Association between exhaled nitric oxide and disease severity in cystic fibrosis

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Background: Nitric Oxide (NO) concentrations in exhaled air are generally increased in asthmatic lung disease. In cystic fibrosis (CF), studies show that NO levels are paradoxically decreased. As NO seems to be important to regulate (anti viral) host defence, bronchomotor control and inflammation, a low NO production or availability might result in a more severe clinical phenotype of the disease. Aim of the study was to investigate the association between NO levels and lung function, infection with P. aeruginosa (PA) and S. aureus and with nutritional status and genetics.

Methods: In 95 clinically stable children with CF (mean age 12.6 yrs (5.3–17.8), M/F 48/47) we measured bronchial (bNO) and nasal exhaled NO (nNO). In a multiple regression model association between NO levels and effect parameters were studied. Effect parameters were available from the annual check-ups of the CF Centre Utrecht.

Results: In the multivariate analysis low nNO was significantly associated with lower values of FEV1 (p < 0.004) and with severe CFTR mutation (p < 0.016). NNO was not associated with infection or nutritional status. BNO was significantly lower in PA positive vs PA negative CF patients (median 11.8 vs 7.9 ppb, respectively, p = 0.03). BNO was not correlated with FEV1, nutritional status or severity of the CFTR mutation.

Conclusion: BNO and nNO seem to be associated with the phenotype and genotype of CF. Patients with more severe phenotype and genotype of CF might lack the potential benefits of NO.

Exhaled nitric oxide is not correlated with inflammation in Cystic Fibrosis

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Background: Exhaled nitric oxide levels are low in patients with cystic fibrosis (CF), despite the chronic inflammation present in the airways.

Aim: The purpose of this investigation was to study exhaled NO (eNO) concentration in children and adolescents with CF, and to evaluate the effect of CF genotype, disease severity, atopic status and respiratory tract infection on this measurement.

Methods: Exhaled NO levels were measured in 36 children and adolescents with CF and 40 healthy age-matched subjects, using a chemiluminesence analyser, according to recently published ERS/ATS guidelines. Spirometry (FEV1 and FVC), CF genotype, bacterial colonization, BMI, white blood cell (WBC) count, C-reactive protein (CRP), total IgE and Schwachman scores were also recorded.

Results: The mean age of patients was 15.2 years, and the mean FEV1 was 69.3% (±23.1) predicted. Exhaled NO was significantly lower (p < 0.001) in CF patients (6.4±3.8 ppb) than in control subjects (13.4±5.3 ppb). FEV1 did not correlate with exhaled NO. No association was observed between eNO values and inflammation markers, Schwachman score, colonization with Pseudomonas aeruginosa, or genotype. Exhaled NO correlated significantly with total IgE (r < 0.0001, r = 0.864).

Conclusions: Despite the airway inflammation that is characteristic of CF, eNO was reduced. There was no association of eNO with infection status, disease severity and genotype. Exhaled NO is not a useful measure of inflammation in CF lung disease.

Predictive factors of sleep hypoxemia in children with cystic fibrosis

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Objective: Cystic fibrosis (CF) patients may develop hypoxemia during sleep. Limited information is available on nocturnal oxygen saturation in CF children with less severe lung disease. The aim of this study was to investigate the degree of nocturnal oxygen desaturation and predictive factors in CF children with normal pulmonary function tests (PFT) or mild to moderate lung disease.

Method: Awake resting and post-exercise SpO2 were measured by pulse oximetry. Each patient had overnight oximetry monitoring at home. Six minute walk test (6MWT), Shwachman-Kulczycki (S-K), Brasfield and computed tomography (CT) scores, blood gas analysis and nutritional status of patients were evaluated.

Results: Twenty-four patients (75% female) with a median age of 9.5 years were included. Nocturnal mean SpO2 was not different according to the severity of lung disease based on PFT. However, lowest SpO2 obtained was lower in children with both mild and moderate lung disease compared to normals (87.4% vs. 91.7%, respectively, p = 0.009). Nocturnal mean SpO2 correlated with S-K (r = 0.80, p < 0.0001), Brasfield (r = 0.56, p = 0.007) and CT scores (r = −0.82, p < 0.0001) as well as PaO2 (r = −0.53, p = 0.021), SaO2 (r = −0.53, p = 0.023), z-score of weight (r = −0.48, p = 0.20) and height (r = −0.45, p = 0.30), there was no correlation with 6MWT. Multiple linear regression analysis with Backward elimination showed that nocturnal mean SpO2 was predicted by S-K scores (B = 0.085, p < 0.0001) and CT scores (B = −0.22, p < 0.0001) while lowest SpO2 was predicted by FEV1 (B = 0.12, p = 0.012).

Conclusions: CF children with normal PFT or mild-to-moderate lung disease may develop sleep hypoxemia and S-K and CT scores are the best predictive factors.

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Conclusions: Despite the airway inflammation that is characteristic of CF, eNO was reduced. There was no association of eNO with infection status, disease severity and genotype. Exhaled NO is not a useful measure of inflammation in CF lung disease.

Pulmonary mechanics in cystic fibrosis (CF) patients awaiting lung transplantation. Evaluation of non invasive mechanical ventilation (NIV)

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The possibility to sustain a spontaneous ventilation can be seen as balance among neurological mechanisms, respiratory muscles strength and work/load relationship determined by lung, thoracic and airways mechanics. In CF patients the increased respiratory work lead to alveolar hypventilation, hypoxemia and hypercapnia. Among patients attending our CF Centre a study has been conducted to evaluate benefits of NIV in patients awaiting lung transplantation. Respiratory mechanical measures have been conducted with heated pneumotacograph (Fleish #2) connected to a pressure transducer of ICU-Lab (KleisTek). 179 patients are currently followed from our CF Centre, median age: 9.26 year. Within this population 33 patients (18.4%) - 17 females, 16 males - have deteriorated pulmonary function (FEV1 < 50%) and they are therefore at risk of organ insufficiency. Respiratory mechanics has been performed on 3 patients awaiting lung transplantation, started with in NIV. We observed a significant decrease of arterial CO2 (p < 0.05), with a significant improvement of acid-base balance (p < 0.05). The decrease of respiratory work, inspiratory effort in spontaneous breathing and the increase of the alveolar ventilation explain improvements in gas exchanges. Respiratory mechanics has evidenced the significant improvement (p < 0.05) of alveolar ventilation (Vt1, Vt2) and the interruption of mechanism of rapid shallow breathing (Ti, Ttot) due to pressure support assured by the NIV. The previous concepts appear even more remarkable if we consider that, by the literature, PCO2 > 50 mmHg is one of main risk factors of death in CF patients awaiting lung transplantation together with FEV1 < 30%, and the need to nutritional interventions.