A Case Study Addressing the Reliability of Polychlorinated Biphenyl Levels Measured at the Time of Breast Cancer Diagnosis in Representing Early-Life Exposure

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Abstract

Background: To date, breast cancer epidemiologic studies have relied on blood or tissue specimens sampled at the time of diagnosis or a few years prior to assess lifetime exposure to polychlorinated biphenyls (PCB). In this study, we evaluated whether such PCB measurements are indicative of early-life levels by reconstructing lifetime toxicokinetic profiles for women included in the CECILE case–control study, using a physiologically based pharmacokinetic (PBPK) model.

Methods: We simulated lifetime toxicokinetic profiles of PCB-153 for 2,134 French women by incorporating information on body weight history, height, pregnancies, and breast-feeding in the PBPK model. Oral dose was calculated by considering measured blood PCB-153 and the temporal trend of environmental contamination. Area under the concentration versus time curve (AUC) for each decade of life and maximum blood concentration (Cmax) were compiled and compared with measured levels, using Pearson partial correlation analyses adjusting for age at diagnosis.

Results: When considering all individuals, simulated AUCs correlated with measured PCBs, with coefficients ranging from 0.735 to 0.981. The weakest correlations were obtained with AUCs for the first decades of life. Stratified analyses suggested that breast-feeding reduces the reliability of late-life blood levels in representing lifetime exposure.

Conclusion: Results of this study suggest that PCB levels measured at the time of diagnosis do not fully represent early-life exposures.

Impact: PBPK-derived estimates of early-life levels circumvent the limitations of current approaches in assessing PCB lifetime exposure and may be used to address hypothesized windows of breast vulnerability (e.g., puberty) in this population. Cancer Epidemiol Biomarkers Prev; 20(2); 281–6. ©2010 AACR.

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