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Review

Ambient air pollution and hypertensive disorders of pregnancy: A systematic review and meta-analysis

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HIGHLIGHTS

- Effects of prenatal air pollution exposure on HDP were examined.
- A meta-analysis was performed on studies published on/after 1980.
- Exposure to NO_2 during the entire pregnancy is associated with HDP and preeclampsia.
- Exposure to Co and O_3 during the first trimester is associated with HDP and preeclampsia.
- In general, our review suggests an association between ambient air pollution and HDP risk.

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ABSTRACT

Hypertensive disorders of pregnancy (HDP, including gestational hypertension, preeclampsia, and eclampsia) have a substantial public health impact. Maternal exposure to high levels of air pollution may trigger HDP, but this association remains unclear. The objective of our report is to assess and quantify the association between maternal exposures to criteria air pollutants (ozone, carbon monoxide, nitrogen dioxide, sulfur dioxide, and particulate matter $\leq$10, 2.5 μm) on HDP risk. PubMed, EMBASE, MEDLINE, Current Contents, Global Health, and Cochrane were searched (last search: September, 2013). After a detailed screening of 270 studies, 10 studies were extracted. We conducted meta-analyses if a pollutant in a specific exposure window was reported by at least four studies. Using fixed- and random-effects models, odds ratios (ORs) and 95% CIs were calculated for each pollutant with specific increment of concentration.

Increases in risks of HDP (OR per 10 ppb = 1.16; 95% CI, 1.03–1.30) and preeclampsia (OR per 10 ppb = 1.10; 95% CI, 1.03–1.17) were observed to be associated with exposure to NO_2 during the entire pregnancy, and significant associations between HDP and exposure to CO (OR per 1 ppm = 1.79; 95% CI, 1.31–2.45) and O_3 (OR per 10 ppb = 1.09; 95% CI, 1.05–1.13) during the first trimester were also observed. Our review suggests an association between ambient air pollution and HDP risk. Although the ORs were relatively low, the population-attributable fractions were not negligible given the ubiquitous nature of air pollution.

1. Introduction

Hypertensive disorders of pregnancy (HDP) including chronic hypertension, gestational hypertension, preeclampsia, and eclampsia are prevalent, accounting for up to 10% of all pregnancies (Duley, 2009). These medical conditions among pregnant women are characterized by high blood pressure, usually after 20 weeks of gestation because blood volume change during pregnancy leads to higher stress on the cardiovascular system (Yoder et al., 2009). HDP is highly associated with increased neonatal and maternal morbidity and mortality (Duley, 2009; Lo et al., 2013). It causes pitting edema, endothelial abnormalities, liver and renal dysfunction, and increased risk of cardiovascular disease, stroke and Type II diabetes later in life of pregnant women (Bauer and Cleary, 2009; Bellamy et al., 2007; Duley, 2009; Wang et al., 2012). In addition,

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maternal HDP also put infants under higher risks of small for gestational age, preterm delivery, low birthweight, and hospitalization for a wide range of neonatal diseases (Allen et al., 2004; Wu et al., 2009a). For example, preeclampsia alone contributes to about 25% of all medically indicated preterm deliveries in the United States (Ananth and Vintzileos, 2006; Goldenberg et al., 2008).

The association between air pollution and increased risk of hypertension in the general population has been reported by many studies (Basile and Bloch, 2012; Coogan et al., 2012; Guo et al., 2010a, 2010b; Sorensen et al., 2012). Although the exact mechanisms underlying the effects of air pollution on blood pressure is yet to be determined, some plausible mechanisms have been suggested in previous studies (Brook and Rajagopalan, 2009). Briefly, there are three non-mutually exclusive pathways that may be responsible for hypertension following exposure to air pollution. The first pathway involves changes in autonomic system balance through interaction of air pollutants with the sympathetic nervous system, thereby increasing blood pressure. The second pathway is an indirect pathway, which involves circulating oxidative stress markers such as cytokines induced by affected body organs, particularly the lung cells. These stress markers may affect blood pressure through changes in endothelial and other hemodynamic function. Lastly, blood pressure may be affected directly by pollutants that enter the vascular system causing vasoconstriction and other vascular dysfunction.

Given the effects that air pollution may have on hypertension in the general population, it is plausible that exposure to air pollution during pregnancy may also increase the risk of HDP through the same mechanisms. Emerging studies have suggested that environmental exposures such as ambient air pollution during pregnancy may play a role in the development of HDP, including gestational hypertension and preeclampsia (Dadvand et al., 2013; Jedrychowski et al., 2012; Lee et al., 2013; Malmqvist et al., 2013; Mobasher et al., 2013; Olsson et al., 2013; Pereira et al., 2013; Rudra et al., 2011; van den Hooven et al., 2011; Vigeh et al., 2011; Vinikoor-Imler et al., 2012; Woodruff et al., 2008; Wu et al., 2009b, 2011; Xu et al., 2013; Zhai et al., 2012). However, inconsistencies and uncertainties remain concerning the effects of specific pollutants and critical exposure periods. To our knowledge, no review or meta-analysis examining the association between air pollution and HDP exists. Given the varied combinations of pollutants (i.e. NO_2, SO_2, $PM_{2.5}$, PM_{10}, O_3, and CO) and exposure periods (i.e. month, trimester, periconception, and other periods), and treatment of exposure as both a continuous and categorical variable, a systematic review of these previous studies is needed. Therefore, we present a systematic review and meta-analysis of 10 studies examining associations between ambient air pollution and HDP. We provide summary estimates of effect by gestational period, quantify heterogeneity, evaluate publication bias, and conduct sensitivity analyses.

2. Materials and methods

2.1. Search methods

Studies were identified using electronic searches of bibliographic databases, and review of reference lists of all relevant papers. The following databases were searched: PubMed, EMBASE, MEDLINE, Current Contents, Global Health, and Cochrane. The Medical Subject Heading (MeSH) terms “hypertension, pregnancy-induced”, “pre-eclampsia”, “eclampsia”, “pregnancy”, “hypertension”, “air pollution”, “particulate matter”, “nitrogen dioxide”, “sulfur dioxide”, “ozone”, and “carbon monoxide” and non-MeSH terms “gestational hypertension”, and “hypertensive disorders of pregnancy” were used in the search. From this search, we selected articles which a) were published in English on/after January 1, 1980; b) were original epidemiologic studies on human live birth; c) had hypertensive disorders of pregnancy, gestational hypertension, preeclampsia, or eclampsia as outcome variables; d) investigated non-occupational non-accidental human prenatal exposure to outdoor air pollution. Since the majority of studies met the inclusion criteria examined exposure to criteria air pollutants, we excluded studies that only examined exposure measured by other surrogate methods such as traffic density data and ecologic assessment (e.g. high vs Low) because the results from these studies cannot be used for effect synthesis (Malmqvist et al., 2013; Vigeh et al., 2011). In addition, since this meta-analysis only focused on the effects of ambient air pollution exposure during pregnancy on HDP, studies with exposure window other than pregnancy period (e.g. periconception) were further excluded (Rudra et al., 2011). Studies available only in abstract form were also excluded as the abstract only provided very limited information about the study (Woodruff et al., 2008). Searches were last updated in September 2013. Relevance of citations for inclusion was evaluated independently by two investigators (SH and HH), differences between whom were resolved by consensus. At first, all identified publications were screened for the eligibility by reviewing the title and abstract based on the inclusion and exclusion criteria. Then, the remaining references were further evaluated by reviewing the full paper. As a result, a total of 270 unduplicated records were identified in the literature search. After review of the title and abstract, 149 studies were excluded due to irrelevant exposure and/or outcome, and 35 non-epidemiologic studies were also excluded. The remaining 86 studies were selected by reviewing the full paper to determine eligibility for inclusion. Nine of them were review, commentary and meeting report, and were further excluded. Sixty-five studies were not considered due to irrelevant exposures and/or outcomes. Finally, ten studies were identified and included in this meta-analysis (Fig. 1).

Data extraction from relevant studies was also conducted independently by two investigators (SH and HH). Each independent reviewer used a standardized data extraction sheet to extract relevant data from these studies. All data entries were confirmed and doubly checked for completeness and accuracy. The following study characteristics were extracted: study design, location, dates of data collection, sample size, outcome, number of cases, distribution of exposure, method of exposure characterization, statistical analysis methods, effect size estimates, covariate adjustment, and conduct of subgroup or sensitivity analyses. Study quality was assessed based on study design, exposure characterization and adjustment for covariates, and sensitivity analyses were conducted where feasible based on these factors. References were managed in Endnote (Thomson Reuters, CA).

2.2. Meta-analysis

We conducted meta-analyses if at least four studies reported the same pollutant and exposure window group. All studies reviewed excluded chronic hypertension in pregnancy from their outcomes, so in this study, we used the restricted definition of HDP which only includes gestational hypertension, preeclampsia, and/or eclampsia. Since different outcomes of HDP were reported in the included studies (i.e. HDP, gestational hypertension, and preeclampsia), we conducted two sets of meta-analysis: 1) for the association between air pollution and preeclampsia and 2) for the association between air pollution and HDP (including HDP, gestational hypertension, and preeclampsia). We used the risk estimates from the fully-adjusted and single-pollutant models presented in each study (Olsson et al., 2013; Xu et al., 2013), and risk estimates from sensitivity analyses were not used. There was one instance where