Cytosolic phospholipase A2 (cPLA2) mediates Pseudomonas aeruginosa-LPS-induced airway constriction of CFTR−/− mice
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Background: Lungs of cystic fibrosis (CF) patients are chronically infected with Pseudomonas aeruginosa. Increased airway constriction has been reported in CF patients but underlining mechanisms have not been elucidated.

Methods: Mice were instilled intranasally with LPS. Airway constriction was assessed using barometric plethysmograph. MIP-2, prostaglandin E2 (PGE2), leukotrienes and AA concentrations were measured in BALF using standard kits and gas chromatography.

Results: LPS induced higher airway constriction and AA release in BALF of CF compared to littermate mice. This was accompanied by increased levels of PGE2, but not those of leukotrienes. However, airway neutrophil influx and MIP-2 production remained similar in both mouse strains. The cPLA2 inhibitor arachidonoyl trifluoro-methyl-ketone (ATK), but not aspirin, which inhibit PGE2 synthesis, reduced LPS-induced airway constriction. LPS induced lower airway constriction in cPLA2−/− mice compared to corresponding littermates. Neither aspirin, nor ATK interfered with LPS-induced airway neutrophil influx or MIP-2 production.

Conclusions: CF mice develop enhanced airway constriction through a cPLA2-dependent mechanism. Airway inflammation is dissociated from airway constriction in this model. cPLA2 may represent a suitable target for therapeutic intervention in CF. Attenuation of airway constriction by cPLA2 inhibitors may help to ameliorate the clinical status of CF patients.

Isolation and characterization of microparticles in sputum from cystic fibrosis patients
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Microparticles (MPs) are membrane vesicles that are released during cell activation and apoptosis. MPs have different biological effects depending on the cell from they originate. Cystic fibrosis (CF) lung disease is characterized by massive neutrophil influx in the airways, their activation and eventually apoptosis. We investigated on the presence and phenotype of MPs in the sputum, a rich noninvasive source of inflammation biomarkers, of acute and intermittent CF adult patients. Spontaneous sputum, obtained from 21 CF patients (10 acute and 11 intermittent) and 7 patients with primary ciliary dishkinesia (PCD), was liquefied with Sputasol. MPs were counted and identified in the supernatants of treated sputum by cytofluorimetry and immunodecoration for leukocyte (CD11a), granulocyte (CD66b), and monocyte-macrophage (CD11b) antigens. CF sputa contained higher number of MPs in comparison with PCD sputa. CD66b and CD11a, but not CD11b, levels in MPs were significantly higher in CF than in PCD. Acute and intermittent patients presented significantly higher levels of CD11a- and CD66b-expressing MPs respect to PCD patients. MPs are detectable in sputa obtained from CF patients and are predominantly of granulocyte origin. The reason for a significantly less presence of granulocyte-derived MPs in PCD as compared with CF patients may be that lung disease in PCD, although similar, is delayed in time as compared with CF. This novel isolation method for MPs from sputum opens a new opportunity for the study of lung pathology in CF.

Comparison of home and hospital intravenous antibiotic therapy for acute pulmonary exacerbations in adults attending a regional cystic fibrosis centre
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Introduction: The aim of this study was to compare home vs. hospital treatment for clinical outcomes in adult patients receiving intravenous antibiotics for acute pulmonary exacerbations.

Methods: Case notes of patients who received intravenous antibiotic treatment for an acute pulmonary exacerbation between 1st September 2008 and 31st August 2009 were reviewed retrospectively. Patients receiving part home/hospital therapy, those on continuous intravenous antibiotic treatment and post lung transplant patients were excluded. The first treatment course for each patient was analysed. Clinical outcome measures included lung function (FEV1, FVC), weight and inflammatory markers (CRP, WCC, neutrophil). Best lung function and weight in 1 year pre treatment were collected.

Results: 124 patients received 248 courses of treatment at home and 73 patients received 151 courses in hospital. No significant differences in treatment length, start FEV1 (hospital vs. home median 39% vs. 43%) or best FEV1 (median 61% vs. 57%). Start inflammatory markers were higher in hospital patients. Significant increase in FEV1 from start to end of treatment (hospital 39% to 53%, p < 0.001, home 43% to 50%, p = 0.04) but greater percentage change in lung function in hospital treated patients (FEV1% vs. 3%, p < 0.001, FVC 11% vs. 4%, p < 0.0001). Baseline weight and BMI lower in hospital treated patients (58 kg vs. 63.9 kg, p = 0.01; 21.2 vs. 22.4, p = 0.02). Median weight gain hospital vs. home 1.1 vs. 0.2 kg, p = 0.003.

Conclusions: Both home and hospital treatment are associated with an increase in lung function, but hospital treatment is superior with a greater percentage increase in lung function and weight.

Efficiency of the inhalational tobramycin therapy in complex antibacterial therapy of lung exacerbation in cystic fibrosis children with chronic Pseudomonas aeruginosa infection
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Introduction: Clinical studies evaluating the rational use of the combination of intravenous and aerosolized antibiotics (AB) in acute lung exacerbations are scarce and conclude that this combination therapy is not superior compared to intravenously administered therapy alone. The aim: compare 3 combinations of AB regimes against Pseudomonas aeruginosa (Pa) in cystic fibrosis (CF) patients with lung exacerbation.

Methods: 108 CF patients (pts) with chronic Pa were prospectively randomized to 14 days of different AB courses: Group A − 32 pts (4–16 yrs) treated with TOBI (16 pts) or Bramitob (16 pts), 300 mg bid in combination with i.v. cefazidime and oral ciprofloxacin; Group B − 39 pts (6–17 yrs) treated with i.v. cefepime and i.v. amikacin; Group C − 37 pts (4–17 yrs) treated with i.v. meropenem and i.v. amikacin.

Results: All AB combinations significantly improved clinical symptoms, lung function and reduced sputum Pa density. Improvement of FVC in A, B and C groups was +27.98%, +24.27% and +31.44%, respectively. Increase of FEV1 was +37.1%, +28.85% and +40.6%, respectively. A group with inhaled tobramycins was significantly superior in decrease of Pa sputum density and even eradication after treatment. In group A there was no growth of Pa sm. in 77.3% of patients, in group B − 45.5%, in group C − 26%. Pa muc. completely disappeared from sputum in group A in 79% of children, in group B − 25.8% and in group C − 29.1%.

Conclusion: Combination of inhaled form of tobramycin with oral ciprofloxacin and i.v. cefazidime for treatment of acute exacerbation in CF pts with chronic Pa infection was superior compared to standard i.v. administered therapy.