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Ambient concentrations of particulate matter and hospitalization for depression in 26 Chinese cities: A case-crossover study

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A R T I C L E I N F O

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A B S T R A C T

Objective: Air pollution with high ambient concentrations of particulate matter (PM) has been frequently reported in China. However, no Chinese study has looked into the short-term effect of PM on hospitalization for depression. We used a time-stratified case-crossover design to identify possible links between ambient PM levels and hospital admissions for depression in 26 Chinese cities.

Methods: Electronic hospitalization summary reports (January 1, 2014–December 31, 2015) were used to identify hospital admissions related to depression. Conditional logistic regression was applied to determine the association between PM levels and hospitalizations for depression, with stratification by sex, age, and comorbidities.

Results: Both $PM_{2.5}$ and PM_{10} levels were positively associated with the number of hospital admissions for depression. The strongest effect was observed on the day of exposure (lag day 0) for PM_{10}, with an interquartile range increase in PM_{10} associated with a 3.55% (95% confidence interval: 1.69–5.45) increase in admissions for depression. For $PM_{2.5}$, the risks of hospitalization peaked on lag day 0 (2.92; 1.37–4.50) and lag day 5 (3.65; 2.09–5.24). The elderly (> 65) were more sensitive to $PM_{2.5}$ exposure (9.23; 5.09–13.53) and PM_{10} exposure (6.35; 3.31–9.49) on lag day 0, and patients with cardiovascular disease were likely to be hospitalized for depression following exposure to high levels of PM_{10} (4.47; 2.13–6.85).

Conclusions: Short-term elevations in PM may increase the risk of hospitalization for depression, particularly in the elderly and in patients with cardiovascular disease.

1. Introduction

Depression is a serious mental disorder that profoundly affects individual quality of life and can impair daily functioning, even leading to suicide (Moscicki, 2001). The prevalence of depression the US has been estimated at 9.0% (CDC, 2010). The estimated prevalence of major depressive disorder in China is 1.6% (2.1% for females and 1.3% for males) (Gu et al., 2013). After the first depressive episode, more than half of patients develop a recurrent or chronic disorder, causing personal suffering and economic problems that are a substantial burden to society (Kleine-Budde et al., 2013). In China, the total cost of depression in 2002 has been estimated at 51,370 million RMB ($6264 million USD) (Hu et al., 2007). Some researchers suggest that prevention is critical in reducing this burden (Cuijpers et al., 2012). Understanding the factors involved in depression is therefore of practical importance.

The onset of depression can be triggered by various factors. Apart from genetic susceptibility, environmental risk factors may contribute to the onset or aggravation of depression. Contributing factors identified in earlier studies include stressful events, such as losing jobs and loved ones (Rashid and Heider, 2008), and physical conditions, such as diabetes (Rustad et al., 2011) and stroke (Saravane et al., 2009). Air

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pollution has also been shown to be involved, which is a heterogeneous mixture of both gaseous pollutants and particulate matter (PM), and especially fine PM ($PM_{2.5}$, particles with an aerodynamic diameter ≤ 2.5 μm), Animal models have shown evidence of the neuropathological effects of exposure to PM (Campbell et al., 2005; Veronesi et al., 2005), and it has been suggested that high concentrations of inhaled air pollutants may reach the brain and cause neuroinflammation (Calderon-Garciduenas et al., 2008). Chronic inflammation has been linked to depression (Brites and Fernandes, 2015). Air pollution may contribute to a depressive mood by inducing dopaminergic neurotoxicity, possibly owing to oxidative stress (Block et al., 2004), as a decrease in dopamine in the central nervous system is one of the underlying pathophysiological mechanisms of depression (Hasler, 2010).

Several studies found a relationship between depression and exposure to PM. Studies conducted in Canada indicated that emergency department visits for depression were associated with exposure to ambient air pollution (Szyszkowicz, 2007; Szyszkowicz et al., 2009, 2016). Lim et al. (2012) reported that increases in PM_{10}, nitrogen dioxide (NO_2), and ozone levels may increase depressive symptoms among the elderly. One prospective cohort study reported a possible association between both long-term $PM_{2.5}$ exposure and depression onset and incident antidepressant use (Kioumourtzoglou et al., 2017). Kim et al. (2016) reported that long-term $PM_{2.5}$ exposure may increase the risk of major depressive disorder.

However, to our knowledge, no published study has investigated the association between PM exposure and depression in China, one of the most polluted countries in the world (Kan et al., 2012). With rapid industrialization and increased energy consumption over the past several decades, air pollution, and especially PM pollution, has become a severe environmental problem in China. Given the public health and economic burden of depression, it is important to determine whether specific air pollutants are linked to an increased risk of depression hospitalization; a better understanding of the underlying mechanisms may lead to evidence-based policymaking for primary prevention and specific interventions. This study investigated the association between ambient concentrations of PM and the number of depression-related hospital admissions in 26 Chinese cities between 2014 and 2015, stratifying by sex, age, and comorbidities.

2. Materials and methods

2.1. Study population

Data on hospital admissions were collected from the electronic hospitalization summary reports of tertiary A hospitals in 26 Chinese cities (Supplementary Fig. 1), which recorded basic demographics (sex and age), dates of admission and discharge, hospitalization and discharge diagnoses in Chinese and their corresponding codes in the 10th revision of the International Classification of Diseases (ICD-10), treatments (mainly surgical information), discharge status (survival, drug allergy, and infection), and hospitalization expenses.

We used ICD-10 codes to identify depression-related admissions between January 1, 2014 and December 31, 2015. These codes included F32 (mild depressive episode), F33 (recurrent depressive disorder), F34.1 (dysthymia), and F41.2 (mixed anxiety and depressive disorder). In total, 19,646 hospital admissions were depression-related.

2.2. Air pollution and meteorological data

Data on air pollution were obtained from the National Air Pollution Monitoring System, which is run by the Chinese Ministry of Environmental Protection. The system fulfills the quality assurance and quality control mandates of the Chinese government through its ambient air-monitoring stations. These stations, ranging in number from 4 to 15 per city, provide hourly air pollution data to the system. We collected records on the levels of $PM_{2.5}$ and PM_{10} (particulate matter < 10 μm in aerodynamic diameter) between January 1, 2014 and December 31, 2015. The daily (24-hour) mean concentrations of pollutants averaged across all the stations in a given city were used as the reading for that city on that day. In addition, the daily (24-hour) average temperature and relative humidity were obtained from the Chinese Meteorological Bureau, allowing for adjustment for weather conditions.

2.3. Study design

To investigate a possible association between ambient PM concentrations and hospitalization for depression, we adopted a time-stratified case-crossover design where cases were used as their own controls (Carracedo-Martinez et al., 2010). With this approach, we were able to adjust for time-invariant characteristics such as age and sex, to ensure unbiased estimates from conditional logistic regression and to avoid time-trend bias (Janes et al., 2005). For each case, the patient's exposure to ambient PM on the day of hospital admission was compared with the exposure on three or four reference days. The reference days were the same days of the week within the same month and year of admission. Using this method, we controlled for the influence of day of week, seasonal and long-term trends, and potential individual-level risk factors (such as sex and genetics).

2.4. Statistical analysis

Pooled analyses were applied in this study; observations from all included cities were combined, and each city was given a special indicator in the dataset. General and clinical characteristics of all 19,646 cases were described, and Spearman's correlation analysis was applied to assess the associations between exposure variables. We then used conditional logistic regression to examine associations between PM concentrations and hospitalizations for depression for each special lag day. Distributed lag non-linear models (DLNM) with three degrees of freedom in the natural cubic splines and a maximum lag of 3 days were used to adjust for the delayed and non-linear effects of temperature and humidity (Goldberg et al., 2011). To control for the meteorological effects on health in different areas, we added interactions between meteorology and the cities to the models. Public holidays were included in the models. The results are described as the percentage of PM concentration increase and the 95% confidence intervals (CIs) in daily admissions for depression per interquartile range (IQR = 75th percentile–25th percentile of air pollutants). We also analyzed the exposure-response association between concentrations of $PM_{2.5}$ and hospitalizations for depression. The DLNM was used to determine the non-linear delayed relationships between exposure and hospitalization for depression.

The models included various lag structures—from the day of hospitalization (lag day 0) up to seven lag days (lag day 7)—to examine the temporal associations of PM concentrations and depression. In addition, we examined the associations with 3-day (lag days 0–2) and 6-day (lag days 0–5) moving mean PM concentrations, to avoid underestimating the effect of pollutants measured by single-day lag models (Bell et al., 2004). In order to explore the impact of PM on depression hospitalization varies across levels of other pollutants, including sulfur dioxide (SO_2), NO_2, and carbon monoxide (CO), two-pollutant models with first order interaction were added in the sensitivity analysis (Carbajal-Arroyo et al., 2011; Winquist et al., 2014).

To determine whether the associations differed by sex and age (< 18, 18–65 and ≥65 years), stratified analyses using a *Z*-test were applied (Altman and Bland, 2003). To examine whether PM exerted different effects on patients with comorbid chronic diseases, we singled out patients who, in addition to a primary diagnosis of depression, had cardiovascular diseases (CVDs, ICD-10 codes I10.x–I15.x, I20.x–I25.x, or I60.x–I69.x), diabetes (E10.x–E14.x), and chronic obstructive pulmonary disease (COPD, J40–J44.x). All analyses were conducted using