Association of Urinary Phenols with Increased Body Weight Measures and Obesity in Children and Adolescents

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Objective To examine the association of urinary levels of the environmental phenol pesticides 2,5-dichlorophenol, 2,4-dichlorophenol, and triclosan with body weight outcomes in children and adolescent participants in the National Health and Nutrition Examination Survey 2007-2010.

Study design We performed multivariate linear and multinomial logistic regressions to analyze the association of body mass index (BMI) z-score, waist circumference (WC), and obesity with urinary pesticide concentration in children and adolescents.

Results After adjustment for covariates, we found a statistically significant positive association ($P < .05$) between both 2,5-dichlorophenol and 2,4-dichlorophenol with BMI z-score, WC, and obesity in children and adolescents. After stratification by age, the significant associations remained only in adolescents (ages 12-19). No associations were found between triclosan and any of the body weight outcomes.

Conclusions We found an association between dichlorophenols and increased body weight measures (BMI z-score, WC, and obesity) in adolescents. However, further studies, such as a longitudinal study, are needed to confirm and elucidate on our findings. *(J Pediatr 2014;165:744-9)*.

Obesity has become an increasingly important public health concern, as the prevalence in children, adolescents, and adults has increased over the past few decades both within the US and worldwide. The most accepted explanation of this rise in obesity is an adoption of an unhealthy diet and lifestyle. However, an increasing body of evidence suggests that exposure to environmental chemicals, known as "obesogens," may increase the risk of obesity both in children and adults.[1-10]

Because of their vast usage throughout the US as well as the rest of the world, pesticides have become ubiquitous in our environment, creating the potential for human exposure through contaminated food, soil, water, air, and other sources. Pesticides have been shown to have many adverse effects in child development including neurologic and metabolic outcomes, such as diabetes and obesity.[7,8] Dichlorophenols are one such category of pesticides; the National Health and Nutrition Examination Survey (NHANES 2007-2010) has detected them in over 90% of the urine samples of participants. 2,5-Dichlorophenol (2,5-DCP) is a metabolite of 1,4-dichlorobenzene (1,4-DCB), which is commonly used in moth balls, room and toilet deodorizers, and as a fumigant insecticide.[9,10] The main source of exposure to 1,4-DCB is through inhalation.[11]

Studies have reported an association between 2,5-DCP and obesity and body mass index (BMI) in children and adolescents[12] and adults.[13] These researchers found a statistically significant increase in the rate of obesity among these populations. The objective of this study was to build on these studies and investigate the correlation between 2,4-dichlorophenol (2,4-DCP), 2,5-DCP, and triclosan (TCS) with not only obesity but with other weight outcomes—BMI z-score and waist circumference (WC), an indication of abdominal fat—using data from NHANES 2007-2010 in children and adolescents (6-19 years old).

Methods

NHANES is a program of cross-sectional, nationally representative surveys of the noninstitutionalized civilian population of the US conducted by the National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (CDC).[14] Beginning in 1999, the survey was conducted continuously and released in 2-year cycles. For our study, we merged the publicly available files for NHANES cycles 2007-2008 and 2009-2010 using the recommendations of NCHS.[15] The

1,4-DCB	1,4-Dichlorobenzene
2,4-DCP	2,4-Dichlorophenol
2,5-DCP	2,5-Dichlorophenol
BMI	Body mass index
CDC	Centers for Disease Control and Prevention
NCHS	National Center for Health Statistics
NHANES	National Health and Nutrition Examination Survey
TCS	Triclosan
WC	Waist circumference

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survey employs a multistage stratified probability sample based on selected counties, blocks, households, and persons within households.

NCHS-trained professionals conducted interviews in participants' homes and extensive physical examinations, which included blood and urine collection, conducted at mobile examination centers. CDC's National Center for Environmental Health, Division of Laboratory Sciences coordinates the National Biomonitoring Program, which offers an assessment of nutritional status and the exposure of the US population to environmental chemicals and toxic substances. All procedures were approved by the NCHS Research Ethics Review Board (Continuation of Protocol #2005-2006 http://www.cdc.gov/nchs/nhanes/irba98.htm), and all participants provided written informed consent.

In the 2007-2008 and 2009-2010 dataset, urinary metabolites of chlorinated phenols and TCS were measured in a randomly selected one-third subsample of persons 6 years and older. For our analysis, we included all participants (age 6-19 years) who had measurements for dichlorophenols and TCS (n = 1603). In addition, participants with missing covariables included in the multivariable-adjusted models were excluded (n = 305). Therefore, the total number of participants in our analyses was 1298.

Spot urine samples were collected from study participants and stored at −20°C until analysis. The urine samples were analyzed by the National Center for Environmental Health, Division of Laboratory Sciences for TCS and 2 chlorophenols: 2,4-DCP and 2,5-DCP using solid phase extraction coupled on-line to high performance liquid chromatography and tandem mass spectrometry.

Urinary 2,4-DCP, 2,5-DCP, and TCS were detected in 90%, 98.5%, and 79% of the samples, respectively. Therefore, as reported in the NHANES dataset, urinary concentrations of 2,4-DCP, 2,5-DCP, and TCS below the level of detection were assigned the limit of detection divided by the square root of 2. To account for variation in dilution in spot urinary samples, urinary creatinine was entered in the analyses as an independent variable as suggested by previous studies.[16,17] Urinary creatinine was determined using a Jaffé rate reaction measured with a CX3 analyzer (Beckman Instruments Inc, Brea, California).[18]

BMI is calculated by the weight divided by height squared (kg/m^2). However, the relation between BMI in children depends on age and sex; therefore, it is more appropriate to calculate the BMI z-score. The BMI z-score is the number of SDs by which a child differs from the mean BMI of children of the same age and sex. Thus, the BMI z-score allows comparison of children of different ages and sexes. Age- and sex-specific BMI z-scores were calculated using the methodology provided by the CDC (http://www.cdc.gov/nccdphp/dnpao/growthcharts/resources/sas.htm).

BMI z-score was then used to classify individuals as overweight and obese defined as BMI greater than or equal to the 95th percentile (obese) or between the 85th and less than the 95th percentile (overweight).

Data on WC (cm) was obtained during the examination. WC was measured at the high point of the right iliac crest at minimal respiration to the nearest 0.1 cm (http://www.cdc.gov/nchs/data/nhanes/nhanes_07_08/manual_an.pdf; http://www.cdc.gov/nchs/data/nhanes/nhanes_09_10/BodyMeasures_09.pdf).

In the regression models, we adjusted for a priori covariates[12,19]: age, race/ethnicity, sex, urinary creatinine, poverty income ratio, calorie intake, and serum cotinine as a biomarker of exposure to environmental tobacco smoke. Race/ethnicity was categorized as non-Hispanic white, non-Hispanic black, Mexican American, other Hispanic, and other. Poverty income ratio is a measure of socioeconomic status and represents the calculated ratio of household income to the poverty threshold after accounting for inflation and family size. Caloric intake was categorized as "normal" and "excessive" based on the US Department of Agriculture calorie intake guidelines by age and sex (http://health.gov/dietaryguidelines/dga2010/DietaryGuidelines2010.pdf). The individual cut-off caloric need was the highest value for the range by age and sex assuming a moderate physical activity level. After stratification by age, we included television, video game, and computer usage for children (ages 6-11 years) and physical activity for adolescents (ages 12-19 years). Information on daily hours of television, video, or computer use was obtained by questionnaire, and the covariate was categorized with a cut point of ≥2 hours/day. Information on physical activity came from the NHANES questionnaire; participants were asked whether they engaged in regular moderate and/or vigorous recreational activities (categorized as yes or no).

Statistical Analyses

Specific sample weights for this subsample were used for analyses to account for the complex sampling design and nonresponse of NHANES. Weights for combined NHANES survey cycles were calculated according to NHANES guidelines.[20] We estimated sampling errors using the Taylor series linearized method. Linear regression analyses were used to investigate the correlation between BMI z-scores and WC and urinary 2,4-DCP, 2,5-DCP, and TCS categorized by weighted quartile distribution. We used multinomial logistic regression models to simultaneously estimate aORs for obesity and overweight status as distinct outcomes (compared with normal/underweight) in association with categorical urinary compounds. In addition to estimating associations for all observations combined, we performed separate analyses stratified by age (6-11 years and 12-19 years). We also assessed possible interactions between pesticides and sex, but because the interaction was not statistically significant, it was not included in the models. SAS 9.3 (SAS Institute, Cary, North Carolina) was used for all statistical analyses and SAS-Callable SUDAAN 10 (Research Triangle Institute, Research Triangle Park, North Carolina) was used to account for the NHANES complex sample design. *P* values from Satterthwaite statistics were presented at the significance level of <.05.

Results

Table I illustrates the weighted characteristics of participants aged 6-19 years from NHANES 2007-2010 included in this

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