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Indoor air pollution affects hypertension risk in rural women in Northern China by interfering with the uptake of metal elements: A preliminary cross-sectional study☆

Bin Wang [a, b, 1], Yibing Zhu [a, b, 1], Yiming Pang [a, b], Jing Xie [a, b], Yongxiu Hao [a, b], Huina Yan [a, b], Zhiwen Li [a, b], Rongwei Ye [a, b, *]

[a] Institute of Reproductive and Child Health/National Health Commission Key Laboratory of Reproductive Health, School of Public Health, Peking University, Beijing, 100191, China
[b] Department of Epidemiology and Biostatistics, School of Public Health, Peking University, Beijing, 100191, China

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ABSTRACT

Coal combustion and passive smoking are two important contributors to indoor air pollution (IAP) in rural areas of northern China. Although the association between outdoor air pollutants and hypertension risk had been widely reported, fewer studies have examined the relationship between IAP and hypertension risk. This study evaluated the association between IAP and hypertension risk in housewives in rural areas of northern China and the potential mediation pathway of metal elements. Our cross-sectional study, conducted in Shanxi Province, China, enrolled 367 subjects without taking anti-hypertensive drugs, including 142 subjects with hypertension (case group) and 225 subjects without hypertension (control group). We collected information on energy use characteristics and lifestyle using questionnaires. An IAP exposure index was developed to indicate the population exposure to coal combustion and passive smoking. Scalp hair samples were collected from the housewives and various trace and major metal elements were measured. Our results revealed that the IAP index was positively correlated with systolic and diastolic blood pressure. A significant association between the IAP index and hypertension risk was found both without [odds ratio (95% confidence interval, CI) = 2.08 (1.30–3.31)] and with [OR (95% CI) = 2.52 (1.46–4.36)] adjustment for confounders. We also observed that the IAP index was positively correlated with the arsenic, lead, and rare earth element levels in hair samples, and negatively correlated with the levels of some other trace elements (*i.e.*, chromium, cobalt, nickel, and tin) and alkaline earth elements (*i.e.*, calcium, magnesium, and barium) with an overall p value of <0.01. We concluded that IAP may contribute to the development of hypertension in rural housewives in northern China, possibly by interfering with the uptake of metal elements.

1. Introduction

Ambient air pollution is an important adverse factor leading to human cardiovascular and cardiopulmonary diseases (Brook, 2008; Hassing et al., 2009; Simkhovich et al., 2009). Epidemiological studies have suggested that the concentration of particulate matter (PM) and its toxic components in ambient air is associated with the incidence of hypertension (Chen et al., 2014; Coogan et al., 2012, 2015; Guo et al., 2010; Sun et al., 2008; Trasande et al., 2015). Coal combustion is an important contributor to indoor air pollution (IAP) in rural areas, especially in developing countries where coal is the primary fuel (Li et al., 2011; Massey et al., 2012). Population exposure to IAP is also affected by lifestyle factors (*e.g.*, kitchen and stove design, frequency of cooking and use of ventilation, and cohabitation with tobacco smokers) (Li et al., 2011; Massey et al., 2013). Li et al. reported that separating the kitchen from the living room and bedrooms, and improving ventilation in living areas when using a stove for heating, were associated with reduced exposure to air pollution and a lower risk of fetal neural tube

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* Corresponding author. Institute of Reproductive and Child Health/National Health Commission Key Laboratory of Reproductive Health, School of Public Health, Peking University, Beijing, 100191, China.
E-mail address: yerw@bjmu.edu.cn (R. Ye).

[1] These authors have equal contributions to this work.

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defects (Li et al., 2011). The level of IAP varies among households and is difficult to monitor. To our knowledge, while the association between outdoor air pollution and hypertension risk had been extensively reported, few studies have examined the relationship between IAP and hypertension risk.

In addition to coal combustion, tobacco smoking, as an important source of IAP, may be a risk factor for hypertension (Li et al., 2015). Approximately 300 million people in China are active smokers; as a consequence, ~540 million people suffer from passive smoking (See: http://www.nhfpc.gov.cn/). Among Chinese women, passive exposure to tobacco smoke may increase their risks of lung cancer and cardiovascular diseases, resulting in elevated morbidity and mortality (Wen et al., 2006). Various pollutants are generated during the combustion of coal and tobacco, including PM, toxic metals, polycyclic aromatic hydrocarbons (PAHs), and PAH derivatives (Massey et al., 2016; O'Connor et al., 2015; Shen et al., 2013). Toxic metals and PAHs are also two important components of PM (Wang et al., 2013, 2016a) and can accumulate in human hair after uptake into human body (Bencko, 1995; Pereira et al., 2004; Schummer et al., 2009). Shanxi Province of China is one of the world-leading coal-producing regions and has an extremely high PAH emission density (Zhang et al., 2007). Previously, we conducted a cross-sectional study of a cohort of housewives recruited from the area with the aim of screening for potential risk factors for hypertension. However, we did not find that hair PAHs were positively associated with the overall hypertension prevalence, suggesting that the organic component of PM does not play a key role in hypertension development. However, we observed that hair arsenic and rare earth element (REE) levels were positively associated with the risk of hypertension (Wang et al., 2017a; Yu et al., 2017a), as well as a decrease in hair alkaline earth elements (AEEs) (Wang et al., 2017b). The inhalation of ambient PM has been reported as an exposure route for various metals entering the human body (Zheng et al., 2010). Therefore, it is necessary to investigate whether the uptake of metals in the body mediates the association between IAP and hypertension development.

Based on our previous studies screening for hypertension risk factors, we planned to conduct a more comprehensive analysis of hair metals and develop an exposure index to evaluate the IAP level. Therefore, the aims of this study were to 1) evaluate the association between IAP and hypertension risk; and 2) investigate the potential effect of IAP on the uptake among various metals in housewives in rural areas of northern China.

2. Materials and method

2.1. Study population

This cross-sectional study was carried out in Pingding County Hospital in Shanxi Province, China. The details of how housewives were recruited were described in our previous study (Wang et al., 2016b). Briefly, women were invited to join the study if they met the following inclusion criteria: 1) long-term local resident ($\geq$10 years); 2) age $\geq$ 30 years; and 3) living conditions stable for the past 10 years. A physical examination, including measurement of height, weight, blood pressure, and heart rate, was performed according to standard protocols by local trained healthcare workers. Blood pressure was measured three times, by experienced physicians, using an appropriate cut-off with a standard mercury sphygmomanometer on the right arm at 2-min intervals following a rest period of least 5 min. Hypertension was defined as a systolic blood pressure $\geq$140 mmHg and/or diastolic blood pressure $\geq$90 mmHg, or a self-reported diagnosis of hypertension requiring treatment with antihypertensive drugs.

Local healthcare workers collected the data during face-to-face interviews. The details of the questionnaire are included in the Supplementary Materials; the instrument included questions about age, occupation, education, active or passive smoking, whether the kitchen was separate from living room/bedroom, the primary fuel used for cooking, frequency of cooking in the kitchen, and heating using a stove during the heating season. If a stove was used for heating during the heating season, the subjects were asked whether it was in the living room/bedroom, what the primary fuel used for heating was, the frequency of ventilation in the living room/bedroom, and the frequency with which exhausted combustion gas was present in the living room. From August 2012 to May 2013, a total of 405 housewives with a valid hypertension diagnosis and completed the survey, were recruited to the study and 398 of them agreed to contribute hair samples for analysis. We excluded all women who were active smokers or had a history of active smoking, as well as those did not provide clear indoor energy use information, were not ethnic Han Chinese and/or were taking anti-hypertensive drugs. Ultimately, 367 subjects were included in our analysis. Our study protocol was approved by the institutional review board of Peking University, and signed consent was obtained from all subjects.

2.2. IAP exposure index and hair metal analysis

Previously, we used an exposure index to evaluate the effects of coal combustion, passive smoking, and lifestyle factors on the risk of various birth defects (Wang et al., 2014). For this study, we developed the IAP exposure index, which considered cooking, an attached kitchen, heating, and passive smoking; full details are provided in the Supplementary Materials. Hair samples grown over the past 2 years were used to determine the long-term intake of various metals. We cut the hair samples into ~0.5-cm length segments, which were washed according to a standard operating procedure described in detail elsewhere (Li et al., 2016). The concentrations of other trace or macro-elements have been reported in our previous studies (Wang et al., 2017a, 2017b; Yu et al., 2017b), including AEEs [*i.e.*, calcium (Ca), magnesium (Mg), barium (Ba), and strontium (Sr)], REEs [(*i.e.*, lanthanum (La), samarium (Sm), europium (Eu), gadolinium (Gd), terbium (Tb), dysprosium (Dy), holmium (Ho), erbium (Er), thulium (Tm), ytterbium (Yb), lutetium (Lu), yttrium (Y), cerium (Ce), praseodymium (Pr), and neodymium (Nd)], and toxic metalloid element [*i.e.*, arsenic (As), noted as a metal in our study for convenience]. In this study, we further analyzed the concentrations of other trace metal elements using inductively coupled plasma-mass spectrometry (ELAN DRC II; PerkinElmer, USA), including chromium (Cr), copper (Cu), cobalt (Co), iron (Fe), manganese (Mn), nickel (Ni), molybdenum (Mo), tin (Sn), zinc (Zn), lead (Pb), and cadmium (Cd). For quality control, standard hair samples (GBW09101a and GBW09101b) were purchased from the National Standard Material Center, China. The measured and certified concentrations of various metal elements in the certified reference human hair were presented in Table S1. It revealed that there were minor differences (<10%) for most of the concerned metals between them, indicating an acceptable recovery rates. The analysis protocol was qualified by China Metrology Accreditation (CMA) and the quantitative analysis was completed in the Central Laboratory of Biological Elements, Peking University Health Science Center.

2.3. Statistical analysis

Demographic information of the cases and controls was compared using Pearson's χ^2 test. Unconditional logistic regression analysis was used to investigate the association between IAP exposure index and the risk of hypertension. The odds ratios with 95% confidence intervals [OR (95% CI)] were calculated, with and without adjusting for confounders, to illustrate the relative