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Acute effects of air pollution on pediatric asthma exacerbation: Evidence of association and effect modification

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ABSTRACT

We investigated the short-term effects of particulate matter with aerodynamic diameter $<10\,\mu g/m^3$ (PM_{10}), sulfur dioxide (SO_2), nitrogen dioxide (NO_2) and ozone (O_3) on pediatric asthma emergency admissions in Athens, Greece over the period 2001–2004. We explored effect modification patterns by season, sex, age and by the presence of desert dust transported mainly from the Sahara area.

We used daily time-series data provided by the children's hospitals and the fixed monitoring stations. The associations were investigated using Poisson regression models controlling for seasonality, weather, influenza episodes, day of the week and holiday effects.

A $10\,\mu g/m^3$ increase in PM_{10} was associated with a 2.54% increase (95% confidence interval (CI): 0.06%, 5.08%) in the number of pediatric asthma hospital admissions, while the same increase in SO_2 was associated with a 5.98% (95% CI: 0.88%, 11.33%) increase. O_3 was associated with a statistically significant increase in asthma admissions among older children in the summer. Our findings provide limited evidence of an association between NO_2 exposure and asthma exacerbation. Statistically significant PM_{10} effects were higher during winter and during desert dust days, while SO_2 effects occurred mainly during spring.

Our study confirms previously reported PM_{10} effects on emergency hospital admissions for pediatric asthma and further provides evidence of stronger effects during desert dust days. We additionally report severe effects of SO_2, even at today's low concentration levels.

1. Introduction

Studies at current levels of pollutants suggest a causal role of pollutants on various adverse health outcomes (Anderson et al., 2004; Holgate et al., 1999; Katsouyanni et al., 2001; Samet et al., 2000). Recent epidemiological research focuses on the health effects of air pollution on potentially sensitive population subgroups such as children and the elderly in order to better understand the mechanisms of action and identify the most susceptible population groups for the protection and improvement of public health (Anderson et al., 2003; Hoek and Brunekreef, 1993; Peters et al., 1999). Potential determinants of children's susceptibility include the continuing process of lung growth and development, incomplete metabolic systems, immature host defences, high rates of infection with respiratory pathogens and activity patterns that increase exposure to air pollution and to volume of inhaled pollutants (Anderson et al., 2004; Holgate et al., 1999).

Epidemiological research on the health effects of air pollution on children has mainly focused on particles, which have been associated with upper and lower respiratory symptoms in children (Atkinson et al., 2001; Halonen et al., 2008; Sunyer et al., 2003; WHO, 2006). Though viral respiratory tract infections are reported as the major trigger for asthma exacerbations in children, an additive or synergistic effect with ambient air pollutants has been considered (Chauhan et al., 2003). Recently, there has been growing demand for more in-depth investigation of the effects of gaseous pollutants and of the possible factors modifying any observed effects.

Following these research lines we have investigated the acute effects of particulate matter with aerodynamic diameter $<10\,\mu$ (PM_{10}) and several gaseous pollutants, namely sulfur dioxide (SO_2), nitrogen dioxide (NO_2) and ozone (O_3), on emergency hospital admissions for asthma-related diagnosis among children aged 0–14 years in Athens, Greece. We explored possible modification patterns by season, sex and age. In addition, Athens, due

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to its metropolitan setting and geographical position, provides an opportune case for the investigation of the health effects of air pollution and windblown desert dust particles, which originate mainly from the Sahara area. Hence, we also investigated whether the presence of windblown Sahara dust modifies the association between PM_{10} and pediatric hospital admissions for asthma.

2. Material and methods

2.1. Data

We collected data on daily counts of pediatric asthma emergency admissions in the three main Children's Hospitals in Athens, covering approximately 85% of pediatric beds of the metropolitan area of Athens, from 2001 to 2004. All of the admissions were for at least one over-night stay. All children admitted with the diagnosis of ''asthma'' (International Classification of Disease (ICD)-9: 493), ''asthmatic bronchitis'' or ''wheezy bronchitis'' (ICD-9: 493.9), aged 0–14 years, living in the greater Athens area were included. Those admitted with the diagnosis of ''acute bronchiolitis'' (ICD-9: 466.1) were excluded (Priftis et al., 2007a). Hospital admissions were classified into two age groups: 0–4 and 5–14 years.

The Athens area forms a basin surrounded by mountains in the north, east and northwest and by the sea on the southwest side. The topography favors atmospheric inversion and the concentrations of the pollutants measured are relatively high. Traffic is the major source of air pollution in Athens European (European Environmental Agency, 2010). The population in the greater Athens area is around 3 million inhabitants, of whom about 400,000 are 0–14 years old (National Statistical Service of Greece, 2001). Daily air pollution measurements were provided by the monitoring network operated by the Ministry of Environment, Energy and Climate Change (Greek Ministry of Environment, 2010). We collected data on PM_{10} (daily average), SO_2 (daily average), NO_2 (1 h max) and O_3 (8 h). We calculated the average daily concentration of the pollutants from monitors that provided data for at least 75% of the days in the analyzed period, as proposed by the multi-city European APHEA project (Short-Term Effects of Air Pollution on Health: an European approach) (Katsouyanni et al., 2001). The number of selected monitoring sites ranged from five in the case of PM_{10} to 14 in the case of NO_2 measurements and covered the whole geographical area of greater Athens. Missing values in the station-specific time-series were replaced by a weighted average from the available stations (Katsouyanni et al., 2001). The final, averaged over stations, time-series of the pollutants were complete, except in the case of SO_2, for which six days (0.4%) with missing data remained. Time-series data on daily temperature (°C, daily mean) and humidity (%, daily mean) were used to control for the potential confounding effects of weather.

Desert dust events, the great majority of which originates from Sahara, generally occur about 30 days per year in Athens, mainly between spring and autumn (Kallos et al., 1997). We identified 110 dust days between 2001 and 2004, using back-trajectory analysis (to locate particles' transport) in combination with a data driven criterion, based on high particle concentrations provided by the fixed monitoring sites. Back trajectory analysis provides maps that indicate the past paths of particles using meteorological data (such as wind velocity and direction) and models. In particular, a certain day was identified as a suspected dust event if air mass transport occurred from Sahara or the Arabian Peninsula (identified through back-trajectories maps) and the rate of the PM_{10} concentration in the most remote fixed monitoring station to a centrally located one exceeded its year-specific median value. There were a few days ($n=44$) identified as suspected desert dust days due to dust transport from Sahara but because of missing measurements of PM_{10} in the remote station we could not uniquely identify these as certified desert dust days. In such cases, a suspected dust event was considered as such in the analysis only if the concentrations of PM_{10} from the available stations exceeded the station and year-specific 90th percentile and high aerosol optical depth values were observed over Athens from the Aqua-MODIS (2010) sensor (http://modis.gsfc.nasa.gov/). MODIS (or Moderate Resolution Imaging Spectroradiometer) is a key instrument aboard the Aqua (EOS PM) satellite that provides daily aerosol optical depth data, as a measure of radiation extinction due to the interaction of radiation with aerosol particles in the atmosphere, primarily due to the processes of scattering and absorption. Our final sample of dust events is in agreement with the expected number of such days from the area's topography (Kallos et al., 1997) and includes all such events that have received media attention and scientific investigation (Kaskaoutis et al., 2008).

2.2. Methods

The pollutant-hospital admissions associations, for each pollutant and subgroup analysis, were investigated using Poisson regression models allowing for over-dispersion, expressed as

$$\log E[Y_t] = \beta_0 + b*\text{Pollutant}_t + s(\text{time}_t, k) + s(\text{temp}_t, k) + s(\text{lag1}(\text{temp}_t), k) + [\text{others}]$$

where $E[Y_t]$ is the expected value of the Poisson distributed variable Y_t indicating the daily admissions count on day t with $\text{Var}(Y_t)=\varphi E[Y_t]$, φ being the over-dispersion parameter, temp_t is the value of mean temperature on day t, lag 1(temp_t) is its lagged effect and Pollutant_t is the pollutant's level on day t. The smooth function s captures the non-linear relationship between the time-varying covariates and calendar time and daily admissions. We used natural splines as smoothing functions. We also included a linear term for daily average humidity and dummy variables for the day of the week effect, public holidays and influenza epidemics. We used the APHEA-2 method for influenza control (Touloumi et al., 2004), including a dummy variable taking the value of one when the seven-day moving average of the respiratory mortality was greater than the 90th percentile of its distribution.

The smooth function of time serves as a proxy for any time-dependent outcome predictors or confounders with long-term trends and seasonal patterns not explicitly included in the model (Touloumi et al., 2004). Hence we removed long-term trends and seasonal patterns from the data to guard against confounding by omitted variables. We controlled for season and long-term trend with a natural cubic regression spline with 1.5 degrees of freedom (d.f.) for each season and year (corresponding to six d.f. per year). This amount of seasonality control has been previously suggested for the analysis of hospital admission data (Zanobetti et al., 2009) and eliminates confounding effects from seasonal and longer-term trends but retains shorter-term fluctuations, part of which may be causally associated with short-term fluctuations in the pollutants. We also included natural splines with three d.f. for temperature on the day of the admission and the day before the admission in the models. To account for non-removable serial correlation in the residuals, autoregressive terms were added into the model as appropriate (Brumback et al., 2000). The levels of the pollutant under investigation on the same day with the admission were included in the model.

To further examine whether the effects of air pollution on pediatric hospital admissions for asthma are spread over several days, we also fitted a separate distributed lag model including the levels of the pollutant on the same day and up to two days before the admission. Our limited choice of lags was based on the medical assumption that an asthmatic response to an environmental agent would be expected to be acute and not extend over several days.

Although the main model choice was based on previous extensive methodological work regarding time-series analysis of the air pollution health effects (Katsouyanni et al., 2009; Samoli et al., 2008) we fitted several models to test the robustness of our findings. Hence, we also applied models with varying degree of seasonality control (using eight or four d.f. per year instead of six) and with more seasonal control during summer holidays (by including an extra term for August). We also tested the sensitivity of the distributed lag models by including a linear term for temperature two days before the event (lag 2), in order to have as many lags for the latter as for the pollutant included in the model.

To investigate potential confounding effects between pollutants, we applied two-pollutant models. Moreover, in order to investigate possible effect modification by season (winter: December through February; spring: March through May; summer: June through July; autumn: September through November), sex and age group we performed separate analysis stratified by these potential modifiers. Finally, we investigated the effect of dust events on asthma admissions using an indicator variable and its interaction with PM_{10} concentrations.

We used R 2.9.2 for the analysis (R 2.9.2 edn. Vienna, Austria). The study was approved by the Ethics Committee of Penteli Children's Hospital.

3. Results

Table 1 presents the distribution of the pediatric hospital admissions included in the analysis. During the study period there were 3601 admissions in total for acute asthma-related diagnoses, with a daily mean of three. 63% of these occurred among males and 72% among children aged less than five years. Asthma admissions revealed a distinct seasonal pattern with a higher number of admissions during winter and lower during summer, when children leave the urban area for summer holidays.

The median level of PM_{10} was 41 $\mu g/m^3$ and of SO_2 14 $\mu g/m^3$ (Table 2), while there were more than 100 days per year that these pollutants exceeded the relevant WHO guidelines (WHO, 2006). The NO_2 median level was 81 $\mu g/m^3$, with only two days overall exceeding the relevant WHO guideline, while O_3 exceeded the corresponding guideline on 251 days and its median was 70 $\mu g/m^3$. The correlations between pollutants ranged from -0.19 (between O_3 and SO_2) to 0.55 (between NO_2 and SO_2).

Table 3 shows the percentage increase in the daily number of all pediatric hospital admissions for asthma associated with 10 $\mu g/m^3$ increase in the analyzed pollutant's levels, for the whole year and by season. In Table 3 the effect estimates are additionally