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Associations between plasma persistent organic pollutant levels and blood pressure in Inuit adults from Nunavik

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ABSTRACT

Background: Recent evidence suggests that exposure to persistent organic pollutants (POPs) increases the risk of hypertension in environmentally exposed populations. High POP levels have been detected in Arctic populations and the exposure is related to high consumption of fish and marine mammals, which represent the traditional diet of these populations.
Objective: We examined the associations between polychlorinated biphenyls (PCBs), organochlorine (OC) pesticides and hypertension among Inuit from Nunavik (Quebec, Canada).
Methods: A complete set of data was obtained for 315 Inuit ≥ 18 years who participated in the "Santé Québec" health survey that was conducted in the 14 villages of Nunavik in 1992. Fourteen polychlorinated biphenyls (PCBs) and 8 OC pesticides or their metabolites were measured in plasma samples using gas chromatography with electron capture detection. Blood pressure (BP) was measured using a standardized protocol and information regarding anti-hypertensive medication was obtained through questionnaires. The associations between log-transformed POPs and hypertension (systolic BP ≥ 140 mm Hg, diastolic BP ≥ 90 mm Hg or anti-hypertensive medication) were analyzed using multiple logistic regressions.
Results: Total PCBs as well as the sum of non-dioxin-like PCBs were significantly associated with higher risk of hypertension. Furthermore, the risk of hypertension increased with higher plasma concentrations of congeners 101, 105, 138 and 187. Models adjusted for BP risk factors became significant after including n − 3 polyunsaturated fatty acids (PUFAs) and further adjustment for lead and mercury did not change the results. Regarding OC pesticides, *p,p′*-dichlorodiphenyldichloroethylene (*p,p′*-DDE) was associated with increased risk of hypertension while inverse associations were observed with *p,p′*-dichlorodiphenyltrichloroethane (*p,p′*-DDT), β-hexachlorocyclohexane (HCH) and oxychlordane.
Conclusions: Some PCB congeners were associated with higher risk of hypertension in this highly exposed population. Most associations became significant after including n − 3 PUFAs in the models. However, the analyses of OC pesticides revealed divergent results, which need to be confirmed in further cohort and experimental studies.

1. Introduction

Exposure to environmental contaminants is of concern in populations who rely on seafood as a way of subsistence since contaminants such as mercury and persistent organic pollutants (POPs) accumulate in predator fish and marine mammals (AMAP, 2011). POPs are chemical compounds that are resistant to biotic and abiotic degradation due to properties such as low water solubility and volatility (Safe, 1994). This group of chemicals includes, among others, the organochlorine (OC) pesticides and the polychlorinated biphenyls (PCBs), which contain mixtures of chlorinated compounds that were manufactured for use as lubricants and coolants in various electrical components. The use of PCBs and some OC pesticides is now banned but they are still widespread in the environment, reaching remote regions with no known local sources of emission (AMAP, 2011). As these chemicals enter the food chain and accumulate in animal tissues, native populations from Arctic regions who consume large quantities of fish and marine mammals are exposed to high POP levels compared to southern populations (Dallaire et al., 2009; Deutch et al., 2004; Van Oostdam et al., 2005). Among Inuit from Nunavik (Quebec, Canada), a decrease

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in POP levels was noticed after the Stockholm convention (Dallaire et al., 2003) but data collected in 2004 revealed that 11% of the adult population still presented total PCB concentrations above the level of concern determined by Health Canada (20 μg/L in whole blood) (Dewailly et al., 2007).

The toxic effects of POPs on the cardiovascular system were firstly reported after an industrial accident that occurred in the town of Seveso, Italy, in 1976, which exposed a large population to substantial amounts of relatively pure 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) (Pesatori et al., 1998). Fifteen years after the accident, Pesatori et al. reported an excess of cardiovascular mortality in the highly exposed area compared to areas with moderate or low exposure (Pesatori et al., 1998). This excess of mortality was mainly due to chronic ischemic heart disease (IHD) in men and hypertensive disease in women.

Other studies conducted in populations without occupational exposure have shown significant associations between PCBs and increased blood pressure (BP) or hypertension, although the associations with individual congeners are not consistent across studies. Goncharov et al. observed significant associations between PCBs and higher blood pressure in two studies conducted among residents of Anniston (Alabama, United States) (Goncharov et al., 2010; Goncharov et al., 2011). In contrast, among the OC pesticides, only β-hexachlorocyclohexane (β-HCH) was significantly associated with increased diastolic BP (Goncharov et al., 2011). Increased hypertension prevalence was also observed by Huang et al. in areas of New York containing hazardous waste sites with POPs (Huang et al., 2006). Also in the United States, Everett et al. observed significant associations between some PCB congeners and higher risk of hypertension among participants in the NHANES 1999–2002 (Everett et al., 2008). Using data from the same health survey, Lee et al. observed increased risk of hypertension across quartiles of PCB 126 in non-diabetic participants (Lee et al., 2007). In addition, Ha et al. reported weak associations between some PCB congeners and newly diagnosed hypertension in men aged ≥40 years (Ha et al., 2009). In contrast, no significant association was observed with levels of OC pesticides (Ha et al., 2009). PCBs have been also associated with higher risk of hypertension in a study conducted among Japan's general population (Uemura et al., 2009). Furthermore, Kreiss et al. observed a significant association between total serum PCBs and high BP in a community-based study including 458 individuals in Triana, Alabama (Kreiss et al., 1981). Significant associations were also observed between POPs and hypertension among Inuit from Greenland although the associations differed by age category (Valera et al., 2013).

In the present study, we aimed to assess the associations between PCBs, OC pesticides and blood pressure in a native population from Quebec (Canada) highly exposed to these contaminants. We also verified the influence of other contaminants (lead and mercury) as well as n−3 polyunsaturated fatty acids (PUFAs), which also reach high levels in this population and have shown protective effects on BP (Valera et al., 2009; Vupputuri et al., 2003; Xun et al., 2010). We hypothesized that increasing PCB levels would be associated with increased risk of hypertension.

2. Methods

2.1. Study population and sampling

Participants in this health survey were adults (≥18 years of age) who inhabited 400 households that were selected randomly from the 1378 households located in the 14 villages of Nunavik (Dewailly et al., 2001a). Total population at the time of the survey was 7078. The 14 villages are scattered along the 1500-km shoreline of Hudson Bay, Hudson Strait, and Ungava Bay (Fig. 1). We performed systematic sampling after sorting the survey base by household address to favor better coverage of the territory and to avoid the selection of next-door neighbors. Furthermore, so that each village would be represented, we stratified the sample by village, with quasi-proportional representation of the number of households in each stratum. Data collection for this survey was achieved between September 17, 1992, and December 1, 1992, by 6 teams, each of which included a nurse and 2–4 Inuit interviewer/interpreters. The study protocol was approved by the Ethics Committee of Maisonneuve-Rosemont Hospital (Montreal). Of the 382 eligible households, 305 (79.8%) had an eligible respondent who agreed to fill out the identification chart and the household questionnaire; therefore, 766 persons aged 18–74 years became admissible to physical examination and biological analyses. Among this group, 518 (67.6%) agreed to participate in this component of the survey, and blood samples were available for 492 (64.4%) of the eligible participants. Informed consent was obtained from all individuals who participated in the survey.

2.2. Data collection

After visiting each village to inform the population that a survey would be conducted, the interviewers visited each household and asked to speak with a person ≥18 years of age to complete the identification chart of the survey. With the information obtained, a main respondent was designated, who then completed a household questionnaire. Individual questionnaires regarding smoking, alcohol consumption, physical activity, cardiovascular disease and treatment were also administered to each participant in the household. Later, participants were asked to attend a clinical visit at the local health center, during which a registered nurse collected blood samples and conducted anthropometric measurements. Waist circumference (WC) was measured using a tape placed horizontally on the curve of the abdomen (Ross et al., 2008). If a curve was not perceptible, the tape was placed horizontally between the last floating rib and the iliac crest. Body mass index (BMI) was calculated by dividing the weight (kg) by the squared height (m). During the clinical visit, BP was measured using mercury sphygmomanometers, 15-inch stethoscopes, and cuffs sized to the subjects' arms. Prior BP measurement, subjects were asked to rest for 5 min and not drink or smoke for at least 15 min. Each subject had three BP readings and means of systolic BP and diastolic BP were calculated using the last two readings.

2.3. Laboratory analyses

Blood samples collected in vial containing EDTA were centrifuged and the plasma transferred in glass vials pre-washed with hexane. Plasma samples were frozen at −20 °C until analysis. For organochlorine analysis, samples were thawed overnight at 4 °C and a 2-mL aliquot was extracted with hexane. The lipid extract was then cleaned-up on Florisil columns and taken to a final volume of 100 μL. Fourteen PCB congeners (IUPAC nos: 28, 52, 99, 101, 105, 118, 128, 138, 153, 156, 170, 180, 183, 187) and 13 chlorinated pesticides or their metabolites (aldrin, α-chlordane, γ-chlordane, *p,p′*-DDT, *p,p′*-DDE, dieldrin, hexachlorobenzene, heptachlor epoxide, β-HCH, mirex, *cis*-nonachlor, *trans*-nonachlor, oxychlordane) were quantified on a HP-5890 series II gas chromatograph equipped with dual-capillary columns and dual Ni-63 electron-capture detectors (Hewlett Packard, Palo Alto, CA). Peaks were identified by their relative retention times obtained on the two columns, using a computer program developed in-house. Quantification was mainly performed on the Ultra-1 column. The limit of detection, based on 3 times the average standard deviation of noise, was 0.02 μg/L for PCB congeners and chlorinated pesticides, with the exception of *p,p′*-DDT and β-HCH which was 0.03 μg/L. The average percentage recoveries were greater than 95% for PCB congeners and ranged from 90 to 103% for chlorinated pesticides. The between-day precision ranged from 3.3 to 7% for PCB congeners and 5.5 to 14.2% for chlorinated pesticides.

The concentration of total plasma lipids was estimated using the formula proposed by Phillips et al. (1989): $TL = 2.27\ TC + TG + 0.623$ where TL is total lipids, TC is total cholesterol and TG is triglycerides, all expressed in g/L. TC and TG were analyzed according to methods of