International Journal of Hygiene and Environmental Health 219 (2016) 566–572

Contents lists available at ScienceDirect

International Journal of Hygiene and Environmental Health

journal homepage: www.elsevier.com/locate/ijheh

Short-term associations between particle oxidative potential and daily mortality and hospital admissions in London

Richard W. Atkinson[a,*], Evangelia Samoli[b], Antonis Analitis[b], Gary W. Fuller[c], David C. Green[c], H. Ross Anderson[a,c], Esme Purdie[c], Chrissi Dunster[c], Layla Aitlhadj[c], Frank J. Kelly[c], Ian S. Mudway[c]

[a] Population Health Research Institute and MRC-PHE Centre for Environment and Health, St George's, University of London, Cranmer Terrace, London SW17 0RE, UK
[b] Department of Hygiene, Epidemiology and Medical Statistics, Medical school, University of Athens, 75 Mikras Asias Str, 115 27 Athens, Greece
[c] MRC-PHE Centre for Environment and Health, King's College London, London, UK

ARTICLE INFO

Article history:
Received 9 March 2016
Received in revised form 3 June 2016
Accepted 3 June 2016

Keywords:
Oxidative potential
Particles
Mortality
Hospital admissions
Time series
Environmental epidemiology

ABSTRACT

Background: Particulate matter (PM) from traffic and other sources has been associated with adverse health effects. One unifying theory is that PM, whatever its source, acts on the human body via its capacity to cause damaging oxidation reactions related to its content of pro-oxidants components. Few epidemiological studies have investigated particle oxidative potential (OP) and health. We conducted a time series analysis to assess associations between daily particle OP measures and numbers of deaths and hospital admissions for cardiovascular and respiratory diseases.

Methods: During 2011 and 2012 particles with an aerodynamic diameter less than 2.5 and 10 μm ($PM_{2.5}$ and PM_{10} respectively) were collected daily on Partisol filters located at an urban background monitoring station in Central London. Particulate OP was assessed based on the capacity of the particles to oxidize ascorbate (OP^{AA}) and glutathione (OP^{GSH}) from a simple chemical model reflecting the antioxidant composition of human respiratory tract lining fluid. Particulate OP, expressed as % loss of antioxidant per μg of PM, was then multiplied by the daily concentrations of PM to derive the daily OP of PM mass concentrations (% loss per m^3). Daily numbers of deaths and age- and cause-specific hospital admissions in London were obtained from national registries. Poisson regression accounting for seasonality and meteorology was used to estimate the percentage change in risk of death or admission associated with an interquartile increment in particle OP.

Results: We found little evidence for adverse associations between OP^{AA} and OP^{GSH} and mortality. Associations with cardiovascular admissions were generally positive in younger adults and negative in older adults with confidence intervals including 0%. For respiratory admissions there was a trend, from positive to negative associations, with increasing age although confidence intervals generally included 0%.

Conclusions: Our study, the first to analyse daily particle OP measures and mortality and admissions in a large population over two years, found little evidence to support the hypothesis that short-term exposure to particle OP is associated with adverse health effects. Further studies with improved exposure assessment and longer time series are required to confirm or reject the role of particle OP in triggering exacerbations of disease.

1. Introduction

Recent comprehensive reviews have concluded that there is sufficient epidemiological, toxicological and mechanistic evidence to link ambient outdoor concentrations of particulate matter (PM) with adverse effects on human health (EPA, 2009; WHO, 2013). Epidemiological time series studies have provided the evidence for associations in urban populations between daily mass concentrations of particles with a median diameter less than 2.5 μm ($PM_{2.5}$) and increased numbers of deaths and hospital admissions from a range of cardiovascular and respiratory diseases within a few days (Atkinson et al., 2014). However, better understanding of the most harmful components, and sources, of the particulate pollution is required in order to better inform policies to protect public health.

* Corresponding author.
E-mail address: atkinson@sgul.ac.uk (R.W. Atkinson).

http://dx.doi.org/10.1016/j.ijheh.2016.06.004

To date, particle characteristics such as size and number, primary *vs.* secondary origin and elemental composition have all been investigated (Atkinson et al., 2015; EPA, 2011; Janssen et al., 2011; Levy et al., 2012; Ruckerl et al., 2011).

Exposure to PM from traffic or other sources is associated with a range of human responses including neutrophilic inflammation, reduced inspiratory capacity, heightened bronchial reactivity, as well as changes in blood viscosity, fibrinogen, C-reactive protein and heart rate variability (HEI, 2010). One unifying theory is that particles elicit these responses by inducing oxidative stress via a range of mechanisms: (a) related to their content of pro-oxidants, such as metals and quinones (Ayres et al., 2008); (b) via the cellular metabolism of polyaromatic hydrocarbons (Baulig et al., 2004); (c) through the induction of acute inflammation, with activation of the phagocytic NADPH oxidase (Hamad et al., 2016); and (d) by depolarisation of the mitochondrial electron transport chain (Ferecatu et al., 2010; Xu et al., 2011). The oxidative potential (OP) of PM may therefore provide a useful, unifying metric for assessing the toxicity of particles in epidemiological studies (Ayres et al., 2008; Kelly and Fussell, 2015).

Because laboratory assessment of particle OP is time and resource intensive, the use of this metric in epidemiological time series studies has been limited to a small number of experimental and panel studies (Delfino et al., 2013; Steenhof et al., 2013; Strak et al., 2012) and a single case-crossover study of COPD/asthma hospital admissions (Canova et al., 2014). The latter found no evidence of an association with particle OP, but was limited to 161 admissions to a single London hospital. In contrast, a study of emergency department visits for asthma/wheezing and congestive heart failure in Atlanta found stronger associations with particle OP than particle mass ($PM_{2.5}$) (Bates et al., 2015). Two recent studies from Canada have estimated the OP of daily $PM_{2.5}$ using regional OP estimates derived from periodic sampling of PM filters and reported stronger associations between $PM_{2.5}$ concentrations and emergency room visits for myocardial infarction and respiratory disease on days with higher particle OP (Weichenthal et al., 2016b; Weichenthal et al., 2016c). A recent cohort study found that adjustment for regional glutathione-related, but not ascorbate dependent, oxidative potential was associated with an increased risk of death and that for lung cancer the association may be stronger than for $PM_{2.5}$ mass concentrations (Weichenthal et al., 2016a). To date, daily measures of particle OP have not been evaluated in a large urban conurbation in relation to daily mortality and admissions from cardiorespiratory diseases. Using laboratory analysis of samples obtained from daily particle measurements made at a monitoring station in Central London, U.K. we derived measures of ascorbate and glutathione-dependent OP for $PM_{2.5}$ and particles with an median diameter less than 10 μm (PM_{10}) and investigated associations with daily numbers of deaths and hospital admissions for cardiovascular and respiratory diseases.

2. Methods

2.1. Health data

Daily counts of deaths from all non-accidental causes (ICD-10 Chapters A-R), cardiovascular (ICD-10 Chapter I) and respiratory causes (ICD-10 Chapter J) for people resident and dying in London, England between January 2011 and December 2012 were constructed from death registrations obtained from the UK Office of National Statistics. For the same time period and using the same ICD-10 codes, daily counts of the numbers of emergency, first episode, hospital admissions for cardiovascular disease and for respiratory diseases stratified by age (0–14, 15–64 and 65+ years) were derived from records of individual admissions obtained from the English Hospital Episode Statistics system.

2.2. Particle oxidative potential measurement

The oxidative potential of particles (PM_{10} and $PM_{2.5}$) was determined by measuring the depletion of the anti-oxidants ascorbate and glutathione from a synthetic respiratory tract lining fluid (RTLF). The synthetic RTLF contains the major low-molecular weight sacrificial antioxidants commonly found on the surface of the lung, at physiologically relevant concentrations and allows analysis of different chemical mechanisms of oxidative damage that PM may inflict on airways. The underlying principle of this assay and the derivation of the OP metrics have been described in detail previously (Godri et al., 2010; Kelly et al., 2011). This method was adapted to perform the analysis on unextracted filters to accommodate the low filter loadings associated with 24 h collections at urban background locations which impact on PM recovery from the filter, but also to avoid potential artifacts being introduced through the extraction procedure.

PM was collected onto Teflon-coated glass fibre filters (Pallfex Emfab^{TM}) using Partisol 2025 samplers (Thermo) using PM_{10} or $PM_{2.5}$ size selective inlets during 2011–12 from the North Kensington background monitoring site (51.521055_ N, 0.213432_W) in Central London. From each filter, 3 × 8 mm discs were punched (Harris Unicore, USA) and transferred into three separate microtubes for analysis. The filter punches were then incubated for 4 h at pH 7.0, 37 °C, with continual mixing throughout, in synthetic RTLF, containing equimolar concentrations (200 μmol/L) of the antioxidants ascorbate, urate and glutathione. Particle free controls to quantify auto-oxidative losses of RTLF antioxidants, and in-house positive (NIST srm 1648a) and negative (M120–an inert carbon black (Cabot Corp., USA) (Zielinski et al., 1999)) control particles were also included to control for batch-to-batch variation. At the end of the incubation period samples were centrifuged for 1-h at 13,000 rpm (4 °C) to remove the filters and any disassociated PM and the supernatant quantified for the remaining concentrations of ascorbate by reverse-phase HPLC with electrochemical detection. The concentration of glutathione remaining in the RTLF at this time point was quantified using the DTNB-enzyme recycling assay. The derivation of the ascorbate and glutathione dependent oxidative potentials was based on the percentage loss of antioxidants relative to the particle free control concentrations at the 4-h time point, normalized for the concentration of PM on the filter punch, i.e. % antioxidant loss per μg. Filter masses were based on pre- and post-weighing following exposures in the field with the masses on the filter punches calculated based on the assumption of equal particle deposition across the filter area. Finally the ascorbate (OP^{AA}) and glutathione (OP^{GSH}) depletion expressed as % loss per μg of PM were multiplied by the ambient daily $PM_{2.5}$ or PM_{10} concentrations to provide daily OP metrics (% loss) expressed per m^3. Measurements for OP^{AA} and OP^{GSH} in PM_{10} and $PM_{2.5}$ were available for 703 and 685 days in the two year study period, the difference in numbers reflecting periods when the samplers were not operating due to technical issues.

2.3. Regulated pollutants and meteorological variables

Hourly average concentrations of PM_{10}, $PM_{2.5}$, nitrogen dioxide (NO_2), sulphur dioxide (SO_2) and ozone (O_3) recorded at the urban background monitoring station at North Kensington during the study period were obtained from the Automatic Urban Rural Network and averaged to give 24-h mean concentrations in μg/m^3 for all pollutants except O_3 for which the 8 h maximum average (WHO, 2006) was computed. The Tapered Element Oscillating Microbalance—Filter Dynamics Measurement System