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Is Hypospadias Associated with Prenatal Exposure to Endocrine Disruptors? A French Collaborative Controlled Study of a Cohort of 300 Consecutive Children Without Genetic Defect.

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Abstract

BACKGROUND:

Numerous studies have focused on the association between endocrine-disrupting chemicals (EDCs) and hypospadias. Phenotype variability, the absence of representative comparison groups and concomitant genetic testing prevent any definitive conclusions.

OBJECTIVE:

To identify the role of occupational and environmental exposures to EDCs in nongenetic isolated hypospadias.

DESIGN, SETTING, AND PARTICIPANTS:

A total of 408 consecutive children with isolated hypospadias and 302 normal boys were prospectively included (2009-2014) in a multi-institutional study in the south of France, the area of the country with the highest prevalence of hypospadias surgery.

OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS:

In patients without AR, SRD5A2, and MAMLD1 mutations, parental occupational and professional exposures to EDCs were evaluated based on European questionnaire QLK4-1999-01422 and a validated job-exposure matrix for EDCs. Environmental exposure was estimated using the zip code, the type of surrounding hazards, and distance from these hazards. Multivariate analysis was performed.

RESULTS:

Fetal exposure to EDCs around the window of genital differentiation was more frequent in the case of hypospadias (40.00% vs 17.55%, odds ratio 3.13, 95% confidence interval 2.11-4.65). The substances were paints/solvents/adhesives (16.0%), detergents (11.0%), pesticides (9.0%), cosmetics (5.6%), and industrial chemicals (4.0%). Jobs with exposure were more frequent in mothers of hypospadiac boys (19.73% vs 10.26%, $p=0.0019$), especially cleaners, hairdressers, beauticians, and laboratory workers. Paternal job exposure was more frequent in the cases of hypospadias (40.13% vs 27.48%, $p=0.02$). Industrial areas, incinerators, and waste areas were more frequent within a 3-km radius for mothers of hypospadiac boys (13.29% vs. 6.64%, $p<0.00005$). Association of occupational and environmental exposures increases this risk.

CONCLUSIONS:

This multicenter prospective controlled study with a homogeneous cohort of hypospadiac boys without genetic defects strongly suggests that EDCs are a risk factor for hypospadias through occupational and environmental exposure during fetal life. The association of various types of exposures may increase this risk.

PATIENT SUMMARY:

Our multi-institutional study showed that parental professional, occupational, and environmental exposures to chemical products increase the risk of hypospadias in children. Copyright © 2015 European Association of Urology. Published by Elsevier B.V. All rights reserved.

KEYWORDS:

Birth defect; Disorder of sex determination; Endocrine-disrupting chemicals; Environment; Hypospadias; Occupation; Pesticides