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Research report

Air pollution as a risk factor for depressive episode in patients with cardiovascular disease, diabetes mellitus, or asthma

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ABSTRACT

Background: There is currently insufficient evidence to confirm the effect of ambient air pollution on mental disorders, especially among susceptible populations. This study investigated the short-term effect of ambient air pollution on the risk of depressive episode and the effect modification across disease subpopulations.

Methods: Subjects who visited the emergency department (ED) for depressive episode from 2005 to 2009 ($n=4985$) in Seoul, Republic of Korea were identified from medical claims data. We conducted a time-stratified case-crossover study using conditional logistic regression. Subgroup analyses were conducted after the subjects were stratified by underlying disease (cardiovascular disease, diabetes mellitus, chronic obstructive pulmonary disease, asthma, and depressive disorder). The risk was expressed as an odds ratio (OR) per 1 standard deviation of each air pollutant.

Results: SO_2, PM_{10}, NO_2, and CO were positively associated with ED visits for depressive episode. The maximum risk was observed in the distributed lag 0–3 model for PM_{10} (OR, 1.120; 95% confidence interval, 1.067–1.176). PM_{10}, NO_2, and CO significantly increased the risks of ED visits for depressive episode in subjects with either underlying cardiovascular disease, diabetes mellitus, asthma, or depressive disorder.

Limitations: Our data may include a misclassification bias due to the validity of a diagnosis determined from medical services utilization data.

Conclusions: SO_2, PM_{10}, NO_2, and CO significantly increased the risk of ED visits for depressive episode, especially among individuals with pre-existing cardiovascular disease, diabetes mellitus, or asthma.

1. Introduction

Unipolar depressive disorder, which was the third leading cause of disease burden in 2004, is projected to become the primary cause of disease burden worldwide by 2030, according to the Global Burden of Disease report (World Health Organization, 2008). Individuals who suffer from mental disorders, including depressive disorder, are at an increased risk for suicide, which is one of the leading causes of death (World Health Organization, 2005). Therefore, depressive disorder has become a major public health challenge.

Ambient air pollution significantly increases the risk of acute myocardial infarction, arrhythmia, stroke, and type 2 diabetes mellitus (DM) (Sun et al., 2010). Recent epidemiological studies have also suggested an association between ambient air pollution and mental disorders such as depression and suicide. These studies have reported a short-term effect of PM_{10}, SO_2, NO_2, and CO on emergency department (ED) visits for depressive disorder (Szyszkowicz et al., 2009) and a long-term effect on depressive symptoms in the elderly (Lim et al., 2012). Consequently, air pollutants, especially particulate matter, may increase the risk of suicide attempt (Szyszkowicz et al., 2010) or suicide (Kim et al., 2010). Depressive symptoms might be associated with inflammatory processes (Raison et al., 2006), which can be induced by air pollutants (Block and Calderon-Garciduenas, 2009). Air pollutants might also cause vascular depression by damaging endothelial vasculature in the brain (Steffens et al., 2003). However, there is currently insufficient evidence to confirm a relationship between air pollution and mental disorders.

Depressive disorder is frequently comorbid with other diseases such as cardiovascular disease (CVD), DM, and asthma (Marshall, 2004; Musselman et al., 1998; Ridker et al., 1997; Stuart and Baune, 2012). Several experimental studies have suggested psycho-endocrine–immune interactions through hypothalamic–pituitary–adrenal (HPA) axis dysregulation and inflammatory

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processes (Reichlin, 1993) to explain the bidirectional association of depression with DM (Stuart and Baune, 2012) or allergic asthma (Marshall, 2004). CVD is also related to depression through HPA axis dysregulation (Musselman et al., 1998) and systemic inflammation (Ridker et al., 1997). Air pollutants may trigger depressive symptoms via inflammatory processes in the brain (Block and Calderon-Garciduenas, 2009), especially among patients with CVD, DM, or asthma who may also have an undiagnosed depressive disorder. Moreover, the association between elevated inflammatory cytokines and the risk of suicide in major depression has been reported (Lindqvist et al., 2009; Nassberger and Traskman-Bendz, 1993). However, most studies on the association between air pollution and mental disorders used secondary data that did not include information about past medical history (Szyszkowicz, 2007; Szyszkowicz et al., 2009). Although one previous study has used a panel data design, researchers did not explore the effect of medication or underlying disease, except CVD, on the association between air pollution and mental disorders (Lim et al., 2012). Therefore, in this study, we investigated the short-term effect of ambient air pollution on ED visits for depressive episode and the interactive effect of ambient air pollution on the risk of depressive episode across disease subpopulations using large representative samples from Seoul, Republic of Korea.

2. Methods

2.1. Study subjects

Subjects who were enrolled in the study visited the ED for depressive episode from January 1, 2005 to December 31, 2009 in Seoul, Republic of Korea. We identified the subjects from medical claims data which were reported to the Health Insurance Review and Assessment Service (HIRA), which is part of the National Health Insurance program of the Republic of Korea. The information identified from the HIRA data included age, sex, diagnosis code (International Classification of Diseases, 10th revision), and the date of the visit (Cho et al., 2013; Kim et al., 2010).

The pre-existing illness of each subject was identified from prior medical services utilization history. However, due to the limitations of these data, we defined pre-existing illness as a disease that had been reported on at least 3 outpatient visits or ≥ 1 hospitalization for the disease during the three years prior to the ED visit. All of the cases were classified into 5 groups: CVD (hypertensive disease [I10–I15], ischemic heart disease [I20–I25], and stroke [I60–I69]), DM (E10–E14), chronic obstructive pulmonary disease (COPD) (J40–J44), asthma (J45–J46), and depressive episode (F32).

2.2. Air pollutants and meteorological variables

The air pollutants that were considered in this study included sulfur dioxide (SO_2), particulate matter with an aerodynamic diameter less than 10 μm (PM_{10}), ozone (O_3), nitrogen dioxide (NO_2), and carbon monoxide (CO). Data were available from 27 recording stations in Seoul from January 2005 to March 2009, 26 stations in April 2009, and 25 stations from May 2009 to the end of the study period. The average daily concentration from these stations was obtained from the Ministry of Environment. The methods of measurement used for each air pollutant were the beta-ray absorption method (PM_{10}), the pulse ultraviolet (UV) fluorescence method (SO_2), the chemiluminescent method (NO_2), the UV photometric method (O_3), and the non-dispersive infrared method (CO). Meteorological data, including temperature, relative humidity, sunlight hours, and air pressure, were obtained from the National Meteorological Office. The period of air pollutant and meteorological data included in the analysis matched the period of ED visits.

2.3. Statistical analysis

To investigate the short-term effect of ambient air pollution on daily ED visits for depressive episode, a time-stratified case-crossover design was used. The case period was defined as the date of each ED visit and the control periods were defined as the same days of the week as the case period within the same month, which allowed for 3 or 4 control days per case day. Unmeasured confounders such as area of residence and socioeconomic status among subjects were controlled by the study design because cases served as their own controls (Janes et al., 2005; Kim et al., 2010).

Cox proportional hazard models were used to estimate the risk of ED visits for depressive disorder due to each air pollutant in both single and distributed lag models. Single lag models were used to explore the association of ED visits with air pollutant levels on the current day, previous day, 2 days, or 3 days prior to the day of a visit (described as lag 0, lag 1, lag 2, and lag 3). However, since ED visits would not only depend on the same day (lag 0) or previous day's (lag 1) effect of air pollutants, we estimated the cumulative effect of air pollution with distributed lag models, which included all air pollutant concentrations from the day of a visit to subsequent specified days in the same statistical model (described as lag0–1, lag0–2, or lag0–3) (Schwartz, 2000). The models included standardized air pollutant concentrations, national holidays, sunlight hours, and the natural cubic spline of the following variables: temperature ($df=30$), relative humidity ($df=15$), and air pressure $df=15$) (Kim et al., 2010). We conducted the same analyses using 1-day to 3-day single lags (lag1, lag2, and lag3) as well as distributed lags (lag0–1, lag0–2, and lag0–3). Subgroup analyses were performed by season (spring, summer, fall, and winter), age (<19, 19–39, 40–64, and ≥ 65 years), sex, and pre-existing illness (CVD, DM, COPD, asthma, and depressive disorder) using the distributed lag model that resulted in the highest risk estimate (lag0–3 for SO_2 and PM_{10} and lag0–2 for the other pollutants). Because air pollutants share common sources and are highly correlated, we also used two-pollutant models that included two pollutants in the same model (PM_{10} with SO_2, PM_{10} with NO_2, PM_{10} with CO, SO_2 with NO_2, SO_2 with CO, and NO_2 with CO) to explore independent effects of air pollutants on the risk of ED visits for depressive episode.

Risk was expressed as an odds ratio (OR) and 95% confidence interval (95% CI) per 1 standard deviation of each air pollutant. We examined statistically significant differences between risk estimates across strata of potential effect modifiers (i.e., the difference between each underlying disease and none of the five diseases) (Altman and Bland, 2003). SAS version 9.3 (SAS institute, Cary, NC) was used to conduct the statistical analyses. All analyses were performed using the HIRA computer systems. The identity of each subject was blinded by the use of a randomly generated identification number.

3. Results

A total of 4985 cases visited the ED for depressive episode during the study period (Table 1). The average age of the study subjects was 44 ± 17, 73.3% were female, and 31.7% had a prior history of depressive disorder.

In the same-day exposure model (lag0), the adjusted OR of PM_{10} was 1.065 (95% CI, 1.032–1.098) per 1 standard deviation (36.70 $\mu g/m^3$) (Fig. 1). All air pollutants were positively associated with ED visits for depressive episode in the lag0 model with the exception of O_3. The associations between air pollutants and the