Office of Science

Research Project Summary

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Exposure of Infants to Endocrine Disruptors

Authors

David Q. Rich[1], Stephen W. Marcella[1], Barry Weinberger [2], Dan Wartenberg[3], Mark Gregory Robson[4], Anna M. Vetrano[2], and Faith Archer[2]

Abstract

Urine collected from pregnant women close to the time of delivery was analyzed for the suspected endocrine disrupting chemicals BPA (bisphenol A) and the metabolites of the common phthalate DEHP. Both of these are commonly found in consumer products. Urine levels of these chemicals were examined for their association with gestational age, anogential distance and genital abnormalities. Statistically significant associations were found between urine levels of both the DEHP metabolite, MEHHP and BPA and gestational age. No clear association was observed between urine levels of DEHP metabolites or BPA and anogenital distance or genital abnormalities. Given the significant national exposure to MEHHP and the evidence that there may be a New Jersey-specific elevation in phthalate exposure, these observations suggest the need for further elucidation of New Jersey specific exposures.

Introduction

There has been increasing evidence that phthalates and bisphenol A (BPA) are endocrine disrupting chemicals in humans. That is, they have the ability to disrupt the endocrine balance particularly during fetal development. Phthalates appear to have anti-androgenic activity as reflected by their association in males with decreased anogential distance, and decreased penile volume and scrotal size. BPA also appears to have both anti-androgenic activity and estrogenic activity. In addition, both phthalates and BPA appear to have the ability to shorten gestation, possibly through their inflammatory properties. In New Jersey, the levels of phthalates in maternal urine prior to scheduled (cesarean) delivery were 5-20 times higher than those in the general US female population (Yan et al., 2009). While it is unclear whether this reflects a general increase in exposure during pregnancy, or an elevation in exposure that is specific to New Jersey, such findings suggest the need for further investigation of exposure to phthalates and BPA for fetal development and infant health.

To address these concerns, this study recruited a cohort of expectant mothers whose pregnancy was judged to be high-risk and who, therefore, attended an obstetric clinic for regularly scheduled pre-pregnancy visits. Maternal urine samples were obtained at the last scheduled obstetric clinic visit and were analyzed for metabolites of DEHP (di(2-ethyl-hexyl) phthalate), BPA, and the principle metabolic conjugates of BPA. These analyses were then compared to measures and observations of the newborns soon after delivery.

Methods

Seventy two expectant mothers attending a high-risk obstetric hospital clinic participated in this study with informed consent and with the approval of the Institutional Review Board of the Robert Wood Johnson-UMDNJ Medical School. Maternal urine samples collected at the last regularly scheduled clinic visit prior to delivery were analyzed for the following metabolites of DEHP: MEHP (mono-(2-ethylhexyl) phthalate); MMP (monomethyl phthalate); MEP (monoethyl phthalate); MBP (monobutyl phthalate); MCHP (monocyclohexyl phthalate); MEHHP (mono(2-ethyl-5-hydroxyhexyl) phthalate); MDP (isodecyl phthalate); MEOHP (mono-n-octyl phthalate); and MNP (monoisononyl phthalate), and for total BPA, BPA sulfate, and BPA glucuronide. At less than 72 hours old, infants were measured for anogenital distance and this measurement was normalized to the infants' body weight. Genital malformations and abnormalities were recorded. Birth weight was recorded and gestational age was determined based on pre-delivery clinic data.

Results

Of the DEHP metabolites measured, MEHP, MEHHP, MEOHP, MEP, MCHP, and MBP were found in maternal urine at quantifiable levels (Figure 1) as were BPA and BPA sulfate. After statistical adjustment for birth parity

and maternal race, each increase in MEHP urine concentration of 5.8 ng/ml-urine, equivalent to the difference in MEHHP concentration between the 75th and 25th percentile of all values found among the 72 women (referred to as the interquartile range), was statistically significantly associated with a decrease in gestational age of 4.2 days (Table 1). Similarly, each increase in BPA of 180.1 ng/ml, equivalent to the interquartile range, was significantly associated with a decrease in gestational age of 1.1 days (Table 1). The effect of MEHHP was more pronounced in male infants than in females, with an increase equivalent to the interquartile range being associated with a significant decrease of 5.1 days. There were no clear associations of anogential distance with any of the chemicals analyzed.

Table 1. Gestational Age Changes: All Subjects (n = 72)

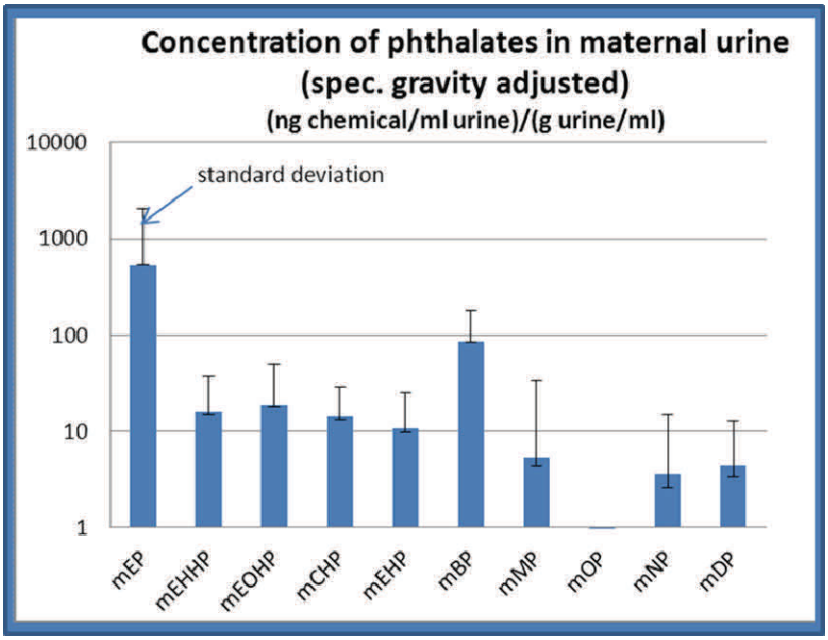
	Unadjusted			Adjusted		
	Change in gestational age (days)*	95% CI	P value	Change in gestational age (days)	95% CI	P value
mEP	0.5	-0.3, 1.3	0.25	0.2	-0.6, 1.0	0.58
mEHHP	-4.6	-8.6, -0.6	**0.02**	-4.2	-7.9, -0.4	**0.03**
mEOHP	-0.5	-2.7, 1.8	0.69	-0.6	-2.7, 1.5	0.58
mCHP	0.8	-4.4, 6.0	0.75	-0.9	-5.7, 3.9	0.71
MEHP	0.4	-1.3, 2.0	0.67	0.4	-1.1, 2.0	0.58
mBP	-1.1	-4.5, 2.3	0.53	-2.1	-5.2, 1.1	0.19
BPA sulf	-0.4	-1.4, 0.6	0.43	-0.5	-1.5, 0.4	0.29
BPA total	-0.7	-1.7, 0.4	0.19	-1.1	-2.0, -0.1	**0.03**

*associated change with an increase in the interquartile range (25-75%ile) for each metabolite.
Abbreviations: CI, confidence interval

Summary and Conclusions

The finding in this study that maternal exposure to both MEHHP and BPA are associated with decreased fetal gestation has not previously been reported. These observations, however, are consistent with limited animal data for phthalate exposure in general and limited human evidence for MEHP. The association of MEHHP with decreased length of gestation is of particular concern since MEHHP is one of the most abundant DEHP metabolites found in the population (http://www.cdc.gov/exposurereport/pdf/FourthReport_UpdatedTables_Mar2013.pdf) and exposure to MEHHP is associated with the use of commercial plastic water bottles and body lotions. For BPA, the finding of decreased gestation is consistent with previous observations in Mexico and China of an association between BPA and premature birth and low birth weight.

These findings are suggestive of adverse effects of phthalates and BPA on pregnancy outcome and are relevant for the population in general. However, in light of the earlier observation that in New Jersey levels of phthalates in maternal urine at the time of delivery was 5-20 higher than in the general (non-pregnant) US female population makes these findings of particular concern to New Jersey. It remains unclear whether this apparent increased phthalate exposure in New Jersey pregnant population reflects New Jersey specific exposures or something more general about phthalate metabolism during pregnancy. Nonetheless, the combination of a possible New Jersey-specific elevation in exposure and the observed adverse effect on gestation of phthalate exposure suggests the need for research to clarify the nature of exposure to phthalates and BPA in New Jersey.



References

Yan X, Calafat A, Lashley S, Smulian J, Ananth C, Barr D, Silva M, Ledoux T, Hore P, Robson MG. (2009). Phthalates Biomarker Identification and Exposure Estimates in a Population of Pregnant Women. Hum Ecol Risk Assess. 15:565-578.

Investigators:

[1]David Q. Rich, ScD, MPH, UMDNJ-School of Public Health (currently, University of Rochester), and Stephen W. Marcella, MD, MPH, UMDNJ-School of Public Health

[2]Barry Weinberger, MD, UMDNJ- Robert Wood Johnson Medical School, Anna M. Vetrano, PhD, UMDNJ-Robert Wood Johnson Medical School and Faith Archer, BS, UMDNJ-Robert Wood Johnson Medical School

[3]Dan Wartenberg, PhD, UMDNJ- Environmental and Occupational Health Science Institute

[4]Mark Gregory Robson, PhD, MPH, DrPH (hc), School of Environmental and Biological Sciences - Rutgers University

Prepared By:

Alan H. Stern, DrPH, DABT, NJDEP, Office of Science

RESEARCH PROJECT SUMMARY

Please send comments or requests to:

Office of Science
Mail code 428-01, P.O. Box 420
Trenton, NJ 0862

Phone: (609)984-6070