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The relationship between urinary BTEX metabolites and residence setting among Korean homemakers: the first Korea National Environmental Health Survey (2009–2011)

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Abstract

Background: Benzene, toluene, ethylbenzene, and xylene (BTEX) are emitted in the combustion or volatilization of hazardous wastes and fossil fuels. Paint, varnishing agents, and cigarette smoke are also sources of BTEX in living environments. Few studies have examined indoor exposure to BTEX using biomarkers, especially in residential settings. In this study, we evaluated the relationship between residence factors and BTEX exposure using biomarkers among Korean homemakers.

Method: We obtained data on 893 non-smoking homemakers older than 19 years from the Korean National Environmental Health Survey (2009–2011). The concentrations of urinary BTEX metabolites (*t*,*t*-muconic acid, hippuric acid, mandelic acid, phenylglyoxylic acid, and total methylhippuric acid) were adjusted using the urinary creatinine. Analysis of covariance (ANCOVA) and logistic regression analysis were used to evaluate the associations between residence parameters and urinary BTEX metabolites.

Results: The geometric mean concentrations of *t*,*t*-muconic acid and methylhippuric acid were significantly higher in the group that had remodeled within the previous 6 months ($p < 0.05$) compared with the no-remodeling group. In logistic regression analyses, the odds ratio for exceeding the median urinary concentration of *t*,*t*-muconic acid was significantly higher in the group that had remodeled compared with the no-remodeling group (OR = 1.591, 95% CI = 1.063–2.382). Urinary methylhippuric acid was significantly associated with residing in a home located within 100 m of a major road (OR = 1.399, 95% CI = 1.071–1.826).

Conclusion: Our study found some significant associations between urinary BTEX metabolites and residence parameters. To find clear associations, additional and more detailed studies are needed.

Trial registration: Not applicable (this study does not include healthcare intervention on human participants).

Keywords: BTEX, Homemakers, Residential settings, Volatile organic compounds

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Background

Benzene, toluene, ethylbenzene, and xylene (BTEX) constitute a subgroup of volatile organic compounds (VOCs) that are used widely in various industries. BTEX is emitted to the environment through the combustion or volatilization of hazardous wastes and fossil fuels [1, 2]. Paint, varnishing agents, and cigarette smoke are sources of BTEX in the home environment [3–5]. The annual worldwide emissions of BTEX to ambient air comprise approximately 34,000 tons of benzene, 11,000 tons of toluene, 2081 tons of ethylbenzene, and 16,000 tons of xylene [6–9].

The hazardous health effects of occupational exposure to BTEX are recognized. The International Agency for Research on Cancer classified benzene as a carcinogen in humans (group 1) causing leukemia [6, 10]. Toluene and xylene have neurotoxic effects, causing neuropathy and psychosomatic symptoms [7, 9, 11, 12]. Acute exposure to high levels of ethylbenzene produces various neurobehavioral symptoms, suggesting central nervous system depressing effects [8, 13, 14]. Non-occupational exposure to BTEX produces another spectrum of health effects. Chronic low-dose exposure to BTEX can cause symptoms such as nausea, cough, wheezing, or worsening asthma [15, 16]. Studies of the occupants of newly built houses found that benzene, toluene, and ethylbenzene increased the odds of developing skin problems such as eczema and atopy [17, 18].

Some researchers have stated that residence setting and the indoor air concentration of BTEX are closely related. An epidemiological study conducted in Canada reported that the indoor air concentration of VOCs including BTEX differed significantly with residence factors such as dwelling type, home renovations, presence of a garage, and smoking status [4]. Other studies of residences reported that the indoor air BTEX concentration is affected by residence factors such as the age of the building, height of the living area, and recent remodeling [19, 20].

These studies demonstrated the possibility of BTEX exposure in the indoor environment by measuring the indoor air concentrations of BTEX. However, indoor exposure to BTEX has not been well studied using biomarkers, especially in relation to residential settings. In this study, we evaluated the relationship between residence factors and the exposure of homemakers to BTEX using biomarkers.

Methods

Study participants

We analyzed data from the first Korean National Environmental Health Survey (KNEHS), which was conducted by the National Institute of Environmental Research (NIER) from 2009 to 2011. The survey was based on national population data from 2005 and a housing census. The study enrolled 6311 participants from 350 districts that were selected in proportion to the distribution of population. Data were collected through interviews and biological sample collection. For this study, we included all subjects who were homemakers and current non-smokers (n = 1406). All subjects were female. Subjects who did not respond to the relevant questions (n = 82) and those who had outlier BTEX concentrations (n = 314) were excluded. Subjects with outlier urinary cotinine-creatinine ratio (CCR) values were also excluded to rule out the effect of environmental tobacco smoke (n = 117). Ultimately, 893 subjects were included in the analysis.

Variables of interest

In this study, age, body mass index (BMI) and monthly household income during the previous year were included as demographic characteristics. Housing parameters include the type of residence, age of the building, recent remodeling, and distance from a major road. Residence type was categorized as 'detached house' or 'multiplex or apartment.' The age of the building was divided into five groups: ≤5, 6–10, 11–15, 16–20, and >20 years. Remodeling was categorized into two groups: 'remodeling in the past 6 months' and 'no remodeling within 6 months.' The distance of the residence from a major road was grouped into two groups: 'within 100 m' and 'more than 100 m away.'

Urinary BTEX metabolites and cotinine

All urinary BTEX metabolites were measured by high-performance liquid chromatography–mass spectrometry (HPLC-MS). Seven BTEX metabolites were included: *t,t*-muconic acid (benzene), hippuric acid (toluene), mandelic acid (ethylbenzene), phenylglyoxylic acid (ethylbenzene), *o*-methylhippuric acid (xylene), *m*-methylhippuric acid (xylene), and *p*-methylhippuric acid (xylene). Solid-phase extraction was performed for all urinary metabolites. After extraction, all samples were eluted. Calibration curves for all metabolite concentrations were plotted using the standard addition method. In the analysis, the limit of detection (LOD) was 3 μg/L for *t,t*-muconic acid, 0.02 mg/L for hippuric acid, 0.005 mg/L for mandelic acid, 0.006 mg/L for phenylglyoxylic acid, 0.004 mg/L for *o*-methylhippuric acid, 0.0038 mg/L for *m*-methylhippuric acid, and 0.003 mg/L for *p*-methylhippuric acid.

Urinary cotinine was analyzed using gas chromatograph-mass spectrometry (GC-MS). After adding internal standard solution to urinary samples, cotinine was extracted by liquid-liquid-extraction using chloroform. The solution was centrifuged and the supernatant was removed. Subsequently, sodium sulfate was added to eliminate residual water. A calibration curve was drawn using the standard addition method, yielding an LOD of 0.3 μg/L.

The target coefficient (R^2) of the calibration curve was ≥0.995 for internal quality control. Concentrations below the LOD were substituted with the LOD divided by the square root of 2. All urinary sample concentrations were adjusted using urinary creatinine concentration.

Statistical analysis

The geometric means of the urinary BTEX metabolites (*t*,*t*-muconic acid, hippuric acid, mandelic acid, phenylglyoxylic acid, and total methylhippuric acid) were calculated according to the demographic characteristics. The concentrations of all metabolites were log-transformed because the distributions were right skewed. Univariate comparisons between variables were performed with Student's *t*-test and analysis of variance (ANOVA). Analysis of covariance (ANCOVA) was used to adjust for age, BMI, and monthly household income. The adjusted odds ratios (ORs) for exceeding the median of the concentration of each urinary metabolite were calculated to evaluate the association between urinary BTEX metabolites and housing characteristics using logistic regression analyses. The logistic model was adjusted for age, BMI, and household income. IBM SPSS ver. 22 for Windows was used for all statistical analysis.

Results

Table 1 presents the demographic distribution and geometric means of the urinary concentrations of the BTEX metabolites. Significant differences in urinary metabolites by age group were observed for *t*,*t*-muconic acid, hippuric acid, mandelic acid, and phenylglyoxylic acid. The phenylglyoxylic acid concentration was significantly higher in the group with low household income group than in the other groups.

Table 2 summarizes the urinary concentrations of BTEX metabolites according to residence factors. Each metabolite concentration was expressed as the geometric mean and standard error with and without adjusting for age, household income, and BMI. The urinary concentrations of mandelic acid and phenylglyoxylic acid were significantly higher in the detached-house group, but this was not significant after the adjustment. The methylhippuric acid concentration differed significantly with the age of the building, even after the adjustment. The *t*,*t*-muconic acid concentration was significantly higher in the recently remodeled group ($p < 0.05$), and remained higher after the adjustment ($p < 0.05$). The adjusted methylhippuric acid concentration was also significantly higher in the recently remodeled group ($p < 0.05$).

Table 3 shows the ORs for exceeding the median of the urinary metabolite concentration by residence settings.

Table 1 Demographic distributions and geometric mean concentrations of urinary BTEX metabolites

	N (%)	*t*,*t*-Muconic acid (μg/g Cr ± SE)	Hippuric acid (g/g Cr ± SE)	Mandelic acid (mg/g Cr ± SE)	Phenylglyoxylic acid (mg/g Cr ± SE)	Methylhippuric acid (mg/g Cr ± SE)
Total	893 (100)	46.80 ± 2.48	0.25 ± 0.01	0.25 ± 0.01	0.26 ± 0.01	0.30 ± 0.27
Age						
19–29	34 (3.8)	38.72 ± 10.07	0.16 ± 0.07	0.21 ± 0.02	0.25 ± 0.04	0.23 ± 0.10
30–39	221 (24.7)	51.92 ± 5.60	0.21 ± 0.01	0.23 ± 0.01	0.22 ± 0.01	0.31 ± 0.05
40–49	173 (19.4)	51.73 ± 5.47	0.27 ± 0.03	0.25 ± 0.01	0.24 ± 0.01	0.27 ± 0.05
50–59	243 (27.2)	46.49 ± 5.13	0.26 ± 0.02	0.26 ± 0.01	0.28 ± 0.01	0.31 ± 0.05
60–69	177 (19.8)	38.66 ± 4.36	0.27 ± 0.02	0.28 ± 0.02	0.32 ± 0.02	0.34 ± 0.07
≥ 70	45 (5.0)	48.49 ± 9.39	0.33 ± 0.04	0.26 ± 0.03	0.30 ± 0.02	0.29 ± 0.12
p-value		0.009	<0.001	0.001	<0.001	0.319
BMI (kg/m^2)						
< 25	580 (64.9)	45.13 ± 3.00	0.25 ± 0.01	0.25 ± 0.01	0.26 ± 0.01	0.30 ± 0.03
≥ 25	313 (35.1)	50.06 ± 4.37	0.24 ± 002	0.25 ± 0.01	0.28 ± 0.01	0.31 ± 0.04
p-value		0.094	0.462	0.936	0.090	0.631
Monthly household income (million won)						
< 1.5	247 (27.7)	46.68 ± 4.55	0.25 ± 0.02	0.26 ± 0.01	0.31 ± 0.01	0.27 ± 0.05
1.5–2.5	225 (25.2)	44.68 ± 4.60	0.24 ± 0.02	0.25 ± 0.01	0.26 ± 0.01	0.33 ± 0.06
2.5–4	271 (30.3)	51.11 ± 4.92	0.25 ± 0.02	0.25 ± 0.01	0.24 ± 0.01	0.30 ± 0.04
≥ 4	150 (16.8)	42.97 ± 5.90	0.27 ± 0.02	0.25 ± 0.01	0.25 ± 0.01	0.32 ± 0.07
p-value		0.192	0.600	0.585	<0.001	0.316

Abbreviations: *SE* standard error, *BMI* body mass index

Table 2 Geometric mean concentrations of urinary BTEX metabolites by housing characteristics

			t,t-Muconic acid (μg/g Cr ± SE)		Hippuric acid (g/g Cr ± SE)		Mandelic acid (mg/g Cr ± SE)		Phenylglyoxylic acid (mg/g Cr ± SE)		Methylhippuric acid (mg/g Cr ± SE)	
Variable	Category	N (%)	Crude	Adjusted*	Crude	Adjusted*	Crude	Adjusted*	Crude	Adjusted*	Crude	Adjusted*
Type of residence	Detached	214 (24.0)	45.93 ± 5.31	46.85 ± 0.06	0.25 ± 0.02	0.24 ± 0.06	0.27 ± 0.01	0.26 ± 0.04	0.29 ± 0.01	0.28 ± 0.04	0.34 ± 0.05	0.32 ± 0.08
	Multiplex or apartment	679 (76.0)	47.08 ± 2.80	46.81 ± 0.03	0.25 ± 0.01	0.25 ± 0.03	0.25 ± 0.01	0.25 ± 0.02	0.25 ± 0.01	0.26 ± 0.02	0.30 ± 0.03	0.30 ± 0.04
	p-value		0.729	0.991	0.734	0.580	0.018	0.173	0.002	0.179	0.235	0.332
Age of building (years)	≤5	53 (5.9)	54.71 ± 8.02	52.09 ± 0.12	0.21 ± 0.03	0.24 ± 0.12	0.26 ± 0.02	0.28 ± 0.08	0.24 ± 0.03	0.25 ± 0.08	0.40 ± 0.08	0.43 ± 0.15
	6–10	175 (19.6)	46.80 ± 6.02	46.57 ± 0.07	0.23 ± 0.02	0.23 ± 0.07	0.25 ± 0.01	0.25 ± 0.04	0.26 ± 0.02	0.27 ± 0.04	0.23 ± 0.04	0.23 ± 0.09
	11–15	175 (19.6)	43.34 ± 5.29	43.16 ± 0.07	0.25 ± 0.02	0.25 ± 0.07	0.25 ± 0.01	0.26 ± 0.04	0.24 ± 0.01	0.25 ± 0.04	0.33 ± 0.06	0.33 ± 0.08
	16–20	197 (22.1)	48.09 ± 5.17	47.80 ± 0.06	0.26 ± 0.02	0.27 ± 0.06	0.25 ± 0.01	0.25 ± 0.04	0.28 ± 0.01	0.28 ± 0.04	0.30 ± 0.06	0.30 ± 0.08
	≥21	293 (32.8)	46.77 ± 4.49	47.66 ± 0.05	0.25 ± 0.02	0.24 ± 0.05	0.25 ± 0.01	0.24 ± 0.03	0.27 ± 0.01	0.26 ± 0.03	0.32 ± 0.06	0.32 ± 0.07
	p-value		0.528	0.645	0.463	0.593	0.985	0.582	0.062	0.175	0.003	0.001
Distance from major road (meters)	≤100	414 (46.4)	46.91 ± 3.24	46.62 ± 0.04	0.24 ± 0.02	0.24 ± 0.04	0.25 ± 0.01	0.25 ± 0.03	0.25 ± 0.01	0.26 ± 0.03	0.32 ± 0.04	0.32 ± 0.06
	>100	479 (53.6)	46.71 ± 3.55	46.99 ± 0.04	0.25 ± 0.01	0.25 ± 0.04	0.25 ± 0.01	0.25 ± 0.03	0.27 ± 0.01	0.27 ± 0.03	0.29 ± 0.04	0.29 ± 0.05
	p-value		0.944	0.890	0.494	0.754	0.918	0.827	0.087	0.191	0.168	0.143
Recent remodeling (6 month)	No	779 (87.2)	46.91 ± 3.24	45.47 ± 0.03	0.24 ± 0.02	0.25 ± 0.03	0.25 ± 0.01	0.25 ± 0.02	0.25 ± 0.01	0.27 ± 0.02	0.32 ± 0.04	0.29 ± 0.04
	Yes	114 (12.8)	56.56 ± 7.67	56.88 ± 1.09	0.24 ± 0.02	0.24 ± 0.08	0.25 ± 0.01	0.24 ± 0.05	0.26 ± 0.02	0.25 ± 0.05	0.37 ± 0.11	0.37 ± 0.10
	p-value		0.018	0.011	0.739	0.699	0.642	0.590	0.518	0.459	0.059	0.046

*Estimated geometric means and *p*-values were calculated by ANCOVA and adjusted for age, BMI, and monthly income
Abbreviation: *SE* standard error

Table 3 Adjusted odds ratios for exceeding the median of each BTEX metabolite by housing characteristics

Variable	Category	*t,t*-Muconic acid Odds ratio* (95% CI)	Hippuric acid Odds ratio* (95% CI)	Mandelic acid Odds ratio* (95% CI)	Phenylglyoxylic acid Odds ratio* (95% CI)	Methylhippuric acid Odds ratio* (95% CI)
Type of residence	Detached	1	1	1	1	1
	Multiplex or apartment	1.145 (0.807–1.165)	1.171 (0.820–1.672)	0.762 (0.536–1.083)	0.724 (0.507–1.034)	0.814 (0.573–1.156)
Age of building	Years	0.996 (0.983–1.009)	1.002 (0.988–1.015)	0.989 (0.976–1.003)	0.992 (0.979–1.006)	0.998 (0.985–1.012)
Distance from major road (meters)	>100	1	1	1	1	1
	≤100	1.129 (0.865–1.474)	0.970 (0.740–1.272)	1.084 (0.830–1.419)	0.819 (0.625–1.074)	1.399 (1.071–1.826)
Remodeling within past 6 months	No	1	1	1	1	1
	Yes	1.591 (1.063–2.382)	0.864 (0.576–1.295)	1.142 (0.766–1.703)	0.879 (0.586–1.320)	1.294 (0.868–1.930)

*Adjusted by age, BMI, and monthly income
Abbreviation: *CI* confidence interval

The group whose residences were within 100 m of a major road had a significantly higher OR for methylhippuric acid compared with the other group (OR = 1.399, 95% CI = 1.071–1.826). The OR for *t,t*-muconic acid was significantly higher in the recent remodeling than in the no-remodeling group (OR = 1.591, 95% CI = 1.063–2.382).

Discussion

Some researchers have evaluated the relationship between the indoor air VOC concentration and residence parameters, including house type and age of the building. One study found that the indoor concentrations of benzene, toluene, and *o*-xylene were lower in apartments than in other types of housing [21]. Another study reported that the total indoor concentration of VOCs, including toluene, ethylbenzene, and xylene, was higher in buildings less than 5 years old compared with other groups [20]. In our study, there were no significant differences by residence type. When evaluated according to building age, the methylhippuric acid concentration was significantly higher in the ≤5-year group and lower in the 6–10-year group, but no significant trend was identified. Differences in building materials, house heating type, cooking style, seasonal variation, and indoor ventilation behavior may influence these outcomes [22–27].

The road environment was studied as potential source of BTEX. Vehicle-fuel additives and non-fuel exhaust contain BTEX, so the ambient air concentration of BTEX in traffic-dense areas with low vehicle speeds is higher than that in rural or suburban areas [28–30]. In our study, although the geometric mean methylhippuric acid concentration did not differ significantly with the distance from a major road, the odds ratio for methylhippuric acid showed an association. Further studies focusing on the road environment may be able to assess the relationship between residing near the road and BTEX exposure more clearly.

Some studies have reported that remodeling a residence is strongly associated with the indoor air concentration of BTEX because of the building materials used in remodeling. Flooring (polyvinyl chloride, rubber, and vinyl) and walls or ceilings (plastic paneling, vinyl wall coverings, and polystyrene foam insulation) can emit various VOCs [31]. Several experimental studies found that flooring and wallpaper significantly increased the indoor total VOC concentration [5, 19, 32]. According to a study that measured the indoor air pollutant concentrations excluding benzene, the indoor total VOC concentration, including toluene and ethylbenzene, was significantly higher in houses that had been remodeled within the previous year [20]. In another study, the indoor benzene concentration in homes that had been remodeled within the previous year was higher than that in those that had not been remodeled [33]. Consistent with these findings, we found an association with BTEX exposure and recent remodeling. Our results revealed that the geometric mean concentrations of *t,t*-muconic acid and methylhippuric acid were significantly higher in the group who had remodeled within the past 6 months. Furthermore, there was a significant association between urinary *t,t*-muconic acid and recent remodeling status.

Although not included as variables in our study, daily cosmetics usage and diet may affect the concentration of metabolites by direct exposure or by deriving metabolites. Nail products such as nail polish or nail polish remover can emit various VOCs including benzene or toluene, and cause significant exposure in conditions lacking efficient ventilation [23, 34]. Other cosmetics like perfumes, washing agents, and hair dyes contain benzyl alcohol, which is metabolized into benzoic acid and

derives hippuric acid [35, 36]. Topical agents like ointments and medication lotions also include benzyl alcohol and benzoic acid [37, 38]. With regard to dietary factors, processed or fermented foods contain preservatives, including sorbic and benzoic acid. Sorbic acid is metabolized into t,t-muconic acid [39, 40], while benzoic acid, which is contained in a variety of supplements such as soft drinks, dairy products, fruits, and spices, can be metabolized into hippuric acid and act as a confounder [41–43].

The strength of our study is that we evaluated BTEX exposure using biomarkers. Several studies have evaluated BTEX emission by measuring the indoor BTEX concentrations directly [19–21, 33, 44]. Although a study previously assessed urinary VOC metabolites including BTEX according to demographics among the U.S population, the metabolites studied were not analyzed according to residential factors [45]. Unlike these studies, we examined the relationships between biomarker levels and responses to a questionnaire about residence factors to evaluate participants' direct exposure according to residence characteristics.

Our study provides useful information about BTEX exposure in humans, as there are no reference values for BTEX biomarkers with non-occupational exposure. Globally, the World Health Organization has set guidelines for controlling indoor air quality; however, these standards do not include reference values for biomarkers [46]. In Korea, the Indoor Air Quality Control in Public-use Facilities Act was revised in 2014, and it includes air concentration standards for indoor air pollutants, including BTEX [47]. However, the current standards for indoor air pollutants do not reflect the relationship between indoor air quality and its health effect [48].

The lack of detailed questions concerning ventilation in the indoor environment or seasonal and diurnal variations was a limitation of our study. In several studies performed in urban areas of major cities, the VOC concentration of ambient air exhibited diurnal variations associated with traffic densities and other activities such as construction [24, 49]. In a study performed in Hong Kong, overall VOC concentrations were lower during the summer season than the winter season, except for toluene and tetrachloroethene, which suggests seasonal differences in the evaporation behavior of fuel, and that the dispersal of pollutant particles affects ambient air concentrations [49]. Another study analyzed indoor air in recently remodeled apartments and found that the concentration of total VOCs was negatively associated with ventilation conditions [44]. Other experimental and epidemiological studies have found that frequent ventilation and longer ventilation times significantly lower the levels of indoor pollutants [22, 25, 50].

Conclusion

We evaluated the relationship between BTEX exposure and residence characteristics using urinary biomarkers, and found a significant association between urinary *t,t*-muconic acid levels and home remodeling within the past 6 months. Methylhippuric acid levels were associated with the distance from a major road. To find clear associations between BTEX exposure and the residential environment, further studies examining detailed variables such as ventilation conditions, seasonal or diurnal variation, cosmetics usage, and dietary factors are needed.

Abbreviations

BMI: Body mass index; BTEX: Benzene, toluene, ethylbenzene, and xylene; CCR: Cotinine-creatinine ratio; CI: Confidence interval; KNEHS: Korean National Environmental Health Survey; NIER: National Institute of Environmental Research; OR: Odds ratio; VOC: Volatile organic compound

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Availability of data and materials

The datasets analyzed during the current study are available on request at the National Institute of Environmental Research, Environmental Health Research Department, http://www.nier.go.kr/NIER/kor/openapi/getEcoHealth.do?menuNo=14018.

Authors' contributions

HHO, DHK and JYR performed the statistical analyses and drafted the article. HKP and CKL searched and assisted the related references. BCS and KHK supported and advised medical view. All of the authors read and approved the final manuscript.

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Haeundae Paik Hospital (IRB No. 2016–05-015).

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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