Science of the Total Environment 409 (2011) 1632–1637

Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

Sources of cadmium exposure among healthy premenopausal women

Scott V. Adams [a,b,*], Polly A. Newcomb [a,b], Martin M. Shafer [c], Charlotte Atkinson [d], Erin J. Aiello Bowles [e], Katherine M. Newton [b,e], Johanna W. Lampe [a,b]

[a] Fred Hutchinson Cancer Research Center, PO Box 19024, M4-B402, Seattle, WA 98109 USA
[b] Department of Epidemiology, University of Washington, Box 357236, Seattle, WA 98195 USA
[c] Environmental Chemistry and Technology Program, University of Wisconsin and Wisconsin State Laboratory of Hygiene, Madison, WI, USA
[d] Department of Oral and Dental Science, Bristol Dental School, Bristol, UK
[e] Group Health Research Institute, Seattle, WA, USA

ARTICLE INFO

Article history:
Received 2 November 2010
Received in revised form 19 January 2011
Accepted 20 January 2011
Available online 17 February 2011

Keywords:
Cadmium
Tofu
Soy
Diet
Smoking
Soybean

ABSTRACT

Background: Cadmium, a persistent and widespread environmental pollutant, has been associated with kidney function impairment and several diseases. Cigarettes are the dominant source of cadmium exposure among smokers; the primary source of cadmium in non-smokers is food. We investigated sources of cadmium exposure in a sample of healthy women.

Methods: In a cross-sectional study, 191 premenopausal women completed a health questionnaire and a food frequency questionnaire. The cadmium content of spot urine samples was measured with inductively-coupled plasma mass spectrometry and normalized to urine creatinine content. Multivariable linear regression was used to estimate the strength of association between smoking habits and, among non-smokers, usual foods consumed and urinary cadmium, adjusted for age, race, multivitamin and supplement use, education, estimated total energy intake, and parity.

Results: Geometric mean urine creatinine-normalized cadmium concentration (uCd) of women with any history of cigarette smoking was 0.43 μg/g (95% confidence interval (CI): 0.38–0.48 μg/g) and 0.30 μg/g (0.27–0.33 μg/g) among never-smokers, and increased with pack-years of smoking. Analysis of dietary data among women with no reported history of smoking suggested that regular consumption of eggs, hot cereals, organ meats, tofu, vegetable soups, leafy greens, green salad, and yams was associated with uCd. Consumption of tofu products showed the most robust association with uCd; each weekly serving of tofu was associated with a 22% (95% CI: 11–33%) increase in uCd. Thus, uCd was estimated to be 0.11 μg/g (95% CI: 0.06–0.15 μg/g) higher among women who consumed any tofu than among those who consumed none.

Conclusions: Cigarette smoking is likely the most important source of cadmium exposure among smokers. Among non-smokers, consumption of specific foods, notably tofu, is associated with increased urine cadmium concentration.

1. Introduction

Cadmium is a heavy metal that has been widely dispersed in the environment as a result of industry and agriculture (Jarup and Akesson, 2009). Non-occupationally exposed persons are exposed to cadmium primarily by smoking tobacco or by eating foods containing cadmium (Jarup and Akesson, 2009). Once inhaled or ingested, cadmium is inefficiently excreted and accumulates primarily in the liver and kidneys (Jarup and Akesson, 2009). Long-term exposure at levels estimated to be achievable by non-occupationally exposed non-smokers can result in impaired kidney function (Jarup, 2003; Satarug et al., 2003). Urine cadmium levels have also been associated with several other health conditions, including osteoporosis (Jarup and Alfven, 2004; Jarup et al., 1998), hypertension (Gallagher and Meliker, 2010), peripheral artery disease (Tellez-Plaza et al., 2010), diabetes mellitus (Schwartz et al., 2003), and cancers including lung, breast and endometrial cancers (Akesson et al., 2008; McElroy et al., 2006; Nawrot et al., 2006).

Tobacco has been documented as the dominant source of cadmium exposure in smokers (McElroy et al., 2007a, 2007b; Pappas et al., 2006; Richter et al., 2009). The tobacco plant readily accumulates cadmium from the soil, which is subsequently released by burning and absorbed through the lungs (Elinder et al., 1983; Pappas et al., 2006; Watanabe et al., 1987). Among non-smokers, direct measurements of cadmium in foods indicate that leafy green vegetables, grains, shellfish, root vegetables, legumes, seeds and nuts, and organ meats are typically considered to be the most significant dietary sources of cadmium (Egan et al., 2007, 2002). However, there is limited empiric data comparing measurement of urine cadmium (uCd) with reported routine consumption of potential dietary sources

* Corresponding author at: Fred Hutchinson Cancer Research Center, 1100 Fairview Ave N, M4-B402, Seattle, WA 98109, USA. Tel.: +1 206 667 6427; fax: +1 206 667 5977.
E-mail address: sadams@fhcrc.org (S.V. Adams).

0048-9697/$ – see front matter © 2011 Elsevier B.V. All rights reserved.
doi:10.1016/j.scitotenv.2011.01.037

(Haswell-Elkins et al., 2007; Hellstrom et al., 2007; McElroy et al., 2007a; Satarug et al., 2010; Vahter et al., 1996).

In this study we combined measurement of urine cadmium with reported smoking habits and dietary data to assess sources of urine cadmium in a sample of healthy premenopausal women in Washington State. We hypothesized that cigarette smoking would be associated with higher urine cadmium in a dose-dependent manner; and that reported usual consumption of foods identified as containing cadmium, such as leafy green vegetables, grains, shellfish, root vegetables, legumes, seeds and nuts, and organ meats would also be associated with elevated urine cadmium.

2. Materials and methods

2.1. Study population and recruitment

The recruitment, exclusion criteria, and clinical protocols of the Equol, Breast, and Bone (EBB) study have been detailed elsewhere (Atkinson et al., 2008a, 2008b). Briefly, premenopausal women aged 40–45 years were recruited from a mammographic screening program within Group Health (GH), an integrated healthcare system in Washington State. Based on self-report, peri and postmenopausal women, women with a history of breast cancer, and women using hormone therapy or oral contraceptives were excluded from the study population; consistent with other goals of the EBB study, women with certain digestive conditions and women using antibiotics were also excluded (Atkinson et al., 2008a, 2008b). Study procedures were approved by the Fred Hutchinson Cancer Research Center (FHCRC) and GH Institutional Review Boards.

2.2. Data collection

Participants completed a health questionnaire, a food frequency questionnaire (FFQ) developed by the Nutrition Assessment Shared Resource of the FHCRC (Patterson et al., 1999), and a study clinic visit during which height and weight were measured. Spot urine samples were collected using standard "clean-catch" procedures. Urine samples were aliquoted and frozen at −70 °C until analysis. Separate aliquots were assayed for creatinine and heavy metals.

2.3. Urine cadmium and creatinine measurement

A panel of 30 elements including cadmium was quantified by sector field inductively coupled plasma mass spectrometry (SF-ICPMS) on a Thermo-Finnigan Element 2 (Thermo Scientific, Waltham, MA) at the Wisconsin State Laboratory of Hygiene (Madison, WI), following quality control procedures similar to those previously described (McElroy et al., 2007a). Urine was diluted in 2% high purity nitric acid containing internal normalization standards, and introduced to the plasma with a low-flow Teflon nebulizer interfaced to an ESI FAST auto-sampler. Isotopes were acquired in peak jumping mode. A series of dedicated samples (molybdenum spiked reference materials and spiked samples) were positioned throughout the analytical sequence to address potential molybdenum oxide interference. A typical SF-ICPMS batch included 20 participant samples, 3 standard reference material aliquots (including National Institute of Standards of Technology 2670a), and multiple quality control samples (duplicates, spikes, check standards and blanks) (McElroy et al., 2007a). The mean of batch-specific reagent blanks was subtracted from the mean of triplicate sample measurements to arrive at the cadmium concentration used for statistical analysis. All participant samples were above the lower limit of quantification of cadmium (0.008 μg/L). Levels of extractable metals (0.5 M nitric acid for 48 h) in un-used urine collection containers and storage/transport vials were also quantified to assess potential contamination biases. Extractable concentrations of cadmium in the urine collection containers (0.0004 ± 0.0002 μg/L, $n = 4$) and storage vials (0.0020 ± 0.0006 μg/L, $n = 9$) were significantly below the method quantification limit of cadmium in urine and therefore judged to be an insignificant source of error.

Urine creatinine was assessed using a colorimetric assay (Atkinson et al., 2008a).

2.4. Smoking

Participants self-reported smoking history. Women who reported smoking less than 100 cigarettes in total were categorized as "never-smokers". Pack-years (py) of smoking was calculated among smokers by multiplying reported average number of cigarettes smoked per day and the reported number of years of smoking, and assuming 20 cigarettes per pack. Women were also categorized as never, former or current smokers; and in a single combined variable: never-smokers; smoker with <10 py; smoker with 10–20 py; or smoker with ≥20 py. Three women who indicated formerly smoking but indicated "social smoking" in place of an average daily number of cigarettes were categorized as former smokers with less than 10 py. No participating women without a personal history of smoking reported current exposure to secondhand smoke in the home.

2.5. Diet

The average weekly consumption of individual food items, total energy intake, and intake of specific nutrients were estimated from food frequency questionnaire (FFQ) responses using the Nutrient Data System for Research software and database developed by the Nutrition Coordinating Center, University of Minnesota, following methods previously reported (Schakel et al., 1997, 1988). In summary, each participant indicated how often she consumed each food item, and a typical serving size (small, medium, or large). A reference measure for a "medium serving" for each food was given on the FFQ. Total medium servings per day of most individual foods items were directly estimated from the response to FFQ items. Consumption of some items (e.g., cold cereals, crackers, and popcorn) were estimated by combining two or more closely related FFQ items, for example, "low-fat" and "regular" items for the same basic food item, as indicated in footnotes to Table 2. Oils used in cooking or as food toppings, salad dressings, and dairy products added to cereals and coffee or tea were not considered as individual food items, but were included in estimation of nutrient and total energy intake (Schakel et al., 1997).

2.6. Statistical analysis

Potential confounding was evaluated for the following set of variables selected *a priori*: age, race, total energy intake, parity, body mass index (BMI), education, and use of mineral or multivitamin supplements. BMI was not included in final multivariable models because no association with urine cadmium was observed. Other potential confounders were included in the final models as parameterized in Table 1, with the exception that total energy intake and age were modeled as continuous variables.

Creatinine-corrected cadmium concentration for each spot urine sample, reported as μg cadmium per g creatinine, was calculated as the measured cadmium concentration divided by creatinine concentration. Creatinine-normalized urinary cadmium concentrations were log-transformed (base 2) to normalize the distribution. The logarithm of creatinine-corrected cadmium was the dependent variable in each multivariable linear regression model.

Linear regression was fit using ordinary least squares regression and robust standard error estimates. Following model fitting, estimates of urine creatinine-corrected cadmium were back-transformed from log-scale, yielding percentage change in uCd per unit change of each independent variable and corresponding 95%