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Polycyclic aromatic hydrocarbons and postmenopausal breast cancer: An evaluation of effect measure modification by body mass index and weight change

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ABSTRACT

Background: Polycyclic aromatic hydrocarbons (PAHs) have been linked to breast cancer in many, but not all, previous studies. PAHs are lipophilic and stored in fat tissue, which we hypothesized may result in constant low-dose exposure to these carcinogens. No previous studies have evaluated whether obesity modifies associations between multiple measures of PAHs and breast cancer incidence.

Methods: This population-based study included 1,006 postmenopausal women with first primary in situ or invasive breast cancer and 990 age-frequency matched controls. To evaluate effect modification by obesity (adult body mass index (BMI, kg/m^2) and weight change) on multiple PAH measures (the biomarker PAH-DNA adducts, and long-term sources active cigarette smoking, living with a smoking spouse, grilled/smoked meat intake, residential synthetic log burning, and vehicular traffic), interaction contrast ratios (ICRs) for the additive scale, and ratio of odds ratios (RORs) with log-likelihood ratio tests (LRT) for the multiplicative scale, were determined using unconditional logistic regression.

Results: BMI modified the PAH-DNA adduct and postmenopausal breast cancer association on the additive (ICR: 0.49; 95% CI: 0.01, 0.96) and multiplicative (ROR: 1.56; 95% CI: 0.91, 2.68) scales. The odds ratio for detectable vs. non-detectable adducts was increased among women with BMI ≥25 (OR=1.34; 95% CI: 0.94, 1.92), but not in those with BMI < 25 (OR=0.86; 95% CI: 0.57, 1.28) (LRT p=0.1). For most other PAH measures, the pattern of modification by BMI/weight gain was similar, but estimates were imprecise.

Conclusions: The association between PAH-DNA adducts and breast cancer incidence may be elevated among overweight/obese women.

1. Introduction

Polycyclic aromatic hydrocarbons (PAHs) are ubiquitous environmental contaminants that result from the incomplete combustion of organic material. Ambient PAH are combustion products of burning organic material. Common exposure sources include motor vehicle exhaust, grilled/smoked food, both active and passive cigarette smoke, and indoor stove and fireplace use (Mumtaz and George, 1995). Tobacco smoke, both active and passive, is a major contributor to ambient PAH exposure (IARC, 2010; White et al., 2016). However, diet may be the most common contributor to PAH exposure in non-smokers (Bostrom et al., 2002; White et al., 2016). The Environmental Protection Agency has determined a list of 16 priority PAHs of which seven PAHs have been classified as probable carcinogens, and the

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International Agency for Research on Cancer has classified PAHs as known carcinogens to the lung (IARC, 2010).

Associations between ambient PAH measures and breast cancer incidence among women are now relatively consistent. Historically, epidemiologic studies between active smoking and breast cancer were inconsistent (Luo et al., 2011b; Reynolds et al., 2004), but a recent meta-analysis of cohort studies reported a modest increase in breast cancer incidence for former and current active smoking (Gaudet et al., 2013) and the US Surgeon General Report states that evidence is suggestive for a causal relationship between active smoking and breast cancer (US Department of Health and Human Services, 2014). Long-term environmental tobacco smoke (ETS) has been more consistently associated with breast cancer incidence (Johnson, 2005; Reynolds et al., 2009; Terry and Rohan, 2002) and the Long Island Breast Cancer Study Project (LIBCSP) reported a doubling of risk for living with a smoking spouse for ≥27 years (Gammon et al., 2004a). PAH-DNA adducts are a biomarker of recent exposure and reflect DNA damage, a step in carcinogenesis. Detectable PAH-DNA adducts, or their proxy, have been consistently linked to breast cancer in previous studies (Gammon et al., 2004b; Li et al., 1999; Rundle et al., 2000b), with one exception (Saieva et al., 2011). Cooking food through grilling and smoking leads to the formation of PAHs (Knize et al., 1999) and has been associated with breast cancer incidence (Steck et al., 2007). Similarly, residential burning of synthetic logs contributes to indoor air pollution and was found to increase breast cancer risk in a case-control study (White et al., 2014). Outdoor air pollution from the combustion of vehicular fuels also contributes to ambient PAH exposure. In the LIBCSP, a validated emissions model assessed exposure to residential traffic-related benzo[*a*]pyrene levels (a PAH used as a proxy for all traffic related PAHs). Women in the top 5% of exposure compared to women below the median had an increased odds of breast cancer (Mordukhovich et al., 2015), consistent with other studies on air pollution exposures and breast cancer (Bonner et al., 2005; Crouse et al., 2010; Hystad et al., 2015; Nie et al., 2007).

PAHs are lipophilic and can be stored in the fat tissue of the breast (Goth-Goldstein, 2010; IARC, 2010). We hypothesized that individuals with higher amounts of body fat may store and metabolize PAHs to a different extent than those with lesser amounts of body fat. The mechanism may be that fat tissue serves as a reservoir where PAHs can accumulate (Mumtaz and George, 1995). It is plausible that PAHs stored in fat tissue are a source of constant low-dose exposure to these carcinogens. One study to date has addressed this issue focusing only on active smoking and obesity (Luo et al., 2011a). Therefore, the aim of the study reported here was to determine if the associations between multiple measures of PAH exposure and breast cancer are modified by multiple measures of body size among postmenopausal women.

2. Methods

This study used case-control resources from the LIBCSP, a population-based study which was designed to examine relationships between environmental exposures and breast cancer in Nassau and Suffolk counties, New York. Detailed methods of the parent case-control study have been described previously (Gammon et al., 2002a). Institutional Review Board approval was obtained from all participating institutions.

2.1. Study population

To be eligible for the LIBCSP, all women had to be English speakers and residents of either Nassau or Suffolk counties in New York at the reference date (the time of diagnosis for cases or identification for controls). Cases were newly diagnosed with first primary in situ or invasive breast cancer between August 1, 1996 and July 31, 1997. Cases were identified through daily or weekly contact with the pathology departments of 31 hospitals in the Long Island-New York City area that diagnose/treat women with breast cancer. Controls were women without a personal history of breast cancer, and were frequency matched to the expected distribution of case women by 5-year age group. Potentially eligible controls were identified by random digit dialing for those under age 65 and from the Health Care Financing Administration for those 65 years of age or older. All participants signed an informed consent form prior to interview.

LIBCSP participants included 1,508 cases and 1,556 controls (82.1% and 62.7% of all eligible subjects, respectively) whose ages ranged from 20 to 98 years. In the study population, the distribution of self-identified race was 93% white, 5% black, and 2% other, which is similar to the distribution in the source population from which it arose at the time of data collection (Gammon et al., 2002a). The study reported here was conducted using the 1,006 cases and 990 controls who were postmenopausal at the reference date. We restricted our ancillary study to postmenopausal women because BMI, a modifier in this analysis, is positively associated with postmenopausal (Carmichael and Bates, 2004), but not premenopausal breast cancer (Cheraghi et al., 2012). As previously reported in the LIBCSP, postmenopausal breast cancer has been associated with parity (Shantakumar et al., 2007b), breastfeeding (Shantakumar et al., 2007b), hormone replacement therapy (HRT) use (Shantakumar et al., 2007a), physical activity (McCullough et al., 2012), postmenopausal BMI (McCullough et al., 2015), and weight gain (Eng et al., 2005).

2.2. PAH exposure assessment

The main case-control questionnaire lasted approximately 120 min, and was administered by trained interviewers to all respondents in their homes. For cases, this occurred on average within 3 months of their first primary breast cancer diagnosis. Additionally, peripheral blood samples were donated at the time of the interview by 73.1% of cases and 73.3% of controls.

Six measures of PAHs were considered in our study: the biomarker PAH-DNA adducts, and long-term sources including active cigarette smoking, residential ETS, grilled/smoked meat intake, residential synthetic log use, and vehicular traffic exposure. Information on active and passive smoking, grilled/smoked meat, synthetic log use, and residential history (used to determine vehicular traffic exposure) were assessed as part of the main case-control questionnaire, whereas the PAH-DNA adducts were assessed using DNA isolated from the blood samples.

2.2.1. Active/passive smoking

Individuals were asked whether they had ever smoked at least 1 cigarette per day for 6 months or longer and were classified as ever smokers (current and former) or never smokers. Passive smoke exposure was assessed as whether individuals ever lived with a smoker, including a smoking spouse. Passive smoke from a spouse was the source of residential ETS of longest exposure duration among LIBCSP participants, and had the strongest association with breast cancer (Gammon et al., 2004a).

2.2.2. Grilled/smoked food intake

As part of the main questionnaire, women were asked to report their consumption of four groups of PAH-containing foods: smoked beef, lamb, and pork; grilled/barbequed beef, lamb, and pork; smoked poultry or fish; and grilled/barbequed poultry or fish. Consumption was averaged over 6 decades of life to determine each individual's average annual intake. This exposure variable was dichotomized into 0–54 and 55+ servings per year based on findings from a previous LIBCSP report (Steck et al., 2007).

2.2.3. Synthetic log use

Individuals were queried about whether they had used an indoor stove or fireplace ≥3 times per year at each of their Long Island residences across the life course, and what material was burned. The