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Original article

Response of biomarkers of inflammation and coagulation to short-term changes in central site, local, and predicted particle number concentrations

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ABSTRACT

Purpose: Previous studies have reported acute (hours–28 days) associations between ambient ultrafine particles (UFP; diameter <0.1) and biomarkers of cardiovascular health using central site data. We evaluated particle number concentration (a proxy measure for UFP) measured at a central site, a local near-highway site and predicted residential concentrations with response of biomarkers of inflammation and coagulation in a near-highway population.
Methods: Participants provided two blood samples for analysis of interleukin-6 (IL-6), high-sensitivity C-reactive protein (hs-CRP), tumor necrosis factor-α receptor II, and fibrinogen. Mixed effect models were used to evaluate the association between PNC levels on the same day, prior 2 days, and moving averages of 3 to 28 days.
Results: Estimated effects on biomarkers of a 5000 unit increase in central site PNC generally increased with longer averaging times for IL-6, hs-CRP, and fibrinogen. Effect estimates were highest for a 28-day moving average, with 91% (95% confidence interval [CI]: 9, 230) higher IL-6 levels, 74% (95% CI: −7, 220) higher hs-CRP levels, and 59% (95% CI: −13, 130) higher fibrinogen levels. We observed no clear trend between near-highway or predicted residential PNC and any of the biomarkers.
Conclusions: Only central site PNC increased blood markers of inflammation while near-highway and predicted residential values did not. We cannot fully explain this result, although differing PNC composition is a possibility. Future studies would assist in understanding these findings.

Introduction

Air pollution is widespread in the urban environment and there is substantial evidence of associations with cardiovascular (CV) morbidity and mortality [1–4]. Three principal pathways have been proposed to explain the adverse CV effects of inhalation of particulate matter: oxidative stress and inflammation, stimulation of the autonomic nervous system, and direct interaction between particles or their components and the CV system [1]. The first pathway, which begins with pulmonary inflammation, progresses to a systemic inflammatory state of oxidative stress, acute phase response, and endothelial dysfunction. Supporting this pathway are observations of associations between particulate matter and markers of systemic inflammation [5–9] and blood pressure [10–12].

The specific components responsible for associations between air pollution and adverse outcomes are yet to be fully defined; however, there is evidence from human, animal, and in vitro studies that ultrafine particles (UFP; diameter <0.1 μm) have causal effects [5,13–17]. UFP have the ability to deposit deep into the lungs, where large surface areas are available for the adsorption of harmful chemicals [14,18,19]. In the urban environment, regional levels of UFP are augmented by contributions from motor vehicle exhaust resulting in both substantial temporal and spatial variability, particularly near busy roadways [20–22].

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Our goal was to examine the effect of short-term exposure to UFP on biomarkers of inflammation and coagulation in a predominately near-highway population. UFP can be reasonably approximated by particle number concentration (PNC) because 80% to 90% of PNC is in the ultrafine range in urban areas [23,24]. We hypothesized that short-term changes in ambient PNC would be related to increases in interleukin-6 (IL-6), high-sensitivity C-reactive protein (hs-CRP), tumor necrosis factor-α receptor II (TNF-RII), and fibrinogen. In most published studies, a single metric is used for PNC exposure, typically from a central site [8,9,25–28]. However, central sites may not represent PNC variation (and therefore exposures) near highways and a neighborhood monitor or predicted residential concentrations [29]. In other studies in which residential measurements have provided the data for exposure, associations of residential PNC and quasi-UFP (diameter <0.25 μm) with blood pressure and inflammatory markers have been identified [6,30]. We evaluated potential associations of PNC measured at a central site, a near-highway monitor, and modeled values with biomarkers of inflammation and coagulation.

Methods

Study area and population

This analysis used data from the Community Assessment of Freeway Exposure and Health (CAFEH) study, a cross-sectional, community-based participatory research study of near-highway air pollution and CV health [31]. The study enrolled residents from three near-highway neighborhoods in Boston, Massachusetts (United States), metropolitan area.

We used data from the Somerville, Massachusetts subsample of CAFEH for this analysis. A detailed description of the study is provided elsewhere [32]. Somerville is a city located to the northwest of Boston whose southeast portion is split by I-93, which carries 150,000 vehicles per day (vpd) and another major roadway, Route-38 (20,000 vpd) [33]. Participants were recruited from three areas based on residential distance to the highway: less than 100 m, 100 to 400 m, and an urban background location greater than 1000 m (Fig. 1). A random sample of addresses within these distance categories was selected for recruitment, and additional participants were recruited from a convenience sample of residents in two senior housing developments. Inclusion criteria were 40 years or older, residing within the study, area and ability to answer a questionnaire in one of five languages (English, Spanish, Haitian Creole, Portuguese, or Chinese). Participants were asked to provide blood samples at two time points approximately 5 months apart. Blood and other clinical data were collected from August 2009 through September 2010. Clinics took place from approximately 6 AM to noon on scheduled days with most clinical visits being from 7 to 11 AM. The study was approved by the Tufts University School of Medicine IRB, and all participants provided informed consent.

Individual level covariates

Data on demographic variables including age, sex, race and ethnicity, employment status, income, and education were collected. Data on factors that may affect exposure to particulate matter including smoking, secondhand smoke, and employment status were also collected. The name and dosage of each participant's prescribed medications during in-home interviews were recorded. A physician categorized medications into those prescribed to manage cholesterol, hypertension, diabetes, and inflammation. The presence of prior or current health conditions including asthma, congestive heart failure, myocardial infarction, rheumatoid arthritis and stroke were identified by self-report.

Exposure measurements

Environmental monitoring used to create the exposure metrics in these analyses are detailed elsewhere [29,34,35]. Ambient measurements of PNC were measured from a rooftop monitor (six floors above street level) at the Countway Library of Medicine of

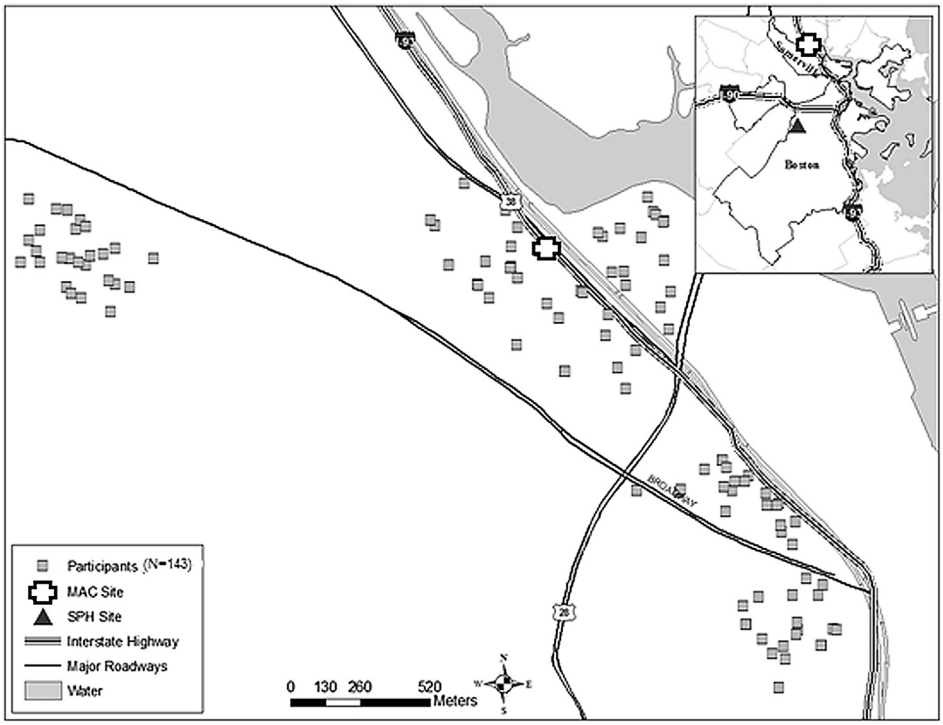

Fig. 1. Study area showing monitoring sites and participant residences.