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Ambient air pollution exposure and risk of migraine: Synergistic effect with high temperature

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ABSTRACT

Background: Migraine is a chronic and agonizing neurological disorder prevalent worldwide. Although its pathogenesis remains unclear, limited evidence exists on the role of air pollution.
Objective: We aimed to assess the association of short-term air pollution exposure with migraine in conjunction with the synergistic effect of temperature.
Methods: We identified 18,921 patients who visited emergency departments (EDs) for migraine as a primary disease in Seoul from the national emergency database between 2008 and 2014. We conducted a time-stratified, case-crossover analysis to compare levels of particles < 2.5 µm ($PM_{2.5}$), particles < 10 µm (PM_{10}), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), ozone (O_3), and carbon monoxide (CO) on ED visit days and those on the control days matched to day of the week, month, and year. We evaluated the synergistic effects of air pollution and temperature using an interaction term.
Results: Higher air pollution levels were significantly associated with risk of migraine over various lag structures. In the best fitting lags, the odds ratio (OR) associated with an interquartile range increase of $PM_{2.5}$, PM_{10}, NO_2, O_3, and CO was 1.031 (95% CI: 1.010–1.053), 1.032 (95% CI: 1.007–1.057), 1.053 (95% CI: 1.022–1.085), 1.034 (95% CI: 1.001–1.067), and 1.029 (95% CI: 1.005–1.053), respectively. The SO_2 effect was positive but not significant (OR 1.019 [95% CI: 0.991–1.047]). The PM effect was significantly stronger on high-temperature days (above the 75th percentile) than on low-temperature days ($PM_{2.5}$, high: OR 1.068, low: OR 1.021, $P_{interact} = 0.03$; PM_{10}, high: OR 1.066, low: OR 1.014, $P_{interact} = 0.02$).
Conclusion: Our study provides new evidence that air pollution exposure may trigger migraine especially on high-temperature days, and this finding may contribute in establishing preventive measures against migraine.

1. Introduction

Migraine is a common, chronic, and agonizing neurological disorder, characterized by recurrent attacks of intense headache and other related symptoms such as nausea (Goadsby et al., 2002; Lipton and Bigal, 2005). The burden of migraine arises from both economic perspectives and the perspective of quality of life (Lipton and Bigal, 2005). A study on health-related quality of life (HRQoL) reported that the effect of migraine on HRQoL corresponded to that of depression and was more severe than that of other chronic diseases such as diabetes and arthritis (Dahlöf, 1993). In South Korea, the number of patients with migraine has been dramatically increasing (from 479,000 in 2010 to 505,000 in 2015), and the medical expenses for migraine have also increased by 34.4% (from USD 39.6 million to 53.2 million).

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Abbreviations

ED	emergency department
HRQoL	health-related quality of life
NEMC	National Emergency Medical Center
NEDIS	National Emergency Department Information System
NI	neurogenic inflammation

Identifying risk factors of migraine is necessary to reduce its increasing burden. Activation of the trigeminovascular system has been identified as a central step in migraine development, but the primary cause has remained unclear (Pietrobon and Striessnig, 2003). Environmental factors including weather conditions, noise, and odors, as well as demographic factors have been considered as risk factors of migraine (Prince et al., 2004; Wöber et al., 2006).

Little is known, however, about the possible role of ambient air pollution on migraine, despite increasing experimental evidence linking air pollution and neurological damage, including neuro-inflammation, neuronal damage, and neurotransmitter changes (Block and Calderón-Garcidueñas, 2009; Pereyra-Muñoz et al., 2006) and epidemiological studies supporting a positive association between air pollution exposure and neurological disease such as Parkinson's disease and stroke (Lee et al., 2017; Shah et al., 2015). Although limited studies have examined the association between ambient air pollution and migraine, the findings have been mixed in this regard. While a study conducted in Edmonton, Canada using a generalized linear mixed model reported a significantly increased risk of migraine associated with exposure to ambient air pollution (Szyszkowicz et al., 2009), this association was not replicated in a study performed in Boston, USA using a case-crossover design (Mukamal et al., 2009).

Furthermore, the synergistic effect of air pollution and temperature on migraine has not been evaluated, although it is biologically possible that they have a joint effect (Gordon, 2003; Ren et al., 2011). A few studies have provided evidence of the synergism between high air pollution levels and high temperature, mainly on risk of mortality by cardiovascular or respiratory diseases (Qian et al., 2008; Stafoggia et al., 2008). The interaction between air pollution and high temperature is of public health interest given the increasing temperatures associated with climate change (Patz et al., 2005).

We therefore studied the effects of short-term exposure to six criteria air pollutants on the risk of migraine in Seoul, South Korea using a time-stratified case-crossover design. We further assessed potential effect modification by temperature.

2. Methods

2.1. Study population

The National Emergency Department Information System (NEDIS) is the largest database for emergency department (ED) information in South Korea, developed by the National Emergency Medical Center (NEMC). The NEMC was established on July 31, 2001 by the Ministry of Health and Welfare in order to coordinate regional and local emergency medical centers and other local emergency medical facilities.

The NEDIS database consists of all cases of ED visits that occurred since 2005 in regional and local emergency medical centers and other local emergency medical facilities, accounting for approximate 76% of the national hospital-based ED visit data. NEDIS data contain individual demographic information (sex, age, type of insurance, and region to which the emergency medical center belongs), ED visit information (ED visit date/time, ED visit route, reason for ED visit [disease, other reason], symptom onset date/time, mechanism of injury [car accident, fall, burn, etc.], patient state on ED arrival [alert, unresponsive], medical information (initial diagnosis [Unified Medical Language System code], results of ED treatment [discharge, transfer, admission, death], and discharge/admission information [final diagnosis on discharge/admission, date and time of discharge/admission]). The data from different emergency medical centers are standardized and combined by NEMC and encrypted for the privacy of patients, physicians, and hospitals.

We obtained information on the study population from NEDIS data for 2008 through 2014, as the NEDIS data have been stabilized since 2008, regarding the participating emergency medical centers. For case definition, the final diagnosis on discharge according to the ICD-10 was used. We collected data from patients who visited the ED for migraine (having the G43 ICD-10 code as a primary discharge diagnosis) that occurred in Seoul. As the largest and capital city of South Korea, Seoul's population accounts for one-fifth of the total population of South Korea, and its population density is 16,189 individuals/km^2. Furthermore, a regular monitoring system for $PM_{2.5}$ was originally established only in Seoul, although monitoring systems in other cities have been developed in recent years. Given the heavy traffic volume and the high population density, Seoul is a suitable city for examining the association between air pollution and the risk of migraine by affording adequate statistical power.

The Institutional Review Board of Seoul National University approved the study protocol (no. E1710/002-004). The need for informed consent was waived because encrypted NEDIS data were provided to protect private information.

2.2. Assessment of air pollution exposure

Seoul consists of 25 districts, which range from 10 to 47 km^2 (mean, 24 km^2). We obtained hourly concentrations of particles < 2.5 μm ($PM_{2.5}$) from 25 monitoring sites, and particles < 10 μm (PM_{10}), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), ozone (O_3), and carbon monoxide (CO) from 27 monitoring sites operated by the Seoul Research Institute of Public Health and Environment. Each district has one monitoring site located centrally within the district (two districts have two monitoring sites for five pollutants except $PM_{2.5}$), and each pollutant was measured with the following methods every 15 min: gravimetry ($PM_{2.5}$), beta-ray absorption (PM_{10}), chemo-luminescence (NO_2), ultraviolet fluorescence (SO_2), ultraviolet photometry (O_3), and nondispersive infrared photometry (CO). These measurements followed the standard protocols established by the Korean Ministry of Environment (MOE, 2011). Because information on patient or ED-specific addresses was not provided for privacy, we constructed city-level measures of air pollution exposure; first, we averaged the hourly concentrations from all monitoring sites for all pollutants. Then, we constructed daily representative values, the 24-hour means for $PM_{2.5}$, PM_{10}, NO_2, and SO_2, and the maximum 8-hour means for O_3 and CO based on the World Health Organization (2006) air quality guidelines.

We calculated paired Pearson's correlations ($N = {}_{25}C_2 = 300$, $N = {}_{27}C_2 = 351$) among site-specific daily concentrations of air pollutants from 25 monitoring sites for $PM_{2.5}$ and 27 monitoring sites for the other pollutants during the study period. All site-specific concentrations were highly correlated with each other from mean 0.725 (SD = 0.079) in SO_2 to mean 0.953 (SD = 0.020) in PM_{10}, showing unimodal distributions, suggesting homogeneity in air pollution levels in the 25 districts within Seoul. Therefore, we decided to use the constructed daily measures of air pollutants as the representatives of ambient air pollution exposure in Seoul.

2.3. Meteorological variables

Seoul is located in the west central part of the Korean Peninsula and has four distinct seasons with a maximum temperature of approximately 32 °C in August and a rainy season during July to August in the temperate zone. Seoul has one weather monitoring station with an automated synoptic observing system, which is located slightly north of