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Blood cadmium concentration and lipid profile in Korean adults

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ABSTRACT

Although animal experiments have shown that cadmium exposure induces alterations in lipid profiles, no epidemiological study of this relationship has been performed. The objective of this study was to evaluate the association between blood cadmium concentration and blood lipid levels in Korean adults. A cross-sectional study comprising participants ($n=3903$) aged 20 years or older from the 2005, 2008, and 2009 Korea National Health and Nutrition Examination Surveys was conducted. Demographic characteristics and dietary intake were obtained from the participants by questionnaire, and cadmium and lipid levels were determined by analysis of blood samples. After adjusting for demographic and dietary factors, blood concentration of cadmium was positively associated with the risk of low high-density lipoprotein cholesterol (HDL-C) in a dose-dependent manner (p for trend <0.001). In addition, the odds ratios (ORs) of a high triglyceride to HDL-C ratio was significantly increased in the high blood cadmium groups [OR=1.36; 95% confidence interval (CI), 1.03–1.79 for fourth quintile and OR=1.41; 95% CI, 1.07–1.86 for fifth quintile] compared with the lowest quintile group. However, high blood cadmium was not associated with a risk of high total cholesterol, high low-density lipoprotein cholesterol, or high triglycerides. These data suggest that an increased cadmium body burden increases the risk of dyslipidemia, mainly due to the increased risk of low HDL-C and the high ratio of triglycerides to HDL-C.

1. Introduction

Cadmium is an important toxic metal that is widely distributed in the general environment and in human foodstuffs from industrial and agricultural sources (Satarug et al., 2003). Exposure to cadmium contributes to the development of numerous adverse health effects and causes a number of diseases, including cardiovascular conditions (Peters et al., 2010; Staessen and Lauwerys, 1993).

Although the detailed mechanism of these toxic effects remains to be elucidated, cadmium is known to disturb numerous cellular functions and damage various cellular structures (Bertin and Averbeck, 2006; Martelli et al., 2006). Cadmium depletes glutathione and protein-bound sulfhydryl groups, resulting in the enhanced production of reactive oxygen species, which induces increased lipid peroxidation (Stohs et al., 2000). In addition, cadmium has a high affinity for biological structures containing sulfhydryl (–SH), carboxyl, and phosphate groups, which inhibit numerous enzymes and disturb some metabolic processes, including lipid metabolism (Rogalska et al., 2009). Several animal studies have indicated that exposure to cadmium may alter lipid metabolism. Cadmium has been reported to cause alterations in the serum and tissue concentrations of some lipid compounds, including total cholesterol (C), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides, causing dyslipidemia in various experimental models of acute and chronic treatment modalities (Larregle et al., 2008; Prabu et al., 2010; Ramirez and Gimenez, 2002; Rogalska et al., 2009; Skoczyńska and Smolik, 1994).

However, findings from experimental animal studies of the association between cadmium and lipid profile have been less consistent; different levels of total C, HDL-C, LDL-C, and triglycerides have been reported following cadmium treatment. Additionally, no known epidemiological study has attempted to elucidate the correlation between cadmium body burden and lipid profile or the prevalence of dyslipidemia. Since the alteration of lipid profile may represent an important and potentially etiological component in the pathogenesis of many disorders, including cardiovascular diseases (Brewer, 2011; Davidson and Toth, 2007), elucidating the correlation between cadmium body burden and dyslipidemia profiles in the human population is vital. Therefore, the aim of the present study was to investigate this association in Korean adults using data from the Korea National Health and Nutrition Examination Survey (KNHANES), a nationally representative survey conducted in the Republic of Korea.

Abbreviations: C, Cholesterol; HDL-C, High Density Lipoprotein Cholesterol; LDL-C, Low Density Lipoprotein Cholesterol; OR, Odds Ratio; CI, Confidence Interval; BMI, Body Mass Index

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2. Materials and methods

2.1. Study population

This study was based on data from the 2005, 2008, and 2009 KNHANES, which were provided by the Korea Centers for Disease Control and Prevention. The sample for KNHANES was selected using a stratified, multistage, cluster-sampling design with proportional allocation based on the National Census Registry. Six hundred sampling units were randomly sampled, and 5974 adults aged 20 years or older were randomly and proportionally selected from these units. Of these 5974 participants, 1826 who did not provide sufficient blood for both lipid and cadmium analysis or had missing responses on the questionnaire were excluded from the analysis. In addition, 245 participants were excluded because they were taking medication for dyslipidemia ($n=219$) or were pregnant ($n=26$). Therefore, the final analysis included a total of 3903 subjects.

2.2. Data collection

The KNHANES included well-established questions to determine the demographic and socioeconomic characteristics of the subjects. These included questions on age, sex, education level, income, physical exercise, smoking habits, and alcohol consumption. Daily energy and nutrient intakes were assessed using 24-h recall and food-intake frequency methods. Height and weight were measured with the participants wearing light clothing and no shoes. Body mass index (BMI) was then calculated as weight (in kilograms) divided by the square of height (in meters).

Blood samples were collected by venipuncture after 10–12 h of fasting. Then, total C, HDL-C, and triglycerides were measured by enzymatic methods with commercially available kits [Bayer Diagnostics or Sekisui Medical (formerly Daiichi)] within 2 h of blood sampling. Cadmium was quantified by Zeeman effect graphite furnace atomic absorption spectrophotometry (Perkin-Elmer AAnalyst 600, Turku, Finland) with a detection limit of approximately 0.30 μg/L. Individuals whose blood concentration fell below the detection limit were assigned a value of the detection limit divided by the square root of 2 (Glass and Gray, 2001). Details of the cadmium analysis have been reported previously (Eum et al., 2008; Lee et al., 2011). For the internal quality assurance and control program, standard reference material was obtained from Bio-Rad (Lyphochek® Whole Blood Metals Control; Hercules, CA, USA) and the coefficient of variation was 14.5% for blood cadmium. External quality control was achieved via participation in an international program set up by the German External Quality Assessment Scheme (G-EQUAS). All blood analyses were carried out by a laboratory certified by the Korean Ministry of Health and Welfare.

The study protocol was approved by the Korean Ministry of Health and Welfare and was conducted in accordance with the Ethical Principles for Medical Research Involving Human Subjects, as defined by the Helsinki Declaration. All study participants provided written informed consent.

2.3. Variable definitions

Dyslipidemia included three lipid abnormalities: decreased HDL-C levels, and increased LDL-C and triglyceride levels. According to the cutoff values for plasma lipids established by the Adult Treatment Panel III guidelines published by the US National Institutes of Health (NCEP, 2002), a low HDL-C level was defined as <40 mg/dL for men and <50 mg/dL for women, a high LDL-C level was defined as ≥ 130 mg/dL, and a high triglyceride level was defined as ≥ 150 mg/dL. LDL-C levels were calculated using the Friedewald formula when triglyceride levels were ≤ 400 mg/dL and were measured directly with commercially available kits (Cholestest® LDL; Sekisui Medical, Tokyo, Japan) when these levels were >400 mg/dL. In addition, the ratio of triglycerides to HDL-C was used as a measure of dyslipidemia, because a ratio greater than 3.8 is known to correlate with LDL-C phenotype B, which is a reliable predictor of the risk of cardiovascular disease (Hanak et al., 2004; Welsh et al., 2010).

As a covariate, education level was categorized as less than a high school diploma, high school diploma, and college or higher. Alcohol consumption was assessed by questioning the subjects about their drinking behavior during the month before the interview. The subjects were asked about their average frequency and amount of alcoholic beverage intake. The average amount and number of alcoholic beverages consumed were converted into the amount of pure alcohol (ethanol) consumed per day.

2.4. Statistical analysis

Means and standard deviations (SDs) or standard errors (SEs) of the demographic and dietary characteristics were calculated according to the quintile of blood cadmium concentration. Estimate statements in linear regression models were used to determine the adjusted mean and 95% confidence intervals (CIs) of each lipid measure with increasing cadmium level. For triglyceride level, based on a normal probability plot, geometric means were used to improve the approximation of a normal distribution. The prevalences of dyslipidemia measures were compared among quintiles of blood cadmium concentration using multivariate logistic regression after adjusting for potentially confounding variables. The presence of a linear trend was evaluated by defining a linear contrast in each linear and logistic regression model. All statistical analyses were conducted using SAS software (version 9.2; SAS Institute, Inc., Cary, NC, USA).

3. Results

This study included 3903 adults aged 20 years or older; their demographic characteristics are presented in Table 1. Mean age, mean BMI, and geometric mean blood cadmium levels of the study population were 46.0 years, 23.7, and 1.16 μg/L, respectively. The basic characteristics and outcomes of the study participants sorted by quintile of blood cadmium concentration are presented in Table 2. As blood cadmium level increased, participants were more likely to be female (p for trend $=0.003$), have a low education level (p for trend <0.001), and participate in less regular physical exercise (p for trend $=0.040$). In addition, blood cadmium level was correlated positively with age (p for trend <0.001), BMI (p for trend $=0.001$), and the amounts of cigarette smoking (p for trend <0.001) and alcohol consumption (p for trend $=0.002$). Average household income and proportion of fat in total energy intake were negatively associated with increased blood cadmium level (p for trend <0.001).

The trends in age- and sex-adjusted mean total C and LDL-C levels were not significantly related to increased blood cadmium concentration, whereas age- and sex-adjusted mean HDL-C, geometric mean triglycerides, and triglyceride to HDL-C ratios were significantly correlated with increased blood cadmium concentration (Table 3). Age- and sex-adjusted mean HDL-C levels were lower among participants with higher blood cadmium concentrations (p for trend <0.001). However, among quintile blood cadmium groups, age- and

Table 1
Demographic characteristics of participants in the Korean population aged 20 years or older.

Characteristics	*N*	%
Sex		
Male	1806	46.3
Female	2097	53.7
Age (years)		
20–39	1491	38.2
40–59	1596	40.9
≥60	816	20.9
BMI		
<18.5	180	4.6
18.5–22.9	1518	38.9
23–25	970	24.9
>25	1235	31.6
Education		
<High school	1295	33.2
High school	1286	32.9
> high school	1322	33.9
Average household income (US$/month)		
<910	1009	25.8
910–1818	1023	26.2
1819–2728	865	22.2
>2728	1006	25.8
Regular exercise		
Yes	2148	55.0
No	1755	45.0
Cigarette smoking		
Never	2199	56.3
Past smoker	771	19.8
Current smoker	933	23.9
Alcohol consumption (g/day)		
0	1367	35.0
>0–5.0	1264	32.4
>5.0	1272	32.6