



Fine particulate matter results in hemodynamic changes in subjects with blunted nocturnal blood pressure dipping



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ABSTRACT

Particulate matter with aerodynamic diameter of $< 2.5 \mu\text{m}$ ($\text{PM}_{2.5}$) is associated with blood pressure and hemodynamic changes. Blunted nocturnal blood pressure dipping is a major risk factor for cardiovascular events; limited information is available on whether $\text{PM}_{2.5}$ exposure-related hemodynamic changes vary with day–night blood pressure circadian rhythms. In this study, we enrolled 161 subjects and monitored the changes in ambulatory blood pressure and hemodynamics for 24 h. The day–night blood pressure and cardiovascular metrics were calculated according to the sleep–wake cycles logged in the subject's diary. The effects of $\text{PM}_{2.5}$ exposure on blood pressure and hemodynamic changes were analyzed using generalized linear mixed-effect model. After adjusting for potential confounders, a $10\text{-}\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ was associated with 1.0 mmHg [95% confidence interval (CI): $0.2\text{--}1.8 \text{ mmHg}$] narrowing in the pulse pressure, 3.1% (95% CI: $1.4\text{--}4.8\%$) decrease in the maximum rate of left ventricular pressure rise, and 3.6% (95% CI: $1.6\text{--}5.7\%$) increase in systemic vascular resistance among 79 subjects with nocturnal blood pressure dip of $< 10\%$. In contrast, $\text{PM}_{2.5}$ was not associated with any changes in cardiovascular metrics among 82 subjects with nocturnal blood pressure dip of $\geq 10\%$. Our findings demonstrate that short-term exposure to $\text{PM}_{2.5}$ contributes to pulse pressure narrowing along with cardiac and vasomotor dysfunctions in subjects with nocturnal blood pressure dip of $< 10\%$.

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1. Introduction

The American Heart Association's scientific statements propose that ambient particulate matter can adversely affect systemic hemodynamics in exposed individuals (Brook et al., 2010). The variation in blood pressure has been a frequently used indicator to evaluate the effects of particulate matter on hemodynamic changes. However, because of inconsistency among the reported results, the effects of short-term particulate matter exposure on blood pressure remains unclear (Brook and Rajagopalan, 2009). The rapid variability in blood pressure on a short-term basis has been proposed to be an important factor contributing to the

disparity in the inconsistent findings of previous studies involving only a single blood pressure measurement (Brook et al., 2010).

Short-term blood pressure variation in response to particulate matter exposure is a complicated physiological response tightly regulated by numerous cardiac and vascular homeostatic mechanisms. An increasing number of studies have demonstrated the influence of short-term exposure to particulate matter on vasomotor dysfunction in human subjects (Dales et al., 2007; Lundbäck et al., 2009; Peretz et al., 2008; Törnqvist et al., 2007; Wu et al., 2010). However, limited data are available to determine the effects of short-term exposure to particulate matter on cardiac contractility, stroke volume, and cardiac output in humans, all of which can contribute to blood pressure change as well as vascular resistance. Two animal studies have reported acute cardiac dysfunction in rats upon exposure to particulate matter (Huang et al., 2010; Yan et al., 2008). More studies are needed to assess the effects of short-term exposure to particulate matter on both cardiac and vascular parameters and subsequent blood pressure changes in human subjects.

Susceptibility is also related to cardiovascular events in an individual upon exposure to particulate matter (Brook et al., 2010).

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However, few clinical predictors are available to address the population vulnerability to subclinical blood pressure changes in response to particulate matter exposure. A sub-cohort study recently reported that blood pressure dipping, a standard day-night blood pressure circadian rhythm, was blunted upon short-term exposure to particulate matter with aerodynamic diameter of $< 10 \mu\text{m}$ (PM_{10}) (Tsai et al., 2012). O'Brien et al. (1998) introduced the dipping/non-dipping classification; the threshold value was a decrease of 10% in nocturnal blood pressure dipping. Such classification appears to have advantages from a clinical standpoint and has been used in several studies to demonstrate target organ damages and cardiovascular risks in non-dippers (i.e., those with nocturnal systolic blood pressure dipping of $< 10\%$) (Bianchi et al., 1994; Kuwajima et al., 1992; Ohkubo et al., 2002; Redon et al., 1994; Rizzoni et al., 1992; Timio et al., 1994; Verdecchia et al., 2012, 1990; Viera et al., 2012). Whether the non-dippers are more susceptible to particulate matter-related cardiovascular risks, however, remains unknown. In this study, we evaluated the difference between the effects of short-term exposure to particulate matter with aerodynamic diameter of $< 2.5 \mu\text{m}$ ($\text{PM}_{2.5}$) on blood pressure and hemodynamic changes in adult dippers and non-dippers using a 24-h ambulatory blood pressure and hemodynamic monitoring method.

2. Materials and methods

2.1. Study population and study protocol

A total of 202 subjects, who were mid- to high-level executives employed at the headquarters of a state-operated enterprise in Taipei City, participated in a cardiovascular health promotion program from July 2002 to September 2002. The health promotion program was conducted during workdays (Monday–Friday) in the office building, which was located in a high traffic area of Xin-Yi Development District of Taipei City. Smoking was prohibited inside the office building. After excluding the subjects with missing data and those who did not provide informed consent or live in the Taipei metropolitan area, 161 subjects were finally recruited in this study; the total participation rate was 79.7%. The study consisted of a clinician interview, self-reported questionnaire, venous biochemistry sampling, and 24-h ambulatory blood pressure and hemodynamic monitoring. The subjects' age, gender, body mass index, physician-diagnosed hypertension, anti-hypertension medication history, and smoking status were obtained via clinician interview and self-report questionnaire, which were performed at the beginning of the study. Venous biochemistry data, including blood sugar, total cholesterol, and triglyceride levels, were collected following a 10-h overnight fast and analyzed in the central laboratory of the National Taiwan University Hospital. Informed consent was obtained from each subject. This study was approved by the Institutional Review Board of National Taiwan University Hospital.

2.2. 24-h Ambulatory blood pressure and hemodynamic monitoring

Following clinician interview and self-reported questionnaire, all subjects were under 24-h ambulatory blood pressure and hemodynamic monitoring using the Dynapulse 5000 system (Pulse Metric Inc., San Diego, CA, USA), which determined the blood pressure by examining pressure waveform changes due to Bernoulli flow effects. The pulse dynamics waveform analysis is a well-approved method for continuous monitoring of systolic and diastolic blood pressure, heart rate, and pulse pressure (Brinton et al., 1997). This method has been applied to derive other hemodynamic parameters including cardiac hemodynamics, such as the maximum

rate of left ventricular pressure rise, stroke volume, and cardiac output (Chio et al., 2007), and vascular hemodynamics, such as systemic vascular compliance and systemic vascular resistance (Brinton et al., 1997). The ambulatory blood pressure monitoring system was mounted on the subject's left arm in the morning (between 8 am and 12 pm) and removed 24 h later. Recordings were performed every 15 min, between 7 am and 10 pm, and every 30 min, between 10 pm and 7 am. The subject's activity during the 24-h ambulatory blood pressure monitoring, including on-duty time, off-duty time, sleep time, and wake up time on the following morning, were logged in the subject's diary. Because Perk et al. (2001) suggested that considering people's actual behavior increases the accuracy of blood pressure determination, the daytime and nighttime blood pressure and hemodynamic parameters for each subject were defined and calculated according to periods of wakefulness and sleep logged in the subjects' diary. Blood pressure dipping was calculated as the daytime minus nighttime average of systolic blood pressure. In comparison with daytime systolic blood pressure, subjects with $\geq 10\%$ and $< 10\%$ reduction in nocturnal systolic blood pressure were classified as dippers and non-dippers, respectively.

2.3. Environmental data

The hourly average mass concentration of $\text{PM}_{2.5}$ exposure was calculated on the day of the study; the data were collected from the Sinjhuang Supersite Station, a fixed-site air quality monitoring station, which is a part of the Taiwan Environmental Protection Agency Air Quality Monitoring Network. The Sinjhuang Supersite Station is located in Sinjhuang Sports Park and is 11.8 km from the subjects' workplace. Toward north of the monitoring station is the main road and the southwestern side is the green boulevard and Sinjhuang Baseball Field. The pollution around the station is primarily due to vehicles on workdays and normal activities on holidays. $\text{PM}_{2.5}$ mass concentrations were measured using the tapered element oscillating microbalance (TEOM) 1400a monitor (R&P, Albany, NY, USA), equipped with a sample equilibrium system Nafion dryer. The scheduled quality control procedures included daily zero and span checks, biweekly precision checks, quarterly multipoint calibration, and data validation. To avoid possible exposure misclassification from spatial variation during the off-duty period, we matched hourly concentrations of $\text{PM}_{2.5}$ to the subject's on-duty period on the examination day based on their diary. To account for meteorological factors on blood pressure and hemodynamics, we also collected meteorological data, including the ambient temperature and relative humidity, from the Sinjhuang Supersite Station.

Fig. 1 illustrates the time course relevant to the blood pressure observations and $\text{PM}_{2.5}$ exposure measurement for all subjects. For example, the on-duty time, off-duty time, sleep time, and wake up time on the following morning for a subject were 0800, 1800, 2200, and 0600, respectively. The daytime blood pressure was from 0800 to 2200, while the nighttime blood pressure was from 2200 to 0600 on the following morning. The hourly $\text{PM}_{2.5}$ concentrations from 0800 to 1800 in the Sinjhuang Supersite Station were matched to $\text{PM}_{2.5}$ exposure during the subject's on-duty period.

2.4. Statistical analysis

Because there were two measures of cardiovascular parameters (i.e., daytime and nighttime), we applied a generalized linear mixed-effect model with a random effect to estimate the effects of $\text{PM}_{2.5}$ exposure on changes in cardiovascular parameters. The models were separately fitted to systolic and diastolic blood pressure, pulse pressure, heart rate, and hemodynamic parameters, including the maximum rate of left ventricular pressure rise, stroke volume, cardiac output, systemic vascular compliance, and systemic vascular resistance. Potential covariates were considered in the mixed models for adjustment, which included individual characteristics (such as age, gender, body mass index, fasting sugar, triglyceride, and total cholesterol levels, history of smoking, hypertension, and hypertension medication) and meteorological factors (temperature and relative humidity). We applied the variable selection technique, 10% change-in-estimate criterion (Rothman et al., 2008), to select potential confounding factors. The covariates, including body mass index, hypertension medication, and gender were finally identified in sequence as adjustment variables. The estimates of the effects of $\text{PM}_{2.5}$ exposure on changes in blood pressure and hemodynamic parameters were expressed as mean values and 95% confidence intervals (CIs) for a $10\text{-}\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$.

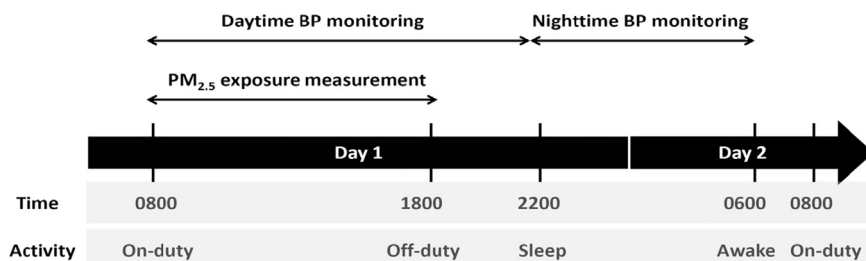


Fig. 1. Time course relevant to personal daytime and nighttime blood pressure (BP) observations and $\text{PM}_{2.5}$ exposure measurement.

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