Environmental Pollution 180 (2013) 246–250

Contents lists available at SciVerse ScienceDirect

Environmental Pollution

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

Health effects of daily airborne particle dose in children: Direct association between personal dose and respiratory health effects

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ARTICLE INFO

Article history:
Received 29 January 2013
Received in revised form
20 May 2013
Accepted 21 May 2013

Keywords:
Alveolar deposited particle surface area
Exhaled nitric oxide
Health respiratory effects
Personal monitoring
Spirometry
Ultrafine particles

ABSTRACT

Air pollution is a widespread health problem associated with respiratory symptoms. Continuous exposure monitoring was performed to estimate alveolar and tracheobronchial dose, measured as deposited surface area, for 103 children and to evaluate the long-term effects of exposure to airborne particles through spirometry, skin prick tests and measurement of exhaled nitric oxide (eNO). The mean daily alveolar deposited surface area dose received by children was 1.35×10^3 mm^2. The lowest and highest particle number concentrations were found during sleeping and eating time. A significant negative association was found between changes in pulmonary function tests and individual dose estimates. Significant differences were found for asthmatics, children with allergic rhinitis and sensitive to allergens compared to healthy subjects for eNO. Variation is a child's activity over time appeared to have a strong impact on respiratory outcomes, which indicates that personal monitoring is vital for assessing the expected health effects of exposure to particles.

1. Introduction

Air pollution is a widespread public health problem associated with several adverse health outcomes ranging from premature mortality to respiratory symptoms and impaired lung function (Kreyling et al., 2006; Pope and Dockery, 2006; Cesaroni et al., 2013). The adverse effects of air pollution on human cardiovascular and respiratory systems have been examined in some cohort studies (Dubnov et al., 2007; Gauderman et al., 2000; Pope et al., 2004; Samet et al., 2000). Both spirometric function and exhaled nitric oxide (eNO), a marker of airway inflammation, have been used as biomarkers of effects on the lower airway (Lee et al., 2011; Rosenlund et al., 2009; Lagorio et al., 2006; Smith et al., 2009; Saito et al., 2004; Steerenberg et al., 1999) and have been shown to be related to exposure to oxides of nitrogen (NO_x), particulate matter less than 2.5 μm in aerodynamic diameter ($PM_{2.5}$) and elemental carbon in a cohort of adolescents in southern California (Gauderman et al., 2004). In that cohort, the forced expiratory volume in one second (FEV_1) was 80 mL less in the city with the highest $PM_{2.5}$ concentration, compared with the city with the lowest $PM_{2.5}$ concentration.

The potential of particles to cause adverse respiratory and systemic health effects is related to their ability to enter the lungs, potentially carrying a number of toxic compounds with them. At present, it is not known which particle size, morphology or chemical components are most strongly related to the negative effects on human health and further research in this field is required. In terms of particle size, attention has shifted between mass (PM_{10} or $PM_{2.5}$), surface area (Giechaskiel et al., 2009; Buonanno et al., 2011a) and particle number concentrations (Franck et al., 2011), whose prevalent contribution is due to ultrafine particles (UFPs), with a diameter less than 100 nm. Recently, interest has focused on UFPs, due to their high deposition fraction, large surface area, chemical composition, potential to translocate to the circulation (Weichenthal, 2012) and their ability to induce inflammation, penetrate into cell membranes (Unfried et al., 2007) and deposit in secondary organs (Semmler et al., 2004), including brain tissue (Calderon-Garciduenas et al., 2004). These effects have received more attention in relation to children, because they inhale a higher dose of airborne particles relative to lung size when compared with adults (Buonanno et al., 2012; Burtscher and Schüepp, 2012) and have an increased breathing frequency compared to adults (Bateson and Schwartz, 2008), causing persistent alterations in distal airway architecture that are characterized by an initial decrease in airway cell proliferation (Lee et al., 2010).

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http://dx.doi.org/10.1016/j.envpol.2013.05.039

Nevertheless, the major difficulty facing epidemiological studies of UFPs is mostly related to the estimation of individual exposure levels. The most common current approach assumes that each person in a given region has the same exposure level, which is often obtained from a few air quality monitors and reflects the mean concentrations in the entire urban area or community. This approach could lead to significant errors in the estimation of individual exposure to air pollutants because the actual exposure is strongly related to the time–activity of the individuals (Buonanno et al., 2011b, 2012a, 2013b). Furthermore, the use of mean air pollution levels smoothes peak air pollution concentrations and thus, may result in unreliable estimates of exposure (Manigrasso et al., 2013). Furthermore, several authors have suggested that short term fluctuations in aerosol concentrations increase morbidity and mortality (Brugge et al., 2007; Strak et al., 2010).

An additional limitation of epidemiological studies is that most of them are focused on the exposure–response, and not on the dose–response relationship and, as a matter of fact, the dose–response relationship represents the main focus of toxicological studies (Sayes et al., 2007). Therefore, in order to compare personal particle dose to such a threshold, an accurate dose evaluation (approaching as much as possible the actual exposure) needs to be carried out. This is a crucial aspect, which can only be solved through personal sampling that is able to measure particle concentrations received by people in every microenvironment they visit during a typical day, and by estimating the corresponding doses.

The work reported in this paper was carried out as part of the international project titled "Ultrafine particle from traffic emission on children health (UPTECH)" (Queensland University of Technology, Brisbane, Australia), which aims to address the lack of epidemiological results on the effects of exposure to UFPs emitted by motor vehicles on children's health in schools (http://www.ilaqh.qut.edu.au/Misc/UPTECH%20Study%20Design.htm). The main aim of this paper is to focus on the individual dose–response relationship for children participating in the study. To this purpose, we estimated the daily dose of alveolar and tracheobronchial deposited surface area by measuring the daily exposure to particle number concentration for each child. A detailed study of each child's daily activity patterns was also conducted based on the Global Positioning Systems (GPS) and diaries carried by each child. In order to evaluate the children's respiratory function, pulmonary function (spirometry), skin prick and eNO tests were performed. As far as we are aware, this is the first time when a direct association between personal dose and respiratory health effects was determined.

2. Materials and methods

2.1. Study population

This study was approved by the Administrative Board of the University of Cassino and Southern Lazio. Written informed consent was obtained from the parents of each child prior to participation in the study. The study population consisted of 103 children, aged 8–11 years, attending schools in the area of Cassino (Central Italy). The children attended three naturally ventilated public schools and the investigations were carried out from December 2010 to December 2011. One rural and two urban schools were considered: a detailed description is reported in Buonanno et al., (2013a).

In addition to individual exposure measurements, a questionnaire was developed for Italian children, based on the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire, to record information on respiratory symptoms, as well as potential confounders and effect modifiers, such as housing conditions, socio-economic status and exposure to environmental tobacco smoke (http://www.ilaqh.qut.edu.au/Misc/UPTECH%20Questionnaire.htm). A time–activity diary was completed by each child, under the supervision of their parents, to record information on potential peak exposure at specific locations and we also asked parents to select the days that were most representative of their child's usual lifestyle. Details of the individual monitoring procedure are reported in Buonanno et al., (2013a).

2.2. Instrumentation and quality assurance

The mobile experimental apparatus comprised of three portable UFP counters (NanoTracer, Philips) equipped with GPS tracking. This device works by diffusion charging, using an electrometer that measures particle number concentration by means of the current induced by previously charged particles collected on a filter inside a Faraday cage (Marra et al., 2010). This instrument provides a measurement of total particle number concentration in the 10–300 nm range, as well as the corresponding number-averaged particle size. Furthermore, an assessment of the deposited particle surface area per unit volume of inhaled air in some regions of the respiratory tract (particularly in the tracheobronchial and alveolar regions) can be estimated on the basis of empirical models (Marra et al., 2010). Consequently, these UFP counters can be useful in monitoring studies because they are able to estimate the dose.

The counters were calibrated at the beginning of the experimental campaign, in order to allow for data quality assurance by comparison with: i) a Condensation Particle Counter (CPC, TSI Model 3775) to measure particle number concentration; ii) a Nanoparticle Surface Area Monitor (NSAM, TSI Model 3550) to assess the human lung-deposited surface area of particles corresponding to tracheobronchial (TB) and alveolar (A) regions of the lung; and iii) a Scanning Mobility Particle Sizer Spectrometer (SMPS, TSI Model 3936) to measure the mean diameter of the particle number size distributions.

Certified respiratory therapists performed spirometry, allergen skin prick tests and estimation of eNO in 75 children attending the three schools.

Spirometry was performed in accordance with the American Thoracic Society/European Respiratory Society guidelines (Miller et al., 2005), using a computerized spirometer (Medgraphics, Cardiorespiratory Diagnostics, St. Paul, Minnesota, USA). Forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), peak expiratory flow rate (PEF or FEF_{MAx}) and forced expiratory flow rate between 25% and 75% of FVC ($FEF_{25-75\%}$) were recorded. For each parameter, the highest of three measurements from acceptable maneuvers was recorded. Results were expressed as a percentage of European Community for Steel and Coal predicted values (Quanjer et al., 1983).

eNO was measured using a handheld electrochemical analyzer (NObreath®, Bedfont Scientific Ltd., Rochester, Kent, UK) that was recently evaluated Antus et al. (2010), according to the American Thoracic Society and European Respiratory Society (American Thoracic Society, 2005) guidelines. Children were asked to inhale ambient air to near total lung capacity and then exhaled for 10 s at a constant flow rate of 50 mL s^{-1} through a disposable mouthpiece into the device. All measurements were performed between 9:00 AM and 12:00 PM. Children did not eat or perform any strenuous physical activity during the 60 min prior to the tests being carried out. Three parallel readings were recorded in order to obtain measurements that were suitable for use in clinical practice (Antus et al., 2010).

Skin prick tests (SPTs) were performed by allergists to assess atopic status. The test was performed according to the standardized ISAAC II protocol (Weiland et al., 2004). The following allergens were tested: dermatophagoides farinae, dermatophagoides pteronyssinus, cladosporium cladosporioides, alternaria tenuis, penicillium mix, cat dander, dog dander, cypress pollen, mixed grasses, olive, lolium perenne, wall pellitory, plantaginaceae, and German cockroach (Stallergenes, Italy). Positive and negative control solutions were also tested. A drop of each solution was placed on the skin (forearm) and the skin beneath each drop was pricked with a needle. Wheal size was measured 20–30 min later as the mean of the largest diameter and its perpendicular. Wheal sizes for allergens that were $\geq$3 mm greater than the negative control were considered positive for that allergen. Children with one or more positive responses to these allergens were regarded as atopic.

2.3. Methodology description

In order to perform individual monitoring, each child kept the NanoTracer device for two days, carrying it with them in all of the microenvironments where he or she spent their time. The children were also asked to record their main activities, indicating the start and end times for each one. Based on these diaries, the corresponding average particle number concentration, diameter, and deposited alveolar and tracheobronchial surface area concentrations were calculated. The dose (in terms of deposited alveolar or tracheobronchial surface area, mm^2) received by each child in each microenvironment/activity was determined by multiplying the alveolar and tracheobronchial surface area concentration ($S_{a,tb}$) of inhaled particles by the time spent (T) in the jth microenvironment and the inhalation rate ($IR_{activity}$) corresponding to the activity carried out (Klepeis, 2006). Then, we summed the partial doses to estimate the daily total deposited alveolar and tracheobronchial surface area (dose), $\overline{S_{a,tb}}$, as reported in Eq. (1).

$$\overline{S_{a,tb}} = \sum_{j=1}^{n} \{IR_{activity} \cdot S_{a,tb} \cdot T\}_j \quad (1)$$

Inhalation rates ($IR_{activity}$) for the different activities were adopted from US EPA estimates (US EPA, 2004) that ranged from 0.3 $m^3\ h^{-1}$ during sleep and resting to 1.4 $m^3\ h^{-1}$ during sporting activities.