IN-UTERO EXPOSURE TO DIOXINS AND DIOXIN-LIKE COMPOUNDS AND ANOGENITAL DISTANCE IN NEWBORNS OF THE RHEA STUDY IN CRETE

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Background and Aims: Maternal exposure to dioxins and dioxin-like compounds has been related to adverse health outcomes in infants (Halldorsson et al 2009). The toxicity of these compounds is mostly traced to their blocking of the aryl hydrocarbon receptor (AhR) in part by modulating estrogen and androgen signaling (Carlson et al 2002). In animals, anogenital distance is used as a measure of fetal androgen action, tracks through life and varies by dose of antiandrogen (Longnecker et al2007). Although anogenital distance is scarcely used in human studies, results show that prenatal phthalate exposure decreases male anogenital distance (Swan et al 2005). We evaluated the association between *in-utero* exposure to dioxins and dioxin like compounds, using the DR-Calux bioassay and anogenital distance in newborns of the Rhea birth cohort in Crete.
Methods: Anogenital distance (AGD: anus to upper penis), anoscrotal distance (ASD: anus to scrotum) and penis width (PW) were measured in 64 boys. Anoclitoral (ACD: anus to clitoris) and anofourchetal distance (AFD: anus to fourchette) were measured in 62 girls. Ratios of anogenital distances divided by body weight were calculated. Maternal blood samples were collected at delivery and dioxin-like activity was measured in plasma using the DR-CALUX bioassay.
Results: Anogenital distances were wider in males (mean AGD= 50,46mm) than females (mean ACD=35,03mm). Plasma dioxin-like activity was negatively associated with AGD in males. The estimated change in AGD per 10 pg CALUX-TEQ/g lipid increase was -1.12mm (95%CI:-2.12,-0.12) and -0.39 mm/kg for the AGD weight ratio (95%CI:-0.74,-0.05) after adjusting for potential confounders. Negative but not statistically significant associations were observed for ASD and PW; no associations were found for ACD or AFD in females.
Conclusions: Male infants may be susceptible to endocrine-disrupting effects of dioxins. This is the first study that appears to replicate in humans, experimental animal evidence used by WHO/FAO for setting recommendations on human dioxin intake.
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