EXPOSURE TO PCBS AND HYPERTENSION IN THE ANNISTON COMMUNITY HEALTH SURVEY

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Abstract

Environmental exposures that may contribute to the development of essential hypertension are not clearly understood. We have studied factors associated with the risk of hypertension in residents of Anniston, Alabama who live near a plant that manufactured polychlorinated biphenyls (PCBs) between 1929 and 1971. A total of 759 Anniston residents had multiple measurements of blood pressure and information on demographic factors, medications, smoking, and exercise collected in 2005-2007. They also provided blood samples for the analysis of 35 PCBs and total serum lipids. Rates of hypertension increased significantly ($p<0.05$) with age, concentrations of serum PCBs and body mass index (BMI) and were higher in African-Americans than in Caucasians. Hypertension was not associated with total serum lipid levels, gender, smoking or frequency of exercise. Odds ratios (ORs) for elevated diastolic blood pressure in relation to total serum PCBs were above four in those not on anti-hypertensive medication (OR=4.49, 95% CI 1.34-14.99) after adjustment for established risk factors for hypertension and were elevated, but to a lesser degree for systolic hypertension (OR=3.87, 95% CI 1.13-13.17).

Introduction

Hypertension is one of the leading causes of death, and is the most important easily recognizable risk factor for stroke, myocardial infarction, heart failure, and peripheral vascular disease.[1] There are a number of reported risk factors, including age, gender, obesity, smoking, elevated serum lipids, co-existing diabetes, high salt intake, a sedentary life style, and stress.[1-2] In the US, African-Americans have a higher incidence of hypertension than do Caucasians. Kreiss et al. first reported an elevated incidence of hypertension in a population exposed to polychlorinated biphenyls.[3] Two recent studies of the general US population, based on the 1999-2000 and 2001-2002 National Health and Nutrition Examination Survey (NHANES) examined associations between hypertension and levels of various persistent organochlorine pollutants (POPs).[4-5] One reported that concentrations of 7 of 10 PCB congeners studied were correlated with hypertension; those with dioxin-like activity had the highest likelihood of having hypertension.[4] The other study examined 21 POPs (three dioxins, three furans, five dioxin-like PCBs, six non-dioxin-like PCBs and four organochlorine pesticides) and reported a statistically significant association between dioxins or furans and hypertension in women, and weaker but still significant associations with dioxin-like and non-dioxin-like PCBs in men.[5]

Anniston, Alabama was the site of a Monsanto production plant that produced PCBs from 1929 until 1971. Elevated levels of PCBs have been found in Anniston residents previously.[6] It has been postulated that significant release and spread of PCBs in Anniston has occurred via air transport and movement of contaminated soils and water.[7-8] To date there has been little systematic study of the health of PCB-exposed residents of Anniston. To further that research, a consortium of universities and community groups was funded by the Agency for Toxic Substances and Disease Registry.

Materials and Methods

Anniston is a city of about 24,000 people, and about 8,000 live in West Anniston, the area closest to the Monsanto plant. A total of 1,110 randomly selected adults (with stratification based on race and residential proximity to the plant) were interviewed. Of these, 772 had blood drawn and blood pressure measurements taken. Eight subjects were excluded due to data quality issues. An additional four subjects were excluded because they had less than three blood pressure measurements, and one subject was excluded because the race listed was neither Caucasian nor African-American. The questionnaire contained information on health status and medications used, as well as socio-demographic information. Three sequential blood pressure measurements were obtained by a nurse at two minute intervals, beginning after the patient had been sitting for five minutes. We compared the means of systolic and diastolic pressures on the first, second and third measurements, and did not find any differences by nested analysis of variance. Therefore, we used the mean value of the three different measurements for each individual.

Analyses of PCBs were performed by the Centers for Disease Control and Prevention's National Center for Environmental Health laboratory using high-resolution gas chromatography/isotope-dilution high-resolution mass spectrometry, as published in detail elsewhere.[9] Serum specimens (2mL) were fortified with $_{13}C^{12}$-labeled internal standards and diluted with concentrated formic acid and water using a 215 liquid handler (Gilson Inc., Middleton, WI) for automation. Automated solid phase extraction (SPE) and silica:silica/sulfuric acid lipid degradation were performed on the Rapid Trace SPE work station (Caliper Life Sciences Inc., Hopkinton, MA). Samples were injected into a Hewlett-Packard 6890 gas chromatograph equipped with a DB-5ms capillary column (30m x 0.25 μm film thickness) coupled to a Thermo Finnigan MAT95 XP mass spectrometer operated in EI mode using selected ion monitoring at 10,000 resolving power. The concentration of each analyte was calculated from its calibration curve. Study specimens were analyzed in batches of 24 specimens intermixed with quality control (n=3) and method blank (n=3) samples. All data were reviewed using comprehensive quality assurance and quality control procedures. Values below the limit of detection (LOD) were set to the LOD divided by the square root of 2. For this study, all PCB levels were recorded using wet weight values and total lipids were included in the model as a separate variable. The LOD for individual congeners ranged between 2.2 pg/g and 63.3 pg/g. Serum cholesterol and triglycerides were determined by the clinical chemistry laboratory at the Jacksonville Medical Center. Total serum lipids were calculated using the formula proposed by Phillips and recently updated by Bernert et al.[10]

Hypertension was defined as either taking antihypertensive medication or elevated systolic (>140 mm Hg) or diastolic pressure (>90 mm Hg) in those not on medication. Multiple logistic regression models were built to contrast associations between PCB tertiles, adjusting for established risk of hypertension. Effect modification by gender was assessed. Adjusted associations between hypertension and PCB levels were assessed separately for individuals taking or not taking antihypertensive medication. Odds ratios and 95% confidence intervals (95% CI) for all logistic regression models were reported.

Results and Discussion

Table 1 shows the selected characteristics of the study population for whom serum organochlorines, lipids and blood pressure measurements were available. The sum of 35 PCBs (total PCBs) are presented for two study groups - participants not on hypertensive medication and those on medication - in addition to age, BMI, gender, and race. Nearly half of the population was taking antihypertensive medication (n=365).

Unadjusted odds ratios for diastolic hypertension contrasting tertiles of serum total PCB concentration showed positive associations with increasing age, serum PCBs, and BMI (normal, overweight and obese) in subjects who were not on anti-hypertensive medication. African-American race was also significantly correlated with rates of hypertension, but the OR was low. There was no statistically significant relationship with total serum lipids, gender, smoking or exercise. Analysis of systolic hypertension showed a similar pattern (data not shown).

Table 2 shows the associations between systolic and diastolic hypertension and total serum PCBs after adjustment for age, BMI, total lipids, gender, race, smoking status and physical activity for the participants not on anti-hypertensive medication. There was a statistically significant elevation in the odds of hypertension for the second (1.24-3.63 ng/g whole weight) and third (3.64-170 ng/g whole weight) tertile of total serum PCBs for diastolic pressure (OR=4.27, 95% CI 1.50-12.15, and OR=4.49, 95% CI 1.34-14.99, respectively). Odds ratios were also elevated for the systolic blood pressure but were somewhat weaker and statistically significant only for the third PCBs tertile (OR=3.05, 95% CI 0.77-12.04 and OR=3.87, 95%CI 1.13-13.17, respectively).

There was no statistically significant relationship with serum PCB levels in the group of subjects who were on anti-hypertensive medication. For diastolic hypertension odds ratios were 0.65 and 0.83 for the second and third tertiles, respectively, while for systolic hypertension the odds ratios were 1.15 and 1.58, respectively. All 95% confidence intervals included 1 (data not shown). We speculate that in this population the anti-hypertensive medication adequately controls diastolic pressure, but does not fully control systolic pressure. Many factors may alter the effectiveness of anti-hypertensive medication. The present study did not collect information to evaluate the effect, if any, of PCBs in patients taking such medications.

Data from the NHANES and studies of a Native American population have provided evidence for an association between serum levels of persistent organic pollutants and diabetes [5, 11] and cardiovascular disease.[12-13] While mechanisms responsible for these associations are still unclear, exposure to PCBs and other dioxin-like compounds results in the induction of a very large number of genes involved in many different pathways.[14] The strong association of hypertension with elevated levels of PCBs in this study suggest that exposure to organochlorines may be a contributing factor in the development of hypertension and warrants further examination of the role of PCBs in cardiovascular diseases, and specifically, the implications for hypertension prevention and treatment.

Acknowledgements
Members of the Anniston Environmental Health Research Consortium include: David Baker, Shirley Baker, Bessie Jones, community representatives; Scott Bartell, UC Irvine; Lain Bian, James Olson, Peter Rogerson, University at Buffalo; Fred Biasini, Russell Foushee, Max Michael, Alan Percy, University of Alabama Birmingham; Anthony DeCaprio, University at Albany; Jane Cash, Martha Lavender, Christie Shelton, Jacksonville State University; Germaine Buck-Louis, NICHD; Howard Frumkin ATSDR/CDC; Mark Hermanson, University of Pennsylvania; Roberto Izquierdo, Paula Rosenbaum, Allen Silverstone, Ruth Weinstock, Upstate Medical University, SUNY; Glenn Johnson, University of Utah; Rhoda Johnson, University of Alabama, Tuscaloosa; Kirsten Moysich, Roswell Park Cancer Institute, and John Stone, Tuskegee University. We also would like to acknowledge Andreas Sjödin, Wayman Turner and Larry Needham at the National Center for Environmental Health, Division of Laboratory Sciences, for their expert chemical analyses for this study.

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Table 1. Selected demographic characteristics of the study participants stratified by the use of anti-hypertensive mediation.

Covariate	No Medication (n=394)	On Medication (n=365)
Age, years: Mean (SD)	47.6 (15.5)	62.8 (11.9)
Sum PCBs, ng/g whole weight: Mean (SD)	4.72 (11.1)	8.78 (12.6)
BMI	29.8 (7.2)	32.9 (7.9)
Gender, n (%): Male	126 (31.9)	104 (28.5)
Female	268 (68.1)	261 (71.5)
Race, n (%) Caucasian	223 (56.6)	184 (50.6)
African-American	171 (43.4)	180 (49.4)

Table 2. Adjusted Odds Ratios [a] and 95% Confidence Intervals for systolic and diastolic hypertension in relation to total PCBs (ng/g whole weight) among study participants not taking anti-hypertensive medication (n=394).

PCBs Tertiles (ng/g whole weight)	Odds Ratios (95% Confidence Intervals) [a]	
	Systolic Hypertension (n=53)	Diastolic Hypertension (n=56)
1. (0.09-1.23)	1.00 (Referent)	1.00 (Referent)
2. (1.24-3.64)	3.05 (0.77-12.04)	4.27 (1.50-12.15)
3. (3.65-170.4)	3.87 (1.13-13.17)	4.49 (1.34-14.99)

a. Adjusted for age, BMI, total serum lipids, gender, race, smoking status, and physical activity.