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Identifi cation of potential chemical risk factors for renal function among Korean women

Habyeong Kang[1], Sunmi Kim[1], Gowoon Lee[1], Inae Lee[1], Jung Pyo Lee[2,5], Jeonghwan Lee[2], Hyunwoong Park[3], Gyuyeon Choi[4], Kyungho Choi[1]
[1]Department of Environmental Health Sciences, Seoul National University, Korea, Republic of
[2]Department of Internal Medicine-Nephrology, SMG-SNU Boramae Medical Center, Korea, Republic of
[3]Department of Laboratory Medicine, SMG-SNU Boramae Medical Center, Korea, Republic of
[4]Department of Obstetrics and Gynecology, Soonchunhyang University College of Medicine, Korea, Republic of
[5]Department of Internal Medicine, Seoul National Univercity College of Medicine, Korea, Republic of

Objectives: Exposure to environmental pollutants (i.e., heavy metals and melamine) has been revealed to damage kidney function. Recently, endocrine disrupting chemicals (EDCs) such as phthalates and bisphenol A have been also suggested as risk factors for chronic kidney diseases (CKD). So far, however, most studies have associated a limited number of urinary chemicals with CKD. In this study, employing Korean female population aged 20-45 years (n=441), potential chemical determinants of the urinary albumin-to-creatinine ratio (ACR) were identified among multiple urinary EDCs.

Methods: The creatinine-adjusted concentration of each chemical in urine was associated with ACR in a linear model adjusted for relevant covariates (single-pollutant model). Then, chemicals with a significant positive association with ACR in the single-pollutant model were included in a multi-pollutant model to evaluate their association with ACR. As a sensitivity analysis, quartile analyses were performed for the subpopulation with normal kidney function (ACR < 9.71 mg/g) to prevent potential reverse causality due to kidney dysfunction. The analyses were replicated with the specific-gravity-adjusted urinary concentrations of the compounds.

Results: In the single-pollutants model, several urinary compounds were significantly associated with ACR. However, in the multi-pollutant model, significant positive associations were observed only for monobutyl phthalate (MBP) and benzophenone-1 (BP-1), which are urinary metabolites of dibutyl phthalate and benzophenone-3, respectively. The significance of the association of these compounds remained as well among the subpopulation with healthy renal function (ACR < 9.71 mg/g) and/or with a different adjustment of urine dilution.

Conclusions: Among the multiple urinary chemicals, MBP and BP-1 consistently and strongly associated with urinary ACR. The observation of this study warrants confirmation in other populations and experimental studies.

Table. Association of creatinine-adjusted urinary chemical concentrations (μg/g creatinine) with urinary albumin-to-creatinine ration (ACR) (mg/g) in the multi-pollutant model (n=441).

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Compound	β (95% CI)	*p*-Value
Monobutyl phthalate	**0.15 (0.06, 0.23)**	**<0.001**
Monoisobutyl phthalate	**0.05 (0.00, 0.10)**	**0.048**
monobenzyl phthalate	**0.09 (0.02, 0.16)**	**0.010**
Di-(2-ethylhexyl) phthalate metabolites	−0.06 (−0.20, 0.08)	0.379
Bisphenol A	0.06 (−0.01, 0.13)	0.108
Benzophenone-1	**0.11 (0.07, 0.16)**	**<0.001**
Methyl paraben	0.04 (−0.03, 0.10)	0.317
Propyl paraben	0.00 (−0.04, 0.04)	0.968

Boldface value represents $p < 0.05$. Both the chemical concentration and ACR were log-transformed. The linear model was adjusted for age, education, region, parity, and urinary cotinine.