BACKGROUND

- Phthalates are synthetic chemicals produced in extremely large volumes for a wide variety of uses in personal care and consumer products, including building materials, food packaging, and medical devices, toys and cosmetics.
- Several in vivo and in vitro studies suggest that phthalates may promote obesity through antiandrogenic effects, antithyroid hormone activities, and/or activation of peroxisome proliferator-activated receptors (PPARs).
- Recently, human studies have been performed to study the association between phthalate exposure and obesity, and some work has shown that concentrations of phthalate metabolites are associated with obesity and insulin resistance in adults.
- Children are known to be more vulnerable to environmental exposure to phthalates, as compared to adults, because of their hand-to-mouth activity, larger surface area to weight ratio, and enhanced metabolic rate. However, studies on the phthalate exposure and obesity/insulin resistance risk in children and adolescents are scarce.
- Urinary phthalate metabolites are the most useful biomarkers, as they are relatively easy to collect and their levels in a single sample reflect the exposure to phthalates over several weeks or months.

PURPOSE

We aimed to examine the associations of urine levels of phthalate metabolites with obesity status (BMI status, body fat %) and metabolic parameters (ALT, lipid profiles, fasting insulin, and HOMA-IR) in Korean girls.

METHODS

- A total of 139 girls (67 overweight cases and 72 controls, aged 6 to 13 yr) were recruited. Anthropometric indices including height, weight, waist circumference were measured and Bioelectrical impedance measures were collected using the Inbody 720 (Biospace 40, Ltd.).
- Fasting blood samples were obtained from the antecubital vein following a 10-hour overnight fast. The fasting plasma concentrations of total cholesterol, low-density lipoprotein (LDL) cholesterol, insulin, glucose, AST, and ALT were measured. The homeostasis model assessment of insulin resistance (HOMA-IR) was calculated using the following formula: fasting plasma glucose (mg dl⁻¹) × fasting insulin (μU/ml⁻¹)/405.
- First morning urine specimens were collected in all subjects, and stored at -20°C until assayed. Phthalate metabolites (MEP, MiBP, MnBP, MEHP, MEHHP, MEOHP, MBzP) were analyzed in selected ion monitoring mode using 7890A GC/7000A QP mass spectrometry (Shimadzu, Kyoto, Japan).
- Associations between phthalate exposure and anthropometric indices/metabolic parameters and their trends were examined by multiple linear regression and logistic regression analyses, respectively.

RESULTS

1. Obesity and urinary concentrations of phthalate metabolites

   Di-2-ethylhexyl phthalate (DEHP) metabolites showed the highest detected concentration (82.5 μg/g creatinine, 100%), and mono-benzyl phthalate (MBzP) showed the lowest detected concentration (6.3 μg/g creatinine, 87.8%). There was no significant difference in the concentrations of all phthalate monoesters between overweight and control girls, however percentage fraction of MEOHP among DEHP metabolites (MEOH%) was significantly lower in overweight girls than in controls.

2. Metabolic parameters and urinary concentrations of phthalate metabolites

   Concentrations of MiBP, MiBP, MEHHP, MEHHP, sum of DEHP metabolites, and sum of high molecular weight phthalates (HMP) were positively associated with serum ALT. Concentrations of MiBP were also positively associated with total cholesterol/LDL cholesterol levels.

   Phthalate metabolite concentrations showed no significant associations with anthropometric indices. After adjusting for age, pubertal stages, and height percentile, MEOHP% was positively associated with waist circumference and MEOHP% was negatively associated with body mass index (BMI) percentile.

3. Indices of insulin resistance and percentage fractions of DEHP metabolites

   After controlling for age and pubertal stages, MEOHP% was positively associated with fasting insulin and HOMA-IR, whereas MEOHP% was negatively associated with fasting insulin and HOMA-IR. However, after further adjustment for BMI percentile, the significant associations were remained only for MEOHP%.

CONCLUSIONS

- Urinary concentrations of phthalate metabolites were not significantly associated with BMI percentile, waist circumference, or percent body fat in Korean girls.
- Urinary concentrations of some phthalate metabolites were positively associated with serum ALT, total cholesterol or LDL cholesterol levels.
- Percentage fraction of MEOHP among DEHP metabolites (MEOH%) was significantly decreased in overweight children than in controls, and it was negatively associated with insulin resistance after controlling for age, pubertal stages, and BMI percentile.
- Prospective studies are needed to determine potential causal links between phthalate exposure and metabolic derangement such as NAFLD and insulin resistance in children.

REFERENCES


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Phthalate exposure and metabolic parameters in Korean girls

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