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Prenatal and postnatal exposures to endocrine disrupting chemicals and timing of pubertal onset in girls and boys: a systematic review and meta-analysis

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Abstract

Background: Globally, the ages at pubertal onset for girls and boys have been decreasing during recent decades, partly attributed to excess body fat accumulation. However, a growing body of literature has recognized that endocrine disrupting chemicals (EDCs) may play an important role in this global trend, but the association has not yet been fully established.

Objective and rationale: EDCs can interfere with normal hormone function and metabolism and play a role in pubertal onset. We aimed to systematically identify and evaluate the current evidence on the timing of pubertal onset in girls and boys following prenatal or postnatal exposures to xenobiotic EDCs.

Search methods: Following PRISMA guidelines, we performed a systematic literature search of original peer-reviewed publications in the PubMed database through a block search approach using a combination of index MeSH and free text search terms. Publications were considered if they covered biomarkers of prenatal or postnatal exposures to xenobiotic EDCs (European Commission's list of category 1 EDCs) measured in maternal or child biospecimen and pubertal onset defined by the progression of the following milestones (and assessed in terms of the following measures): menarche (age), thelarche (Tanner staging) and pubarche (Tanner staging), in girls, and genital stage (Tanner staging), testicular volume (ml) and pubarche (Tanner staging), in boys.

Outcomes: The literature search resulted in 703 references, of which we identified 52 publications fulfilling the eligibility criteria for the qualitative trend synthesis and 23 publications for the meta-analysis. The qualitative trend synthesis provided data on 103 combinations of associations between prenatal or postnatal exposure to EDC compounds groups and puberty outcomes and the meta-analysis enabled 18 summary risk estimates of meta-associations.

Wider implications: Statistically significant associations in the qualitative trend synthesis suggested that postnatal exposure to phthalates may be associated with earlier thelarche and later pubarche. However, we did not find consistent evidence in the meta-analysis for associations between timing of pubertal onset in girls and boys and exposures to any of the studied xenobiotic EDCs. We were not able to identify specific pre- or postnatal windows of exposure as particularly critical and susceptible for effects of EDCs. Current evidence is subject to several methodological challenges and inconsistencies and evidence on specific exposure-outcome associations remains too scarce to firmly confirm EDC exposure as a risk factor for changes in age of pubertal onset in the general child population. To create a more uniform foundation for future comparison of evidence and to strengthen pooled studies, we recommend the use of more standardized approaches in the choice of statistical analyses, with exposure transformations, and in the definitions and assessments of puberty outcomes. The impact of mixtures of EDC exposures on the association also remains unestablished and would be valuable to elucidate for prenatal and postnatal windows of exposure. Future large, longitudinal epidemiological studies are needed to clarify the overall association.

Keywords: endocrine disrupting chemicals; genital stage; menarche; postnatal exposure; prenatal exposure; pubarche; puberty; testicular volume; thelarche.

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