Göteborg, 2016

Exhaled particles for monitoring of airway inflammation
Sampling and analysis of endogenous particles from breath

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i sal Hamberger, Arbets- och miljömedicin, Medicinaregatan 16A, Göteborg, torsdagen den 8 december 2016 kl. 9:00

av
Per Larsson

Fakultetsopponent:

Professor Jan Johansson

Institutionen för neurobiologi, vårdvetenskap och samhälle.
Karolinska Institutet, Stockholm

Avhandlingen baseras på följande delarbeten

I. Larsson P, Mirgorodskaya E, Samuelsson L, Bake B, Almstrand AC, Bredberg A, Olin AC. Surfactant protein A and albumin in particles in exhaled air. *Respiratory Medicine 106: 197-204, 2012.*

II. Larsson P, Lärstad M, Bake B, Hammar O, Bredberg A, Almstrand AC, Mirgorodskaya E, Olin AC. Exhaled particles as markers of small airway inflammation in subjects with asthma. *Clinical Physiology and Functional Imaging 2015. DOI: 10.1111/cpf.12323.*

III. Larsson P, Bake B, Wallin A, Hammar O, Almstrand AC, Lärstad M, Ljungström E, Mirgorodskaya E, Olin AC. The effect of exhalation flow on endogenous particle emission and phospholipid composition. *Submitted manuscript 2016.*

IV. Mirgorodskaya E, Larsson P, Koca H, Kim JL, Bake B, Ljungström E, Holm M, Olin AC, Exhaled surfactant protein A and albumin in a healthy Swedish population. *Manuscript.*

SAHLGRENSKA AKADEMIN
INSTITUTIONEN FÖR MEDICIN

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Sampling and analysis of endogenous particles from breath

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Abstract

Non-invasive collection methods suitable for studying the composition of the respiratory tract lining fluid (RTLF) in small airways are currently not readily available. The overall aim of this thesis was to contribute to the development of a non-invasive method for sampling of RTLF with the purpose of studying airway inflammation.

As we breathe small particles of liquid are formed from the RTLF. These particles follow the airstream during exhalation and can be sampled from the exhaled breath using the PExA method. A micro sample of RTLF can thus be obtained by sampling these particles.

Methods for measuring surfactant protein A (SP-A) and albumin in exhaled particles (PEx) were developed. The methods were used to study the effect of birch pollen exposure in a group of individuals with mild asthma and birch pollen allergy. During birch pollen season the PEx mass concentration was reduced while no significant effect on SP-A or albumin concentrations in PEx was observed. Alteration in particle amount seem to reflect change in bronchial motor-tone. In a middle aged population without lung diseases, reference intervals (RI) for SP-A and albumin weight percent concentration (wt%) in PEx was calculated to 1.9-5.3 wt% and 3.6-11.2 wt% (90% RI), respectively. SP-A concentration in PEx was not associated with age, gender, anthropometry, atopy or particle production, whereas albumin concentration in PEx was associated to age, atopy and particle production.

Particle formation was studied with aim to understand and facilitate optimal particle collection. Particles exhaled with a maximal forced exhalation contained very low amounts of the major surfactant lipid (dipalmitoylphosphatidylcholine) compared to particles exhaled by a slow and deep exhalation/inhalation manoeuvre. This suggests that particle formation, including efficiency and formation site, can be controlled by selecting an appropriate breathing manoeuvre.

The PExA method is a promising non-invasive method for measuring proteins and lipids in RTLF collected from small airways. Further biomarker development studies are necessary to facilitate the method application in clinical studies.

Keywords: Exhaled particles, respiratory tract lining fluid, inflammation

ISBN: 978-91-628-9961-5 (TRYCK) http://hdl.handle.net/2077/44869
ISBN: 978-91-628-9962-2 (PDF)