Neutrophil elastase: its activity and content, the levels of anti-elastase in children with bronchopulmonary diseases

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Purpose of research: Assessing the system of neutrophil elastase (NE) – the activity and content of antiproteases (anti-NE) in children with congenital bronchial pathology (CBP), lung pathology (CLP) and cystic fibrosis (CF).

Methods: 59 patients, 1–17 years, were studied, all with CB&P and CF. Control Group (C) included 10 children with no somatic pathology. The NE activity was judged by the intensity of division of N-metoxysuccinyl–ALA–ALA–PRO–VAL–L–Nitroanilide on the DU 530 Beckman spectrometer. The content of NE and anti-NE was determined by immuno-enzymic method.

Results: The highest NE levels (5 times higher than those in the C) were demonstrated in patients with CBP; patients with CLP demonstrated somewhat lesser levels and the CF patients showed still lesser levels. The CF patients’ levels of NE were 2.5–3 times higher than those in the C in all cases (p < 0.05–0.01).

Ne level in groups showing considerable differences in the enzyme content did not differ much from the C. It was only in patients with CLP that the NE activity was 2 times lower than in the C, while in others it slightly exceeded the C data. The level of anti-NE in CF patients was 2 times higher than in C and CB&P.

Conclusion: It was found that the NE amounts and activity in the C was relatively on the same level. In CBP and CLP patients, the amount of NE was 10 and 5 times (respectively) higher than the data for the activity of the enzyme, while in the CF patients, it was only 3 times higher, with the level of anti-NE being 2 times lower than in other groups, which, evidently, is the reason for overproduction of viscous bronchial secretion in CF cases.

Cytokine pattern in broncho-alveolar lavage in children with Cystic Fibrosis and infection with Pseudomonas aeruginosa

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Background: It has been shown in broncho-alveolar lavage (BAL) of children with cystic fibrosis (CF) that TH2 cytokines are elevated. This is especially true for patients with chronic PA infection. However, it is unclear whether a Th-2 type profile predisposes for – or is a consequence of PA infection. We investigated whether children with acute PA infection display a distinct cytokine profile in the lung.

Methods: The cytokine pattern was assessed in 68 children (32 boys, 36 girls; median age 6.08 years), 47 children with CF and 21 controls (11 children following lung transplantation, 10 children with recurrent pulmonary infections). Bronchoscopy was performed under general anaesthesia and the last aliquot of standard BAL (3x1 ml/kg/bodyweight; NaCl 0.9%) was used for analysis. Cytokines and chemokines (IL-6, -8, -13, -17, IFN-γ, TARC) were measured via multiplex sandwich ELISA. Univariate analysis to investigate differences with regard to age, sex, PA-infection and correlations with lung function parameters and age were performed for each cytokine.

Results: CF-patients displayed significantly increased IL-6, -8, -13 and 17 levels in lavage fluid. Cytokine expression did not correlate directly with age or lung function parameters. PA-infection did not significantly impact cytokine expression.

Conclusion: Although cytokine expression was augmented in the CF-group our data suggest indirectly that children with acute PA infection may not display a different cytokine profile per se that predisposes to chronic PA. These results need to be confirmed in a prospective setting.

Airway Ca^{2+}-activated Cl^- channel (CaCC) activity is normal in mClCa3-deficient mice

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Defective CFTR-mediated CaCC secretion plays a central role in the pathogenesis of cystic fibrosis (CF) lung disease. Functional studies documented that airway epithelia express alternative Ca^{2+}-activated Cl^- channels (CaCC), which have been proposed as a therapeutic target to compensate for lack of CFTR activity in CF patients. However, the molecular identity of CaCC has not been unequivocally identified. The goal of this study was to determine the role of mClCa3 (gob-5) as a putative candidate for the endogenous CaCC. To determine the role of mClCa3 in Ca^{2+}-activated Cl^- secretion, we performed transepithelial measurements of ion transport in freshly excised tracheal tissues from mClCa3-deficient mice and wild-type littermates using perfused Ussing chambers. Further, we performed immunohistochemistry and histology to compare mClCa3 localization and pulmonary morphology in mClCa3-deficient and wild-type mice. We demonstrate that basal CaCC (bumentaide-sensitive Isc) and Ca^{2+}-activated Cl^- secretion (UTP-induced Ics) were not altered in mClCa3-deficient mice compared to wild-type controls. Further transepithelial Na^+ absorption and cAMP-induced Cl^- secretion were normal in mClCa3-deficient mice. Lack of pulmonary expression of mClCa3 was confirmed by immunohistochemistry in mClCa3 deficient mice, but did not result in a spontaneous lung disease phenotype. Our results argue against a role for mClCa3 in Ca^{2+}-activated Cl^- secretion in the murine lung.

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