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Short-term effects of particle size fractions on circulating biomarkers of inflammation in a panel of elderly subjects and healthy young adults☆

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ABSTRACT

Systemic inflammation biomarkers have been associated with risk of cardiovascular morbidity and mortality. We aimed to clarify associations of acute exposure to particulate matter (PM_{10} (PM < 10 μm), $PM_{2.5\text{-}10}$ (PM 2.5–10 μm), $PM_{2.5}$ (PM < 2.5 μm), $PM_{1\text{-}2.5}$ (PM 1–2.5 μm), and PM1 (PM < 1 μm)) with systemic inflammation using panels of elderly subjects and healthy young adults.

We followed a panel of 44 nonsmoking elderly subjects living in a retirement home and a panel of 40 healthy young adults living in a school dormitory in Tehran city, Iran from May 2012 to May 2013. Blood biomarkers were measured one every 7–8 weeks and included white blood cells (WBC), high sensitive C-reactive protein (hsCRP), tumor necrosis factor-soluble receptor-II (sTNF-RII), interleukin-6 (IL-6), and von Willebrand factor (vWF). We measured hourly indoor and outdoor exposure to PM_{10}, $PM_{2.5\text{-}10}$, $PM_{2.5}$, $PM_{1\text{-}2.5}$, and PM_1 mass concentration to derive weighted averages of personal exposure based on simultaneously collected time-activity data. The random intercept linear mixed effects model was used for data analysis.

We observed significant positive associations for WBC and IL-6 with exposure to PM_{10}, $PM_{2.5\text{-}10}$, $PM_{2.5}$, $PM_{1\text{-}2.5}$, and PM_1; sTNF-RII with $PM_{2.5}$, $PM_{1\text{-}2.5}$, and PM_1; hsCRP with $PM_{2.5}$ and PM_1; and vWF with PM_{10} and $PM_{2.5\text{-}10}$, $PM_{2.5}$, and $PM_{1\text{-}2.5}$ mass concentration in elderly subjects from the current-day and multiday averages. For healthy young adults, we found significant positive associations for WBC and IL-6 with exposure to PM_{10}, $PM_{2.5\text{-}10}$, $PM_{2.5}$, and $PM_{1\text{-}2.5}$, but no with PM_1. The results showed that increase of hsCRP, sTNF-RII, and vWF were not significantly associated with any of the PM sizes investigated in the healthy young subjects.

Our results provided some evidence that short-term exposure to PM_{10}, $PM_{2.5\text{-}10}$, $PM_{2.5}$, $PM_{1\text{-}2.5}$, and PM_1 was associated with inflammation and coagulation blood markers, but associations were depended on PM size and also differed across the various time lag.

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1. Introduction

Air pollution is a major issue for the global community and has a wide range of adverse effects on human health (Rückerl et al., 2011). Numerous studies have shown that environmental exposure to particulate matter (PM) is associated with increase in cardiovascular hospitalization and mortality (Cosselman et al., 2015; Pope III and Dockery, 2006). Although biological mechanisms related to the PM exposure and cardiovascular diseases have not been fully illustrated, toxicological studies have demonstrated that PM may induce inflammatory and oxidative stress and prothrombotic responses mediated through vascular endothelial cells, leukocytes, and platelets, with expression of inflammatory cytokines, cellular adhesion molecules, and coagulation factors (Brook et al., 2010).

PM_{10} (PM < 10 μm) deposited in lungs activate inflammation with 1) generation of pro-inflammatory cytokines by macrophages that have phagocytized coarse particles, and 2) induction of chemokine production by the pulmonary epithelium (Fujii et al., 2001; Valavanidis et al., 2008; Wang et al., 2015). The mediators released by alveolar macrophages can influence both local and systemic inflammatory responses (Brook et al., 2010; Cosselman et al., 2015; Newby et al., 2014). Fine and especially ultrafine particles are quickly absorbed and may pass directly into the blood stream, thus causing a direct insult to the cardiovascular system and other organs distant from the lungs (Polichetti et al., 2009; Zhang et al., 2016). Numerous epidemiological studies have found that risk of heart and vasculature diseases is associated with increased blood levels of circulating markers of systemic inflammation such as white blood cells (WBC), high sensitive C-reactive protein (hsCRP), tumor necrosis factor-soluble receptor-II (sTNF-RII), interleukin-6 (IL-6), and von Willebrand factor (vWF) (Brook et al., 2010; Chen et al., 2015; Hampel et al., 2015). These markers, associated with cardiovascular diseases CVDs, are commonly investigated in PM studies and were selected to show short-term effects of various PM size fractions on circulating markers, providing a more comprehensive understanding of biological pathways linking PM exposure with CVDs.

Exposure assessment is a critical step in epidemiologic studies. People are exposed to PM in outdoor and especially in indoor environments where people spend more than 90% of their time (Nazaroff and Goldstein, 2015). Generally, epidemiologic studies on the acute effects of air pollution often rely on air pollution data from a single central monitoring station. Thus, personal exposures in outdoor and indoor environments (Delfino et al., 2008) are not well captured as exposure also depends on proximity to emissions sources. Moreover, actual exposure is strongly dependent on the individual time activity patterns (Almeida-Silva et al., 2015).

Many studies focus on only one particle size fraction, $PM_{2.5}$ (PM < 2.5 μm). However, experimental evidences have found that PM of smaller sizes (e.g. PM < 1 μm in diameter) can as well affect the level of inflammation and oxidative stress (Lane et al., 2016; Ntziachristos et al., 2007). Indeed, the relevant pathways of biologic action may differ across PM of different sizes. However, simultaneous assessment of effects of various PM size fractions such as PM_{10}, $PM_{2.5\text{-}10}$ (PM 2.5–10 μm), $PM_{2.5}$, $PM_{1\text{-}2.5}$ (PM 1–2.5 μm), and PM1 (PM < 1 μm) on circulating biomarkers are sparse(Chen et al., 2015; Karottki et al., 2015), thus, it is still unknown how the association between PM and circulating markers differs by particle size. Some toxicological studies indicate that coarse particles are more strongly associated with inflammation and coagulation than $PM_{2.5}$ (Adar et al., 2015). Personal characteristics such as age may as well determine the health relevance of the various exposures. Indeed studies investigating associations of PM mass concentrations and circulation biomarkers in the elderly (Delfino et al., 2010; Rückerl et al., 2014) and in healthy young adults (Chuang et al., 2007; Ghio et al., 2003; Rich et al., 2012; Thompson et al., 2010; Wu et al., 2012) are not fully consistent.

In this study, we hypothesized that exposure to PM_{10}, $PM_{2.5\text{-}10}$, $PM_{2.5}$, $PM_{1\text{-}2.5}$, and PM_1 would be associated with increased biomarkers of systemic inflammatory responses in the healthy young adults and the elderly subjects. To investigate these acute responses, we carried out a study involving repeated measurements of PM_{10}, $PM_{2.5\text{-}10}$, $PM_{2.5}$, $PM_{1\text{-}2.5}$, and PM_1 exposures and circulating biomarkers (WBC, hsCRP, sTNF-RII, IL-6, and vWF) in a panel of elderly subjects living in a retirement home and of healthy young adults living in a school dormitory in Tehran, the capital of Iran. Tehran is the largest metropolitan area in western Asia. About 9 million residents of this city are regularly exposed to severe air pollution including smog episodes where schools were closed due to air pollution. Despite the significance of PM pollution in Tehran, there is little information on effects of PM on human health in this area.

2. Materials and methods

2.1. Study participants and design

The study design consisted in two parallel panel studies, one among healthy young adults and one among elderly subjects. The panel approach with repeated measurements comes with the advantage of each participant acting as his or her own control, thus, individual characteristics that do no vary over time will not confound the acute effect associations of interest. We recruited 44 non-smoking elderly volunteer subjects included men and women (>65 years of age) living in a retirement home and 40 healthy, non-smoking male high school students between 15 and 18 years of age living in a school dormitory in the city of Tehran who had consent to take part in the study.

Detailed information about the study sites can be found in our previous publications (Hassanvand et al., 2014, 2015). Briefly, the retirement home and school dormitory were located in central urban area of Tehran. The retirement home is located about 650 m away from a major freeway and the school dormitory was approximately 200 m away from a major freeway and 1.1 km away from the retirement home. Of 60 elderly volunteers, 10 were not eligible, 3 died, and 3 had insufficient biomarker data due to exclusions for frequent infections, leaving 44 subjects. Of 45 healthy young volunteers, 3 were not eligible, and 2 had insufficient biomarker data due to exclusions for frequent infections, leaving 40 subjects.

Between May 2012 to May 2013, the healthy young and the elderly participants were recruited to take part in six blood draws scheduled every seven to eight weeks on the same day of the week and the same time of the day (Wednesday afternoons between 13:00–15:00) to control day-of-week effects and circadian rhythm. Each participant contributed six blood draws ($n = 240$ (40×6) and 264 (44×6) total samples, respectively, for the healthy young and the elderly subjects). We chose longer time periods between the measurements to possibly increase the variability in PM concentrations which tend to show seasonal patterns. At each step of blood sampling, participants were visited by a physician and data on health status, medication use and disease was collected and subsequently venous blood samples were drawn. We did not take blood during times with acute infectious illnesses. Finally, we used participants with six complete blood samples.

All participants provided written informed consent prior to participating in the study. The Research Ethics Boards of Tehran University of Medical Sciences approved the study protocol.

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