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Hourly differences in air pollution on the risk of asthma exacerbation

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ABSTRACT

We investigated the association between hourly differences in air pollution and asthma exacerbation in Korea using asthma-related emergency department data and verified seasonality and demographic modifiers with an hourly temporal resolution. We applied time-stratified case-crossover adjusted for weather and influenza; the lag was stratified as 1–6, 7–12, 13–18, 19–24, 25–48, and49–72 h. Odds ratios (95% confidence interval) per interquartile range increase were 1.05 (1.00–1.11) after 1–6 h for $PM_{10-2.5}$ and 1.10 (1.04–1.16) after 19–24 h for O_3. Effect size was 1.14 (1.06–1.22) at a 1–6 h lag in spring for $PM_{10-2.5}$, and 1.25 (1.03–1.51) at a 25–48 h lag in winter for O_3. O_3 effects were age- and low socio-economic status-modified at a 7–12 h lag [1.25 (1.04–1.51)]. Increased $PM_{10-2.5}$ and O_3 increased the risk of asthma exacerbation; the effect of $PM_{10-2.5}$ was most immediate.

1. Introduction

Several studies have suggested a complex etiological pathway for asthma (Reed, 2006; Clougherty et al., 2007; Su et al., 2013). Air pollution is one of environmental factors that may be involved in the pathogenesis of the disease, but the health effects of pollutants seem to vary according to time-dependent variations in the concentration, particle size, and nature of the pollutants (Feo Brito et al., 2007; Mohr et al., 2008).

Among several air pollutants, the concentration of ozone (O_3) varies widely during the day because O_3 is formed via photochemical reactions and strong sunlight accelerates this reaction. Thus, the concentration of O_3 tends to be high during the day and in spring or summer. However, the seasonal health effects of O_3 are not clearly understood, as some studies have in fact suggested that the effects of O_3 are greater in cold weather than in hot weather (Wong et al., 1999; Linn et al., 2000; Pattenden et al., 2010), while other studies have demonstrated synergistic effect of high temperature and O_3 levels in summer months (Pattenden et al., 2010).

The presence of particulate matter (PM) in the air is an important consideration, particularly the source and the fraction size. Particles of aerodynamic diameter <10 μm (PM_{10}), 2.5–10 μm ($PM_{10-2.5}$), or <2.5 μm ($PM_{2.5}$) arise from different sources and have different health effects. For instance, in Seoul, Korea, $PM_{2.5}$ levels were influenced by both local urban activities and region-scale transport, and the 3 major contributors of $PM_{2.5}$ were secondary nitrate, secondary sulfate and gasoline-fueled vehicles (Heo et al., 2009).

To date, most studies have investigated the association between air pollutants and their health effects on a daily timescale, but rarely at a finer temporal resolution. For instance, a large multicenter study that analyzed the association between daily and 3-h average concentrations of air pollutants and emergency department (ED) visits for cardiac and respiratory conditions suggested that increases in levels of PM_{10} and $PM_{2.5}$ were associated with a nearly 3- and over 4-fold higher frequency, respectively, of asthma-related ED visits during the warm season than the whole year (Stieb et al., 2009). Of the different air pollutants tested in that study, O_3 showed a consistent association with ED visits for respiratory conditions.

The present study was designed to quantify the effect of increases in the levels of two air pollutants, PM of various fraction sizes (PM_{10}, $PM_{10-2.5}$, $PM_{2.5}$), and O_3, on asthma exacerbations in a short timescale. Asthma-related ED visits were chosen as the outcome measure to assess asthma exacerbations, and hourly data on air pollutant ambient concentrations were collected. We also

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analyzed the effect of seasons and demographic characteristics on the association between air pollutant levels and asthma exacerbations after adjusting for meteorological variables.

2. Methods

2.1. Study population

This study was conducted between January 1, 2008, and December 31, 2011 in Seoul, South Korea, and was approved by the Institutional Review Board of Seoul National University, School of Public Health (IRB No. 64-2013-12-04).

ED visit data were obtained from the National Emergency Department Information System (NEDIS) of the National Emergency Medical Center. NEDIS has access to 137 hospitals in 7 metropolitan cities from 9 provinces in Korea, of which 31 hospitals are in Seoul. We analyzed data from 29 hospitals in Seoul.

ED visit data were coded and classified according to the discharge diagnosis for asthma using International Classification of Disease 10th Revision (ICD-10, asthma, J45). Patients of all ages and either gender were enrolled during the study period. The hospital address was used as a proxy for patient address. For each ED visit, the following data were collected from the NEDIS: time and date of onset of the asthma attack, ED discharge diagnosis, gender, age, and the socio-economic status (SES). The SES was inferred from the type of medical coverage of each patient. Patients with national health insurance were considered to be from high SES, and those with state medical aid to be from low SES. Only the ED visits recorded within 12 h between the onset of asthma symptoms (patient-reported time) and the registered time of arrival at the ED were enrolled.

2.2. Measurement of particulate matter in the air

Data on the hourly average concentrations for PM_{10} ($\mu g/m^3$), O_3 (parts per billion [ppb]), and NO_2 (ppb) were collected from the National Institute of Environmental Research. PM_{10} concentrations $>200\ \mu g/m^3$ were excluded from the analysis because extremely high levels were considered a result of the occurrence of Asian dust (Hashizume et al., 2010). Data on the hourly concentrations of $PM_{2.5}$ were obtained from the Research Institute of Public Health and Environment of the Seoul metropolitan government. The data for $PM_{10-2.5}$ were calculated by subtracting concentration values for $PM_{2.5}$ from those of $PM_{10.}$ However, data on the hourly measurements of $PM_{2.5}$ were available only for 2010; and hence, $PM_{10-2.5}$ data could be inferred only for this year. The mean and interquartile range (IQR) concentrations were determined for each air pollutant for the entire study period and for different time strata such as seasons, or as required for the analysis. The durations of the four seasons were defined as, March–May for spring, June–August for summer, September–November for fall, and December–February for winter.

The delayed time (h) between the hour at which there was an IQR increase in the concentration of an air pollutant ($\mu g/m^3$) and the onset of asthma exacerbation (patient-reported) was called the lag, which was stratified in time blocks as 1–6 h, 7–12 h, 13–18 h, 19–24 h, 25–48 h, and 49–72 h (17) and used moving average lag structures defined as a multi-time average of exposures.

2.3. Confounding variables

Weather data, including hourly mean temperatures (°C), relative humidity (%), and air pressure (hPa) were obtained from the Korean Meteorological Administration and recorded as averages for 1–24 h for a single day. A given day's rain was expressed as a binary variable, and days with precipitation >0 mm were identified as rainy days. The weekly influenza patient proportion was calculated as the number of influenza-related clinic visits divided by the total number of clinic visits, on the basis of data obtained from the Korean Centers for Diseases Control and Prevention.

2.4. Sensitivity analyses

Several sensitive analyses were performed to check the robustness of our main findings. First, the time window allowed between the onset of asthma exacerbation and the arrival at ED was chosen after exploring windows of 6 h, 12 h, and 24 h. All 3 time windows showed comparable consistency for effect size and lag effect of the different pollutants. The window of 12 h was considered reasonable to account for a patient to become aware of the symptoms and access the ED, both of which may get delayed if the exacerbations occurred at late night or very early morning.

Secondly, the effect of the pollutants on ED visits was assessed using single pollutant and multi-pollutant models to confirm agreement between the 2 models. In the multi-pollutant model, the effects of $PM_{10,}$ $PM_{10-2.5}$, and $PM_{2.5}$ were analyzed independently after adjusting for levels of O_3 and NO_2, and the effect of O_3 was estimated after adjusting for concentrations of PM_{10} and NO_2. The effect size and lag effect of PM_{10}, $PM_{10-2.5}$, $PM_{2.5}$, and O_3 were checked for consistency between the single and multi-pollutant models.

Lastly, the effect size (the change in the number of asthma-related ED visits corresponding to an IQR increase in the level of an air pollutant) was assessed by each air pollutant, first on an hourly average basis, and then compared with the effect size if the air pollutant concentration values were averaged over fixed delayed time (lag) defined as, 1–6 h, 7–12 h, 13–18 h, 19–24 h, 25–48 h, and49–72 h. These moving averages were considered reasonable to summarize the data and are presented.

2.5. Statistical analysis

Descriptive analyses were used to assess the distribution of age, gender, SES, and temporal characteristics of the visit (i.e., season, duration between symptom onset and ED visit. Air pollutant concentrations and all the meteorological variables were treated as continuous variables and controlled for in the models, except for rain, which was treated as a binary variable.

We applied case crossover analysis with fixed time strata of the calendar month and year in which the asthma exacerbation occurred. The day on which asthma exacerbation occurred was considered the case day, and all other instances of the same day of the week as the case day were considered control days. Exposure and confounder data for the hour of the onset of asthma exacerbation on the case day were compared with those at the same hour on control days (Bhaskaran et al., 2011). For instance, if the onset of asthma exacerbation occurred at 11:00 on the 10th of March, then the 10th of March was assigned to be a case day; a time window such as 1–6 h was set to be from 05:00 to 10:00 and the average concentrations of the pollutants during this time window was considered the exposure of the case day. For the control days (the 3rd, 17th, 24th, and 31st of March), the average concentrations during the same timeframe, 05:00 to 10:00, were set to be the exposure of the control days. The case-crossover study design automatically controlled for time-invariant individual level confounders, such as gender and age, and comparisons were made within individuals between case and control days by exposure levels. Conditional logistic regression was used to quantify the effect of air pollutants on asthma exacerbations using ED visit data to evaluate effect modification by confounders.

The effects of an IQR increase in the pollutant concentration were investigated in terms of moving averages in the 6 lag periods