URINARY BISPHENOL A LEVELS AND EXPOSURE ASSESSMENT IN THE KOREAN POPULATION

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Introduction

Bisphenol A (BPA) is a high-volume industrial chemical used in the global production of polycarbonate plastics and epoxy resins, which are used in food and drink containers as well as baby bottles[1]. Due to its broad applications, BPA has been detected in human blood, urine and breast milk as well as environmental substances, including water, indoor and outdoor air, and dust[2-3]. Indeed, exposure to high concentrations of BPA can result in a variety of harmful effects, including reproductive toxicity through an endocrine disruption mechanism[4-7]. In this study, we estimated the representative BPA concentrations in urine of the Korean population and attempted to elucidate the demographic characteristics potentially influencing its concentrations. We also evaluated BPA exposure from estimated daily intakes through food and urinary BPA concentrations.

Materials and methods

Study subjects. The Korean Research Project on Integrated Exposure Assessment to Hazardous Materials for Food Safety (KRIEFS) project was performed by the Ministry of Food and Drug Safety (MFDS) from 2010 to 2012, and was a nationwide study that evaluated integrated exposure to hazardous materials through the intake of foods, oriental medicine, and health supplements. The survey categorized the subject based on ages like adult, child and adolescent, and infants. For the adults, minimum numbers of samples were allotted according to regions, gender, and ages to extract them using a method of square root percentage quota based on distribution ration of population. Meanwhile, for child and adolescent, and infants, the survey employed a cluster sampling method centering on schools or organizations in three of four main areas by each city.

The subjects were individually interviewed by trained technicians using standard protocols. A questionnaire was developed for this study that included questions on age, education, income, smoking status, alcohol consumption and dietary intake

Exposure assessment. The exposure has been assessed by the estimated exposure from urinary BPA, 24-hour recall (24HR) and food frequency questionnaire (FFQ). To analysis the estimated BPA exposure, we used a unit dose of BPA associated with the 24-h average urinary BPA concentration[8]. For the analysis of food group intakes of the 24HR and FFQ, we used 12 food categories (Grains, Sugars, Beans, Vegetables, Fruits, Meats, Fish and

Table 1. Demographic characteristics in the study subjects

Variables	N[a]	% (95% CI)
Sex	2044	
Male	993	48.58 (46.41-50.75)
Female	1051	51.42 (49.25-53.59)
Age group (years)	2044	
0 – 2	82	4.01 (3.16-4.86)
3 – 6	417	20.40 (18.65-22.15)
7 – 12	258	12.62 (11.18-14.06)
13 – 18	215	10.52 (9.19-11.85)
19 – 29	196	9.59 (8.31-10.87)
30 – 39	223	10.91 (9.56-12.26)
40 – 49	230	11.25 (9.88-12.62)
50 – 59	236	11.25 (10.16-12.93)
60 ≤	187	9.15 (7.90-10.40)
Education[b]	1076	
< High school	274	25.46 (22.86-28.07)
= High school	372	34.57 (31.73-37.42)
> High school	430	39.96 (37.03-42.89)
Household income (US $/month)	1926	
< 2,000	550	28.56 (26.84-30.58)
2,000 – 3,000	481	24.97 (23.04-26.91)
3,000 – 4,000	428	22.22 (20.36-24.08)
> 4000	467	24.25 (22.33-26.16)
Smoking status[c]	1256	
Never smoker	861	68.55 (65.98-71.12)
Former smoker	160	12.74 (10.89-14.59)
Current smoker	235	18.71 (16.55-20.87)
Alcohol consumption[c]	1260	
< 1 time per week	734	58.25 (55.53-60.98)
1 time per week	275	21.83 (19.54-24.04)
2 – 3 times per week	166	13.17 (11.30-15.04)
≥ 4 times per week	85	6.75 (5.36-8.13)

[a]Sample size; [b]Includes subjects > 18 years old; [c]Includes subjects > 12 years old

shells, Milk and dairy products, Beverages, Alcohol Drinks, Seasonings and Seaweeds). BPA intake was calculated by 95th percentile BPA concentration in each item.

Statistical analyses. Statistical analyses were performed using the software Stata 12.0 (StataCorp, College Station, Texas). We calculated geometric means (GMs) with 95% confidence intervals (CIs) for urinary BPA. We also used minimum, maximum and 95 percentile values to describe the distributions of BPA. The comparison of means was performed by Student's t test or ANOVA following multiple-comparison tests using the Duncan's method. Multiple regression analyses were performed to determine the influencing factors for urinary BPA.

Results and discussion

Table 1 shows demographic characteristics of the subjects who had their urinary BPA concentrations measured. This study included a total of 2044 eligible subjects. The subjects were evenly divided between males and females (48.58% and 51.42%, respectively). Approximately75% in adults had at least received a high school education and approximately 72% of the subjects had a monthly household income of > $2,000.

Creatinine pre-adjusted and adjusted urinary BPA concentrations are shown in Table 2. The GM of pre-adjusted (adjusted) urinary BPA concentrations was 1.83 μg/L (2.01 μg/g creatinine) in overall age, and there was no statiscal difference (pre-adjusted p=0.1289; adjusted p=0.9186, respectively) of BPA concentrations among male

Table 2. Geometric mean (95% CI) of urinary BPA concentrations by demographic characteristics

Variables	Creatinine pre-adjusted (μg/L)	Creatinine adjusted (μg/g creatinine)	Creatinine (mg/dL) GM (95% CI)
Total	1.83 (1.75-1.91)	2.01 (1.93-2.11)	0.91 (0.89-0.93)
Sex			
Male	1.90 (1.78-2.03)	1.87 (1.74-2.01)	1.02 (0.98-1.05)
Female	1.76 (1.66-1.87)	2.16 (2.04-2.28)	0.82 (0.79-0.85)
p value	0.1289	0.9186	
Age group (years)			
0 – 2	3.79 (2.89-4.97)	7.33 (5.70-9.42)	0.52 (0.47-0.57)
3 – 6	2.98 (2.71-3.28)	4.03 (3.70-4.40)	0.74 (0.71-0.77)
7 – 12	1.88 (1.68-2.11)	2.09 (1.88-2.32)	0.90 (0.85-0.96)
13 – 18	1.73 (1.55-1.92)	1.20 (1.07-1.34)	1.44 (1.34-1.55)
19 – 29	1.94 (1.67-2.26)	1.55 (1.37-1.76)	1.25 (1.15-1.36)
30 – 39	1.49 (1.30-1.70)	1.60 (1.40-1.82)	0.94 (0.87-1.01)
40 – 49	1.31 (1.15-1.49)	1.41 (1.26-1.59)	0.93 (0.86-0.99)
50 – 59	1.34 (1.19-1.51)	1.58 (1.41-1.76)	0.85 (0.79-0.91)
60 ≤	1.23 (1.08-1.41)	1.53 (1.33-1.74)	0.81 (0.75-0.87)
p value	< 0.0001	< 0.0001	
Education[a]			
< High school	1.22 (1.09-1.36)	1.47 (1.31-1.65)	0.83 (0.78-0.88)
= High school	1.39 (1.24-1.55)	1.62 (1.45-1.79)	0.86 (0.82-0.91)
> High school	1.65 (1.51-1.80)	1.50 (1.39-1.62)	1.10 (1.04-1.16)
p value	0.3436	0.0495	
Household income (US $/month)			
< 2,000	1.69 (1.55-1.84)	1.88 (1.73-2.04)	0.90 (0.86-0.94)
2,000 – 3,000	1.90 (1.72-2.09)	2.23 (2.02-2.46)	0.85 (0.81-0.89)
3,000 – 4,000	2.11 (1.91-2.32)	2.26 (2.05-2.50)	0.93 (0.88-0.99)
> 4000	1.78 (1.63-1.93)	1.82 (1.67-1.98)	0.97 (0.93-1.03)
p value	0.1202	0.0046	
Smoking status[b]			
Never smoker	1.48 (1.39-1.57)	1.51 (1.43-1.60)	0.98 (0.94-1.02)
Former smoker	1.39 (1.19-1.64)	1.29 (1.10-1.51)	1.08 (1.00-1.17)
Current smoker	1.45 (1.27-1.66)	1.40 (1.24-1.59)	1.03 (0.96-1.11)
p value	0.8371	0.5741	
Alcohol consumptio[b]			
< 1 time per week	1.51 (1.40-1.62)	1.49 (1.39-1.59)	1.02 (0.97-1.06)
1 time per week	1.35 (1.20-1.51)	1.39 (1.27-1.54)	0.97 (0.90-1.04)
2 – 3 times per week	1.58 (1.39-1.80)	1.54 (1.37-1.74)	1.02 (0.94-1.11)
≥ 4 times per week	1.32 (1.02-1.71)	1.34 (1.02-1.76)	0.98 (0.88-1.10)
p value	0.4306	0.4259	

[a]Includes subjects > 18 years old; [b]Includes subjects > 12 years old

(1.90 μg/L, 1.87 μg/g creatinine) and female (1.76 μg/L, 2.16 μg/g creatinine). The levels of urinary BPA decreased according to the age groups (p<0.0001). Urinary BPA concentration was highest in these aged 0-2 (3.79 μg/L, 7.33 μg/g creatinine). However, there was no statiscal difference of urinary BPA levels according to education, household income, smoking status and alcohol consumption (Table 2). In creatinine adjusted BPA concentrations, there were statistically significant differences according to the age group, education and income ($p < 0.05$)

Multi regression analysis revealed a positive association between creatinine pre-adjusted urinary BPA concentration and age ($\beta = -0.0868$, $p < 0.001$) after adjusteing for the other covariates, whereas there was no significant association between creatinine adjusted urinary BPA concentration and covariates (Table 3).

Table 3. Contributing factors to urinary BPA levels by multiple regression analysis in the study subjects

Variables[a]	Creatinine pre-adjusted		Creatinine adjusted	
	β	*p* value	*β*	*p* value
Sex	- 1.1252	0.107	- 0.0616	0.923
Age	- 0.0868	< 0.001	- 0.0362	0.087
Education[b]	- 0.2696	0.128	- 0.1032	0.522
Household income	- 0.0471	0.688	- 0.0201	0.851
Smoking status[c]	- 0.2567	0.525	- 0.2672	0.467
Alcohol consumption[c]	- 0.5291	0.079	- 0.3228	0.239
	$R^2 = 0.0188$		$R^2 = 0.0063$	

[a]Sex (1=male and 2=female), age (years), education (1=below high school, 2=high school and 3=over high school), income (1=below $2,000, 2=$2,000 to $3,000, 3=$3,000 to $4,000 and 4=above $4,000), smoking (1=never smoker, 2=former smoker and 3=current smoker), alcohol consumption (1=below 1 time per week, 2=1 time per week, 3=2~3 times per week and 4=above 4 times per week); [b]Includes respondents > 18 years old; [c]Includes respondents > 12 years old

Table 4 shows estimated daily BPA intakes through food and urinary BPA concentrations. In 24HR and FFQ, we used 12 food categories and 95th percentile BPA concentration in each item. To assess the BPA exposure estimated with urinary BPA concentrations, we converted urinary BPA concentration into the daily BPA intake by using a unit dose of BPA associated with the 24-h average urinary BPA concentration. In overall ages, GM (95th percentile) BPA exposures in 24HR, FFQ and estimation through urinary BPA concentrations were 0.023 (0.140), 0.032 (0.130) and 0.045 (0.215) μg/kg bw/day, respectively. No difference was observed between male and female. Even conservatively estimated BPA exposures were lower than 1% of European Food Safety Authority (EFSA) tolerable daily intake (TDI) 50 μg/kg bw/day. When age was treated as a categorical variable, GM of BPA exposure exhibited a decrease with age (Fig. 1). The maximum levels of 24HR, FFQ and estimation through urinary BPA concentrations were 0.735, 0.607 and 4.824 μg/kg bw/day, respectively. These exposure levels also were lower than EFSA TDI

Table 4. The evaluations of BPA exposure through dietary intake and estimated with urinary BPA concentrations (unit: . μg/kg bw/day)

	24-h Recall[b]		FFQ[c]		Estimation[a]		*p* value	EFSA TDI[c] (%)
	GM (95% CI)	95th	GM (95% CI)	95th	GM (95% CI)	95th		
Total	0.023 (0.022-0.024)	0.140	0.032 (0.031-0.033)	0.130	0.045 (0.043-0.047)	0.215	< 0.0001	0.090 (0.43)
Male	0.022 (0.021-0.024)	0.131	0.031 (0.029-0.033)	0.128	0.045 (0.042-0.048)	0.218	< 0.0001	0.090 (0.44)
Female	0.024 (0.022-0.025)	0.141	0.033 (0.031-0.035)	0.130	0.046 (0.043-0.049)	0.213	< 0.0001	0.092 (0.43)
p value	0.1233		0.1080		0.5305			

[a]24-hour diet recall; [b]Food Frequency Questionnaire; [c]50 μg/kg bw/day, compared with GM (95th) of estimated BPA exposure

Overall, BPA exposure is well below the current TDI of 50 μg/kg bw/day. However, children ages 0-6 are higher than the other ages. This trend may be explained in relation to possible BPA exposure route of each age group. Children's mouthing of PVC containing toys and other plastic materials may be the cause of high concentration of BPA in urine[9-10].

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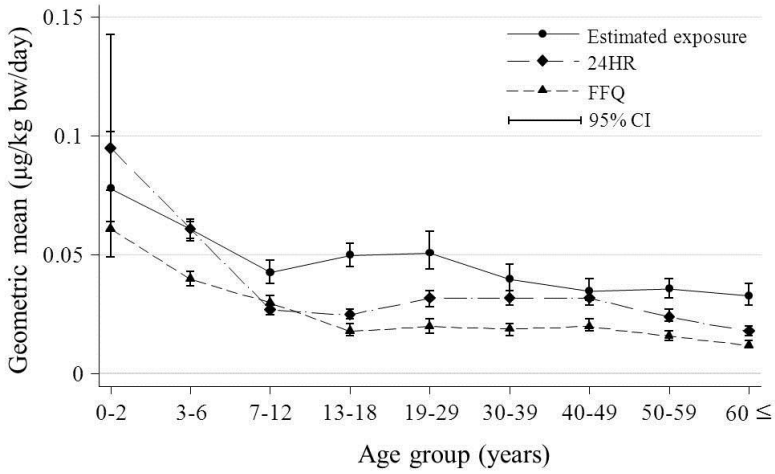

Fig 1. Differences in the age-related changes in BPA exposure

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