records of patients hospitalized between April 2009 and March 2010 who received colistimethate sodium (colistin) i.v. We collected data on their weight, drug dosage, ADRs reported during the treatment, and associated treatments. Data of 308 patients were reviewed for a total of 445 hospitalizations. We identified 30 patients treated on 35 episodes. Mean dose was 124,000 U/kg/die. Nine patients experienced an ADR. They had received 121,000 U/kg/die (range 44,500–199,000 U/kg/die) for a total of 445 hospitalizations. We identified 30 patients treated on 35 episodes. Nine patients experienced an ADR. They had received 121,000 U/kg/die (range 44,500–199,000 U/kg/die). This dose was not statistically different from the dose received by patients (26) who did not experience ADRs (121,800 U/kg/die; range 49,800–109,000 U/kg/die). The main reactions were neurologic (such as paresthesia, dysthesia and weakness) and nephrotoxic (petercreatinemia): all were reversible. We did not find an increased rate of renal effects when aminoglycoside were associated.

**Conclusions:** IV colistin is still a valuable drug in the treatment of pulmonary exacerbations in CF. However ADRs are frequent and not necessarily dose-dependent. At the time we support the view that treatment should start with a low dosage with stepwise increases but large, prospective trials are warranted to study other factor risks in cystic fibrosis patients.

**62** Pseudomonas aeruginosa bacteraemia in patients with cystic fibrosis during acute exacerbations

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During chronic respiratory infections, patients with cystic fibrosis (CF) suffer more or less frequently from acute exacerbations (AEs) which are characterized by several clinical symptoms including increased cough and sputum production. It has been proposed that the symptoms of an AE are largely due to the incidental release of planktonic bacterial organisms from biofilms which are present in airways of virtually all infected CF patients. We assessed this hypothesis in an open prospective clinical study, in which we determined P. aeruginosa DNA by nested PCR and qPCR in blood specimens of 43 CF patients, chronically infected with P. aeruginosa, obtained during AE and 10 to 14 days after antibiotic treatment, when the patient was clinically stable. The majority of CF patients (72%) had a positive blood PCR for P. aeruginosa. Positive P. aeruginosa PCRs were observed in 68% of the patients during AEs, and in 22% of clinically stable patients. qPCR revealed the presence of ~104 bacterial cells per ml of blood during AE which was significantly greater than levels in clinically stable CF patients. Nested PCR for Escherichia coli and Prevotella intermeda were negative in all cases. We conclude that AEs are correlated with a release of P. aeruginosa from infected airways into the blood stream. These results provide a novel rational for antibiotic therapy during AEs in CF.

**63** I-neb Insight Online – a telemedicine-based system to monitor true adherence to nebulizer therapy in adult cystic fibrosis patients: a preliminary analysis

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I-neb Insight Online is a telemedicine-based patient management system for use with the I-neb AAD System to monitor patient adherence to treatment, compliance with correct use and cleaning of the I-neb AAD System device. The I-neb AAD System is equipped with a patient logging system (PLS) that records device use. True Adherence (TA) is calculated using % adherence to prescribed regimen x % compliance with correct use / 100 and is an important indicator of patients’ use of the device [1]. Forty-four patients with cystic fibrosis completed a 13 week handling study in which they were asked to upload treatment data from home on a weekly basis. Prescription updates were initiated by the patient or clinician. Data was analyzed and presented online in graphs so that patients, clinicians and patient support programme personnel could manage the patients’ treatments. Prescribed use was analyzed using a graph of 1 week resolution and combined with PLS data to calculate adherence. Average patient TA for 38 patients over 13 weeks was categorized into 3 groups of low (<50%), medium (50–79%) and high (≥80%) [2]. Average TA was high in 11 patients and was medium and low in 21 and 6 patients respectively. Mean week 1/week 13 TA values for high, medium and low adherence groups were: 89%/88%, 78%/67% and 46%/52%. TA improved or remained unchanged in 45% of patients. This study shows that this technology can identify those with low or variable TA, which could direct adherence interventions.

**Reference(s)**