Haddam et al. Environmental Health 2011, 10:37
http://www.ehjournal.net/content/10/1/37

ENVIRONMENTAL HEALTH

RESEARCH Open Access

Confounders in the assessment of the renal effects associated with low-level urinary cadmium: an analysis in industrial workers

Nahida Haddam[1,2], Sekkal Samira[1], Xavier Dumont[3], Abdesselem Taleb[1], Dominique Lison[3], Vincent Haufroid[3] and Alfred Bernard[3*]

Abstract

Background: Associations of proteinuria with low-level urinary cadmium (Cd) are currently interpreted as the sign of renal dysfunction induced by Cd. Few studies have considered the possibility that these associations might be non causal and arise from confounding by factors influencing the renal excretion of Cd and proteins.

Methods: We examined 184 healthy male workers (mean age, 39.5 years) from a zinc smelter (n = 132) or a blanket factory (n = 52). We measured the concentrations of Cd in blood (B-Cd) and the urinary excretion of Cd (U-Cd), retinol-binding protein (RBP), protein HC and albumin. Associations between biomarkers of metal exposure and urinary proteins were assessed by simple and multiple regression analyses.

Results: The medians (interquartile range) of B-Cd (μg/l) and U-Cd (μg/g creatinine) were 0.80 (0.45-1.16) and 0.70 (0.40-1.3) in smelter workers and 0.66 (0.47-0.87) and 0.55 (0.40-0.90) in blanket factory workers, respectively. Occupation had no influence on these values, which varied mainly with smoking habits. In univariate analysis, concentrations of RBP and protein HC in urine were significantly correlated with both U-Cd and B-Cd but these associations were substantially weakened by the adjustment for current smoking and the residual influence of diuresis after correction for urinary creatinine. Albumin in urine did not correlate with B-Cd but was consistently associated with U-Cd through a relationship, which was unaffected by smoking or diuresis. Further analyses showed that RBP and albumin in urine mutually distort their associations with U-Cd and that the relationship between RBP and Cd in urine was almost the replicate of that linking RBP to albumin

Conclusions: Associations between proteinuria and low-level urinary Cd should be interpreted with caution as they appear to be largely driven by diuresis, current smoking and probably also the co-excretion of Cd with plasma proteins.

Introduction

Cadmium (Cd) is a widespread pollutant that accumulates in the soil, the food chain and ultimately in the human body. Other major sources of exposure to Cd are cigarette smoking and the use or production of Cd in various industrial settings. Cd is a highly toxic metal which at high doses can cause damage on virtually all organs and biological systems. At current human exposure levels in the industry or environment, it is assumed that Cd primarily damages the kidneys and especially the proximal tubular cells where the metal selectively concentrates. The hallmark of Cd nephrotoxicity is an increased urinary excretion of low-molecular-weight (LMW) proteins such as β_2-microglobulin, retinol-binding protein (RBP) or protein HC. This increased excretion of LMW proteins in urine referred to as "tubular proteinuria" results from a defective protein reabsorption by the damaged tubular cells [1-3].

Studies among industrial workers and populations living in heavily polluted areas have clearly shown that Cd causes tubular dysfunction in a dose-dependent manner, the tubular proteinuria developing only when the renal

* Correspondence: Alfred.bernard@uclouvain.be
[3]Unit of Toxicology and Applied Pharmacology, Catholic University of Louvain, Brussels, Belgium
Full list of author information is available at the end of the article