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Combined effect of urinary monohydroxylated polycyclic aromatic hydrocarbons and impaired lung function on diabetes

Jian Hou [a,b,1], Huizhen Sun [a,b,1], Lili Xiao [a,b], Yun Zhou [a,b], Wenjun Yin [a,b], Tian Xu [a,b], Juan Cheng [a,b], Weihong Chen [a,b,*,2], Jing Yuan [a,b,*,3]

[a] Department of Occupational and Environmental Health, School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, Hangkong Road 13, Wuhan, 430030 Hubei, PR China

[b] Key Laboratory of Environment and Health, Ministry of Education & Ministry of Environmental Protection, and State Key Laboratory of Environmental Health (Incubating), School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, Hangkong Road 13, Wuhan, 430030 Hubei, PR China

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ABSTRACT

Associations of type 2 diabetes with exposure to polycyclic aromatic hydrocarbons and reduced lung function have been reported. The aim of the present study was to investigate effect of reduced lung function and exposure to background PAHs on diabetes. A total of 2730 individuals were drawn from the Wuhan-Zhuhai (WHZH) Cohort Study (n=3053). Participants completed physical examination, measurement of lung function and urinary monohydroxylated polycyclic aromatic hydrocarbons (OH-PAHs). Risk factors for type 2 diabetes were identified by multiple logistic regression analysis, and the presence of additive interaction between levels of urinary OH-PAHs and lower lung function was evaluated by calculation of the relative excess risk due to interaction (RERI) and attributable proportion due to interaction (AP). Urinary OH-PAHs levels was positively associated with type 2 diabetes among individuals with impaired lung function ($p<0.05$). Forced expiratory volume in one second (FEV1, odd ratio (OR): 0.664, 95% confidence interval (CI): 0.491–0.900) and forced vital capacity (FVC, OR: 0.693, 95% CI: 0.537–0.893) were negatively associated with diabetes among individuals. Additive interaction of higher urinary levels of OH-PAHs and lower FVC (RERI: 0.679, 95% CI: 0.120–1.238); AP: 0.427, 95% CI: 0.072–0.782) was associated with diabetes. Exposure to background PAHs was related to diabetes among individuals with lower lung function. Urinary levels of OH-PAHs and reduced lung function had an additive effect on diabetes.

1. Introduction

The rapid increase in the prevalence of type 2 diabetes mellitus (T2DM) is becoming a global health problem. The International Diabetes Federation estimated that the global prevalence of diabetes was 381.8 million in the year 2013, and that number was expected to rise to 591.9 million by the year 2035 (Guariguata et al., 2014). Contribution of diabetes to global all-cause deaths was estimated to be one in twelve of adults worldwide (Group, 2015). Recent data from a China National Diabetes Prevalence Survey have shown that the age-standardized prevalence of total diabetes and prediabetes accounted for 92.4 million and 148.2 million adults, respectively (Kim et al., 2013). China has a fairly large proportion (approximately 25%) of diabetes patients in the worldwide (Chan et al., 2014). Accumulating evidence suggest that various factors are associated with burden of diabetes, including environmental and genetic factors as well as changes in individual lifestyle. Exposure to air pollution increased risks of lung function impairment and incident diabetes in addition to increased prevalence of chronic obstructive pulmonary diseases (COPD) and exacerbations of the patients (Eze et al., 2015). However, the

Abbreviations: AP, attributable proportion due to interaction; BMI, body mass index; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; MLR, multiple logistic regression; NO_2, nitrogen dioxide; OHNa, hydroxynaphthalene; OHFlu, hydroxyfluorene; OHPh, hydroxyphenanthrene; 1-OHP, 1-hydroxypyrene; PAH, polycyclic aromatic hydrocarbons; RERI, the relative excess risk due to interaction; 95% CI, confidence interval

* Corresponding authors at: Department of Occupational and Environmental Health, Ministry of Education & Ministry of Environmental Protection, and State Key Laboratory of Environmental Health (Incubating), School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, Hangkong Road 13, Wuhan, 430030 Hubei, PR China.

E-mail addresses: wchen@mails.tjmu.edu.cn (W. Chen), jyuan@tjh.tjmu.edu.cn (J. Yuan).

[1] These authors contributed equally to this work.
[2] Co-corresponding author.
[3] First corresponding author.

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conflicting results for considering reduced lung function as a risk for diabetes were reported as well. Studies reported that reduced lung function was related to incident of diabetes (Klein et al., 2010; Kwon et al., 2012). Moreover, individuals with certain lung diseases relating to airflow obstruction (such as COPD and asthma) were at risk for diabetes (Papaiwannou et al., 2014; Song et al., 2010). However, COPD and asthma were not associated with prediabetes and diabetes, respectively (Rana et al., 2004; Yamane et al., 2013). Lung function decline was presented commonly before the development of diabetes (Yeh et al., 2011). The close relationship between the restrictive impairment of lung function and incident diabetes might partially due to inflammation in the body (Wannamethee et al., 2010). Reduced lung function was considered as an important risk for low-grade systemic inflammation (Gan et al., 2005). Multiple studies have indicated that alteration of endothelial function, overactivity of the sympathetic nervous system as well as alteration in mitochondria and brown adipocytes functions were linked to air pollution-related diabetes, which may contribute to an increased risk of the developing diabetes (Hectors et al., 2011; Krämer et al., 2010; Rajagopalan and Brook, 2012).

Short term and chronic exposure to air pollutants in the living and occupational environments can cause adverse respiratory and cardiovascular events, leading to increased risk for respiratory and cardiovascular diseases including lung function decline, asthma, myocardial infarction and heart failure (Mannucci et al., 2015; Zhou et al., 2016). Polycyclic aromatic hydrocarbons (PAHs) are a group of approximately 10,000 compounds, such as benzopyrene, fluoranthene and naphthalene. PAHs are produced by incomplete combustion of carbon containing materials from outdoor and indoor sources, including automobiles, industries, smoke from burning wood, charcoal, tobacco and cooking oil fume (Kim et al., 2013), duing to the highly mobile physico-chemical properties of PAHs in the environment. PAHs were ubiquitously detected in air, water, soil and sediment (Kim et al., 2013), thus, urinary levels of PAHs metabolites were often used as indicators to assess internal exposure of PAHs in the human body.

Recent studies showed that urinary levels of monohydroxylated polycyclic aromatic hydrocarbons (OH-PAHs) were associated with either reduced lung function or increased risk of developing diabetes (Alshaarawy et al., 2014; Yang et al., 2014; Zhou et al., 2016). Of them urinary level of 1-hydroxypyrene (1-OHP) was widely used to reflect PAHs exposure level in the body. However, urinary levels of OH-PAHs have been used in investigating adverse health effects of PAHs, including reduced lung function, oxidative DNA damage and diabetes (Alshaarawy et al., 2013; Fan et al., 2012; Li et al., 2012; Yang et al., 2014). This is due to the reason that currently available technological methods for urinary OH-PAHs (Onyemauwa et al., 2009). Urinary levels of OH-PAHs can provide more individual accuracy estimation of overall PAHs exposure, and decrease in the bias in determination of internal exposure level of PAHs rather than urinary1-hydroxypyrene (1-OHP) as a single indicator. Moreover, a dose-response relationships between urinary levels of OH-PAHs (such as hydroxyfluorene and hydroxyfluorene) and reduced lung function were found among the occupational workers and general population (Hu et al., 2012; Zhou et al., 2016).

Studies reported that nitrogen dioxide (NO_2), another important pollutant, was related to reduced lung function among the adults (Adam et al., 2015; Rice et al., 2013). It deteriorated lung function and marginally modified association of traffic-related NO_2 level (emitted per square kilometer each year) and diabetes (Vossoughi et al., 2014). The aims of the present study were to investigate associations between environmental exposure to PAHs and reduced lung function with the prevalence of diabetes, and to determine whether the association between impaired lung function and type 2 diabetes was modified by urinary OH-PAHs levels among participants based on the baseline data of the Wuhan-Zhuhai (WHZH) Cohort Study.

2. Materials and methods

2.1. Study population

Considering an obvious difference in air quality between Wuhan city and Zhuhai city, a total of 2730 Wuhan residents from the Wuhan-Zhuhai (WHZH) Cohort Study were included in the present study, after excluding those with missing information on lung function (n=61), body mass index (BMI, n=36), urinary PAHs levels (n=246) and blood biochemical data (n=10) and family history of diabetes (n=16).

Data were collected on sociodemographic characteristics (such as age, gender and educational attainment level), occupational history, lifestyle (including active and passive smoking, physical activity) as well as personal and family medical histories by the questionnaires. Educational attainment level was classified into three levels: less than high school, higher school and completed a university degree or above. Definitions of smoking and drinking were described elsewhere (Yang et al., 2014). Leisure-time physical activity was defined as more than 600 metabolic equivalent (MET)-min per week, otherwise defined as leisure-time physical inactivity (Hallal et al., 2012). MET-minutes (MET-min) per week was calculated (MET coefficient of activity × duration (min per time) × frequency (times per week)) based on the compendium of physical activities according to the descriptions of previous studies (Ainsworth et al., 2011; Ng et al., 2009). Body mass index (BMI) was the ratio of weight (in kilograms) to height (in meters) squared. Individual with a BMI <24 kg/m^2 was defined as non-obese, and those with a BMI of 24–27.9 kg/m^2 as overweight or a BMI of a ≥ 28 kg/ m^2 as obese, according to the Chinese criteria (Bei-Fan, 2002). Individuals with a fasting plasma glucose value of more than 7.0 mmol/L or self-reported physician-diagnosed diabetes or taking hypoglycemic agents were considered as diabetes patients. Poor lung function is a generic term including at least obstructive lung dysfunction (OLD) and restrictive lung dysfunction (RLD) (Mannino et al., 2003; Mannino et al., 2005). Individuals with self-reported asthma, bronchitis and emphysema, and COPD or forced expiratory volumes in 1 second (FEV1)/forced vital capacity (FVC) ratio $<70\%$ were defined as OLD. RLD was defined as FEV1/FVC ratio $\geq 70\%$ plus FVC $<80\%$, otherwise defined as normal lung function. Each participants completed a physical examination, including anthropometry measurements (including height, weight, waist and hip circumference) and blood biochemical test (such as blood glucose and triglyceride) according to the standard methods.

The study was approved by Medical Research Ethics Committee of Tongji Medical College, Huazhong University of Science and Technology. Written informed consent was obtained from all participants before starting the study.

2.2. Levels of urinary OH-PAHs

We used a gas chromatography-mass spectrometry to measure urinary levels of twelve OH-PAHs, including 1-hydroxynaphthalene (1-OHNa), 2-hydroxynaphthalene (2-OHNa), 2-hydroxyfluorene (2-OHFlu), 2-hydroxyfluorene (9-OHFlu), 1-hydroxyphenanthrene (1-OHPh), 2-hydroxyphenanthrene (2-OHPh), 3-hydroxyphenanthrene (3-OHPh), 4-hydroxyphenanthrene (4-OHPh) and 9-hydroxyphenanthrene (9-OHPh) and 1-OHP, 6-hydroxychrysene (6-OHChr) and 3-hydroxybenzo[a] pyrene (3-OHBaP) as described previously (Li et al., 2012). Briefly,