Air Pollution and Emergency Department Visits for Hypertension in Edmonton and Calgary, Canada: A Case-Crossover Study

Robert D. Brook¹ and Termeh Kousha²

BACKGROUND
Ambient air pollutant exposures have been associated with a wide variety of cardiovascular events; however, few studies have evaluated their impact upon acute emergency department (ED) visits for hypertension.

METHODS
The purpose of this study was to examine the associations between ED visits for hypertension and ambient air pollution concentrations among 6,532 patients during the period of January 2010 to December 2011 in Edmonton and Calgary, Alberta, Canada. The associations were evaluated using a case-crossover design.

RESULTS
Odds ratios and their 95% confidence interval have been calculated for 1 unit increase in their interquartile range for lags (the time between air pollutant measurement and exposure–response) 0–8 days. During the cold season, statistically significant positive results were observed for SO₂, among lag days 4–6 and 8 for females and lag days 5 and 6 for males. Moreover, statistically significant positive results were observed for NO₂ on lag day 7 for females and for PM₁₀ on lag days 5 and 7, for females and lag day 6 for males. During the warm season, statistically significant positive results were observed for O₃ on lag days 3 and 4 and for SO₂ on lag days 2 and 8 for females.

CONCLUSIONS
These findings support the hypothesis that recent exposures to ambient levels of several air pollutants can be capable of elevating blood pressure to a clinically significant extent such that it leads to ED visits for hypertension.

Key words: air pollution; blood pressure; Alberta; case-crossover; emergency department visit; hypertension.

doi:10.1093/ajh/hpu302

The association between air pollution and hospital admissions for respiratory diseases is well-established.¹⁻⁷ During the past decade a wide array of studies have shown that air pollution is additionally related to excess cardiovascular morbidity and mortality.¹⁻¹² Though there may be many mechanistic explanations,¹¹⁺⁻¹² mounting evidence supports the hypothesis that exposures to various air pollutants are capable of causing clinically significant elevations in blood pressure (BP), whether acute or chronic in nature.¹ Not only is hypertension the most important risk factor for cardiovascular morbidity (i.e., stroke, heart failure, and coronary heart disease), but also it is leading underlying cause of global mortality.¹³⁻¹⁵ An important pathway whereby air pollutants might trigger acute morbidity is via rapid elevation of BP. In addition to potentially promoting sudden cardiovascular events (e.g., strokes), acute elevations in BP may also prompt an urgent care visit specifically in regards to the higher BP level per se or a variety of potentially associated symptoms (e.g., headache).

Few previous studies have directly examined the relationship between air pollutants and the acute morbidity (e.g., emergency department (ED) visits) specifically related to hypertension.¹¹⁺⁻¹⁶,¹⁷ In a case-crossover (CC) study in Edmonton, Canada, we showed an association between short-term exposures to several ambient air pollutants and ED visits for hypertension during a 10-year period among 5,365 patients.¹¹ The main finding in this study was that significant increases in the risk for ED visits for hypertension occurred in association with higher levels of ambient PM₁₀ (particulate matter smaller than about 10 micrometers), PM₂.₅ (particulate matter smaller than about 2.5 micrometers), NO₂, and SO₂ a few days earlier and there was no significant relationships for other gaseous copollutants.¹¹ These observations suggest that, even at relatively low ambient concentrations frequently encountered in Canadian cities, short-term exposures to increases in these common pollutants are capable of causing “clinically meaningful” prohypertensive responses.

In another CC study in Beijing, China, SO₂ and NO₂ were also found to be significantly associated with ED visits for hypertension (n = 1,491).¹⁶ Their study showed that 10 μg/m³ increase in SO₂ and NO₂ were significantly associated with emergency room visits for hypertension. Another study
in Beijing area study, PM$_{2.5}$ was also found to be related to an increased risk for ED visits for hypertension.$^{17}$

While many studies have shown that air pollution exposure can rapidly raise BP,$^{9,12}$ few reports have demonstrated that this prohypertensive response translates into a clinically meaningful health effect over the short-term such as an ED visit related to hypertension per se.

In this context, the aim of this study was to expand on the prior studies by investigating the associations between ambient air pollution exposures and 6,532 ED visits for hypertension during the period from January 2010 to December 2011 in Edmonton and Calgary, Alberta, Canada.

MATERIALS AND METHODS

Study population

Health data were retrieved from the National Ambulatory Care Reporting System (NACRS; See CIHI Website: www.cihi.ca). ED visits for hypertension were retrieved from the NACRS using the International Classification of Diseases, tenth revision (ICD-10) code I10, during the period of January 2010 to December 2011 in Edmonton and Calgary, Alberta, Canada.

Environmental data

The environmental data were obtained from Environment Canada. (See NAPS Web site: http://www.etc-cte.ec.gc.ca/NapsData). We used patient-specific 3-digit residential postal codes to identify the closest NAPS stations for each patient. For air pollutants, we considered only the NAPS stations within 35 km of each patient’s residential postal code centroid. The daily average values of ozone (O$_3$), nitrogen dioxide (NO$_2$), particulate matter with an aerodynamic diameter less than 2.5 µm (PM$_{2.5}$), and sulfur dioxide (SO$_2$) were calculated by averaging over all the stations within 35 km of each patient’s postal code centroid. We eliminated the patients who lived further than 35 km to all the stations from the study. We retrieved hourly data for temperature and relative humidity for Edmonton and Calgary from Environment Canada. We calculated the daily levels for temperature and relative humidity by averaging hourly data over 24-hour periods. For temperature and relative humidity, we have considered only meteorological stations within 100 km of each patient’s residential postal code centroid. If more than 1 station was available for a patient, the daily values of all stations were averaged.

Statistical methods

A CC design was used in this study.$^{18}$ ED visits were used to represent health outcomes and were analyzed as separate individual events. Ambient air pollutant concentrations, temperature, and relative humidity were expressed as daily mean values. We incorporated the concept of lag time into their exposure definition, i.e., the time between air pollutant measurement and exposure–response relationships between exposure to air pollutants and ED visit for hypertension. All components, air pollutants and meteorological factors, in the models were lagged by the same number of days, from 0 (same day visit) to 8 days.

In order to do a multicity study, statistical analysis we applied a time stratified CC design.$^{19}$ In this methodology, cases served as their own controls on a set of predefined control days proximate to the time they became cases. Because cases are the perfect match for themselves in personal characteristics (i.e., age, race, etc.), the CC method demonstrated utility and benefits for epidemiological studies of air pollution.$^{20}$

A $P$ value less than 0.05 was considered statistically significant in all analyses. The generated results were reported as odds ratios (ORs) and their 95% confidence intervals (CI). For the first stage of analysis, ORs for O$_3$, NO$_2$, PM$_{2.5}$, and SO$_2$ were calculated separately for each city by using the PROC PHREG producer in SAS EG v.4.2. In this model, air pollutants and meteorological factors were lagged by the same number of days, from 0 to 8. The controls were matched to case periods by day of week for the case period (day) and the control periods were determined as other days in the same month and year; for each case, 3 or 4 controls were presented. In the second stage of this study, we combined the estimates to generalize an overall effect relevant to 2 cities. This stage of the study required a meta-analysis of the estimates and their standard errors to achieve a pooled effect estimate. Assuming that individual effect size estimates represent the same underlying parameter and effect estimates are weighted by the inverse of their variance, pooled estimators, and their standard errors using a fixed-effects model were calculated. Moreover, based on an assumption that individual effect size estimates reflect potentially different underlying parameters, random-effects model was also calculated.$^{21}$ Meta-analysis and meta-regression were performed using the R language.$^{22}$

RESULTS

Figure 1 shows frequency (counts) for all hypertension ED visits by sex and age, from 0 years to 100 years of age. The patients of 100 years old age and older are represented on the graph as 100 years of age (i.e., by one point). Table 1 shows the frequency of visits by different age groups, sex, season: cold months (October-March) and warm months.
(April–September) and by city. The number of visits for females was almost 1.5 times more than males. Also, more than half (55%) of the ED visits for hypertension occurred for the age group 60 and older. Table 2 shows the descriptive air pollution statistics and the characteristics of relative humidity and temperature by cities.

The results of pooling estimates for hypertension among the 2 cities are presented in Figure 2 for males (left panel) and females (right panel) for cold seasons. ORs and their 95% CI have been calculated for 1 unit increase in interquartile (IQR = 75th percentiles−25th percentiles) value of air pollutants. The IQR values are 10.66 ppb, 13.42 ppb, 5.37 ppb, respectively, for daily means of NO\(_2\), O\(_3\), PM\(_{2.5}\), and SO\(_2\). During the cold season, statistically significant positive results were observed for SO\(_2\) among lag days 4–6 and 8, OR = 1.108 (95% CI: 1.040, 1.177); P = 0.00201, OR = 1.077 (1.009, 1.144); P = 0.00436, OR = 1.061 (1.000, 1.126); P = 0.0280 and OR = 1.068 (1.005, 1.131); P = 0.03912, respectively, for females and lag days 5 and 6 OR = 1.074 (1.000, 1.148); P = 0.00032, OR = 1.068 (1.000, 1.140); P = 0.00471, respectively, for males. Moreover, statistically significant positive results were observed for NO\(_2\) on lag day 7, OR = 1.140 (1.052, 1.228); P = 2.92 × 10\(^{-10}\) for females and for PM\(_{2.5}\) on lag days 5 and 7, OR = 1.068 (1.006, 1.129); P = 0.00006 and OR = 1.068 (1.000, 1.122); P = 0.00043 for females and lag day 6 OR = 1.076 (1.003, 1.150); P = 0.00731 for males. During the warm season, statistically significant positive results were observed for O\(_3\) on lag days 3 and 4, OR = 1.134 (1.000, 1.275); P = 0.00629 and OR = 1.138 (1.000, 1.277); P = 0.00224 and for SO\(_2\) on lag days 2 and 8, OR = 1.080 (1.022, 1.138); P = 0.0139 and OR = 1.052 (1.000, 1.110); P = 0.00182, respectively, for females. There were no statistically significant positive results for males during the warm seasons.

### Hypertension among patients with one or more health conditions

Patients with diabetes are at higher risk of dying during heat waves,\(^{23}\) and the rates of cardiovascular death have been shown to be increased in those exposed to elevated levels of PM pollution.\(^{24,25}\) In order to analyze for a possible increased susceptibility for air pollution-induced ED visits for hypertension among individuals with diabetes, as well as several other selected cardiovascular diseases, we considered patients who suffered from one (or more) of the followings health conditions as a secondary disease: diabetes (ICD-10 code: E10-15), dysrhythmia (ICD-10 code: I47-49), congestive heart failure (ICD-10 code: I50), atherosclerosis (ICD-10 code: I70), chronic obstructive pulmonary disease (COPD) (ICD-10 code: J40-J44, J47), pneumonia (ICD-10 code: J12-18, P23), upper respiratory infections (ICD-10 code: J00-J06, J30-J39), and asthma (ICD-10 code: J45). Because of the small sample size of this study, we considered both 2 cities and all genders together (N = 467 patients 58%)

### Table 1. Frequency of ED visits by type, sex, age group, season (cold (October–March) and warm (April–September)), and by city

<table>
<thead>
<tr>
<th>Sex</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>2,688</td>
<td>41</td>
</tr>
<tr>
<td>Female</td>
<td>3,844</td>
<td>59</td>
</tr>
<tr>
<td>Age groups</td>
<td></td>
<td></td>
</tr>
<tr>
<td>[0, 29]</td>
<td>215</td>
<td>3</td>
</tr>
<tr>
<td>[30, 59]</td>
<td>2,766</td>
<td>42</td>
</tr>
<tr>
<td>60+</td>
<td>3,551</td>
<td>55</td>
</tr>
<tr>
<td>Season</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cold</td>
<td>2,849</td>
<td>44</td>
</tr>
<tr>
<td>Warm</td>
<td>3,683</td>
<td>56</td>
</tr>
<tr>
<td>City/region</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calgary</td>
<td>3,632</td>
<td>56</td>
</tr>
<tr>
<td>Edmonton</td>
<td>2,900</td>
<td>44</td>
</tr>
<tr>
<td>Total</td>
<td>6,532</td>
<td></td>
</tr>
</tbody>
</table>

### Table 2. Descriptive air pollution statistics by cities and characteristics of relative humidity and temperature

<table>
<thead>
<tr>
<th>City</th>
<th>Variable</th>
<th>Minimum</th>
<th>Median</th>
<th>Maximum</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calgary</td>
<td>NO(_2) (ppb)</td>
<td>1.4</td>
<td>13.2</td>
<td>47.0</td>
<td>11.8</td>
</tr>
<tr>
<td></td>
<td>O(_3) (ppb)</td>
<td>2.3</td>
<td>22.0</td>
<td>42.3</td>
<td>13.5</td>
</tr>
<tr>
<td></td>
<td>PM(_{2.5}) (ug/m(^3))</td>
<td>2.4</td>
<td>10.1</td>
<td>138.4</td>
<td>5.0</td>
</tr>
<tr>
<td></td>
<td>SO(_2) (ppb)</td>
<td>0.0</td>
<td>1.0</td>
<td>4.0</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>Humidity (percentage)</td>
<td>16.1</td>
<td>61.7</td>
<td>99.4</td>
<td>24.8</td>
</tr>
<tr>
<td></td>
<td>Temperature (celsius)</td>
<td>−26.7</td>
<td>6.1</td>
<td>21.6</td>
<td>12.44</td>
</tr>
<tr>
<td>Edmonton</td>
<td>NO(_2) (ppb)</td>
<td>2.4</td>
<td>10.8</td>
<td>44.0</td>
<td>8.7</td>
</tr>
<tr>
<td></td>
<td>O(_3) (ppb)</td>
<td>1.4</td>
<td>21.5</td>
<td>50.1</td>
<td>13.6</td>
</tr>
<tr>
<td></td>
<td>PM(_{2.5})</td>
<td>2.2</td>
<td>8.1</td>
<td>156.3</td>
<td>5.6</td>
</tr>
<tr>
<td></td>
<td>SO(_2) (ppb)</td>
<td>0.0</td>
<td>0.9</td>
<td>10.9</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>Humidity</td>
<td>13.9</td>
<td>71.6</td>
<td>29.9</td>
<td>19.6</td>
</tr>
<tr>
<td></td>
<td>Temperature</td>
<td>−27.7</td>
<td>6.6</td>
<td>20.4</td>
<td>15.1</td>
</tr>
</tbody>
</table>

Abbreviation: IQR, interquartile.
females, 42% males). ORs and their 95% CI were calculated for 1 unit increases in all 4 pollutants on lag days 0 up to 30 to analyze the short- and long-term exposures for the 4 pollutants. There were no statistically significant results; however the results trended in the positive direction for all 4 pollutants irrespective of lag.

**DISCUSSION**

Our findings demonstrate several significant associations between recent exposures during the past week to gaseous as well as particulate air pollutants and the risk for ED visits for hypertension in Edmonton and Calgary, Alberta, Canada. We have seen seasonal and sex differences in our output. The sex differences in output could be due to different sample size (as one can see in Table 1, the number of visits for females were almost 1.5 times more than males). During the warm season O₃ concentration were higher than cold season (mean in warm season is 26.6 vs. 16.6 ppb in cold season), which explains why the effect of O₃ was much higher during the warm season. Also for pollutant NO₂, concentration were higher during the cold season (mean in warm season is 9.5 vs. 19.9 ppb in cold season), which explains why the effect of NO₂ was much higher during the cold season.

While many pollutants on several lag days were not significantly related to ED visits, the direction of risk on most days favored positive associations. IQR is actually a low level of absolute air pollution concentration and if the responses in the population are indeed linear, then the much higher levels throughout the developing world (impacting >3 billion people) is extremely important from a public health standpoint. Overall, these current findings agree with previous published studies which have examined the association between air pollution and ED visits for hypertension, and cardiovascular disease. Our new results add to the growing evidence that acute air pollution exposures may be capable of disrupting cardiovascular physiology and hemodynamic enough to trigger clinically-relevant elevations in BP warranting ED visits for hypertension.

We have previously reviewed the potential mechanisms underlying the increase in BP induced by air pollution. These pathways are presumably responsible for disrupting arterial hemodynamics and thus prompting the ED visits observed in this study. We hypothesize that, acute activation of the sympathetic nervous system and/or impaired vascular endothelial-dependent vasodilation are the most likely biological mechanisms. However, since this is an association study, the actual causes of the ED visits for hypertension related to air pollution exposures cannot be determined.

**Prior studies**

We are aware of at least 3 prior papers evaluating the impact of air pollution on ED visits for hypertension. In a similar CC study in Edmonton, Canada from April 1992 to March 2002, we showed an association between ambient air pollutants and ED visits for hypertension among 5,365 patients. Our previous study results showed that SO₂, NO₂, and PM₁₀ on lag 3 days and PM₂.₅ on lag 6 days were significantly associated with ED visits for hypertension. In a CC design the authors found positive relations between both PM₁₀ and PM₂.₅ and ED visits for hypertension on lag 2 days. Another CC study in Beijing, China, among 1,491 ED visits for hypertension between January 2007 and December 2007, SO₂ and NO₂ were significantly associated with ED visits for hypertension. In a CC study in Beijing, China, among 1,491 ED visits for hypertension between January 2007 and December 2007, SO₂ and NO₂ were significantly associated with ED visits for hypertension.
Sensitive groups

In order to analyze for a possible effect of comorbidities on the risk of ED visits for hypertension due to air pollution, diabetes as well as several other cardiovascular diseases were considered. While the risks were not significant, the general pattern we observed was similar to some prior studies evaluating the effect of comorbidities.\textsuperscript{34,35} Though we did not find statistically significant evidence to support effect modification or susceptibility to pollutants in subgroups, in our study we believe further studies appropriately powered to investigate subgroup characteristics are warranted to evaluate this issue.

Limitations

Numerous pollutants and lag-time periods were evaluated. Given the multiple associations evaluated, it is possible that some of the positive findings represent Type I errors. Nevertheless, during winter months the effect for SO\textsubscript{2} (both sexes) and NO\textsubscript{2} (females) at later lag periods appears consistent. While fewer significant associations were observed, the overall trend in effect for PM\textsubscript{1.5} appears positive as well during later lag periods. The associations of air pollution O\textsubscript{3} appeared less consistent. Given that our current results are supported by previous reports,\textsuperscript{11,16,17} we believe the overall observations of a delayed risk (strongest 5–8 days following exposures) for ED visits for hypertension in relation to exposures to specific air pollutants is a plausible finding, not likely caused by Type I errors. It is also important to note that a number of the \(P\) values are highly significant which lends further support for the veracity of many of the observed associations. Regardless, we must acknowledge that this study was exploratory in its very nature given the numerous associations being tested and our findings should be considered hypothesis-generating and thereby serve as the basis to support future studies to corroborate our observations. Second, it seems unlikely that there would be higher rates of visits for hypertension without actual elevations in BP levels occurring among the patients (i.e., visits coded erroneously as hypertension but without underlying BP elevations). Unfortunately, the underlying mechanisms responsible cannot be established by this type of epidemiological study. While several plausible pathways that produce prohypertensive responses have been demonstrated for particulate matter,\textsuperscript{9,12} few similar data exist for the gaseous pollutants NO\textsubscript{2} and SO\textsubscript{2} which showed stronger relationships in our study. More investigation is required to elucidate how these latter pollutants might be capable of triggering BP elevations or if they are serving as a proxy for sources of exposure to specific pollutant mixtures (e.g., traffic for NO\textsubscript{2} and coal combustion for SO\textsubscript{2}).

Small ORs may still pose large public health risks

The ORs per IQR change in air pollution in this study are not large. This is principally due to the low absolute concentrations of air pollutants in Canada which are some of the lowest levels in the world. These small absolute health effects in relation to exposures are biologically expected and yet the associations remain highly important from a public health standpoint since these small risks impact millions of people in a continuous manner.\textsuperscript{12} Our study demonstrated small ORs for hypertension ED visits in relation air pollution; however, the population attributable fraction (PAF) may still be larger compared to other more potent risk factors. Billions of people are exposed across the world to pollution levels that can be many fold higher than in Canada.\textsuperscript{13} In support of this contention, a study on the public health importance (i.e., PAF) of the triggers of myocardial infarctions identified that the ever-present small risks of PM outweigh the impacts of risk factors with much larger ORs (e.g., cocaine usage).\textsuperscript{36} This suggests that while the ORs are not large, the public health impact is indeed likely highly relevant.

CONCLUSIONS

The findings of this study support our hypothesis that ambient levels of air pollution are capable of elevating BP to a level that leads to an ED visit for acute hypertension. Given the worldwide epidemics of hypertension and elevated levels of air pollution, this relationship is not only important to residents of Calgary and Edmonton, but also maybe of global importance. Further studies are warranted to better understand the linkages between hypertension and air pollution.

ACKNOWLEDGMENTS

The authors thank Dr Mieczyslaw Szyszkowicz for helpful discussion, suggestions, and advice in the methodology. The authors acknowledge Environment Canada for providing the air pollution data from the National Air Pollution Surveillance (NAPS) network that was used in this study.

DISCLOSURE

The authors declared no conflict of interest.

REFERENCES

Brook and Kousha


10. Szyszkwicz M, Rowe BH, Brook RD. Even low levels of ambient air pollution are associated with increased emergency department visits for hypertension. Can J Cardiol 2012; 28:360–366.


