Cod: 8.1001

IN UTERO DIOXIN EXPOSURE AND OBESITY IN THE SEVESO SECOND GENERATION

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Introduction

In animal studies, maternal exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) has been related to decreased body weight of offspring from birth through adulthood, suggesting a role for dioxin-like compounds in metabolism and obesity later in life.1-7 Several epidemiologic studies have examined effects of in utero exposure to dioxin-like compounds on child growth and obesity with inconsistent results.8-14

The Seveso Women's Health Study (SWHS) of women exposed to TCDD during or before their child-bearing years is unique.15 Initial, individual-level TCDD exposure measures are available for this first generation cohort.16,17 Nearly 40 years after the Seveso explosion, data collection to follow-up the second generation of the SWHS cohort is almost complete. We aim to examine the relation of in utero TCDD exposure with obesity among all SWHS children. Here, we report preliminary results to date for adult children 18 years and older.

Materials and Methods

We included 403 children who were 18 years or older with complete follow-up data. We calculated continuous body mass index (BMI) as kg/m2 and categorical BMI (underweight, <18.5 kg/m2; normal, 18.5-24.9 kg/m2; overweight, 25.0-29.9 kg/m2; obese, ≥30.0 kg/m2).18 We defined in utero TCDD exposure as initial TCDD concentration measured in maternal serum collected soon after the explosion. TCDD levels were log-transformed and included as a continuous variable. We used linear regression to examine the relation of serum TCDD with BMI and logistic regression to examine the relation with obesity. For all outcomes, we considered effect modification by sex.

Results and Discussion

The 403 children (215 female, 188 male) were an average of 28.6 (±6.0) years of age at follow-up. In utero TCDD exposure based on initial maternal serum TCDD level is high (median=53.7 ppt), with a wide range (3-5,710). The average BMI for the 403 children was 23.6 (±3.7) kg/m2, with 24.3% classified as overweight and 7.4% classified as obese. In age-adjusted models, a 10-fold increase in maternal serum TCDD concentration was associated with decreased BMI among daughters (adj-β = -0.40, 95% CI -0.79, -0.01), but not sons (adj-β = 0.05, 95% CI -0.28, 0.37) (p-interaction = 0.09). Also among daughters, after adjusting for age, a 10-fold increase in maternal serum TCDD was associated with reduced odds of obesity (adj-OR = 0.71, 95% CI 0.46, 1.11), which was not observed in sons (adj-OR = 1.20, 95% CI 0.84, 1.70) (p-interaction = 0.07).

Fully adjusted results for the complete Seveso second generation cohort, including the children who are less than 18 years, will be presented. In addition, we will present results using TCDD exposure extrapolated to the pregnancy.

These preliminary results provide evidence to support the chemical obesogen hypothesis, that in utero exposure to endocrine disrupting compounds may alter risk of obesity later in life. In this case, we observe a decreased risk of obesity in daughters exposed to TCDD.

Acknowledgements

We gratefully acknowledge field staff, N. Gelpi and C. Siracusa, for data collection at Hospital of Desio. This study was supported by grants R01 ES07171 and 2P30-ESO01896-17 from the National Institute of Environmental Health Sciences, R82471 from the U.S. Environmental Protection Agency, and 2896 from Regione Lombardia and Fondazione Lombardia Ambiente, Milan, Italy.

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