International Journal of Hygiene and Environmental Health 216 (2013) 467–471

Contents lists available at SciVerse ScienceDirect

International Journal of Hygiene and Environmental Health

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

Association between urinary concentrations of bisphenol A and type 2 diabetes in Korean adults: A population-based cross-sectional study

Kisok Kim[a,*], Hyejin Park[b]

[a] Department of Pharmacy, Keimyung University, Daegu, Republic of Korea
[b] Department of Epidemiology and Health Promotion, Kyungpook National University, Daegu, Republic of Korea

ARTICLE INFO

Article history:
Received 14 February 2012
Received in revised form 6 July 2012
Accepted 26 July 2012

Keywords:
Bisphenol A
Type 2 diabetes
KNHBS
Demographic characteristics

ABSTRACT

Bisphenol A (BPA) is a synthetic phenolic compound to which the general public may be exposed via consumer products and environmental contamination. We assessed the association between urinary BPA concentration and the prevalence of type 2 diabetes. This cross-sectional study included Korean adult participants ($n = 1210$) aged 40–69 years and was based on the 2009 Korean National Human Biomonitoring Survey. Demographic characteristics and medical history of type 2 diabetes were collected from the participants by questionnaire, and BPA levels were determined by analysis of urine samples. The mean age of the participants was 53.4 years and 41.6% were men; the prevalence of type 2 diabetes differed according to demographic characteristics. The geometric mean urinary BPA levels of participants with and without type 2 diabetes were 2.03 and 2.40 ng/mL, respectively. Among BPA quartiles, no clear association was found between BPA levels and type 2 diabetes. Although the adjusted odds ratio of type 2 diabetes was slightly increased for participants in the upper BPA quartile, the association was not statistically significant. These findings suggest that a high body BPA burden may not be associated with an increased prevalence of type 2 diabetes in Korean adults.

Introduction

Bisphenol A (2,2′-bis[4-hydroxyphenyl]propane; BPA) is one of the chemicals produced in the greatest volume worldwide, with over 6 billion pounds produced and over 100 tons released into the atmosphere each year (Vandenberg et al., 2009). BPA is the base compound for the manufacture of polycarbonate plastic and epoxy resins, which are used in baby bottles, water bottles, food storage containers, and dental sealants (Arenholt-Bindslev et al., 1999; Calafat et al., 2005; Howe et al., 1998; Sajiki and Yonekubo, 2003). BPA has also been detected in a variety of food and environmental substances, including water, wastewater, indoor and outdoor air, and dust (Loganathan and Kannan, 2011; Tsai, 2006; Vandenberg et al., 2007).

Low BPA doses have shown hormone-like effects and toxicities on the brain, reproductive system, and metabolic processes, including alterations in insulin homeostasis, in animal models (Cabaton et al., 2011; Richter et al., 2007; Salian et al., 2011). Several animal studies have suggested that exposure to BPA may contribute to or exacerbate the development of type 2 diabetes (Alonso-Magdalena et al., 2005; Ropero et al., 2008). However, findings from epidemiologic studies of the association between BPA and type 2 diabetes have been less consistent; recent population-based studies of data from the US National Health and Nutritional Examination Survey (NHANES) found that US adults with higher BPA levels were more likely to have diabetes (Lang et al., 2008; Shankar and Teppala, 2011). However, a study of Chinese adults did not confirm this association (Ning et al., 2011). Race/ethnicity may be an important source of variation; for example, no report has found a correlation between BPA exposure and type 2 diabetes among Korean adults, based on a nationwide survey. In addition, the urinary BPA concentration of Koreans was reported to be higher than those of people from several other Asian countries, including China, India, and Japan (Zhang et al., 2011). Therefore, the aim of this study was to investigate this association in Korean adults using data from a nationwide survey.

Materials and methods

Study population

This population-based, cross-sectional survey was conducted between August and September 2009 and included

Abbreviations: BMI, body mass index; BPA, bisphenol A; CI, confidence interval; OR, odds ratio.

* Corresponding author at: Department of Pharmacy, Keimyung University, 1000 Shindang-dong, Daegu 704-701, Republic of Korea. Tel.: +82 53 580 5932; fax: +82 53 580 5164.
E-mail address: kimkisok@kmu.ac.kr (K. Kim).

1438-4639/$ – see front matter © 2012 Elsevier GmbH. All rights reserved.
http://dx.doi.org/10.1016/j.ijheh.2012.07.007

biomonitoring for exposure to a range of environmental chemicals among the adult population (18–69 years of age) of the Republic of Korea. Participants were recruited by census block – stratified, multistage cluster sampling based on the National Census Registry. The number of census blocks was determined by the population of each city, and 100 census blocks were then selected randomly. Of the selected subjects in the census blocks, 1870 individuals completed interviews without missing data and provided urine samples (87.4% overall response rate). For this type 2 diabetes study, we restricted participation to those aged 40 and over ($n = 1210$). The study was supervised by the Korean Food and Drug Administration, and the study protocol was approved by the Asan Medical Center (Seoul, Korea) Institutional Review Board and conducted in accordance with the ethical principles for medical research involving human subjects, as defined by the Helsinki Declaration. Study participants provided written informed consent.

Data collection

Selected subjects were invited to a public health centre in the designated census block for an interview and collection of a urine sample. Data were gathered about participants' sex, age, education, income, cigarette smoking, and current residence in face-to-face interviews. Height and weight were measured while subjects were wearing light clothing and no shoes. Body mass index (BMI) was calculated as weight (in kilograms) divided by height (in metres squared). Spot urine samples were collected at different times throughout the day and creatinine levels were used to correct for urine dilution. The criteria for type 2 diabetes were based on self-reported and doctor-diagnosed type 2 diabetes. Education was categorised as less than a middle-school diploma, and high school or higher. Monthly household income was categorised as <1 million Korean won (1150 KRW is approximately equal to one US dollar), 1–3 million Korean won, and >3 million Korean won. Subjects were classified as underweight ($BMI < 18.5$), normal weight ($18.5 \leq BMI < 23.0$), overweight ($23.0 \leq BMI < 25.0$), or obese ($BMI \geq 25.0$) according to the World Health Organization (WHO) definitions for Asian populations. The sample was also divided into "never" and "ever" groups according to cigarette smoking history.

Analysis of BPA

Analyses of urine samples were performed at the Korean Institute of Science and Technology (Seoul, Korea) using a method combining liquid–liquid extraction and gas chromatography (GC) coupled with mass spectrometry (MS) (Kim et al., 2011). In brief, urine samples were thawed at room temperature and vortex mixed. Next, 2 mL aliquots were transferred to tubes and spiked with 10 μL BPA-d_{16} (1 μg/mL). After gentle mixing, samples were added to 50 μL glucuronidase/arylsulfatase solution (in 0.2 M sodium acetate buffer, pH 5.2), and hydrolysis was allowed to proceed at 55 °C for 3 h. After cooling to room temperature, the samples were added to a 5% K_2CO_3 solution and extracted with methyl tert-butyl ester. The dried extracts were then derivatised with 50 μL bis-(trimethylsilyl) trifluoroacetamide/trimethylchlorosilane (100:1, v/v) mixture at 60 °C for 30 min. Samples were analysed using GC–MS systems with GC and mass-selective detectors (Models 6890 and 5975; Agilent Technologies Inc., Wilmington, DE, USA) connected to an Ultra-2 column (25 m × 0.2 mm internal diameter, 0.33 μm film thickness; Agilent Technologies Inc.).

Linearity was checked from 0.1 ng/mL to 200 ng/mL with a correlation coefficient of 0.997. Recovery was performed by adding known amounts of the standards to achieve concentrations of 87.4–109.0%. The intra- and inter-day accuracy and precision were investigated by determining the analyte in the seven replicates during a single day and by duplicating the experiments for 5 consecutive days. The intra-day accuracy was 91.2–114.5% with a precision of 5.2–11.2%, and inter-day accuracy was 96.4–108.4% with a precision of 3.8–6.7%. The limit of detection (LOD) and limit of quantification (LOQ) under the chromatographic conditions were determined at signal-to-noise ratios (S/N) of 3 and 10, respectively. The LOD was 0.05 ng/mL and the LOQ was 0.20 ng/mL. Individuals ($n = 33$) whose urinary concentrations fell below the LOD were assigned a value of LOD/2 (Cole et al., 2009).

Statistical analyses

Geometric means with 95% confidence intervals (CIs) for urinary BPA concentrations were calculated by taking the antilog of the mean of the natural log-transformed values. Based on a normal probability plot, geometric means were used to improve the approximation of a normal distribution. Estimate statements in the linear regression model were used to determine the adjusted geometric mean of urinary BPA. Among quartiles of urinary BPA concentration, odds ratios (ORs) with 95% CIs for the prevalence of type 2 diabetes compared with the reference were calculated using multivariate logistic regression analysis after adjusting for potentially confounding variables. We evaluated the differences in categorical variables between groups using the Mantel–Haenszel chi-squared test. The difference between normal and type 2 diabetes subgroups in mean values and the presence of a linear trend among quartiles of urinary BPA subgroups was evaluated by a survey t-test and by defining a linear contrast in each of the general linear models, respectively. All statistical analyses were conducted using SAS software (ver. 9.2; SAS Institute, Inc., Cary, NC, USA).

Results

This study included a total of 1210 eligible subjects aged 40–69 years. The mean age of participants was 53.4 years and 41.6% of the sample was male. The prevalence of type 2 diabetes by demographic characteristics is presented in Table 1. A total of 99 participants had been diagnosed with type 2 diabetes; the prevalence of type 2 diabetes was correlated positively with age ($p < 0.001$) and BMI ($p = 0.001$), and associated negatively with education level ($p < 0.001$) and household income ($p < 0.001$). Cigarette smoking and place of residence were not significantly associated with the prevalence of type 2 diabetes.

The geometric mean urinary BPA concentrations in Korean adults aged 40–69 years were 2.03 ng/mL (95% CI, 1.92–2.14 ng/mL) among those not diagnosed with type 2 diabetes and 2.40 ng/mL (95% CI, 2.04–2.82 ng/mL) among those diagnosed with type 2 diabetes (Table 2). Urinary BPA levels in non-diabetic and diabetic participants were similar across population subgroups. However, in females and participants aged 50–59 years, urinary BPA levels were significantly higher in type 2 diabetes groups than in normal participants ($p < 0.05$). In addition, BPA levels of urban residents were significantly higher in those who reported diagnoses of type 2 diabetes ($p = 0.013$). Though the difference was not statistically significant, after adjustment for age and sex, mean BPA concentrations appeared higher in those who reported diagnoses of type 2 diabetes (Fig. 1).

Table 3 shows the prevalence and ORs for the association of type 2 diabetes risk with quartiles of urinary BPA levels. The prevalence and ORs of type 2 diabetes revealed no clear association with BPA levels. Although the OR of type 2 diabetes increased with urinary BPA concentration in both crude (model 1) and adjusted (models 2–4) models, this trend was not statistically significant.