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Domestic airborne black carbon levels and 8-isoprostane in exhaled breath condensate among children in New York City ☆

Maria Jose Rosa [a,*], Beizhan Yan [b], Steven N. Chillrud [b], Luis M. Acosta [a], Adnan Divjan [a], Judith S. Jacobson [c], Rachel L. Miller [a,d], Inge F. Goldstein [c], Matthew S. Perzanowski [a]

[a] Department of Environmental Health Sciences, Mailman School of Public Health, Columbia University, 722 W 168th Street, 11th floor, New York, NY 10032, United States
[b] Lamont-Doherty Earth Observatory, Columbia University, Comer Building, Rm 203, Palisades, NY 10964, United States
[c] Department of Epidemiology, Mailman School of Public Health, Columbia University, 722 W 168th Street, R732, New York, NY 10032, United States
[d] Division of Pulmonary, Allergy, Critical Care Medicine, Department of Medicine, Columbia, University College of Physicians and Surgeons, 630 W 168th Street, PHE-101, New York, NY 10032, United States

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ABSTRACT

Background: Exposure to airborne black carbon (BC) has been associated with asthma development, respiratory symptoms and decrements in lung function. However, the mechanism through which BC may lead to respiratory symptoms has not been completely elucidated. Oxidative stress has been suggested as a potential mechanism through which BC might lead to adverse health outcomes. Exhaled breath condensate (EBC) allows for the non-invasive collection of airway lining fluid containing biomarkers of oxidative stress like 8-isoprostane, a stable by-product of lipid peroxidation. Therefore, we sought to characterize the association between domestic airborne BC concentrations and 8-isoprostane in EBC.

Materials and methods: Seven- and eight-year-old children participated in an asthma case–control study in New York City. During home visits, air samples and EBC were collected. Seven day averages of domestic levels of particulate matter <2.5 μm ($PM_{2.5}$), BC and environmental tobacco smoke (ETS) were measured. Urea and 8-isoprostane were measured by liquid chromatography tandem mass spectrometry (LC/MS/MS) in EBC.

Results: In univariate models, $PM_{2.5}$ and BC, but not ETS, were significantly associated with increases in 8-isoprostane in the EBC ($\beta=0.006$ and $\beta=0.106$ respectively, $p<0.05$ for both). These associations remained statistically significant for both $PM_{2.5}$ and BC after adjustment for covariates. In a co-pollutant model including $PM_{2.5}$, BC and ETS, only BC remained a statistically significant predictor of 8-isoprostane ($p<0.05$).

Conclusions: Our findings suggest the BC fraction of PM might contain exposure relevant to increased oxidative stress in the airways.

1. Introduction

Exposure to airborne particulate matter (PM), diesel exhaust particles (DEP) and combustion by-products has been implicated in asthma development and morbidity (Clark et al., 2010; Jung et al., 2012). Early life exposure to traffic-related air pollutants and living in proximity to point sources that contribute to airborne PM have been associated with elevated risk of asthma in young children (Clark et al., 2010). Proximity to roadway has been associated with increased asthma prevalence and report of wheeze in children living in southern California (McConnell et al., 2006). Indoor levels of PM were found to be associated with development of wheeze at ages 5–7 years in an inner-city cohort in New York City (NYC) (Jung et al., 2012). However the effect of these exposures on underlying biological processes in the airways that may lead to these outcomes has not been completely elucidated.

Recently, black carbon (BC) has been proposed as a more suitable surrogate for DEP exposure than PM, given its association with the volume of diesel traffic and not car traffic (Cornell et al., 2012; Lena et al., 2002). DEP are thought to be responsible for a

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*Correspondence to: Department of Preventive Medicine, Icahn School of Medicine at Mount Sinai, One Gustave L. Levy Place, Box 1057, New York, NY 10029, United States. Fax: +1 212 996 0407.
E-mail addresses: maria.rosa@mssm.edu (M.J. Rosa), yanbz@ldeo.columbia.edu (B. Yan), chilli@ldeo.columbia.edu (S.N. Chillrud), la181@columbia.edu (L.M. Acosta), ad708@columbia.edu (A. Divjan), jsj4@columbia.edu (J.S. Jacobson), rlm14@columbia.edu (R.L. Miller), ifg2@columbia.edu (I.F. Goldstein), mp2217@columbia.edu (M.S. Perzanowski).

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large portion of the detrimental effects of traffic-associated PM (Sydbom et al., 2001). Truck route density was also a strong predictor of wintertime BC and domestic level BC in two different studies (Clougherty et al., 2013; Cornell et al., 2012). In addition, burning of residual fuel oil, used extensively in apartment and commercial heating in NYC, is a significant source of airborne BC (Clougherty et al., 2013; Cornell et al., 2012). Previous epidemiological studies have found associations between BC exposure and adverse respiratory outcomes. In a birth cohort in British Columbia, central site levels of BC, but not $PM_{2.5}$, early in life were associated with increased risk of childhood asthma diagnosis (Clark et al., 2010). Local BC levels estimated through a spatio-temporal land-use regression model were associated with decrements in lung function measures in women living in East Boston (Suglia et al., 2008). In NYC adolescents, increases in school levels of BC were associated with acute respiratory symptoms, including increased wheeze, chest tightness and shortness of breath (Patel et al., 2010).

Despite growing evidence linking BC exposure and respiratory illness, the mechanism through which BC may lead to these adverse respiratory effects has not been completely elucidated. One of the potential mechanisms is oxidative stress. 8-isoprostane, which belongs to the family of F2-isoprostanes and is a by-product of the free radical-catalyzed peroxidation of arachidonic acid, can be measured in exhaled breath condensate (EBC). It has been used as a surrogate marker of oxidative stress in multiple studies, and found to be elevated in the presence of asthma, cystic fibrosis and chronic obstructive pulmonary disease (Baraldi et al., 2003; Montuschi et al., 2000a, 1999, 2000b). Exposure to combustion fly ash particles, as a model for particulate matter exposure, also has been shown to induce generation of reactive oxygen species (ROS) in lung murine and primary human macrophages (Fritsch-Decker et al., 2011). In this particular study, murine macrophages that were incubated with a low dose of fly ash particles had a time dependent increase in 8-isoprostane concentrations (Fritsch-Decker et al., 2011).

The measurement of 8-isoprostane in the airways also can aid in the study of airborne exposures. Recently, researchers in China found positive associations between central site levels of $PM_{2.5}$ and 8-isoprostane, measured in EBC collected from healthy young adults (Huang et al., 2012). In another recent study, 1–5 day averages of BC measured at NYC high schools were associated with increased levels of 8-isoprostane measured in EBC in adolescents enrolled at the schools (Patel et al., 2013). Spatial variability and temporality have been shown to be significant predictors of BC concentrations in NYC, stressing the importance of understanding local exposure patterns (Clougherty et al., 2013). Therefore, we sought to characterize the association between short-term domestic measures of BC, and additionally $PM_{2.5}$ and environmental tobacco smoke (ETS), another known pollutant associated with oxidative stress (Kostikas et al., 2013; Noakes et al., 2007) and 8-isoprostane measured in EBC as a surrogate marker of oxidative stress in a cohort of children living in NYC. We hypothesized that increased levels of all three of these measures of pollutant exposure would be associated with increased levels of 8-isoprostane in EBC.

2. Materials and methods

2.1. Study cohort

Participants ($N=350$) were enrolled in the New York City Neighborhood Asthma and Allergy Study (NYC NAAS) and enrollment has been previously described (Olmedo et al., 2011). In brief, the NYC NAAS is a case–control asthma study of 7–8 years old children living in NYC whose parents were recruited through the Health Insurance Plan of New York (HIP), a middle-income insurance provider. Neighborhoods were selected based on zip code level asthma prevalence among 5-year-old children as reported by the NYC Department of Health and Mental Hygiene (2003). Neighborhoods in the Bronx, Brooklyn, Queens and Manhattan with asthma prevalence of 3–9% were defined as lower asthma prevalence neighborhoods (LAPN) and those with asthma prevalence of 11–18% as higher asthma prevalence neighborhoods (HAPN). Cases were defined based on parental report of symptoms, including responses to the International Study of Asthma and Allergy in Childhood (ISAAC) wheeze module. Children were classified based on whether the parent reported at least one of the following for the child in the 12 months prior to administration of the questionnaire: 1) wheeze, 2) being woken at night by cough without having a cold, 3) wheeze with exercise or 4) report of asthma medication use. Children who did not meet any of these criteria were classified as controls. Demographic characteristics were obtained through questionnaires administered during home visits. Columbia University Institutional Review Board procedures for consent and assent were followed.

2.2. Domestic pollutant assessment

$PM_{2.5}$ was collected by sampling air in the child's home at 1.5 L/min for 7 days. BC and ETS were quantified on the filter using a recently validated multi-wavelength optical absorption technique developed for Teflon filters utilizing a modified Lawless method (Yan et al., 2011). The optical device used consisted of a balanced deuterium tungsten halogen light source (DH-2000-BAL), an integrating sphere (ISP-50-8-R), a lab-made filter holder, and an Ocean Optics USB4000-VIS-NIR miniature fiber-optic spectrometer. Children's home addresses were geocoded and linked to a previously described GIS database (Lovasi et al., 2009). The density of buildings burning residual oil and the truck route density in a 500-m Euclidean radius were examined as potential predictors due to a previously seen association between these two variables and domestic BC levels (Cornell et al., 2012). In order to examine neighborhood level exposures, annual averages of $PM_{2.5}$ and elemental carbon (EC), which is representative of the same carbonaceous fraction as BC and are considered comparable, were obtained from the NYC Community Air Survey for 2009 and assigned to each participant based on their United Hospital Fund (UHF) ID.

2.3. Exhaled breath condensate collection and analysis

EBC was collected using the R-tube system (Respiratory Research Inc., Charlottesville, VA) during the home visit *before* the start of the 7 days air monitoring session due to logistical issues. Exhaled breath is condensed as it passes through a collection chamber within a cold (-20 °C) aluminum sleeve. Children were seated and instructed to form a complete seal around the mouthpiece and breathe at a normal rate for 10 min. The breath condensate was aliquoted and stored at -80 °C until analyses. The measurement of biomarkers in EBC stems from the idea that airway lining fluid droplets become aerosolized during exhalation (Kharitonov and Barnes, 2002). However, there is extreme and variable dilution of droplets from airway lining fluid (Effros et al., 2003). Urea, which exists under homeostatic regulation in the body, has been previously used as a marker of dilution in EBC (Effros et al., 2003). Urea and 8-isoprostane were measured in 150 randomly chosen EBC samples by liquid chromatography tandem mass spectrometry (LC/MS/MS) using a Thermo Finnigan TSQ Quantum system (Thermo Fisher Scientific, Waltham, MA) at the Lamont-Doherty Earth Institute. Due to a transient problem with the assay, 8-isoprostane levels could not be measured in one batch of 14 samples. Because there was not enough EBC volume in storage, these samples could not be assayed again and were excluded from analyses. Of these 14 samples, 6 (42.9%) were from participants classified as controls while the remaining 8 (57.1%) were from participants classified as cases.

2.4. Statistical analyses

Complete data was available for 130 participants. Data were analyzed using generalized estimating equations models with an exchangeable correlation matrix and a robust estimator covariance structure (SPSS 18, Chicago, IL). Children were matched by UHF ID to account for spatial correlation within neighborhoods. All three pollutants were analyzed as continuous predictors and were not logarithmically transformed in order to make the estimates more easily interpretable. 8-isoprotane and urea concentrations were natural log transformed; therefore the association between the pollutants and biomarkers is interpreted as a percent change. Potential covariates were included in the model if their presence produced a greater than 10% change in beta. Final models were adjusted for case control status, sex, African American race, heating season (defined as October 1st–April 30th) and urea concentrations. BC, $PM_{2.5}$ and ETS were analyzed both as separate predictors of 8-isoprostane and in a co-pollutant model.