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Associations between size-fractionated particulate air pollution and blood pressure in a panel of type II diabetes mellitus patients

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ABSTRACT

Little is known regarding how the size distribution of particulate matter (PM) air pollution influences its effect on blood pressure (BP), especially among patients with diabetes. The objective of this study was to explore the short-term associations between size-fractionated PM and BP among diabetes patients. We scheduled 6 repeated BP examinations every 2 weeks from 13 April 2013 to 30 June 2013 in a panel of 35 type 2 diabetes mellitus patients recruited from an urban community in Shanghai, China. We measured real-time PM concentrations in the size range of 0.25 to 10 μm. We used linear mixed-effect models to examine the short-term association of size-fractionated PM and BP after controlling for individual characteristics, mean temperature, relative humidity, day of the week, years with diabetes and use of antihypertensive medication. The association with systolic BP and pulse pressure strengthened with decreasing diameter. The size fractions with the strongest associations were 0.25 to 0.40 μm for number concentrations and ≤2.5 μm for mass concentrations. Furthermore, these effects occurred immediately even after 0–2 h and lasted for up to 48 h following exposure. An interquartile range increase in 24-h average number concentrations of $PM_{0.25–0.40}$ was associated with increases of 3.61 mm Hg in systolic BP and 2.96 mm Hg in pulse pressure. Females, patients younger than 65 years of age and patients without antihypertensive treatment were more susceptible to these effects. Our results revealed important size and temporal patterns of PM in elevating BP among diabetes patients in China.

1. Introduction

According to the Global Burden of Metabolic Risk Factors for Chronic Diseases, in 2010, high blood pressure (BP) was the leading risk factor for cardiovascular diseases, chronic kidney disease, and diabetes throughout the world, leading to more than 40% of deaths from these diseases worldwide. The mortality burden of cardiometabolic risk factors has shifted from high-income to low- and middle-income countries (The Global Burden of Metabolic Risk Factors for Chronic Diseases, 2014). As the largest developing country, China has witnessed a gradual increase in the prevalence of both cardiometabolic diseases and risk determinants (Yang et al., 2010). For example, the estimated prevalence of diabetes among a representative sample of adults in China was 11.6% and the prevalence of pre-diabetes was 50.1% (Xu et al., 2013). Therefore, identifying the potential risk factors for diabetes is important to reduce the disease burden.

Numerous epidemiological studies have demonstrated the short-term associations between elevated ambient air pollution and increased risks of adverse cardiovascular events (Koulova and Frishman, 2014; Mustafic et al., 2012). However, the underlying mechanisms have not been well established. Previous studies have suggested that increased arterial BP may be largely responsible for the cardiovascular effects associated with PM exposure (Brook and Rajagopalan, 2009). Diabetes itself increases the risk of hypertension because of chronic autonomic dysregulation, endothelial dysfunction and the systematic inflammatory state, and PM exposure also leads to higher BP through the same pathway (Hoffmann et al., 2012). Therefore, PM-mediated BP elevation may be involved in the development of diabetes and increases the vulnerability of diabetes patients to the hazardous exposure to PM (O'Neill et al., 2005; Zanobetti and Schwartz, 2002).

PM consists of discrete particles that range in size over several orders of magnitude, including inhalable particles (≤10 μm in aerodynamic diameter, PM_{10}), coarse particles ($PM_{2.5–10}$), fine particles (≤2.5 μm in aerodynamic diameter, $PM_{2.5}$), and ultrafine particles (≤0.1 μm in aerodynamic diameter, $PM_{0.1}$). Particle size is an important determinant of the site and efficiency of deposition in the respiratory tract, and an indicator of chemical composition and source (Araujo and Nel, 2009; Peng

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et al., 2009). Therefore, the effect of PM on BP varies considerably by its diameter. However, among the size fractions of PM, only the effects of $PM_{2.5}$ and PM_{10} have been widely examined in previous studies. Little is known about how the size distribution of PM influences its effect on BP, especially for PM ≤1 μm in aerodynamic diameter.

Therefore, the objective of this longitudinal panel study was to explore the associations between short-term exposures to size-fractionated PM and arterial BP among a panel of type II diabetes mellitus (T2DM) patients in Shanghai, China.

2. Materials and methods

2.1. Study design

Shanghai comprises urban and sub-urban districts and counties, with a total area of 6341 square kilometers (km^2), and had a population of 23.8 million at the end of 2013. In this study, we recruited 35 T2DM patients from Tianping Community, which is located in the central urban area (Xuhui District) of Shanghai with a total area of 2.68 km^2 and a population of 86,000. We measured both the environmental and health data from the Tianping Community Health Service Center (TCHSC).

The inclusion criteria for this study included: doctor-diagnosed T2DM, permanent residents of Tianping Community, more than 40 years of age, and no history of smoking, alcoholism or severe chronic cardiopulmonary diseases. We scheduled 6 follow-up visits every 2 weeks from 13 April 2013 to 30 June 2013. The subjects were randomly divided into 4 subgroups and were invited to take part in BP examinations on one day of two weekends at a 2-week interval to capture day-to-day variations in levels of PM and BP. Each examination was conducted at the same time of the same day of week to exclude any circadian rhythms. We used a self-administered questionnaire to collect personal information including name, address, age, sex, education status, income level, blood glucose level, recent history of medication, and activity patterns 3 days before the scheduled body examination. Height and weight were measured at the first follow-up to calculate the body mass index (BMI). This study was approved by the Institutional Review Board of the School of Public Health, Fudan University, and informed consent was provided by each participant.

2.2. BP measurement

A physician of TCHSC performed standardized resting BP measurements during each visit. Briefly, participants rested in a sitting position in a quiet room for at least 10 min before left upper arm BP was measured using a mercury sphygmomanometer at least three times with a 2-min minimum interval between measurements. In most cases the second and third sets of readings were averaged to calculate the systolic BP (SBP) and diastolic BP (DBP) (Rioux et al., 2010). However, if the difference between the SBP or DBP values of the second and third measurements was >5 mm Hg, the BP was considered unstable, and another 1 to 3 measurements were taken until the difference between the last two measurements was ≤5 mm Hg. The pulse pressure (PP) was calculated as the difference between the average SBP and DBP values.

2.3. Environmental data

Real-time (one value per 5 min) ambient particle number concentrations (PNCs) were measured using the Environmental Dust Monitor 365 (GRIMM; Grimm Aerosol Technik GmbH & Co. KG, Ainring, Germany) installed on the rooftop of the building of TCHSC (approximately 20 m high). There were no apparent emission sources (including arterial streets) or tall buildings around TCHSC. This instrument allows for continuous measurements of PNC with 30 size channels ranging from 0.25 to 32 μm. Ultrafine particles (PM smaller than 0.1 μm) were not measured in this study due to the limitation of our instruments. Considering the very small number concentrations of particles > 1 μm in diameter, we only analyzed PNCs in the range of 0.25 to 1.0 μm in this analysis. To avoid any issues associated with multiple comparisons, we combined the size fractions into larger strata. These PNC strata included 0.25–0.40, 0.40–0.65 and 0.65–1.0 μm.

To evaluate the effects of PM above 1 μm in diameter, we obtained real-time particle mass concentrations (PMC) of PM_{10} and $PM_{2.5}$ and concentrations of four gaseous pollutants from the nearest government-owned monitoring station in Huangpu District, which was approximately 2.5 km away from the TCHSC. We also calculated $PM_{10-2.5}$ by subtracting $PM_{2.5}$ from PM_{10}. Methods based on tapered element oscillating microbalance (TEOM), ultraviolet fluorescence, chemiluminescence, infrared absorption and ultraviolet absorption were used to measure PMC, sulfur dioxide (SO_2), nitrogen dioxide (NO_2), carbon monoxide (CO) and ozone (O_3), respectively. The TEOM™ Series 1400ab Continuous Ambient Particulate Monitor (Thermo Fisher Scientific Inc.) was used to measure $PM_{2.5}$ and PM_{10}. Models 100A, 200A, 300, and 400A made by API Inc. were used to continuously monitor SO_2, NO_2, CO, and O_3, respectively.

We obtained daily mean temperature and mean relative humidity data from a weather station approximately 2 km from TCHSC.

2.3.1. Statistical analysis

Environmental and health data were linked by the time of the subject's BP measurements. We used linear mixed-effect models to examine the association of size-fractionated PM and BP. This model allows each subject to serve as his or her own control over time, and adjustment for within-subject covariates that do not change over time. BP measurements were entered as dependent variables without log-transformation because they almost followed the normal distribution via initial inspection. Fixed-effect independent variables include air pollutants, as well as covariates to adjust for their potential confounding effects. These covariates include individual characteristics (age, sex, BMI, income, antihypertensive medication and years with T2DM), daily mean temperature, daily mean relative humidity, and an indicator variable of "day of the week". The variable of antihypertensive medication includes three levels: "none", "calcium antagonists", and "angiotensin converting enzyme inhibitor". Finally, we incorporated a random intercept for each subject to account for the correlation among multiple BP measurements collected for the same participant.

After the main model was established, we introduced PNC or PMC at each size range in single-pollutant models. To fully explore the lag structures for PM's short-term effects on BP, we examined the models using multiple periods preceding BP measurements, i.e., single lags of 0–2 hour (h), 3–6 h, 7–12 h, 13–24 h, 25–48 h and 49–72 h. We did not evaluate lags of longer than 72 h because few short-term studies found that air pollution's effects could last longer than 3 days (Dominici et al., 2006; Mustafic et al., 2012; Urch et al., 2005). We adjusted a priori for the confounding effects of ambient temperature and relative humidity using the moving average of the same day of BP examination and the previous 3 days.

We performed stratification analyses to explore the effect modifications by individual characteristics including age, sex, BMI, income, antihypertensive treatment and years with T2DM. To allow for stratification analyses, we dichotomized these variables.

As a sensitivity analysis, we fitted two-pollutant models to evaluate the robustness of our results after controlling for simultaneous exposure to gaseous pollutants (SO_2, NO_2, CO and O_3).

Statistical tests were two-sided, and p-values of ≤0.05 were considered statistically significant. All analyses were conducted in R software (Version 2.15.3, R Foundation for Statistical Computing, Vienna, Austria) using "lme4" package. The results were presented as the change of BP and its 95% confidence intervals (CIs) associated with an interquartile range (IQR) increase of PM concentrations.