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Associations of organochlorines with endogenous hormones in male Great Lakes fish consumers and nonconsumers ☆

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Abstract

This study investigated the relationships of steroid and thyroid hormones with total noncoplanar polychlorinated biphenyls (PCBs), total toxic equivalents (TEQs) from dioxins-like organochlorines, and dichlorodiphenyl dichloroethene (DDE) in 56 male frequent and infrequent Great Lakes sport caught fish consumers. Significant negative associations were found for triiodothyronine (T_3), thyroxine (T_4), thyroid stimulating hormone (TSH), and sex hormone binding globulin (SHBG)-bound testosterone with PCBs, for TSH with total TEQs, and for estrone sulfate with DDE, adjusting for age, body mass index, and medication use. Follicle-stimulating hormone, luteinizing hormone, free testosterone, and SHBG were not significantly associated with organochlorines. Models that accounted for exposure to both PCBs and TEQs predicted T_4, estrone sulfate, and SHBG-bound testosterone better than models that included either PCBs or TEQs alone, with the lowest hormone levels occurring in the participants with both higher PCB levels and lower TEQ levels.

These data suggest that exposure to PCBs, dioxin-like organochlorines, and DDE, alone and potentially in combination, may be associated with effects on the endocrine system in adult males. Further studies should help delineate specific exposure effects and effects of exposures to other common environmental contaminants alone and in combination with PCBs.

Keywords: Dioxin; PCB; Thyroid; Testosterone; Estrone sulfate

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1. Introduction

Polychlorinated biphenyls (PCBs), dioxins, furans, and dichlorodiphenyl dichloroethene (DDE) are widespread environmental pollutants that are routinely detected in human tissue samples (ATSDR, 1998, 2000, 2002). Dioxins, furans, and some PCB congeners contribute to dioxin-like toxic equivalents (TEQs) and activate the arylhydrocarbon (Ah) receptor (van den Berg et al., 1998). Background exposure to dioxins, PCBs, and DDE in humans is predominantly through diet, and concentrations of blood organochlorines (OCs) are often highly correlated (Turyk et al., 2005). However, health effects, including changes in hormonal balance from exposure to OCs may be attributed to combined rather than single exposures. Animal studies have shown decreases in thyroid hormones and some steroid hormones following exposure to PCB and dioxin congeners (van Birgelen et al., 1992, 1995; Corey et al., 1996; Kato et al., 1998). In general, human studies have found decreased levels of thyroxine (T_4) in heavy consumers of fish (Persky et al., 2001, 2002; Hagmar et al 2001a), while a trend toward increased levels of T_4 has been noted in the few studies of persons exposed to dioxin-like chemicals (Murai et al., 1987; Ott et al., 1994; Calvert et al., 1999). The studies, however, have not always been consistent and have not, in general, examined interactive effects. In humans, the effects of PCBs and dioxins on steroid hormones have been less studied than their effects on thyroid hormones.

Previous investigations of a cohort of Great Lakes fish consumers have shown that PCB, DDE, dioxin, and furan levels were significantly correlated with age, body mass index (BMI), gender, and frequency of Great Lakes sport caught fish (GLSCF) consumption (Hanrahan et al., 1999; Falk et al., 1999) and that PCBs were associated with lower levels of T_4 and free T_4 index (FTI) in women and T_4 and sex hormone binding globulin (SHBG)-bound testosterone in men (Persky et al., 2001). In this paper we extend our analysis to examine the effects of exposure to dioxin-like chemicals on thyroid and steroid hormones in a subgroup of 56 men from the Great Lakes cohort. In addition, the effects of concurrent exposure to dioxin-like organochlorines, noncoplanar PCBs, and DDE on endogenous hormones are investigated. Since the levels of these three types of organochlorines are highly correlated, variance inflation factors are used to evaluate the effects of multicolinearity on the analyses involving multiple organochlorines.

2. Methods

The full study protocol and related protocols and Institutional Review Board approval information have been previously published (Anderson et al., 1996; Hanrahan et al., 1999; Falk et al., 1999; Persky et al., 2001). All subjects gave written informed consent prior to any study. Approximately 1800 charter boat captains on Lakes Michigan, Huron, and Erie and 1200 referent participants who reported eating less than six meals of Great Lakes sport fish in each year of the last 12 years completed a telephone survey in 1993–1994. Blood samples were donated by 445 captains and 100 referents and tested for noncoplanar PCBs and DDE. A subsample was selected for dioxin, furan, and coplanar PCB analysis. All of the 100 referents were selected. The captains were stratified by state of residence, age range, and gender and a random sample was selected from each strata in the same frequency as the 100 referents (Falk et al., 1999). Of the 438 participants with stored serum after organochlorine analysis, 309 consented to participate in the hormone study. Participants with a history of thyroid disease, diabetes, other endocrine problems, prednisone therapy, current oral contraceptives or hormone replacement therapy, or missing data were excluded for a final group of 179 males and 51 females. The study group for this report is the 56 males who had measurements available for dioxins, furans, coplanar PCBs, noncoplanar PCBs, DDE, and hormones. One referent male was excluded because his total TEQ exposure was greater than 3 standard deviations below the mean total TEQs, but inclusion of this participant did not change our conclusions.

Serum hormone measurements and quality assurance and quality control procedures have been previously described (Persky et al., 2001). Thyroid hormone analyses for triiodothyronine (T_3), T_4, free T_4 index (FTI), and thyroid-stimulating hormone (TSH) were performed by SmithKline Beecham Clinical Laboratories (Van Nuys, CA). Steroid hormone measurements for luteinizing hormone (LH), follicule-stimulating hormone (FSH), testosterone, SHBG, SHBG-bound testosterone, free testosterone, and estrone sulfate were performed by the Immunoassay Core Facility Laboratory of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University.

Serum samples were analyzed for DDE and 89 PCB congeners at the Wisconsin State Laboratory of Hygiene (Madison, WI) or the Michigan Department of Community Health (Lansing, MI). The PCB congeners were represented by 62 peaks using the capillary column gas chromatography with the electron capture detection method (Burse et al., 1990). Dioxin-like organochlorines, including 8 dioxins, 10 furans, and 4 coplanar PCB congeners, were measured according to the high-resolution mass spectrometric method of Patterson et al. (1987). Detailed descriptions of the laboratory protocol have been published elsewhere (Hanrahan et al., 1999; Falk et al., 1999).

Summed TEQs were determined by adding the TEQs of dioxins, furans, coplanar PCBs, and monoortho PCBs 105, 114, 118, 123, 157, and 167; PCB156 was not measured. The TEQ for each congener is the product of the toxic equivalency factor (TEF) and the concentration in pg/g lipid (van den Berg et al., 1998). Total PCBs is the sum of all noncoplanar PCBs in ng/g lipid. Lipid-standardized