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Original article

A panel study of airborne particulate matter composition versus concentration: Potential for inflammatory response and impaired pulmonary function in children

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Abbreviations:
CI, confidence interval; ELISA, enzyme-linked immunosorbent assay; IL, interleukin; IQR, interquartile range; NO_2, nitrogen dioxide; PEF, peak expiratory flow; PM, particulate matter; PM_{10}, particulate matter smaller than 10 μm; $PM_{2.5}$, particulate matter smaller than 2.5 μm; SO_2, sulfur dioxide; SPM, suspended particle matter

ABSTRACT

Background: The relationship between airborne particulate matter (PM) and pulmonary function in children has not been consistent among studies, potentially owing to differences in the inflammatory response to PM, based on PM types and sources. The objective of this study was to investigate the effect of airborne PM on pulmonary function in schoolchildren and its potential for an inflammatory response.
Methods: Daily morning peak expiratory flow (PEF) was measured in 339 schoolchildren in February 2015. Interleukin (IL)-8 production was assessed in THP1 cells stimulated by airborne PM collected every day during the study period, and these IL-8 concentrations are described as the daily IL-8 levels. A linear mixed model was used to estimate the association between PEF values and the daily levels of suspended PM (SPM), PM diameters smaller than 2.5 μm ($PM_{2.5}$), and IL-8.
Results: The daily IL-8 levels were significantly associated with those of SPM and $PM_{2.5}$. A 0.83 μg/mL increase in IL-8 levels was significantly associated with a −1.07 L/min (95% confidence interval, −2.05 to −0.08) decrease in PEF. A 12.0 $\mu g/m^3$ increase in SPM and a 10.0 $\mu g/m^3$ increase in $PM_{2.5}$ were associated with a −1.36 L/min (−2.93 to 0.22) and −1.72 L/min (−3.82 to 0.36) decreases in PEF, respectively. There were no significant relationships between PEF, SPM, and $PM_{2.5}$.
Conclusions: These findings suggest that the effects of airborne PM on pulmonary function in schoolchildren might depend more on the pro-inflammatory response than the mass concentration of the PM.

Introduction

Although numerous epidemiological studies have documented significant associations between airborne particulate matter (PM) and pulmonary function,[1–3] not all studies have found a relationship.[4–6] In particular, a European multicenter study was unable to consistently detect an association between airborne PM and pulmonary function, despite the wide range of climatic conditions and pollutant mixes encountered across the sites.[6] Thus, the effects of PM on pulmonary function and respiratory symptoms are not the same across studies.

Airborne PM is usually categorized based on particle size, as PM_{10} or $PM_{2.5}$, which represents median aerodynamic diameters of smaller than 10 μm or 2.5 μm, respectively.[7,8] Although PM is a mixture of solids and liquid droplets that form from various substances and float in the air,[9] previous studies have primarily focused on mass concentrations of PM_{10} or $PM_{2.5}$ to estimate the

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relationship between airborne PM and pulmonary function. However, various components of PM can influence the subsequent pro-inflammatory cytokine response,[10] and the inflammatory potential of PM is heterogeneous regarding city and season.[11–14] The discordant results between studies investigating the association between airborne PM and pulmonary function might be attributable to the disparity of inflammatory responses to different compositions of PM.

Exposure to airborne PM increases the interleukin (IL)-8 concentration in bronchial lavage fluid and elevates IL-8 mRNA expression in bronchial biopsy tissue in healthy and asthmatic subjects.[15] Additionally, IL-8 is one of the most important neutrophil chemotaxins present within the lower respiratory tract.[16] Neutrophils mainly migrate to the lungs in patients with asthma during the acute inflammatory phase after exposure to PM.[17] Patients with asthma experienced an asymptomatic reduction in pulmonary function and an inflammatory response after walking along an urban road for only 2 h in a previous study, suggesting an increase in the number of neutrophils in the airway.[18] Therefore, exposure to airborne PM may augment neutrophilic airway inflammation depending on IL-8 production.

Nevertheless, for the association between airborne PM and health, including respiratory disorders, the quantity of PM is the most important factor. However, the effects of airborne PM on pulmonary function may be related to the production of pro-inflammatory cytokines, especially IL-8, depending on the PM types and sources. This study aimed to investigate the association between pulmonary function in schoolchildren and the daily levels of IL-8 production in the presence of PM.

Methods

Study design

In this panel study, the peak expiratory flow (PEF) of schoolchildren was monitored daily in the morning in February 2015 in Matsue, the capital city of Shimane Prefecture, southwest Japan. This city has a population of approximately 200,000 and covers an area of 530.2 km^2. Students aged 10–12 years in four of the 35 elementary schools in Matsue City in 2015 were enrolled. These four elementary schools were within 10 km of each other, and all subjects lived within a 1-km radius from the schools. All children went to school on foot and were potentially exposed to air pollutants.

Sex, height, weight, and the presence of asthma, allergic rhinitis, allergic conjunctivitis, atopic dermatitis, and food allergies were recorded in February 2015. Because the influence of airborne PM exposure on pulmonary function may differ depending on the presence of allergic diseases, asthma and allergic diseases were collected. The subjects were considered to have asthma if they met any of the following criteria in the previous 12 months: diagnosis of asthma by a pediatrician, presence of wheezing, use of asthma medication, or a visit to a hospital for asthma. The subjects were considered to have allergic rhinitis, allergic conjunctivitis, atopic dermatitis, and/or food allergy if they met any of the following criteria in the previous 12 months: diagnosis of any of these conditions by a pediatrician, use of medication for any of these conditions, or a visit to a hospital for any of these conditions. The study was approved by the institutional ethics committee (Ethics Committee of the Faculty of Medicine, Tottori University, Approval Number 2473), the Matsue City Board of Education, and the Parent Teacher Association of each elementary school. The children and their parents were informed of the study by the teachers and provided written consent.

Recording of daily morning peak expiratory flow

The children and teachers were taught how to measure PEF before study initiation. From February 2, 2015 to February 27, 2015, all children measured their PEF daily in the morning using a peak flow meter (Mini-Wright, Harlow, England, American Thoracic Society scale). The children recorded their best PEF value from three attempts between 8 AM and 9 AM.

Measurement of air pollutant levels

Suspended PM (SPM) is defined under the National Air Quality Standard as any particle with a diameter <10 μm with a 100% cut-off.[19] In Japan, the Japanese Ministry of the Environment monitors SPM levels instead of PM_{10}. The concentrations of SPM, $PM_{2.5}$, sulfur dioxide (SO_2), nitrogen dioxide (NO_2), and ozone in Matsue City were obtained from the Japanese Ministry of the Environment, which monitors these values. Meteorological variables such as daily temperature, humidity, and atmospheric pressure were obtained from the Japan Meteorological Agency. These data were used to examine the associations between changes in PEF and air pollutant levels. Daily average levels of air pollutants (SPM, $PM_{2.5}$, SO_2, NO_2, and ozone) were calculated from 6 AM of one day to 5 AM of the next day.

Preparation of airborne particles and endotoxin concentrations

In one of the four schools, airborne PM was collected from February 1, 2015, to February 28, 2015, on a 20 × 25-cm quartz filter (2500QAT-UP; Tokyo Dylec, Tokyo, Japan) at a flow rate of 1000 L/min by using a high-volume air sampler (HV-1000R; Shibata, Tokyo, Japan) for 24 h from 6 AM to 6 AM the following day. Before sampling, to remove endotoxins from the filters, the filters were sterilized using dry heat at 240 °C for 30 min. To extract the collected PM from the filter, 40 mL endotoxin-free distilled deionized water (Sterile water endotoxin free; Wako Pure Chemicals, Osaka, Japan) was used with an ultrasonic apparatus (BRANSONIC2800; Emerson Japan, Atsugi, Japan) for 60 min.[20] The extraction liquids were filtered through 10 μm filters (pluriStrainer 10 μm; pluriSelect, Leipzig, Germany) to remove PM >10 μm in diameter. PM <10 μm in diameter in the dissolving solution was sterilized at 121 °C for 30 min in an autoclave (Tomy SX-300; Tomy, Tokyo, Japan) and stored in a freezer at −70 °C to prevent growth of bacteria and fungi. The concentrations of endotoxin in these extraction liquids collected between February 1, 2015 and February 28, 2015 were calculated with the Limulus color KY test (Wako Pure Chemicals) according to the manufacturer's protocols with endotoxin-free 96-well plates (Toxipet plateLP; Seikagaku, Tokyo, Japan). Samples were run in triplicate and read using an automated ELISA reader (Model 680, Bio-Rad, Philadelphia, USA). The concentrations of endotoxin are described as daily endotoxin levels.

Cell culture and measurement of IL-8 production

THP1 (ATCC® TIB-202™) human monocyte cell lines were cultured in Roswell Park Memorial Institute medium 1640 containing 10% (v/v) fetal bovine serum, 0.05 mM 2-mercaptoethanol, 100 U/mL penicillin, 100 μg/mL streptomycin, and 0.5 μg/mL amphotericin B at 37 °C and 5% CO_2 and in a humidified cell culture incubator. IL-8 release stimulated by collected PM liquid was calculated using the calculations in previous studies.[10,21,22] THP1 cells (1×10^5 cells/450 μL/tube) in an endotoxin-free tube (pirotube; Seikagaku, Tokyo, Japan) were exposed for 24 h at 37 °C with solvent only (negative control) or 50 μL of each PM <10 μm dissolving solution collected between February 1, 2015 and February