Environmental Research 166 (2018) 588–594

Contents lists available at ScienceDirect

Environmental Research

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

Exploring the association between polycyclic aromatic hydrocarbons and diabetes among adults in the United States

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ARTICLE INFO

Keywords:
Polycyclic aromatic hydrocarbons
Diabetes
Environmental pollutants

ABSTRACT

Objective: To explore the association between polycyclic aromatic hydrocarbons (PAHs) and diabetes and to determine whether effects are heterogeneous when examined by body mass index (BMI).

Methods: Cross-sectional data from 8664 participants were analyzed from the National Health and Nutrition Examination Survey for years 2005–2014. Multivariable logistic regression was used to explore the association between urinary biomarkers of PAHs and diabetes. All models were adjusted for age, sex, race, poverty-income ratio, and serum cotinine.

Results: When compared with the lowest quintiles of exposure, the highest quintiles of exposure to 2-hydroxynaphthalene, 2-hydroxyfluorene, 9-hydroxyfluorene, 2-hydroxyphenanthrene, and a summed variable of all low molecular weight PAHs (aOR = 1.73; 95% CI: 1.17–2.55) showed a positive association with diabetes. Stratified analyses by BMI indicated that the positive association between PAHs and diabetes was found among both normal weight and obese participants.

Conclusions: High levels of exposure to PAHs are positively associated with diabetes in the U.S. general population and these effects are modified by BMI. These findings suggest the importance of strong environmental regulation of PAHs to protect population health.

1. Introduction

With multiple, protective environmental regulations being rapidly overturned in the U.S., it is important for public health practitioners and policymakers to have access to up-to-date evidence for advocacy and decision-making. An argument often cited for the current rollback of several protective environmental policies is that the evidence is inconsistent or unclear. However, it is well-documented that environmental pollutants are directly associated with many chronic diseases (Alhamdow et al., 2017; Zhang et al., 2016; Stec et al., 2018; Feng et al., 2014; Liu et al., 2016). Therefore, this research study explores the association between exposure to the environmental pollutants known as polycyclic aromatic hydrocarbons (PAHs) and the outcome of diabetes in the general U.S. adult population.

PAHs are lipid-soluble chemicals primarily released through manufacturing and other industrial processes that result from the incomplete combustion of gas, oil, and coal (Agency for Toxic Substances and Disease Registry (ATSDR), 2015). Additional environmental sources include forest and brush fires, volcanoes, and petroleum seeps (Abdel-Shafy and Mansour, 2016). PAHs are ubiquitous toxic pollutants, with high melting and boiling points and low vapor pressures that decrease with increased molecular mass (Bandeira and Meneses, 2013). These properties affect absorption and retention within both the environment and the human body (Bandeira and Meneses, 2013). Humans can be exposed to PAHs through contaminated water and air, particularly from sources such as automotive emissions, smoke from wood-burning stoves, jet aircraft exhausts, tobacco smoking or exposure to secondhand smoke, and food such as grilled and charred meats (Agency for Toxic Substances and Disease Registry (ATSDR), 2015; Abdel-Shafy and Mansour, 2016). The Agency for Toxic Substances and Disease Registry includes multiple PAHs (e.g., Benzo(a) pyrene, hydroxylated Polycyclic Aromatic Hydrocarbons, and Benzo(b) fluoranthene) in the top ten chemicals currently on the priority list of hazardous substances, which is based upon factors such as toxicity and likelihood of human exposure (Agency for Toxic Substances and Disease Registry (ATSDR), 2017).

Previous studies have linked PAH exposure to breast cancer (Korsh et al., 2015), lung cancer (Armstrong et al., 2004), cardiovascular disease (Alshaarawy et al., 2016), DNA disruptions (Kim et al., 2016), and recently diabetes (Alshaarawy et al., 2014). The Centers for Disease

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https://doi.org/10.1016/j.envres.2018.06.041
Received 8 February 2018; Received in revised form 15 June 2018; Accepted 19 June 2018

Control and Prevention (CDC) estimate that more than 30 million people living in the United States have diabetes and about 95% of those cases are composed of type 2 diabetes (Centers for Disease Control and Prevention, 2018). Risk factors for type 2 diabetes are well-known and include increasing age, overweight and obesity, and African American, Hispanic, American Indian, or Alaska Native race/ethnicity (Centers for Disease Control and Prevention, 2017).

Age, sex, and race, all of which are non-modifiable factors, are also likely to influence exposure to PAHs through modes such as occupational hazards, active smoking, and/or secondhand smoke exposure. Being overweight or obese is a risk factor for diabetes (Centers for Disease Control and Prevention, 2017) and PAHs are highly lipid-soluble (Kim et al., 2016). However, it is unlikely that there would be differential exposure to PAHs between individuals with a low body mass index (BMI) versus a high BMI. After being ingested, inhaled, or absorbed through the skin, PAHs are primarily metabolized by the liver and kidney, and are then excreted in bile and urine (Agency for Toxic Substances and Disease Registry (ATSDR), 2008). In addition, detectable levels of PAHs have been identified in almost all internal organs, especially those with high amounts of adipose tissue (Abdel-Shafy and Mansour, 2016). The lipophilic properties of PAHs vary by length of exposure, route of exposure, and concentration, and may act synergistically with individual risk factors and comorbidities to increase the severity of impacts on the human body (Abdel-Shafy and Mansour, 2016; Agency for Toxic Substances and Disease Registry (ATSDR), 2015). As PAHs are stored in adipose tissue until they are expelled through normal bladder and gastrointestinal functions (Agency for Toxic Substances and Disease Registry (ATSDR), 2015), it is plausible that PAHs may be more persistent in individuals with a higher BMI, which may affect the odds of diabetes in comparison with those who have a lower BMI.

Prior evidence has shown an association between ambient air pollution and incident diabetes (Andersen et al., 2012; Kramer et al., 2010; Coogan et al., 2012; Chen et al., 2013), diabetes-related hospitalizations (Zanobetti et al., 2014), and diabetes-associated mortality (Raaschou-Nielsen et al., 2013; Samoli et al., 2014) as well as an association between persistent organic pollutants and diabetes prevalence (Lee et al., 2006). Furthermore, the specific association between PAHs and cardiometabolic health risk, including diabetes, has been examined in the general, U.S. population (Alshaarawy et al., 2014; Ranjbar et al., 2015), but new information is now available about PAHs for which data were not previously collected. Specifically, NHANES data have now been collected for urinary concentrations of 9-hydroxyfluorene, and new evidence from other data sources has been published which aids in understanding the process by which PAHs are associated with diabetes through joint effects with obesity, but further investigation is warranted (Hou et al., 2017; Yang et al., 2017). In addition, since PAHs moderately persist in the environment (Connell, 2005; Whitehead et al., 2014), recent data would be expected to detect a higher cumulative exposure in the general population. The objective of this study was to explore the association between exposure to PAHs and the outcome of diabetes in the U.S. general population and to determine whether effects are heterogeneous when examined by body mass index.

2. Methods

2.1. Data source

Data were acquired from the National Health and Nutrition Examination Survey (NHANES) for years 2005–2014 (Centers for Disease Control and Prevention, 2017). The exposure of interest was any exposure to the following nine PAHs as measured by urinalysis in a Mobile Examination Center (MEC) for NHANES: 1-hydroxynaphthalene, 2-hydroxynaphthalene, 2-hydroxyfluorene, 3-hydroxyfluorene, 9-hydroxyfluorene, 1-hydroxyphenanthrene, 2-hydroxyphenanthrene, 3-hydroxyphenanthrene, and 1-hydroxypyrene. During the 2005–2012 NHANES survey cycles, urinary metabolites of PAHs were determined using gas chromatography-tandem mass spectrometry; subsequently, liquid chromatography-tandem mass spectrometry was implemented in the 2013–2014 survey cycle (Wang et al., 2017). To account for variation in urine sample volume, exposure variables were corrected for urinary creatinine in all analyses by dividing each of the PAHs (ng/L) by urinary creatinine (mg/dl) and multiplying by 0.01 to result in nanograms of PAHs per gram of creatinine (ng/g) (Alshaarawy et al., 2014; Xu et al., 2013; Everett et al., 2010). The outcome of interest was diabetes defined as laboratory-confirmed glycohemoglobin levels $\geq 6.5\%$, self-reported diagnosis of diabetes by a physician, and/or self-reported insulin use. Information for the potential confounders of age, sex, race, and poverty-income ratio were collected by NHANES representatives via self-reported questionnaire. Body measures, including BMI, and laboratory-confirmed serum cotinine were obtained in the MEC by trained NHANES representatives.

2.2. Potential confounders

To prevent both over-adjustment bias and unnecessary adjustment, a causal diagram was generated based upon a thorough review of the literature to aid in identifying a minimum set of covariates that have the potential to affect both the exposure and the outcome (Greenland et al., 1999; Schisterman et al., 2009). Statistical adjustments were made for demographic factors including age as a continuous variable and sex as a dichotomous variable. Since being a racial minority is associated with both the exposure (Houston et al., 2014) and the outcome (Centers for Disease Control and Prevention, 2017), race was included as a nominal variable, which was categorized as Non-Hispanic White, Non-Hispanic Black, Mexican American and Other Hispanic, and Other Race, including Multi-Racial. Because persons living in low-income areas are exposed to higher levels of environmental pollutants than their counterparts in higher-income areas (Schraufnagel et al., 2013; Krieger et al., 2014), statistical adjustments were made for poverty-income ratio, defined as a dichotomous variable for individuals above or below the federal poverty threshold. Since active smoking and exposure to secondhand smoke are major contributors of exposure to PAHs (Li et al., 2017; Oliveira et al., 2017; Zhou et al., 2017) and are independently associated with diabetes (Zhu et al., 2017; Liu et al., 2018; White et al., 2018), adjustments for serum cotinine as a continuous variable were included in all models. A sensitivity analysis was conducted utilizing history of smoking (i.e., "Have you smoked at least 100 cigarettes in your entire life?") as a covariate.

2.3. Statistical analyses

The exposure distribution for each PAH was divided into quintiles and the lowest exposure level (quintile 1) was designated as the reference group. Since low molecular weight PAHs exist mainly in vapor form, human exposure occurs through inhalation; in contrast, high molecular weight PAHs exist almost entirely in particulate form and are thus often ingested or absorbed through the skin in addition to inhalation (Alshaarawy et al., 2014; Juhasz et al., 2000; Elovaara et al., 1995). As such, the metabolism of low and high molecular weight PAHs is likely different. Furthermore, it is expected that the resulting health effects of cumulative exposure to PAHs is different than exposure to one, single PAH; as such, a summed variable of all low molecular weight PAHs was created for analysis and included the following PAHs: 1-hydroxynaphthalene, 2-hydroxynaphthalene, 2-hydroxyfluorene, 3-hydroxyfluorene, 9-hydroxyfluorene, 1-hydroxyphenanthrene, 2-hydroxyphenanthrene, and 3-hydroxyphenanthrene. 1-hydroxypyrene was not included in the summed variable as it is the only PAH with a high molecular weight. The diabetes outcome was coded dichotomously as a yes/no variable.

Multivariable logistic regression was conducted to ascertain the