Environment International 89–90 (2016) 185–192

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Exposure to multiple sources of polycyclic aromatic hydrocarbons and breast cancer incidence

Alexandra J. White [a,*], Patrick T. Bradshaw [b], Amy H. Herring [c], Susan L. Teitelbaum [d], Jan Beyea [e], Steven D. Stellman [f], Susan E. Steck [i], Irina Mordukhovich [a], Sybil M. Eng [f], Lawrence S. Engel [a], Kathleen Conway [a], Maureen Hatch [j], Alfred I. Neugut [f,g], Regina M. Santella [h], Marilie D. Gammon [a]

[a] Department of Epidemiology, University of North Carolina, Chapel Hill, NC, USA
[b] Department of Nutrition, University of North Carolina, Chapel Hill, NC, USA
[c] Department of Biostatistics, University of North Carolina, Chapel Hill, NC, USA
[d] Department of Preventive Medicine, Ichan School of Medicine at Mt. Sinai, New York, NY, USA
[e] Consulting in the Public Interest (CIPI), Lambertville, NJ, USA
[f] Department of Epidemiology, Columbia University, USA
[g] Department of Medicine, Columbia University, USA
[h] Department of Environmental Health Sciences, Columbia University, USA
[i] Department of Epidemiology and Biostatistics, University of South Carolina, Columbia, SC, USA
[j] Division of Cancer Epidemiology and Genetics, Radiation Epidemiology Branch, National Cancer Institute, Bethesda, MD, USA

ARTICLE INFO

Article history:
Received 27 October 2015
Received in revised form 3 February 2016
Accepted 4 February 2016
Available online xxxx

Keywords:
Breast cancer
Polycyclic aromatic hydrocarbons
Smoking
Environmental tobacco smoke
Grilled meat
Indoor air
Outdoor air

ABSTRACT

Background: Despite studies having consistently linked exposure to single-source polycyclic aromatic hydrocarbons (PAHs) to breast cancer, it is unclear whether single sources or specific groups of PAH sources should be targeted for breast cancer risk reduction.
Objectives: This study considers the impact on breast cancer incidence from multiple PAH exposure sources in a single model, which better reflects exposure to these complex mixtures.
Methods: In a population-based case-control study conducted on Long Island, New York ($N = 1508$ breast cancer cases/1556 controls), a Bayesian hierarchical regression approach was used to estimate adjusted posterior means and credible intervals (CrI) for the adjusted odds ratios (ORs) for PAH exposure sources, considered singly and as groups: active smoking; residential environmental tobacco smoke (ETS); indoor and outdoor air pollution; and grilled/smoked meat intake.
Results: Most women were exposed to PAHs from multiple sources, and the most common included active/passive smoking and grilled/smoked food intake. In multiple-PAH source models, breast cancer incidence was associated with residential ETS from a spouse (OR = 1.20, 95%CrI = 1.03, 1.40) and synthetic firelog burning (OR = 1.29, 95%CrI = 1.06, 1.57); these estimates are similar, but slightly attenuated, to those from single-source models. Additionally when we considered PAH exposure groups, the most pronounced significant associations included total indoor sources (active smoking, ETS from spouse, grilled/smoked meat intake, stove/fireplace use, OR = 1.45, 95%CrI = 1.02, 2.04).
Conclusions: Groups of PAH sources, particularly indoor sources, were associated with a 30–50% increase in breast cancer incidence. PAH exposure is ubiquitous and a potentially modifiable breast cancer risk factor.

1. Introduction

Breast cancer is the most commonly diagnosed cancer among women in the U.S. (American Cancer Society, 2014). Experimental research suggests that polycyclic aromatic hydrocarbons (PAHs) induce mammary tumors (IARC, 2010), but associations in women are understudied. Humans are exposed to PAHs across the life course from multiple sources, including cigarette smoking, environmental tobacco smoke (ETS), diet, indoor and outdoor air pollution (Boström et al., 2002). PAHs are formed from the incomplete combustion of organic material and are confirmed carcinogens to the human lung (IARC, 2010).

Previous population studies have observed positive associations between short-term PAH biomarker concentrations (*i.e.*, PAH-DNA

* Corresponding author at: Department of Epidemiology, CB#7435, McGavran-Greenberg Hall, University of North Carolina, Chapel Hill, NC 27599-7435, USA.
E-mail address: whitea@unc.edu (A.J. White).

http://dx.doi.org/10.1016/j.envint.2016.02.009
0160-4120/

adducts) and breast cancer incidence (Gammon et al., 2004b; Li et al., 2002; Rundle et al., 2000). However, it is unclear from biomarker studies which PAH sources are the predominant contributors to these associations. As long-term carcinogen exposure is considered to be most relevant, other studies have considered single PAH exposure sources and have found increases in breast cancer risk with active cigarette smoking (Gaudet et al., 2013), long-term residential ETS (Gammon et al., 2004a; Laden and Hunter, 1998; Morabia et al., 1996), indoor air pollution from burning synthetic logs (White et al., 2014), outdoor air pollution (Bonner et al., 2005; Crouse et al., 2010; Lewis-Michl et al., 1996; Mordukhovich et al., 2016; Nie et al., 2007; Raaschou-Nielsen et al., 2011), and intake of grilled and smoked foods (Di Maso et al., 2013; Fu et al., 2011; Steck et al., 2007).

Our understanding of the impact of PAHs on breast cancer may be improved if these multiple sources are considered simultaneously (2015). The relative contribution of PAH sources to an individual's exposure is unknown (Boström et al., 2002). Tobacco smoke is likely the largest contributor (Menzie et al., 1992), but diet is the predominant source among non-smokers (Boström et al., 2002). However, carcinogenic potency is hypothesized to vary by route of exposure (Menzie et al., 1992), metabolic pathway and type of PAH (Boström et al., 2002). Thus, it is unclear whether certain sources, groups of sources, or all PAH sources should be targeted for breast cancer risk reduction.

The study reported here aims to consider, in a single hierarchical regression model, the impact of multiple long-term PAH sources on breast cancer incidence. Variables from the same exposure source (for example, different measures of grilled/smoked meat intake) are highly correlated. A hierarchical regression approach permits the consideration of multiple PAH source exposures in a single multivariable model, while accounting for similar sources of the PAH exposures. Additionally, with a single statistical model we are able to estimate the OR for groups of PAH sources, or PAH exposure profiles, based on contrasting *a priori* defined exposure groups of interest.

2. Methods

The study reported here builds upon the population-based case-control resources of the Long Island Breast Cancer Study Project (LIBCSP), for which extensive methods have been previously published (Gammon et al., 2002). IRB approval was obtained from all relevant institutions. Written signed informed consent was obtained from all participants.

2.1. Study population

The cases are English-speaking female residents of Long Island, New York who were diagnosed with their first primary *in situ* or invasive breast cancer between August 1st, 1996 and July 31st, 1997. Cases were identified using rapid case ascertainment. Controls were women without a history of breast cancer who were frequency matched on the expected 5-year age distribution of the cases. Controls were identified using random digit dialing for those <65 years of age and by using Health Care Finance Administration Rosters for those 65 years of age and older.

2.2. PAH exposure sources assessment

Five binary PAH exposure sources were assessed across the life course. Active smoking, residential ETS, grilled/smoked meat intake, and indoor wood-burning stove/fireplace use were assessed by structured questionnaire (Gammon et al., 2004a; Steck et al., 2007; White et al., 2014) with a trained interviewer, and vehicular traffic exposure was assessed using a validated historical geographic model (Beyea et al., 2006; Mordukhovich et al., 2016). Continuous variables required categorization because associations with breast cancer were neither non-linear nor log-linear and were dichotomized in order to facilitate interpretation and scaling in the hierarchical regression across PAH sources.

Active smoking (ever, never) was defined as smoking at least 1 cigarette per day for 6 months or longer, and current active smoking (yes, no) was defined as smoking within the last 12 months prior to diagnosis or referent date for controls (=date of identification). Smoking prior to first birth (yes, no) was determined by using age at first birth and age at which participant first starting smoking. Participants were asked if they had lived with a smoker to determine ETS exposure (yes, no) and their relationship to that person to evaluate if they lived with a smoking spouse (yes, no). Indoor stove/fireplace use was defined as having used a stove/fireplace in a Long Island residence for at least 3 times per year (yes, no) and whether or not participants burned wood (yes, no) and/or synthetic logs (yes, no).

Continuous variables for the PAH sources were dichotomized using cutpoints that best reflected previous associations observed with breast cancer incidence (Mordukhovich et al., 2016; Steck et al., 2007). Frequency of intake of grilled/smoked meat was assessed for six decades across the life course. Lifetime intake was defined as the average servings consumed per year based on quantile distributions of consumption in the controls, as follows: for total grilled/barbecued and smoked meats (<55 servings/year, 55+ servings/year); grilled/barbecued beef, pork and lamb (<14, 14+ servings/year); and smoked beef, pork and lamb (<22, 22+ servings/year). The geographic model for vehicular traffic exposure incorporated historical U.S. vehicular PAH emissions data, information on traffic and transportation patterns, Long Island meteorological variables and pollutant dispersion factors to determine vehicular traffic exposure in 1995, the year prior to LIBCSP recruitment (low risk = <95th percentile, high risk = ≥95th percentile). Previously, we found the association with breast cancer to be limited to the top 5% of those exposed to vehicular traffic (Mordukhovich et al., 2016).

2.3. Confounder assessment

A directed acyclic graph was used to identify a minimally sufficient set to control for confounding (Glymour and Greenland, 2008) (Supplemental Fig. I).

The odds ratios were adjusted for the following covariates, which were assessed by structured questionnaire (Gammon et al., 2002): age at menarche (≤12, >12 years); parity (nulliparous, parous); lifetime alcohol intake (non-drinkers, <15 g/day, 15 g-30 g/day, ≥30 g/day); education (high school graduate or less, some college, college or post-college); income (<$34,999, $35,000–$69,999, ≥$70,000); and the frequency matching factor, 5-year age group.

2.4. Statistical analysis

To examine the associations between the main PAH sources and PAH groups and breast cancer risk, 12 binary PAH exposure variables were considered. For our primary analysis, these 12 variables were characterized according to five exposure sources: (1) active smoking: ever active smoking, current active, smoking prior to first pregnancy; (2) residential ETS: any residential ETS, residential ETS from spouse; (3) indoor stove and/or fireplace use: any stove/fireplace use, wood burning, synthetic log burning; (4) diet: total grilled/barbecued and smoked meats, smoked beef, pork and lamb and grilled/barbecued beef, pork and lamb; and (5) vehicular traffic. Estimating associations with the PAH exposure variables by these five exposure sources facilitates understanding which of these sources to prioritize for reduction from a public health standpoint.

All models were specified in a Bayesian framework and we calculated posterior means for the ORs and corresponding 95% posterior credible intervals (CrI, the Bayesian analog to a confidence interval)