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Global association between ambient air pollution and blood pressure: A systematic review and meta-analysis☆

Bo-Yi Yang [a], Zhengmin Qian (Min)[b], Steven W. Howard [c], Michael G. Vaughn [d], Shu-Jun Fan [e], Kang-Kang Liu [a], Guang-Hui Dong [a, *]

[a] *Guangzhou Key Laboratory of Environmental Pollution and Health Risk Assessment, Department of Preventive Medicine, School of Public Health, Sun Yat-sen University, Guangzhou 510080, China*
[b] *Department of Epidemiology, College for Public Health and Social Justice, Saint Louis University, Saint Louis 63104, USA*
[c] *Department of Health Management and Policy, College for Public Health and Social Justice, Saint Louis University, Saint Louis 63104, USA*
[d] *School of Social Work, College for Public Health and Social Justice, Saint Louis University, Saint Louis 63104, USA*
[e] *Guangzhou Center for Disease Control and Prevention, Guangzhou 510440, China*

A R T I C L E I N F O

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A B S T R A C T

Although numerous studies have investigated the association of ambient air pollution with hypertension and blood pressure (BP), the results were inconsistent. We performed a comprehensive systematic review and meta-analysis of these studies. Seven international and Chinese databases were searched for studies examining the associations of particulate (diameter<2.5 µm ($PM_{2.5}$), 2.5–10 µm ($PM_{2.5\text{-}10}$) or >10 µm (PM_{10})) and gaseous (sulfur dioxide (SO_2), nitrogen dioxide (NO_2), nitrogen oxides (NO_x), ozone (O_3), carbon monoxide (CO)) air pollutants with hypertension or BP. Odds ratios (OR), regression coefficients (β) and their 95% confidence intervals were calculated to evaluate the strength of the associations. Subgroup analysis, sensitivity analysis, and meta-regression analysis were also conducted. The overall meta-analysis showed significant associations of long-term exposures to $PM_{2.5}$ with hypertension (OR = 1.05), and of PM_{10}, $PM_{2.5}$, and NO_2 with DBP (β values: 0.47–0.86 mmHg). In addition, short-term exposures to four (PM_{10}, $PM_{2.5}$, SO_2, NO_2), two ($PM_{2.5}$ and SO_2), and four air pollutants (PM_{10}, $PM_{2.5}$, SO_2, and NO_2), were significantly associated with hypertension (ORs: 1.05–1.10), SBP (β values: 0.53–0.75 mmHg) and DBP (β values: 0.15–0.64 mmHg), respectively. Stratified analyses showed a generally stronger relationship among studies of men, Asians, North Americans, and areas with higher air pollutant levels. In conclusion, our study indicates a positive association between ambient air pollution and increased BP and hypertension. Geographical and socio-demographic factors may modify the pro-hypertensive effects of air pollutants.

1. Introduction

Hypertension and high blood pressure (BP) have been ranked as the leading cause of death and disability worldwide, accounting for over 10.7 million deaths per year (Forouzanfar et al., 2015). In recent years, average BP levels have decreased worldwide. However, people in developing countries have experienced an increase in BP levels and hypertension prevalence, presumably related to lifestyle changes and increasingly deteriorating environmental conditions (Danaei et al., 2011). In parallel, ambient air pollution has also become the largest global environmental health threat (World Health Organization, 2015; Giorgini et al., 2016). Mechanistic evidence indicates that the inhalation of several air pollutants could trigger autonomic nervous system imbalance, and cause systemic inflammation, endothelial dysfunction and DNA methylation disruption (Bellavia et al., 2013; Furuyama et al., 2009; Geiser and Kreyling, 2010; Miller, 2014; Perez et al., 2015; Seaton et al., 1995; Perera et al., 2011). It has therefore been speculated that air pollution may contribute to hypertension pathogenesis. During the past few decades, many human epidemiological studies have evaluated the relationships of long-term and short-term exposure to ambient air pollutants with hypertension and BP levels (Giorgini

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* Corresponding author. Department of Preventive Medicine, School of Public Health, Sun Yat-sen University, 74 Zhongshan 2nd Road, Yuexiu District, Guangzhou 510080, PR China.
E-mail address: donggh5@mail.sysu.edu.cn (G.-H. Dong).

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Abbreviations

BP	blood pressure
β	correlation coefficient
CO	carbon monoxide
DBP	diastolic blood pressure
NO_2	nitrogen dioxide
NO_x	nitrogen oxides
O_3	ozone
OR	odds ratio
PM_{10}	particulate matter with an aerodynamic diameter ≤10 μm
$PM_{2.5-10}$	particulate matter with diameter 2.5–10 μm
$PM_{2.5}$	particulate matter with diameter <2.5 μm
SBP	systolic blood pressure
SO_2	sulfur dioxide

et al., 2016; Brook and Rajagopalan, 2009; Cai et al., 2016; Liang et al., 2014; Zhang et al., 2016a). However, results were inconsistent due to variations in study design, population characteristics, exposure duration, air pollutant concentrations, exposure assessments, as well as BP measurements, which make these findings difficult to interpret and prevent specific suggestions to policy makers.

Systematic review and meta-analysis are widely used methods in environmental health epidemiology, enabling researchers to quantitatively synthesize data across studies endeavoring to offset the challenge of small sample size, to solve uncertainty from single studies, and to highlight research gaps. Until now, three meta-analyses have been conducted to pool the long-term and short-term effects of ambient air pollutants on hypertension or BP (Cai et al., 2016; Liang et al., 2014; Zhang et al., 2016b). However, the meta-analyses by Liang et al. (2014) and Zhang et al. (2016b) only investigated the effects of particulate air pollutants (diameter <2.5 μm ($PM_{2.5}$) and <10 μm (PM_{10})) on BP levels, without covering other main air pollutants such as sulfur dioxide (SO_2), nitrogen dioxide (NO_2), nitrogen oxides (NO_x), ozone (O_3), and carbon monoxide (CO). The most recent meta-analysis by Cai et al. (2016) involved seven air pollutants (O_3, CO, NO_2, NO_x, SO_2, PM_{10} and $PM_{2.5}$), yet it only focused on hypertension (but not BP) and had apparent flaws such as missing important studies (e.g. Fuks et al., 2014) and inadvertently including two studies with different study aims (ischemic stroke (Oudin et al., 2011) and acute coronary syndrome (Qorbani et al., 2012)).

To provide researchers and healthcare professionals with more comprehensive estimates of the effect of long-term and short-term exposure to ambient air pollution on hypertension and BP levels, we systematically retrieved all relevant studies to date and conducted a meta-analysis of the literature that was specifically designed to overcome the limitations of the three aforementioned meta-analytic reviews.

2. Methods

2.1. Search strategy

The systematic review and meta-analysis was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) guidelines (Supplemental Table 1). We systematically searched three English databases (PubMed, Embase, ISI Web of Science) and four Chinese databases (China National Knowledge Infrastructure, Chongqing VIP Chinese Science and Technology Periodical, China Biological Medicine, and wanfang) for pertinent literature published before 25 May 2017. The search strategies were based on combinations of keywords concerning ambient air pollutants (air pollution, particulate matter, air pollutants, particles, sulfur dioxide, nitrogen oxide, nitrogen dioxide, ozone, and carbon monoxide) and hypertension (hypertension, high blood pressure, hypertensive, blood pressure, systolic blood pressure, and diastolic blood pressure) (detailed search strategies are listed in Supplemental Table 2). Language was restricted to Chinese and English. We also manually searched the reference lists of included studies as well as relevant review articles for additional articles.

2.2. Eligibility criteria and study selection

Studies were included if they met the following criteria: (1) explored the associations of long-term exposure (≥30 days) and short-term exposure (<30 days) to ambient air pollution with hypertension or BP; (2) cohort, cross-sectional, case-crossover, time-series, case-control, or panel studies; (3) the definition of hypertension included systolic blood pressure (SBP) ≥140 mmHg or diastolic blood pressure (DBP) ≥90 mmHg, self-reportedly taking antihypertensive medicine, self-report of doctor-diagnosed hypertension, or categorized by the International Classification of Disease (10th revision for hypertension, ICD10: I10 or ICD9: 401); (4) reported quantitative estimates and their 95% confidence intervals (CIs) or standard errors (or sufficient data to calculate these estimates); (5) for duplicate publication, the paper that provided the most detailed information was included.

All references identified from the databases were downloaded into a reference manager (NoteExpress 3.2, Aegean Software, Beijing, China). We deleted duplicates directly from the initial records using the software, and the remaining articles were screened for eligibility using the following two steps. First, titles and abstracts of all publications were reviewed for eligibility. Then, for the remaining references marked as potentially eligible, full texts were further evaluated (Fig. 1). The study selection was performed by two independent investigators and any disagreements were resolved by discussion.

2.3. Data extraction

The following data were extracted from eligible studies: authors, publication year, study setting, study design, year of study, age, gender proportion, health status of the study participants, mean concentrations of air pollutants, assessment of air pollution exposure, lag patterns, blood pressure measurement method, definition of hypertension, estimates (odds ratio (OR), correlation coefficient (β), risk ratio, or hazard ratio) and their corresponding 95% confidence interval (CI) or standard error, sample size, and covariates. For each study, the data were independently extracted by two authors, and conflicts were adjudicated by a third author. For studies without enough data for pooling, efforts were made to obtain the raw data by contacting original authors (Liu et al., 2016).

2.4. Quality assessment

The quality of each study was independently assessed by two investigators. Any disagreement was resolved by consensus after discussion. Cross-sectional studies were assessed using the Joanna Briggs Institute (JBI) meta-analysis of statistics assessment and review instrument. Cohort, panel, and case-crossover studies were assessed using Newcastle Ottawa Scale (NOS). Each study was evaluated on a JBI score from zero to 20, or an NOS score from zero