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690 - ASSOCIATIONS BETWEEN PRENATAL EXPOSURE TO PFAS AND ORGANOCHLORINE CHEMICALS AND EARLY PUBERTAL DEVELOPMENT: A METABOLOMIC STUDY IN THREE EUROPEAN COHORTS

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Resumen

Background/Objectives: Per- and polyfluoroalkylated substances (PFAS) and organochlorine compounds (OCs) are endocrine-disrupting chemicals that interfere with key metabolic and hormonal pathways. Prenatal exposure may alter endocrine system programming and impact pubertal development. We investigate the association between prenatal exposure to that chemicals and early pubertal development among children using metabolomics to inform underlying mechanisms.

Methods: PFAS and OCs (dichlorodiphenyldichloroethylene [DDE], hexachlorobenzene [HCB], polychlorinated biphenyls [PCB] 138, 153, 180) levels were determined in first-trimester maternal plasma/serum samples from three European cohorts: INMA (Spain); EDEN (France); MoBa (Norway). The metabolome was characterized in urine and serum of corresponding children (6-11 years). Pubertal development of children (294 girls, 343 boys) was assessed at age 8-11 using the parent-reported Pubertal Development Scale (PDS). Sex-specific generalized linear mixed models with Poisson distribution evaluated associations between biomarkers (PFAS, OCs, metabolites) and probability of being in pubertal stage 2+ (PDS dichotomized: stage 1 [prepuberty] vs. 2+ [puberty]). Multivariate regression models characterized links between pollutants and metabolites.

Results: No statistically significant associations were observed between prenatal exposures to the chemicals and risk of early puberty onset. Stratified analyses revealed prenatal DDE exposure was associated with increased risk of earlier puberty (RR = 1.29; 95%CI: 1.00-1.67) among overweight/obese girls. Perfluorononanoic acid (PFNA) exposure appeared significantly associated with higher risk of earlier puberty among boys with overweight/obesity (RR = 2.20; 95%CI: 1.22-3.96). In contrast, in girls with normal weight, PCB-180 and HCB (RR = 0.83; 95%CI: 0.69-0.99; RR = 0.92; 95%CI: 0.85-0.99, respectively) showed inverse associations with early puberty risk. Serum metabolomic fingerprints rich in sphingolipids and phosphatidylcholines were inversely associated with early puberty risk and prenatal PCB exposure particularly among boys.

Conclusions/Recommendations: The analyses revealed differential associations between prenatal PFAS and OCs exposure and earlier puberty, indicating potential effect modification by adiposity status on metabolic-disrupting effects of these chemicals. Metabolomic profiles suggest potential metabolic pathways underlying these associations.