

Urinary Clara cell protein and alpha 1-microglobulin – biomarkers of changes in kidney and airway function

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ABSTRACT

Validated biomarkers are useful tools for screening large populations. The benefit of screening may be improved risk assessment or early indications of adverse effects before detection or onset of symptoms. Screening is valuable in studies of environmental exposures and their effects on human health, for example after exposure to air pollution and toxic metals in our daily environment. The overall aim of this thesis was to optimize sampling of urinary Clara cell 16 kDa protein (CC16) and alpha 1-microglobulin (A1M) and test them as biomarkers of changes in kidney and airway function.

For optimized sampling of urinary CC16 and A1M, timed or creatinine-corrected first morning samples are preferable. This is the time of day when the variation in excretion due to influence of urine flow and daily activities is low. For all urinary CC16 sampling, men should discard the first 100 ml to wash out post-renal excretion of CC16 before collection.

Urinary and serum CC16 were tested as biomarkers of changes in the permeability of the respiratory epithelium. This was examined after exposure to wood smoke for 4 hours and compared with a session of filtered clean air for 4 hours. Exposure to wood smoke significantly increased serum CC16 after 20 hours and there was tendency towards increased urinary CC16.

Both urinary CC16 and A1M are sensitive to changes in tubular function and were analysed together with another tubular biomarker, retinol-binding protein (RBP), in the urine of small children with urinary tract infection (UTI). Clara cell 16 kDa protein was significantly higher in children with upper UTI compared with children with lower UTI. Also, the association between decreased uptake of dimercaptosuccinic acid (DMSA) and increased excretion of CC16 was strong. There was no difference in A1M excretion between upper and lower UTI.

In patients with community-acquired pneumonia (CAP), urinary CC16 was increased compared with the control group. By contrast, serum CC16 was decreased in patients with CAP. The increase in urinary CC16 was probably due to fever-related proteinuria since urinary A1M and RBP were also increased. The decrease in serum CC16 could be explained by increased renal excretion. Also, asthma, chronic obstructive pulmonary disease (COPD) and smoking (known to decrease serum CC16) were common among patients with CAP.

In conclusion, this thesis demonstrates that both CC16 and A1M are useful biomarkers of tubular renal function. There is also a possibility to use urinary CC16 as an airway biomarker in screening studies of air pollution under the right conditions, using optimal sampling methods.

Key words: biomarker, Clara cell 16 kDa protein (CC16), alpha 1-microglobulin (A1M), ambient air pollution, renal function, pyelonephritis, children

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- I. **Andersson L., Lundberg PA., and Barregard L**
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J Appl Toxicol 2007 Jan; 27: 60–66
- II. **Andersson L., Haraldsson B., Johansson C., and Barregard L**
Methodological issues on the use of urinary alpha-1-microglobulin in epidemiological studies.
Nephrol Dial Transplant 2008; 23: 1252–1256
- III. **Barregard L., Sällsten G., Andersson L., Almstrand AC., Gustafson P., Andersson M., and Olin AC**
Experimental exposure to wood smoke: effects on airway inflammation and oxidative stress.
Occup Environ Med 2008; 65: 319–324
- IV. **Andersson L., Preda I., Hahn-Zoric M., Hanson LÅ., Jodal U., Sixt R., Barregard L., and Hansson S**
Urinary proteins in children with urinary tract infection.
Pediatr Nephrol 2009; 24: 1533–1538
- V. **Andersson L., Strålin K., and Barregard L**
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