LAY ABSTRACT

TITLE: Pre-pubertal and Pubertal Endocrine Disrupting Chemicals Exposure and Breast Density among Chilean Adolescents

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SCIENTIFIC ABSTRACT (words: 250)

Background: During puberty mammary tissue undergoes rapid development, which provides a window of heightened susceptibility of breast composition to the influence of endogenous and exogenous hormones. Exposure to endocrine disrupting chemicals (EDCs) may affect breast development and composition and the risk of developing breast cancer in adulthood.

Methods: We evaluated the associations between breast density and urinary concentrations of phenols and phthalates collected at Tanner 1 (B1) and Tanner 4 (B4) in 200 Chilean girls. Total breast volume (BV), fibroglandular volume (FGV), and percent dense breast (%FGV) were evaluated at B4 using dual x-ray absorptiometry. Generalized estimating equations were used to analyze the association between concentrations of EDC biomarkers across puberty and breast density.

Results: The geometric mean %FGV was 7% higher among girls in the highest relative to the lowest tertile of monocarboxyisooctyl phthalate (1.07; 95% CI: 1.01-1.14). Monoethyl phthalate (MEP) concentrations at B4 were positively associated with FGV (highest vs lowest tertile: 1.22; 95% CI: 1.06-1.40). Bisphenol A displayed a u-shaped association with FGV; girls in the middle tertile had at least 10% lower FGV than girls in the lowest or highest tertiles. Monocarboxyisononyl phthalate showed a non-linear association with BV. No other statistically significant associations were observed.

Conclusions: Our results suggest that the developing breast tissue is susceptible to select EDCs during childhood and adolescence.
**Impact:** This study may spur further investigations into environmental influences on breast development during puberty, and how shifts in pubertal breast density track through the life course to modify breast cancer risk.

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A higher proportion of tissue relative to fat in the breast (greater breast density) is strongly linked with increased breast cancer risk. During puberty, the breast tissue develops rapidly in response to changing levels of hormones in the body. Phenols and phthalates are types of synthetic chemicals that can disturb a person’s own hormone system. These chemicals are commonly found in plastics, personal care products, adhesives, detergents, pharmaceuticals, and building materials, such as vinyl flooring. We investigated for the first time the potential impact of these chemicals on adolescent breast composition. We measured the levels of 26 phenols and phthalates in the urine of 200 girls in Santiago, Chile, during childhood (ages 6.7-9.6 years) and adolescence (ages 9.4-13.1 years). Adolescent breast composition was measured using a very low dose x-ray method. One of the phthalates influenced total breast volume, while a few other chemicals, including bisphenol and additional phthalates, influenced dense (breast tissue) volume and/or the percent dense breast (proportion of total breast volume that is breast tissue). Taken together, the results of our study suggest that exposure to some phthalates and phenols during childhood and adolescence may affect the composition of the developing breast. These changes may occur at levels typical of everyday exposures. Future studies will be useful to determine whether these changes in adolescent breast density influence breast composition in adulthood to impact breast cancer risk. This work was supported by National Institutes of Health grant R01CA158313 from the National Cancer Institute, and by the Breast Cancer and the Environment Research Program (BCERP) award U01ES026130 from the National Institute of Environmental Health Sciences and the National Cancer Institute.