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Association of polycyclic aromatic hydrocarbons metabolites and risk of diabetes in coke oven workers☆

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A B S T R A C T

Elevated polycyclic aromatic hydrocarbons (PAHs) metabolites have recently been linked to increased risk of diabetes in the general population, but little is known about the risk of diabetes due to high pollution levels of PAHs exposure. We aimed to examine whether occupational exposure to PAHs would be one of the important risk factors for diabetes in the coke oven workers. A total of 1472 coke oven workers with complete data were qualified for the present study. We measured 12 urinary monohydroxy polycyclic aromatic hydrocarbons (OH-PAHs) by gas chromatography–mass spectrometry (GC-MS). Multiple logistic regression was used to evaluate the associations between urinary OH-PAHs and risk of diabetes, with adjustment for the potential confounders. We found that elevated urinary 4-hydroxyphenanthrene (4-OHPh) was significantly associated, in a dose-dependent manner, with increased risk of diabetes ($P_{trend} = 0.003$). Compared with individuals with 4-OHPh in the lowest quartile, the adjusted odds ratio (OR) of diabetes among those in the highest quartile was 2.80 (95% CI = 1.37–5.71). In stratified analysis, the association was more prominent in those who were smokers, overweight (BMI ≥24 kg/m^2), with longer working years (≥20 years) and worked at coke oven settings. In addition, high levels of 4-OHPh combined with longer working years or overweight had a joint effect on the risk of diabetes. Our data suggested that elevated 4-OHPh was dose-responsive associated with increased risk of diabetes in the coke oven workers. The risk assessment of diabetes related to occupational PAHs exposure should take working years and BMI into consideration.

1. Introduction

Because of economic development, nutrition transition, and rapid changes in lifestyle, the prevalence of diabetes is increasing sharply in China (Murray et al., 2012; Xu et al., 2013). During the past 30 years, the overall prevalence of diabetes has increased from less than 1% to 11.6% in the Chinese adult population, accounting for 113.9 million Chinese adults with diabetes (Xu et al., 2013).

Diabetes is a chronic and complex disease determined by genetic and environmental factors. Many environmental factors such as persistence organic pollutants (POPs), heavy metal, and particulate matter are related to the risk of diabetes (Airaksinen et al., 2011; Feng et al., 2015; Liu et al., 2016). Polycyclic aromatic hydrocarbons (PAHs) are ubiquitous contaminants in general environment and certain occupational settings. They can be by-products in processes involving automobile exhaust, coal burning, cigarette smoking, home cooking, and industrial production

Abbreviations: ANOVA, One way analysis of variance; BMI, body weight index; GC-MS, gas chromatography–mass spectrometry; NHANES, National Health and Nutritional Health Survey; OHNa, hydroxynaphthalene; OHFlu, hydroxyfluorene; OHPh, hydroxyphenanthrene; 1-OHP, 1-hydroxypyrene; 6-OHChr, 6-hydroxychrysene; 3-OHBaP, 3-hydroxybenzo[a]pyrene; OH-PAHs, monohydroxy polycyclic aromatic hydrocarbons; ΣOH-PAHs, total concentration of all PAH metabolites; PAH, polycyclic aromatic hydrocarbon.

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processes (Bostrom et al., 2002). Two recent studies, including one from our lab, established an association between PAHs and diabetes in general population (Alshaarawy et al., 2014; Yang et al., 2014). Given this relation exist in general population, we speculate that the relation may be amplified among coke oven workers, probably because they are exposed to the high levels of PAHs — the predominant contaminants of coke oven emissions produced during incomplete combustion of coal. However, no study has investigated the association of diabetes with occupational exposure to PAHs. China is the world's largest producer and consumer of coal, with more than 400,000 employees working in the coke oven plant (Hu et al., 2006). Therefore, we aimed to examine the relation of PAHs-diabetes in coke oven workers, and whether the association could be modified by different characteristics or health status.

2. Methods

2.1. Study population

The study population consisted of 1628 coke oven workers who worked at least 1 year in a coking plant in Wuhan city, China (Wang et al., 2016). We excluded participants with missing information on fasting blood glucose (n = 134) or covariates included in the multivariate model (n = 22). Finally, a total of 1472 participants with complete data were included in the current study. Information on demographic variables (age, sex, education, and marital status), lifestyle habits (e.g. smoking status, drinking status and physical activity), health status, occupational history, and medication were obtained by trained reviewers using standardized questionnaires. Subjects who had smoked an average of more than 1 cigarette per day for more than 1 year in their lifetime were defined as smokers; otherwise, they were considered as non-smokers. Those who had drunk alcohol beverage at least once a week for more than 6 months were defined as drinkers; otherwise, they were considered as non-drinkers. Physical activity was defined as those who regularly took at least 20 min of exercise per day during leisure time over the previous 6 months. Education was classified into 3 groups: less than high school graduate, high school graduate, and college or beyond. Pre-shift referred to be at the beginning of dayshift, and post-shift referred to be at the end of nightshift. The anthropometric data including body height, weight, waist circumference, and hip circumference were obtained by direct measurements. BMI was calculated as weight in kilograms divided by height in meter-squared. A fasting blood sample was collected for examination of blood lipids and blood glucose. In addition, a spot morning 20 mL pre-shift or post-shift urine sample from each participant was collected in sterile conical tubes and stored at −80 °C prior to laboratory analysis. The protocol was reviewed and approved by the Ethics and Human Subject Committee of Tongji Medical College, and all participants provided the written informed consent.

2.2. Definition of normoglycemia, impaired fasting glucose and diabetes

According to the American Diabetes Association guidelines (ADA, 2014), participants were defined as diabetics if they were treated with diabetes medications, or had a fasting blood glucose concentration ≥7.0 mmol/L, or self-reported physician-diagnosed diabetes. Impaired fasting glucose (IFG) was defined as a fasting glucose concentration between 5.6 and 6.9 mmol/L, absence of previously diagnosed diabetes, and absence of hypoglycemic medication. Participants with a negative self-report of diabetes, fasting glucose <5.6 mmol/L, and the absence of glycemic control medication were defined as normoglycemia.

2.3. Measurement of urinary PAH metabolites and creatinine

We determined 12 urinary PAH metabolites [1-hydroxynaphthalene (1-OHNa); 2-hydroxynaphthalene (2-OHNa); 2-hydroxyfluorene (2-OHFlu); 9-hydroxyfluorene (9-OHFlu); 1-hydroxyphenanthrene (1-OHPh); 2-hydroxyphenanthrene (2-OHPh); 3-hydroxyphenanthrene (3-OHPh); 4-hydroxyphenanthrene (4-OHPh); 9-Hydroxyphenanthrene (9-OHPh); 1-hydroxypyrene (1-OHP); 6-hydroxychrysene (6-OHChr); 3-hydroxybenzo[a]pyrene (3-OHBaP)] by gas chromatography-mass spectrometry (GC-MS, Agilent, Santa Clara, CA) as described previously (Li et al., 2012). Briefly, 3.0 mL urine of each individual was extracted for measurement and each sample was determined in triplicate to elevate measurement accuracy. The standard curve was rerun after 100 samples were determined, and about 10% of the total samples were designated for quality control. The identification and quantification of urinary PAHs metabolites were based on retention time, mass-to-charge ratio, and peak area using a linear regression curve obtained from separate internal standard solutions. The limits of detection (LOD) for urinary PAHs metabolites were in the range 0.1–0.9 μg/L; default values were replaced with LOD/2. The concentration of urinary creatinine was examined by a Randox Daytona fully automated clinical chemistry analyzer (Furuno electric Co., Ltd, Japan) according to the colorimetric methods of Jaffe's (Taussky, 1954). Valid urinary PAH metabolite concentrations were calibrated by levels of urinary creatinine and expressed as micrograms per millimole creatinine (μg/mmol creatinine). Because 6-OHChr and 3-OHBaP were below the limits of quantification, they were excluded in the further analysis.

2.4. Statistical analysis

The differences of demographic characteristics by diabetes status were evaluated by One way analysis of variance (ANOVA) for continuous variables and Chi-square test for categorical variables. Difference on PAHs metabolites levels of different diabetes status were evaluated by using Mann-Whitney's *U* test. The trend for log-transformed PAHs metabolites levels in different diabetes status groups was tested by using simple linear regression. Multivariate logistic regression was conducted to evaluate the associations between urinary PAH metabolites and diabetes, with adjustments for potential covariates including working years, sex, BMI, smoking status, drinking status, physical activity, education, workshift, work sites, family history of diabetes, total cholesterol, and triglycerides. Stratified analyses were also performed by smoking status (smoker vs. nonsmoker), BMI (<24 vs. ≥24 kg/m^2), working years (<20 vs. ≥20 years), and work site (office vs. adjunct workplaces vs. coke oven). Additionally, for urinary 4-OHPh, we further conducted multivariate logistic regression models to examine the combined effects of urinary PAH metabolites quartiles and working years (<20 vs. ≥20 years) or BMI (<24 vs. ≥24 kg/m^2) on the risk of diabetes. All data were analyzed with SPSS version 12 and a two-sided $P < 0.05$ was considered statistically significant.

3. Results

3.1. Characteristics of the study population

Table 1 presented the basic characteristics of the coke oven workers according to the diabetes status. The prevalence of diabetes was 7.8% in the total study population of 1472 participants. The mean age of the participants was 42.8 ± 8.1 years, and the majority was male (88.8%). As expected, subjects with diabetes were more likely to be older, obese, have longer working years and

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