Exhaled NO and small airway function in asthma and cystic fibrosis

Akademisk avhandling
som för avläggande av medicine doktorsexamen vid Sahlgrenska Akademin vid Göteborgs Universitet kommer att offentligen försvaras i föreläsningssal 1, Drottning Silvias Barn och Ungdomssjukhus, Göteborg

Fredagen den 11 juni 2010, klockan 9.00
av
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Legitimerad läkare

Fakultetsopponent:
Professor Lennart Nordvall
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Uppsala Universitet, Sverige

Avhandlingen baseras på följande delarbeten:

I. **C Keen**, A-C Olin, Å Edentoft, E Gronowitz and B Strandvik**.** Airway nitric oxide in patients with cystic fibrosis is associated with pancreatic function, pseudomonas infection and polyunsaturated fatty acids. *CHEST*, 2007; 131(6):1857-1864

II. **C Keen**, A-C Olin, S Eriksson, A Ekman, A Lindblad, S Basu, C Beermann and B Strandvik. Supplementation with fatty acids influences the airway nitric oxide and inflammatory markers in patients with cystic fibrosis. *Journal of Pediatric Gastroenterology and Nutrition,* 2010; 50(5):537-544.

III. **C Keen**, P Gustafsson, A Lindblad, G Wennergren and A-C Olin. Low levels of exhaled nitric oxide are associated with impaired lung function in cystic fibrosis. *Pediatric Pulmonology,* 2010; 45(3):241-248.

IV. **C Keen,** A-C Olin, G Wennergren, F Aljassim and P Gustafsson: Exhaled NO, small airway function and airway hyper responsiveness in paediatric asthma. (*Submitted)*

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Exhaled NO and small airway function in asthma and cystic fibrosis

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Background: Asthma and cystic fibrosis (CF) are chronic inflammatory airway disorders known to involve the peripheral airways. Non-invasive tests sensitive to peripheral airway function and inflammation are therefore of high priority. Multiple breath inert gas washout (MBW) is a test sensitive to small airway function and exhaled nitric oxide (NO) reflects airway inflammation in asthma.
Aim: To use exhaled NO in combination with MBW to assess the contribution of small airway inflammation and dysfunction in paediatric asthma and CF in order to potentially allow for earlier intervention and more successful management of these conditions in the future.
Results: CF subjects had reduced levels of nasal and exhaled NO. All but three children with CF had abnormally elevated LCI. Low levels of NO were associated with impaired airway function, chronic infection with *Ps. Aeruginosa,* severe genotypes and the fatty acid deficiency characteristic for CF subjects. Low levels of alveolar NO, albeit not lower in CF than in healthy controls, were associated with increased systemic inflammation and chronic bacterial airway colonisation.
LCI, S_{cond}, and S_{acin} were all significantly elevated in children with asthma and S_{cond} was the marker that most significantly differentiated the asthmatic children from the healthy controls. Increased S_{cond} was associated with increased levels of exhaled NO and airway hyper-responsiveness and S_{acin} correlated with alveolar NO.
Conclusions*:* This thesis provides further evidence of small airway involvement in both paediatric asthma and CF. The findings of clinically significant dysfunction of the small conducting airways in paediatric asthma and the associations between small airway dysfunction, increased levels of exhaled NO and airway hyper-responsiveness are novel findings. In CF, low levels of exhaled NO are linked to small airway dysfunction. These findings provide new exciting insights into the pathology and pathophysiology of paediatric asthma and CF and may allow for earlier and better targeted interventions.

Keywords: asthma, children, cystic fibrosis, flow independent exhaled nitric oxide, multiple breath inert gas washout, polyunsaturated fatty acids.

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