RELATIONSHIPS BETWEEN URINARY PHTHALATE METABOLITES AND POTENTIAL BIOMARKERS OF INFLAMMATION AND OXIDATIVE STRESS FROM NHANES 1999-2006

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Background and Aims: Phthalate exposure has been associated with a wide range of adverse health outcomes in epidemiologic studies, and one hypothesized mechanism is potentially through induction of inflammation and oxidative stress. We recently reported associations between urinary phthalate metabolites and levels of serum gamma glutamyltransferase (GGT), an indicator of oxidative stress, and C-reactive protein (CRP), a marker of inflammation. In this study we expanded our analysis to investigate associations with other potential markers of oxidative stress (bilirubin) and inflammation (alkaline phosphatase, absolute neutrophil count [ANC], ferritin, and fibrinogen). We hypothesized that higher phthalate metabolite concentrations would be associated with elevations in the inflammation markers and decreases in bilirubin, an indication of increased oxidative stress.
Methods: In this exploratory analysis, we combined data from the National Health and Nutrition Examination Survey (NHANES) collected between 1999 and 2006 and performed multivariable regression analyses.
Results: After adjustment for covariates we found ANC to be significantly and positively associated with the metabolites mono-n-butyl phthalate (MnBP), mono-benzyl phthalate (MBzP), mono-(3-carboxypropyl) phthalate (MCPP), mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), mono-2-ethyl-5-carboxypentyl phthalate (MECPP), and a combined measure of the dibutyl phthalate metabolites ($p < 0.05$). We also observed significant positive associations between alkaline phosphatase levels and the metabolites MnBP, MBzP, MCPP, MEHHP, mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP), mono-isobutyl phthalate (MiBP), mono-(carboxynonyl) phthalate (MCNP), and the aforementioned combination measure ($p < 0.05$). Lastly, bilirubin was significantly and inversely associated with the metabolites MnBP, mono-(2-ethyl)-hexyl phthalate (MEHP), MBzP, MCPP, MEHHP, MEOHP, MiBP, MECPP, and the combined DBP metabolites ($p < 0.0001$).
Conclusions: Concentrations of some urinary phthalate metabolites are associated with increases in ANC and alkaline phosphatase levels, as well as decreased bilirubin levels, which may be indicative of increased inflammation and oxidative stress. These markers may be useful in other studies of low-dose exposure to environmental contaminants in NHANES and other datasets.