Ambient ozone concentration and emergency department visits for panic attacks

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ABSTRACT

The effect of ambient air pollution on panic disorder in the general population has not yet been thoroughly elucidated, although the occurrence of panic disorder in workers exposed to organic solvents has been reported previously. We investigated the association of ambient air pollution with the risk of panic attack-related emergency department visits. Using health insurance claims, we collected data from emergency department visits for panic attacks in Seoul, Republic of Korea (2005–2009). Daily air pollutant concentrations were obtained using automatic monitoring system data. We conducted a time-series study using a generalized additive model with Poisson distribution, which included spline variables (date of visit, daily mean temperature, and relative humidity) and parametric variables (daily mean air pollutant concentration, national holiday, and day of the week). In addition to single lag models (lag1 to lag3), cumulative lag models (lag0–1 to lag0–3) were constructed using moving-average concentrations on the days leading up to the visit. The risk was expressed as relative risk (RR) per one standard deviation of each air pollutant and its 95% confidence interval (95% CI). A total of 2320 emergency department visits for panic attacks were observed during the study period. The adjusted RR of panic attack-related emergency department visits was 1.051 (95% CI, 1.014–1.090) for same-day exposure to ozone. In cumulative models, adjusted RRs were 1.068 (1.029–1.107) in lag0-2 and 1.074 (1.035–1.114) in lag0-3. The ambient ozone concentration was significantly associated with emergency department visits for panic attacks.

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1. Introduction

Concern about neuropsychiatric effects of air pollution is growing. Recent epidemiological studies reported positive associations between ambient air pollution and mental health problems such as suicidal behaviour (Kim et al., 2010; Szyszkowicz et al., 2010) and depression (Cho et al., 2014; Lim et al., 2012; Szyszkowicz et al., 2009). These associations have been substantiated by numerous animal experiments showing systemic inflammation following air pollution exposure, resulting in neuroinflammation and changes in neurotransmitter levels including dopamine and serotonin (Gonzalez-Pina et al., 2008; Gonzalez-Pina and Paz, 1997; Sirivelu et al., 2006; Veronesi et al., 2005). Another animal study showed that ozone-induced lung inflammation may affect stress response-related brain regions (e.g., the amygdala) through vagal afferent nerves (Gackiere et al., 2011). Together with depression, anxiety affects the neurotransmitters and brain regions that are impacted by air pollution, and depression and anxiety share a common pathophysiology (Weiss et al., 1994). Nonetheless, ambient air pollution's effect on anxiety has been minimally investigated.

Among anxiety disorders, panic disorder is a major mental health challenge because it causes chronic psychosocial

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impairment and decreased quality of life (Markowitz et al., 1989). According to the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-V), panic disorder criteria include recurrent unexpected panic attacks. A previous study reported that the lifetime panic disorder prevalence is about 2.0%, whereas panic attacks are 9.0% (Wittchen and Essau, 1993). A more recent epidemiological study revealed that the lifetime panic attack prevalence reached 22.7% in the United States (Kessler et al., 2006). A panic attack is characterized by cardiopulmonary symptoms such as shortness of breath, sudden palpitations, and chest pain and may be frequently followed by emergency department visits (Buccelletti et al., 2013). Regarding its aetiology, in addition to the genetic components, panic disorder is associated with psychological stress, but is not essentially bound to a situation compared to other anxiety disorders such as phobias (Schmidt et al., 2014).

Although little evidence exists linking environmental pollution and panic disorder, several studies reported the occurrence of anxiety disorders including panic disorder in workers exposed to organic solvents (Dager et al., 1987; Morrow et al., 2000; Visser et al., 2011). However, ambient air pollution's effect on panic disorder in the general population has not been well studied. Thus, we investigated the risks of panic disorder related to ambient air pollution using national representative data.

2. Methods

2.1. Study participants

We collected medical record data on individuals who visited the emergency department in 2005–2009 in Seoul, Republic of Korea. These data were obtained from the Health Insurance Review and Assessment Service (HIRA), a part of the National Health Insurance program of the Republic of Korea. The HIRA information included age, gender, diagnosis code, and date of the visit. The diagnosis of 'panic disorder without agoraphobia' (F41.0) was made according to the International Classification of Diseases, 10th revision (ICD-10). Because we focused on emergency cases in which the differentiation of panic disorders from panic attacks was unlikely to be taken into account, we defined "emergency department visit for panic attack" as an emergency case with F41.0.

To identify susceptible populations, we selected underlying illnesses associated with air pollution and panic disorder, identified from the patients' previous medical care utilization history. Due to the data limitations, we defined underlying illnesses as those diseases reported on at least three outpatient visits or resulting in one or more hospitalizations during the 3 years prior to the emergency department visit. The underlying illnesses included hypertensive disease (I10–I15), ischemic heart disease (I20–I25), stroke (I60–I69), chronic lower respiratory diseases (J40–J47), diabetes mellitus (E10–E14), panic disorder (F41.0), and depressive disorder (F32).

This study was approved by the Institutional Review Board of Yonsei University Health System (approval number 4-2014-0471), Seoul, Republic of Korea. The requirement of informed consent was waived because of using secondary data.

2.2. Air pollutants and meteorological variables

The air pollutants considered in this study were particulate matter <10 μm (PM_{10}), sulphur dioxide (SO_2), nitrogen dioxide (NO_2), ozone (O_3), and carbon monoxide (CO), and their levels were measured continuously every hour by the Ministry of Environment. Seoul has 27 measuring stations, and the daily pollutant concentrations were calculated as the average values from these stations. The pollutant measurement methods were as follows: beta-ray

absorption method (PM_{10}), pulse UV fluorescence method (SO_2), chemiluminescent method (NO_2), UV photometric method (O_3), and non-dispersive infrared method (CO). Meteorological data, including temperature and relative humidity, were obtained from the National Meteorological Office and collected continuously every hour from one station in Seoul. The air pollutant and meteorological data was collected over the same time period as the emergency department data.

2.3. Statistical analysis

To investigate the short-term effects of daily air pollutant exposure levels on emergency department visits for panic attacks, we conducted a time-series study using a generalized additive model with a Poisson distribution (Hastie and Tibshirani, 1990). This semi-parametric model included spline variables (date of visit, daily mean temperature, and relative humidity) and parametric variables (daily mean air pollutant concentration, national holiday, and day of the week). The date of the visit was modelled as a cubic spline, and the degree of freedom (*df*) was selected by generalized cross validation criterion optimization (Hastie et al., 1990, 1993). The daily number of emergency department visits, national holidays, and day of the week (Monday to Sunday) were considered the dependent variables. The daily mean temperature (cubic spline, $df = 30$) and relative humidity (cubic spline, $df = 15$) were included as meteorological confounders. In addition to same-day exposure (lag0), we performed analyses using single lag models (lag1, lag2, and lag3) to account for previous days' exposure. In addition, cumulative lag models (lag0–1, lag0–2, and lag0–3) were constructed by averaging pollutant concentrations on the days leading up to and including the day of the visit. Following stratification by age, gender, underlying illness, and season, we performed the same lag0–3 model analyses. The risk was expressed as relative risk (RR) per increment in one standard deviation for each air pollutant and its 95% confidence interval (95% CI).

SAS version 9.3 (SAS Institute, Cary, NC) was used to conduct the statistical analyses. All analyses were blinded to the study participants' identity by encoding identification numbers.

3. Results

The study period was 1826 days (2005–2009), and there were 2320 emergency department visits for panic attacks in Seoul,

Table 1
General characteristics of emergency department visits for panic attacks from 2005 to 2009 in Seoul, Republic of Korea.

Variables		No. of cases (%)	
Total visits		2320	(100.0)
Age (years)	<40	1101	(47.5)
	≥40	1147	(49.4)
Gender	Men	1066	(45.9)
	Women	1182	(50.9)
Season	Spring	618	(26.6)
	Summer	712	(30.7)
	Fall	563	(24.3)
	Winter	427	(18.4)
Underlying illness	Cardiovascular disease[a]	775	(33.4)
	Chronic lower respiratory diseases (J40-J47)	672	(29.0)
	Diabetes mellitus (E10-E14)	286	(12.3)
	Panic disorder (F410)	868	(37.4)
	Depressive disorder (F32)	926	(39.9)

The number of missing age, gender, and underlying illness values is 72 (3.1%).
[a] Cardiovascular disease refers to hypertensive disease (I10–I15), ischemic heart disease (I20–I25), and stroke (I60–I69).