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Low-level cadmium exposure in Toyama City and its surroundings in Toyama prefecture, Japan, with references to possible contribution of shellfish intake to increase urinary cadmium levels

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Abstract

Objectives: This study was initiated to examine if exposure to cadmium (Cd) was high also outside of the previously identified Itai-itai disease endemic region in the Jinzu River basin in Toyama prefecture in Japan.
Methods: Morning spot urine samples were collected in June–August 2004 from 651 adult women (including 535 never-smokers) in various regions in Toyama prefecture, and subjected to urinalyses for cadmium (Cd), α_1-microglobulin (α_1-MG), β_2-microglobulin (β_2-MG), *N*-acetyl-β-D-glucosaminidase (NAG), specific gravity (SG or sg) and creatinine (CR or cr). Three months later, the second urine samples were collected from those with elevated Cd in urine (e.g., ≧4 μg/g cr), together with answers to questionnaires on shellfish consumption.
Results: The geometric mean (GM) Cd, α_1-MG, β_2-MG and NAG (after correction for CR) for the total participants were 2.0 μg/g cr, 2.4 mg/g cr, 104 μg/g cr and 2.8 units/g cr, respectively; further analysis with never-smoking cases only did not induce significant changes in these parameters. Analyses of the second urine samples from the high Cd subjects showed that there was substantial decrease (to about a half) in Cd in the 3-month period, and that the decrease was accompanied by reduction in α_1-MG and NAG (β_2-MG did not show elevation even in the first samples). The urinalysis results in combination with the results of the questionnaire survey suggest that the high urinary Cd was temporary and might be induced by intake of shellfish that is edible whole.
Conclusions: The overall findings appear to suggest that Cd exposure in Toyama populations (outside of the Itai-itai disease endemic region) was at the levels commonly observed on the coast of the Sea of Japan, and that the Cd level in urine might be

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modified by the intake of some types of seafood. Further studies are necessary to elucidate the relation of urinary Cd with seafood intake.

Keywords: *N*-acetyl-β-D-glucosaminidase; Adult women; Cadmium; α_1-Microglobulin; β_2-Microglobulin; Population in Toyama; Urine

1. Introduction

The outbreak of Itai-itai disease, a chronic cadmium poisoning in a suburb of the City of Toyama, the capital of Toyama prefecture, Japan, followed environmental exposures (primarily via foods) to cadmium (Cd) at high levels (Environment Agency, 1972; International Programme on Chemical Safety, 1992a,b; Ikeda et al., 2004). Whereas the endemic of the disease was localized in the Jinzu River basin region (Aoshima, 1987), it is of both scientific as well as public health concern to know if the high exposure to Cd has been observed also among residents outside of the region in the prefecture.

It is well established that long-term exposure to Cd even at low levels may induce renal tubular dysfunction and that urinary Cd level is a reliable marker of environmental exposure to Cd (International Programme on Chemical Safety, 1992a,b; Schaller, 1996). With regard to monitoring of the possible health effects among the populations exposed, α_1-microglobulin (α_1-MG), β_2-microglobulin (β_2-MG) and *N*-acetyl-β-D-glucosaminidase (NAG) in urine are commonly used markers of tubular dysfunction (e.g., Kawada, 1995). The present study was initiated to obtain answers to the above-mentioned question through the analysis of Cd and tubular dysfunction markers in urine of residents in the prefecture.

2. Materials and methods

2.1. Subjects of the present analyses

The Ethics Committee of Kyoto Industrial Health Association approved the study protocol. In June–August 2004, working women (with no potential risk of exposure to hazardous substances including metals such as Cd and lead) were invited to participate in this study after presentation of the study purpose at the time of a routine health examination in workplaces (which was provided once a year as a part of occupational health service to workers). In practice, 651 adult women volunteered. Each of them provided her written informed consent, offered a morning spot urine sample, and filled questionnaires on items including the date of birth, the place of residence, previous diseases, smoking habits, and job history. None of the participants was from the Itai-itai disease endemic region.

Because smoking is a substantial non-occupational source of exposure to Cd (e.g., Watanabe et al., 1983), only never-smokers were selected in some cases of analyses based on the answers to the questionnaires. Among the 651 participants, 535 women reported as never-smokers (never-smoking ratio: 82%), whereas 75 and 27 women were current and ex-smokers, respectively. Remaining 14 subjects did not give clear answers on their smoking habits and they were taken as if they were smokers.

The average ages of both the total and the never-smoking women were about 40 years (Table 1). A majority of the 535 never-smokers was in the age range of 30s (37%), 40s (26%) or 50s (20%).

Three months later (i.e., in September–November 2004), 26 women with high Cd in first urine samples (i.e., ≧10 μg Cd/l as observed values, or ≧8 μg Cd/g cr) were asked to offer the second urine samples, together with giving answers to short questionnaires on whether or not it was the season for them to consume such specific kinds of seafood as small squids, oysters and scallops (which were edible as whole including viscera) at the times of the first and the second urine sampling. In practice, 18 women (the high Cd group) responded by offering the second urine samples and answers to the questionnaires. In addition, 8 women with relatively high Cd (5–10 μg/l as observed values, or 4–8 μg/g cr as Cd after correction for creatinine; the second high Cd group) offered the second urine samples and questionnaire answers. Separately, 9 women with unelevated levels of Cd in urine at the first examination (1.3 μg Cd/l or Cd/g cr as GM for both observed values and the values after correction for creatinine; the