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Blood cadmium by race/hispanic origin: The role of smoking☆

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ABSTRACT

Background: There have been increasing concerns over health effects of low level exposure to cadmium, especially those on bones and kidneys.
Objective: To explore how age-adjusted geometric means of blood cadmium in adults varied by race/Hispanic origin, sex, and smoking status among U.S. adults and the extent to which the difference in blood cadmium by race/Hispanic origin and sex may be explained by intensity of smoking, a known major source of cadmium exposure.
Methods: Our sample included 7,368 adults from National Health and Nutrition Examination Survey (NHANES) 2011–2014. With direct age adjustment, geometric means of blood cadmium and number of cigarettes smoked per day were estimated for subgroups defined by race/Hispanic origin, smoking status, and sex using interval regression, which allows mean estimation in the presence of left- and right-censoring.
Results: Among never and former smoking men and women, blood cadmium tended to be higher for non-Hispanic Asian adults than adults of other race/Hispanic origin. Among current smokers, who generally had higher blood cadmium than never and former smokers, non-Hispanic white, black, and Asian adults had similarly elevated blood cadmium compared to Hispanic adults. A separate analysis revealed that non-Hispanic white adults tended to have the highest smoking intensity regardless of sex, than adults of the other race/Hispanic origin groups.
Conclusions: The observed pattern provided evidence for smoking as a major source of cadmium exposure, yet factors other than smoking also appeared to contribute to higher blood cadmium of non-Hispanic Asian adults.

1. Introduction

Cadmium at high doses can decrease bone mineral density and cause kidney dysfunction (Satarug et al., 2010). Cadmium has been determined to be a human carcinogen, causing lung cancers and associated with kidney and prostate cancer (IARC, 1993; Ju-Kun et al., 2016). An association between high level exposure to cadmium and breast cancer has also been reported in multiple studies (Larsson et al., 2015). An important source of cadmium exposure is cigarette smoking, but foods such as potatoes, rice, wheat, soybean, shellfish and organ meat also are sources (ATSDR, 2012). In the United States, characteristics such as Asian ancestry (CDC, 2015), female sex, smoking status, and older age (Adams and Newcomb, 2014; CDC, 2015; Mortensen et al., 2011) are associated with higher cadmium body burdens. Differences in blood cadmium between Asians and other racial groups in the U.S. have been reported scarcely (CDC, 2015; McKelvey et al., 2007). Additional knowledge on racial difference in cadmium exposure may facilitate further research on the avoidable sources of exposure to cadmium, thereby contributing to the efforts to prevent adverse health effects induced by cadmium. We explored sex-specific differences in blood cadmium between race/Hispanic origin groups by smoking status and examined the extent to which the difference may be explained by smoking intensity.

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2. Methods

2.1. Data source and measurements

We used data on race/Hispanic origin, sex, age at screening, blood cadmium, and self-reported smoking status and intensity from the National Health and Nutrition Examination Survey (NHANES) 2011–2014. The final response rates for the exam component for adults were 64.5% and 63.7% for 2011–12 and 2013–2014, respectively (CDC, 2012, 2014). The entire sample from 2011 to 12 and a 1/2 subsample from 2013 to 14 of adults, both of which were selected to be representative of the adult U.S. population in terms of race/Hispanic origin, sex, age, and income levels through a multistage probability design (Johnson et al., 2014), were targeted for blood cadmium measurements. Eligible for inclusion were 8,123 non-Hispanic white, non-Hispanic black, non-Hispanic Asian and Hispanic adults aged 20 and over, of whom 755 had missing data. Missing data were: 622 for blood cadmium; 151 for number of cigarette smoked (former and current smokers, and 9 missing smoking status (the total exceeds 755 because some participants were missing more than one variable). The remaining adults with complete data (n=7,368) formed the analytic sample.

2.2. Variables

Blood cadmium was measured using inductively coupled plasma mass spectrometry, with limits of detection (LODs) 0.16 and 0.10 μg/L in 2011–12 and 2013–14, respectively, by the Environmental Health laboratory at CDC (CDC, 2012, 2014). We used three mutually-exclusive smoking status categories: never (reported < 100 cigarettes smoked during one's lifetime); former (do not currently smoke); or current (currently smoke some or all days). Self-reported average number of cigarettes smoked per day before quitting for former smokers or in the last 30 days for current smokers was used as a measure of smoking intensity. Serum cotinine was used to assess the validity of self-reported smoking status for NHANES 2011–2012; serum cotinine data were not available for NHANES 2013–2014. A serum cotinine > 10 ng/mL was taken as biochemical evidence of recent active smoking (during the last 5 days prior to examination) (Pirkle et al., 1996): 4.0% of self-reported never smokers; 8.6% of self-reported former smokers; and 92.2% of self-reported current smokers had serum cotinine > 10 ng/mL.

2.3. Statistical methods

Age-adjusted geometric means of blood cadmium and number of cigarettes smoked for subgroups defined by race/Hispanic origin, smoking status, and sex, were estimated with direct age adjustment in the following 4 steps: 1, log-transformation; 2, estimation of within-subgroup age-specific means, i.e., three age group-specific means (age groups of 20–39, 40–59, 60 and over) (Klein and Schoenborn, 2001) within each subgroup; 3, estimation of subgroup means with direct age adjustment; 4, back-transformation of subgroup specific means. There were: 72 within-subgroup age-specific means and 24 subgroup means for blood cadmium; 48 within-subgroup age-specific means and 16 subgroup means for number of cigarettes smoked, which was reported by former and current smokers only. Both blood cadmium and number of cigarettes smoked were right skewed (which justified log-transformation) and censored (blood cadmium values below the LOD were left-censored, and number of cigarettes smoked reported as ≤1 or ≥95 were left- and right-censored, respectively). To properly handle the censoring, interval regression (Conroy, 2005) was used in step 2. A single interval regression model, weighted with examination weights for 2011–2012 and 1/2 sub-sample special weights for 2013–2014, was fit to the entire analytic sample to estimate within-subgroup age-specific means. In step 3, an age-adjusted mean for each subgroup was calculated as a linear combination of coefficients from step 2 with standard proportions for 3 age groups (Klein and Schoenborn, 2001) used as scalars. In step 4, the age-adjusted means from step 3 were back-transformed to obtain age-adjusted geometric means (referred to as "means" hereafter). Results obtained in step 3 were used for pairwise comparisons by Wald test at significance level of 0.05. We used "svy" estimation of Stata 13 (StataCorp, 2013), allowing variance estimation suitable for complex survey design.

2.4. Sensitivity analysis

We performed a sensitivity analysis, in which reported age-adjusted subgroup mean and standard error estimates of blood cadmium were compared with the corresponding estimates based on an alternative approach that ignored left-censoring (i.e., using the data with < LOD values substituted with LOD/(√2) and fitting linear regression model in place of interval regression). Additionally, for each of the 72 pairwise comparisons of age-adjusted means we performed, reported statistical significance (as well as relative difference in the two estimated geometric means, calculated as "higher estimate" divided by "lower estimate") was compared with the counterpart based on the alternative approach. These pairwise comparisons include: 36 sex and smoking status-specific comparisons by race/Hispanic origin; 12 race/Hispanic origin and smoking status-specific comparison by sex; and 24 sex and race/Hispanic origin comparisons by smoking status.

3. Results

Age-adjusted blood cadmium means by race/Hispanic origin, smoking status, and sex ranged from 0.16 μg/L (95% confidence interval [CI]: 0.15, 0.17) to 1.10 μg/L (95% CI: 0.98, 1.23) (Fig. 1 and Table 1). All subgroup means had satisfactory precision of relative standard errors < 30% (data not shown in tabular form). Within each sex-race/Hispanic origin group, current smokers had 2–4 times higher mean blood cadmium than former smokers, who in turn had up to 60% higher mean blood cadmium than never smokers. Among current smokers, Hispanic adults tended to have lower mean blood cadmium than adults of the other race/Hispanic origin, and there were no differences between non-Hispanic white, non-Hispanic black and non-Hispanic Asian adults. Among never and former smokers of the same sex, however, mean blood cadmium was almost always higher in non-Hispanic Asian adults compared to adults of other three race/Hispanic origin groups ($p < 0.001$ for all pairwise comparisons except for non-Hispanic Asian vs. non-Hispanic black formerly-smoking males with $p=0.7$). Within most smoking status-race/Hispanic origin groups, women had higher mean blood cadmium levels than men.

Non-Hispanic white former and current smokers tended to smoke the most among men. Among currently smoking women, non-Hispanic white women also had the highest mean number of cigarettes smoked. Among formerly smoking women, non-Hispanic white, non-Hispanic black and non-Hispanic Asian women had similar mean number of cigarettes smoked, and Hispanic women had fewer cigarettes than non-Hispanic white and black women. Among former smokers, women tended to have smoked fewer cigarettes than men, but no consistent difference by sex was seen among current smokers.

We used a sensitivity analysis with the aim to document discrepancies between the blood cadmium results based on the approach used and the alternative approach, in which values below LOD were substituted with LOD/(√2), ignoring censoring. We found that the non-Hispanic white male never smoker subgroup, which had the highest < LOD proportion, had the most pronounced discrepancies in estimation of an age-adjusted mean and its standard error; the highest ratio of alternative to reported mean, 1.27; and the lowest ratio of alternative to reported standard errors, 0.53. Fig. 2 is a graphical depiction of these results as a plot of "alternative-reported" relative differences of point estimates for each sex, race/Hispanic origin vs. < LOD proportion.