POLYCHLORINATED BIPHENYLS AND THYROID HORMONES IN THE ANNISTON COMMUNITY HEALTH SURVEY

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Introduction

Thyroid hormones thyroxine (T4) and triiodothyronine (T3) are essential for normal development and physiologic function in humans.[1] Environmental toxicants including polychlorinated biphenyls (PCBs) may disturb the regulation of the thyroid hormone delivery to cells and tissues, which is controlled by the pituitary gland hormone thyrotropin (TSH) and feedback systems.[2] This has been a topic of intense interest.[3] Environmental exposures to polychlorinated biphenyls (PCBs) have been associated with the decreases in level of T3 and T4.[3] A few studies also observed changes in TSH.[4-6] Overall, the results from studies of higher quality and better design on associations among PCBs and thyroid hormones remained inconclusive.[3] The prevalences of hypo- and hyperthyroidism have been found to be higher among women than among men,[7] and the associations between PCB exposure and thyroid hormone concentrations may vary by sex.[5]

In the city of Anniston, Alabama, Monsanto Chemical Company operated a PCB production facility from 1932 to 1971 that manufactured all commercial and experimental Aroclors used in the United States. It is estimated that more than half of the total US production of PCBs occurred at this facility. High historical levels of PCBs were reported in both the environment and people in the area.[8] The present cross-sectional study was conducted by the Anniston Environmental Health Research Consortium in 2005-7 to address some of the community health concerns about PCBs. We reported earlier on associations between PCBs and diabetes, hypertension, and blood pressure.[9-11] The present study aimed to examine associations among the sum of PCBs and levels of T4 and TSH in the study participants from Anniston.

Materials and Methods

Study Design and Population

3,320 households were randomly selected from a commercial list of all residential sites within the city limits. Out of 1,823 households that were successfully contacted, from which one adult per household was randomly selected, 1,110 individuals agreed to participate in the survey. Of these 1,110 respondents, 774 visited the study office and provided a fasting blood sample for measurements of thyroid hormones, glucose, PCBs and lipid levels, and had their height, weight, waist circumference and blood pressure measured using a standardized protocol. Demographic information, medical and family history, self-reported health behaviors and health conditions, and individual medications were recorded. The study was reviewed and approved by the appropriate Institutional Review Boards.

Laboratory and Statistical Analyses

The 35 major ortho-substituted PCB congeners were measured by the Division of Laboratory Sciences at the Centers for Disease Control and Prevention's National Center for Environmental Health using high-resolution gas chromatography/isotope-dilution high-resolution mass spectrometry.[12] Study specimens were analyzed in batches of 24 intermixed with quality control (QC, n=3) and method blank (n=3) samples. Serum total lipids were calculated using the enzymatic "summation" method using triglyceride and total cholesterol measurements.[13] We summed the serum concentrations of 35 PCB congeners for each participant and then log-transformed these sums. Values below the detection limit were substituted with the congener-specific limit of detection divided by the square root of 2. The sum of PCBs was divided into quartiles, with the first quartile serving as the referent category. Quartile cut points were based on values from the entire group of participants with valid whole weight PCB measurements (n=765).

Serum T4 and TSH were analyzed by the Endocrine Laboratories at the University of Southern California.[14,15] The sufficient volume samples and quality control yielded usable results for 744 participants. The normal ranges were 4.5 to 12.5 μg/dL for T4 and 0.3 to 3.0 mIU/L for TSH, as reported by the laboratory.

We excluded 52 individuals who were using thyroid medication, as determined by nurse review of subjects' medications. A positive family history of thyroid disease was defined as any thyroid disease in siblings, parents, grandparents, aunts or uncles. Multivariable logistic regression models were used to estimate odds ratios of abnormally high or low T4 and TSH and the 95% confidence intervals. Models were adjusted for serum total lipids, age, sex, race, body mass index (BMI) categories (defined as BMI <25, 25-29, ≥30), and family history of thyroid disease.

Results and Discussion

Forty-seven percent of participants self-identified as African-American (the rest were White) and 69% were female (Table 1). The mean age was 54.3 years, ranging from 18 to 93. Approximately 30% of participants had less than a high school education, 40% were high school graduates without college and most had low income (data not shown). Most participants (51%) had an elevated BMI (≥30 kg/m^2). T4 was above normal range in 6.5% and lower than normal range in 0.7% of participants. For TSH, 17% of participants had results above normal, while 0.9% were below normal. A Chi-square test of proportions showed White participants were more likely to have above-normal TSH than were African-Americans; this association was reflected in the adjusted logistic regression model for above-normal TSH (results not shown).

Table 1. Selected demographic characteristics and serum concentrations of PCBs and thyroid hormones (mean ± SE or percent) of Anniston Community Health Survey (ACHS) participants for whom thyroid data are available.

Characteristic	Female (n=476)	Male (n=215)	Total (n=691)
	Mean ± Std. Error		
Age in years	54.0 ± 0.7	55.0 ± 1.0	54.3 ± 0.6
Sum of 35 PCBs, wet weight (ng/g)	6.79 ± 0.61	6.44 ± 0.68	6.68 ± 0.47
	Percentage (non-missing)		
African-American	46.9%	46.5%	46.7%
BMI classification			
Normal < 25	21.6%	24.1% [a]	22.4%
Overweight 25-29	22.9%	34.4%	26.5%
Obese ≥ 30	55.5%	41.5%	51.2%
Sum of 35 PCBs, wet weight (ng/g)			
Quartile I (0.11-1.43)	27.5%	21.9%	25.8%
Quartile II (1.43-3.28)	21.6%	30.7%	24.5%
Quartile III (3.28-7.41)	25.2%	25.6%	25.3%
Quartile IV (7.41-170)	25.6%	21.9%	24.5%
TSH (reference range: 0.3-3.0			
Above reference range	18.9%	14.0%	17.4%
Below reference range	0.84%	0.93%	0.87%
TT4 (reference range: 4.5-12.5			
Above reference range	7.14%	5.12%	6.51%
Below reference range	0.63%	0.93%	0.72%

[a] $p<0.05$ for female participants compared with male participants, using Chi-square test of independence.
Quartile ranges for the sum of 35 PCBs (ng/g, wet weight) are based on the whole ACHS sample (n=765).
A response of don't know or refusal is counted as missing. Missing 3 observations for BMI.
Participants taking thyroid medication were excluded (n=52).

Logistic regression results showed lower odds of having a TSH concentration above the reference range among participants with higher serum PCB concentrations (adjusted OR = 0.73, 95% CI 0.55-0.98) (Table 2). This relationship was statistically significant after adjustment for several possible risk factors but was not significant prior to adjustment. The odds of having below-normal TSH were observed to decrease non-significantly with PCB exposure before and after adjustment. A statistically insignificant increase in the likelihood of increased T4 with PCB exposure was observed in results from the adjusted logistic regression on participants with T4 within or above the reference range. Results were ambiguous and non-significant for the odds of having below-normal T4, which were seen to increase with PCB exposure in an unadjusted analysis but decrease after adjustment. Small sample sizes for those with T4 or TSH lower than the normal range limit the inferences that can be made from these analyses.

Table 2. Odds ratios for TSH and TT4 status of ACHS participants per unit increase in the natural log of sum of serum concentrations of 35 PCB congeners.

Thyroid hormone status	*n* above or below reference range / *n* total in analysis	Unadjusted OR (95% C.I.)	Adjusted OR[b] (95% C.I.)
TSH			
Above reference range	120 / 685	0.87 (0.75 – 1.02)	0.70 (0.52 – 0.95)
Below reference range	6 / 571	0.78 (0.41 – 1.45)	0.77 (0.24 – 2.52)
TT4			
Above reference range	45 / 686	1.00 (0.79 – 1.27)	1.07 (0.73 – 1.58)
Below reference range	5 / 646	1.30 (0.64 – 2.62)	0.87 (0.30 – 2.54)

Table 3. Odds ratios for TSH and TT4 status of ACHS participants by quartiles of the summed serum concentrations of 35 PCB congeners.

Thyroid hormone status	*n* above or below reference range / *n* total in analysis	Quartile I 0.11-1.43 ng/g, wet weight	Quartile II 1.43-3.28 ng/g, wet weight		Quartile III 3.28-7.41 ng/g, wet weight		Quartile IV 7.41-170 ng/g, wet weight	
		Referent quartile	Unadj. OR (95% C.I.)	Adjusted OR[b] (95% C.I.)	Unadj. OR (95% C.I.)	Adjusted OR[b] (95% C.I.)	Unadj. OR (95% C.I.)	Adjusted OR[b] (95% C.I.)
TSH above reference range	120 / 685	1.00	1.89 (1.11-3.22)	1.28 (0.64-2.55)	0.77 (0.42-1.40)	0.56 (0.25-1.28)	0.97 (0.54-1.73)	1.00 (0.40-2.52)
TT4 Above reference range	45 / 686	1.00	0.72 (0.30-1.73)	0.82 (0.28-2.37)	0.95 (0.42-2.15)	1.00 (0.33-3.00)	0.89 (0.39-2.04)	0.88 (0.25-3.13)

[b] Adjusted for age (years), race, sex, family history of thyroid disease (yes/no), BMI classification (normal, overweight, or obese), serum total lipid concentration (mg/dL).

Serum concentrations of 35 PCB congeners (ng/g, wet weight) were summed for each participant; natural logarithm was taken for this sum. Reference range for TSH: 0.3-3.0 miU/L; reference range for total T4: 4.5-12.5 µg/dL. Variables missing observations: BMI classification (3), family history of thyroid disease (50). Of those participants for whom thyroid data were available and who were not taking thyroid medication, only five had serum TT4 concentrations below the reference range and only six had serum TSH concentrations below the reference range, Because of these small sample sizes, we did not estimate odds ratios for these groups by quartile of 35 summed PCBs. Participants taking thyroid medication were excluded (n=52).

We investigated the association of PCB levels with the prevalence of thyroid hormone abnormalities in a community with high environmental exposures to PCBs. In results from adjusted logistic regression on all

participants combined, we observed lower odds of having above-normal TSH among participants with higher serum PCB concentrations. This preliminary result is in agreement with several studies that showed inverse associations between serum TSH and PCBs.[4-6] However, when we estimated odds ratios by quartile of summed PCB concentration, we observed an elevated odds ratio for having above-normal TSH in the second quartile. With the relationships between PCB exposure and the levels of thyroid hormones and TSH still inconclusive, additional research is warranted in this area. Further analysis of these data will include review of all thyroid hormone values, medication, and other available data in order to establish clinical diagnoses for all participants, as well as investigation of possible effects of race, sex, and BMI on abnormal thyroid hormone or TSH levels.

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