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Bioaerosol exposure and circulating biomarkers in a panel of elderly subjects and healthy young adults

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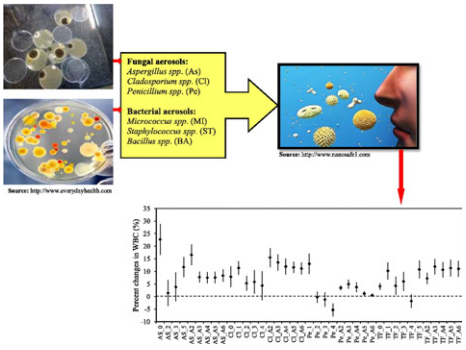
HIGHLIGHTS

- Exposure to bioaerosols increases the level of biomarkers both in elderly and healthy young subjects.
- Associations were stronger in the healthy young adults.
- Pooled results confirm the hypothesis that bioaerosols induced blood markers.

GRAPHICAL ABSTRACT



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ABSTRACT

Numerous studies have found that risk of cardiovascular diseases is associated with increased blood levels of circulating markers of systemic inflammation. We investigated associations of acute exposure to bioaerosols (bacteria and fungi) with blood markers of inflammation and coagulation using panels of elderly subjects and healthy young adults. We conducted a panel study of 44 nonsmoker elderly subjects in a retirement communities and a panel study of 40 healthy young adults living in a school dormitory within Tehran city, Iran. Blood sample biomarkers were measured weekly over 6 weeks and including high sensitive C-reactive protein (hsCRP), tumor necrosis factor-soluble receptor-II (sTNF-RII), von Willebrand factor (vWF), white blood cells (WBC) count and interleukin-6 (IL-6). We found significant positive associations for IL-6 and WBC with exposure to *Aspergillus* spp. (As), *Cladosporium* spp. (Cl), *Penicillium* spp. (Pe), total fungi (TF) and *Micrococcus* spp. (MI); vWF with Cl and MI; sTNF-RII with *Staphylococcus* spp. (ST) in healthy young adults from the current-day and multiday averages. For elderly subjects, we observed significant positive associations for hsCRP, sTNF-RII and WBC with exposure to MI, but not with ST and total bacteria (TB). Our results showed the strongest significant positive associations for IL-6 with MI, ST and TB in elderly people. In addition, IL-6 was also positively associated with

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As, Cl and Pe in elderly. Also, the results showed that increase of vWF was significantly associated with bacterial and fungal aerosols, except *Bacillus* spp. (BA) at some lags in elderly subjects. Pooled results support the pivotal role of bioaerosols in increasing the level of some of inflammatory biomarkers, especially IL-6 and WBC in healthy young adults but possibly also in elderly people.

1. Introduction

Human exposure to particulate matter (PM) is one of the most pressing topics in modern-day public health (Nelin et al., 2012). In addition, extensive epidemiological research links ambient air pollution, especially PM with increased cardiovascular events such as cardiovascular mortality and morbidity (Araujo and Nel, 2009; Bräuner et al., 2008; Brook et al., 2010; Huttunen et al., 2012; Nelin et al., 2012; Pelucchi et al., 2009; Valentino et al., 2016). These harmful health effects are suggested to be mediated by systemic inflammation (Huttunen et al., 2012; Nelin et al., 2012; Thompson et al., 2010). Several epidemiological and experimental studies have shown that exposure to PM increases levels of inflammatory markers circulating in blood, especially CRP, IL-6, and sTNF-RII (Delfino et al., 2010; Delfino et al., 2009; Hampel et al., 2015; Huttunen et al., 2012; Langrish et al., 2012; Rückerl et al., 2007; Rückerl et al., 2014). CRP, IL-6 and sTNF-RII act as predictors of cardiovascular events (Pai et al., 2004). PM is divided into three groups, such as: coarse (aerodynamic diameter between 2.5 and 10 μm), fine (particles with an aerodynamic diameter smaller than 2.5 μm), and ultrafine particles (have a diameter <0.1 μm) (Brook et al., 2010; Nelin et al., 2012). Bioaerosols, as a class of airborne pollutants, are particulate matter that contain one or more compounds of biological origin and comprise 5–50 (30% on average) of the aerosols larger than 0.2 μm (Blais-Lecours et al., 2015; Faridi et al., 2015; Ghosh et al., 2015; Perrino and Marcovecchio, 2016; Walser et al., 2015). This includes viable and non-viable bacterial and fungal spores, bacterial and fungal products (endotoxins, mycotoxins, peptidoglycans, β (1, 3)-glucans), viruses, pollen grains, fur fibres, airborne algae, plant debris, and fragments of microbial insects, animal and human skin (Blais-Lecours et al., 2015; Ghosh et al., 2015; Perrino and Marcovecchio, 2016; Walser et al., 2015). Bacterial and fungal aerosols, as the most important bioaerosols, are an inseparable part of the human societies and mainly present in most enclosed environments (Brook et al., 2004; Faridi et al., 2015; Ghosh et al., 2015; Goudarzi et al., 2016; Jones and Harrison, 2004). Bacterial and fungal aerosols have an aerodynamic diameter of 2.5 (Brook et al., 2004) and 1–30 μm (Faridi et al., 2015; Ghosh et al., 2015), respectively (Ghosh et al., 2015). In reality, bacteria are $PM_{2.5}$ and a part of fungal spores are PM_{10} (Blais-Lecours et al., 2015; Brook et al., 2004; Després et al., 2012). Both the upper and lower respiratory systems are affected by bacterial and fungal aerosols (Blais-Lecours et al., 2015; Després et al., 2012; Faridi et al., 2015; Pastuszka et al., 2000), hence their health assessment is highly essential. The occurrence of bioaerosols had been recognized in atmospheric PM samples since the second half of 19th century, but these parts of PM received less attention than others (Després et al., 2012; Perrino and Marcovecchio, 2016). These parts of PM not only in the atmospheric PM samples have presence, but also in about 5 to 34% of indoor PM can be attributed (Ghosh et al., 2015; Mandal and Brandl, 2011; Perrino and Marcovecchio, 2016). Health hazards of bioaerosols are divided into two categories, including: non-infectious diseases (e.g. hypersensitivity, allergies, and asthma) and infectious diseases (e.g. legionellosis, tuberculosis and anthrax) (Ghosh et al., 2015). Although numerous studies have been performed to assess the association of the physical and chemical characteristics of PM (Brucker et al., 2013; Delfino et al., 2010; Delfino et al., 2009; Delfino et al., 2008; Rückerl et al., 2007; Ruckerl et al., 2006; Steinvil et al., 2008) and pollutant gases (Delfino et al., 2009; Rückerl et al., 2007; Rückerl et al., 2014; Ruckerl et al., 2006; Steinvil et al., 2008; Thompson et al., 2010) with circulating biomarkers, few of those have been evaluated the association between bioaerosols and circulating biomarkers (Purokivi et al., 2001).

In this study, we hypothesized that exposure to bioaerosols (bacteria and fungi) would be associated with increased circulating biomarkers in the healthy young adults and the elderly subjects. To assess these acute responses, we carried out a study involving repeated measurements of bioaerosol exposures and circulating biomarkers (hsCRP, sTNF-RII, vWF, WBC and IL-6) in a panel of healthy young adults living in a school dormitory and elderly subjects living within a retirement home in Tehran, the capital of Iran. Tehran is the largest city of Iran with a population of approximately nine million people and has one of the most polluted atmosphere in the world (Hassanvand et al., 2014; Hassanvand et al., 2015; Hassanvand et al., 2017; Hoseini et al., 2016). In recent years, residents of this city have been exposed to severe air pollutant, especially PM and composition of PM, frequently exceeding the ambient air quality standards. Despite the significance of PM in Tehran, there is no information on effects of bioaerosols, as a class of PM, on human health.

2. Methods

2.1. Study participants and design

Two-prospective panel study in Tehran, Iran, including healthy young adults and the elderly subjects (>65 years of age) were recruited from May 2012 to May 2013. In the repeated measurement design, each subject serves as her or his own control. Elderly subjects (44 non-smokers) lived in a retirement home and healthy young adults (40 non-smokers, high school students, and 15–18 years of age) were living within a school dormitory in the city of Tehran, Iran.

Detailed information on the study sites could be found in our previous publication (Faridi et al., 2015). Briefly, the retirement home and school dormitory were located in central urban area of Tehran. Of 60 elderlies, 16 ones were excluded (10 were not eligible, 3 died, and 3 had insufficient biomarker data due to frequent infections), leaving 44 subjects. Of 45 healthy young volunteers, 5 ones were excluded (3 were not eligible, and 2 had insufficient biomarker data due to frequent infections), leaving 40 subjects. Table 1 provides summary data on the blood markers by study and descriptive characteristics of the subjects of each panel study. Over a 12-month period, participants were followed to take part in up to six blood withdrawals scheduled every seven to eight weeks on the same weekday (Wednesday afternoons) and the same time (13:00–15:00) to control circadian variation and weekly effects. Each participant contributed six blood withdrawals ($n = 240$ (6×40) and 264 (6×44) total samples for the healthy young and the elderly subjects, respectively). This approach was intended to increase the chance of having more variability in bioaerosol concentration. At each step of blood withdrawal, participants were visited by a physician and data on health status, medication use and disease was collected and subsequently venous blood samples were drawn. Over this study, blood markers of subjects with acute infectious illnesses were excluded.

2.2. Measurement of blood biomarkers

We took 10-ml blood sample from each subject in each time and kept on ice packs before centrifugation. Samples of venous blood were centrifuged by a refrigerated centrifuge for 15 min and then immediately stored at −70 °C before assay. Biomarkers of hsCRP, sTNF-RII, vWF and IL-6, were determined in plasma and WBC were measured in