

**207 Respiratory pathogens in patients with cystic fibrosis. Reviewing the past 15 years**

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**Objectives:** To describe the prevalence and sensitivity of bacterias isolated in respiratory secretions of controlled children in the cystic fibrosis Unit of our hospital between the year of 1995–2009.

**Methodology:** We included 59 patients with cystic fibrosis, from where we selected one sputum culture per month and the sensitivity to positive cultures.

**Results:** 4264 sputum cultures were studied, of whom 1997 have been positive with 2606 bacterias. We discovered an increasing of samples as well as a decrease in the quantity of positive cultures, with 66.7% of positive cultures in 1995 and 29.7% in 2009. The most common bacterias were: *Staphylococcus aureus* (1078), *Pseudomonas aeruginosa* (512), *Burkholderia cepacia* complex (440) and Enterobacteriaceae (163). We have observed a decrease in *Pseudomonas aeruginosa*, *Burkholderia cepacia* complex and an increased of *Staphylococcus aureus* and *Stenotrophomonas*. The *Burkholderia cepacia* complex, *Stenotrophomonas* and *Achromobacter* have shown high resistance to antibiotics, and *Pseudomonas aeruginosa* has a resistance less than 5–10% against colimycin, tobramycin and ciprofloxacin.

**Conclusions:** *Staphylococcus aureus* and *Pseudomonas aeruginosa* continue being the most common bacterias present in patients with cystic fibrosis. We associated the decrease in the prevalence of *Pseudomonas aeruginosa* with implementation of newborn screening, better treatment guidelines and more effective control of cross infection. The emergence of new pathogens such as *Stenotrophomonas* and *Achromobacter* is smaller, but important, because together with the *Burkholderia cepacia* shows resistance to usual antibiotics.

**208\* Value of flexible bronchoscopy and bronchoalveolar lavage in the eradication of *Pseudomonas aeruginosa* in cystic fibrosis children**

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**Background:** Current strategies of *P. aeruginosa* eradication are based on microbiological surveillance by samples obtained from upper respiratory airways. However, these do not reliably predict its bronchial presence in young CF children.

**Hypothesis:** Bronchoalveolar lavage (BAL) obtained by flexible bronchoscopy could give reliable information and avoid the inappropriate suppression of eradication treatment.

**Objectives:**

1. To assess BAL in children in whom oropharyngeal or sputum cultures remain negative from the beginning of inhaled treatment.
2. To study the relationship among infection and inflammation across the cytology of BAL.
3. To evaluate safety and side-effects of the test.

**Methods:** Prospective study of CF children (1997–2009) with repeatedly negative cultures during the year after first *P. aeruginosa* isolation. Performance of flexible bronchoscopy with BAL previously to the withdrawal of inhaled treatment.

**Results:** 36 bronchoscopies were carried out on 30 patients (64% female, 34% male). Medium age of first isolation was 33 months. BAL cultures were positive in 11 cases (30.5%). There were no differences between sex, age of diagnosis or first isolation and kind of eradication treatment. Neutrophilic inflammation was significantly greater in positive BAL samples ( $p < 0.001$ ). Adverse events reported were clinically minor as cough (39%), temporary desaturations  $< 90\%$  (13.8%) and fever (2.7%).

**Conclusions:** Bronchoscopy in CF children reveals a significant prevalence of previous undetected infection, therefore it should be carried out as previous control of the ending of eradication treatment. It is a safe technique and the cytology of BAL correlates infection and inflammation.

**209\* Comparative efficacy and safety of four randomized regimens to treat early *Pseudomonas aeruginosa* infection in children with cystic fibrosis**

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**Background:** Chronic *Pseudomonas aeruginosa* (Pa) infection worsens the prognosis of patients with Cystic Fibrosis (CF). Early Pa infection may be amenable to eradication. We investigated the benefits and harms of 4 anti-pseudomonal antibiotic treatments in CF children at their first Pa positive respiratory culture.

**Methods:** In a multicenter trial, CF children ages 1–12 years were randomized to receive treatment on a scheduled quarterly basis (cycled therapy) or if Pa was recovered from quarterly respiratory cultures (culture-based therapy), for a total of 6 quarters. At each cycle, participants received inhaled tobramycin (300 mg BID) for 28 days, with either oral ciprofloxacin (15–20 mg/kg BID) or oral placebo for 14 days. The primary endpoints were time to pulmonary exacerbation and proportion of Pa-positive respiratory cultures.

**Results:** 304 subjects (76 participants in each of the 4 groups) qualified for inclusion. There were no differences in exacerbations between cycled and culture-based groups (HR 0.95, 95% CI 0.54, 1.66) or between ciprofloxacin and placebo (HR, 1.45, 95% CI 0.82, 2.54). There were no differences in the relative odds of Pa-positive cultures comparing cycled vs. culture-based group (OR 0.89, 95% CI 0.58, 1.37) or ciprofloxacin vs. placebo (OR 0.80; 95%CI 0.58, 1.09). Adverse events were similar in all groups.

**Conclusions:** More intensive prophylactic (cycled) inhaled aminoglycoside treatment did not reduce exacerbations or prevalence of Pa positive cultures compared with an approach based on microbiological findings. There were no benefits of adding ciprofloxacin. There were no concerns with regard to drug toxicity or emergence of resistant pathogens.

**210 Efficacy and safety of tobramycin and colistin for inhalation in children with cystic fibrosis from Moscow region**

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It is known that inhaled antibiotic therapy (AB) delays pulmonary progression and quality of life in cystic fibrosis (CF) patients with *Pseudomonas aeruginosa* infection (Pa). Since 2009 Bramitob, TOBI, Colistin are registered in Russia. Before this period our patients received i.v. forms of gentamycin and tobramycin for inhalation treatment.

**Aim:** Compare 3 Pa- inhaled antibiotic treatments in CF patients with first isolate and chronic Pa infection.

**Method:** Bramitob group – 21 patients (6–18 years) all with chronic infection, TOBI group – 11 patients (3–15 years) 2 of them with first isolate and 9 with chronic infection, Colistin – 9 patients (0–15 years) 6 of them with first isolate and 3 with chronic infection.

**Result:** In Bramitob group eradication of Pa was in 7/21 patients, in TOBI group in 1/2 of patient with first isolate and in 6/9 with chronic infection, in Colistin group in 4/6 of patients with first isolate and in 2/3 children with chronic Pa infection. In most of our patients we revealed improvement of lung function and nutritional status and decrease in number of exacerbations of chronic bronchopulmonary process.

**Conclusion:** Equal clinical efficiency and safety of Bramitob, Colistin and TOBI was shown. Russian CF patients have the opportunity to receive anti-pseudomonas inhalation treatment according to the European standards now.