American Journal of Emergency Medicine (2009) 27, 391–396

The American Journal of Emergency Medicine

www.elsevier.com/locate/ajem

Original Contribution

Air pollution and daily ED visits for migraine and headache in Edmonton, Canada

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Received 23 August 2007; revised 4 March 2008; accepted 5 March 2008

Abstract

Background: A variety of environmental factors have been identified as possible triggers for migraine and other headache syndromes.

Objective: We analyzed associations between air pollution and emergency department (ED) visits for migraine and headache.

Methods: Analysis was based on 56 241 ED visits for migraine and 48 022 ED visits for headache to Edmonton hospitals between 1992 and 2002. A Poisson model of counts hierarchically clustered by day of week, month, and year was applied using generalized linear mixed models. Temperature and relative humidity were included as covariates.

Results: Females accounted for 78.5% of migraine visits and 56.3% of headache visits. An interquartile range (IQR) increase (6.2 $\mu g/m^3$) in daily average particulate matter of median aerodynamic diameter less than 2.5 μm ($PM_{2.5}$) was associated with increases in visits of 3.3% for migraine (95% confidence interval [CI]: 0.6-6.0), lagged 2 days, and 3.4% for headache (95% CI: 0.3-6.6), lagged 0 days, among females in the cold season (October-March). $PM_{2.5}$ was also associated with cold season migraine visits among females at lag 0 and 1 day ($P < .1$). In the warm period (April-September), a 2.3-ppb IQR increase in sulfur dioxide was associated with a 2.5% increase in migraine visits (95% CI: 0.3-4.6) among females, whereas a 12.8-ppb IQR increment in nitrogen dioxide was associated with a 6.8% increase in headache visits (95% CI: 1.5-12.5) for males.

Conclusions: Findings provide preliminary evidence of an association between air pollution and ED visits for migraine and nonspecific headache. Findings were most consistent for particulate matter.

Migraines represent an important public health concern. According to a report in a longitudinal study in Canada, it was estimated that migraines account for more than 7 million lost working days annually [1]. In the United States, migraines cause the loss of approximately 150 million work days per year at an estimated lost labor cost of $13 billion [2]. In Canada, an estimated 2.6 million adult females and nearly 1 million adult males have migraines, whereas only about one half of these individuals have been diagnosed by a physician [3]. When attacks are severe, they often precipitate visits to the emergency department (ED) for diagnosis and management.

Studies on migraine have investigated a variety of pathophysiological mechanisms. The link between air pollutants or other environmental factors and migraine or other headaches has not been accepted widely by clinicians, although stressors, including noise, have been identified as

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doi:10.1016/j.ajem.2008.03.013

Table 1 Frequency of ED visits for migraine and headache by age group and sex

Age, y	Migraine	%	No. of females	No. of males	Headache	%	No. of females	No. of males
<20	2810	5.0	1874	936	7483	15.6	3686	3796
20-<30	13 064	23.2	10 034	3030	8098	16.9	4903	3195
30-<40	20 357	36.2	16 425	3932	9592	20.0	5848	3744
40-<50	24 233	25.3	11 370	2863	7567	15.8	4490	3077
50-<60	4325	7.7	3267	1058	5060	10.5	2812	2248
60-<70	1166	2.1	935	231	3843	8.0	1818	2025
70-<80	242	0.4	188	54	3746	7.8	1854	1892
≥80	44	0.1	39	5	2633	5.5	1619	1014
Total	56 241	100	44 132	12 109	48 022	100	27 031	20 991

Data were gathered in Edmonton from April 1, 1992, to March 31, 2002.

possible triggers [4], and weather is frequently identified as a trigger by migraine sufferers [5]. Neurogenic switching, in which exposure to irritants produces an afferent signal that triggers a distant response, potentially in a different organ system, has been hypothesized as a mechanism through which neurogenic inflammation triggered by air pollution exposures may cause migraine headache [6,7]. Exposure to CO affects neurogenic inflammation and, by consequence, may generate migraine attacks [8]. A study conducted on a group of 32 patients having various headache types in Turin, Italy, showed a correlation between headaches and exposure to CO and NO_2 [9].

This study is based on 10-year daily summarized counts of ED visits in which migraine and nonspecific headache are analyzed separately. The goal of this work was to examine the hypothesis that exposure to ambient air pollutants may trigger migraine or headache attacks.

1. Methods

The study population consisted of people serviced at 5 EDs from Edmonton area hospitals within the Capital Health region in Edmonton and St Albert, Alberta (Canada), between April 1, 1992, and March 31, 2002. Each hospital has a full-service ED with inpatient beds and provides 24-hour service. They are staffed by full-time emergency physicians. The overall catchment size covered by the hospitals is estimated at approximately 1.5 million individuals. Emergency department visits were identified based on a discharge diagnosis using the International Classification of Diseases 9th revision, of migraine, rubric 346 [10], and of headache, rubric 784 [10]. Each ED visit within Capital Health is coded by experienced medical record nosologists using the triage information, nursing notes, ED records, and consultation notes. The sample consisted of 2 946 714 ED visits during the 10-year period.

In total, the analysis is based on 56 241 ED visits for migraine and on 48 022 ED visits for headache during a span of 3652 days. The ED visits for migraine and headache represented approximately 1.9% and 1.6%, respectively, of all recorded and diagnosed ED visits to these hospitals during the study period. The study was approved by the University of Alberta Health Research Ethics Board (panel B), and the data were transferred to the Health Canada team following de-identification. No patient contact was made, and patients could not be traced.

Environment Canada supplied hourly data for selected weather variables: relative humidity, temperature (dry bulb), and atmospheric pressure (sea level). For our study, we created a daily average of 24 measurements to represent values of these variables. Because many findings have implicated weather fluctuations as a major factor in migraine/headache triggers [5], we included these variables in our models as a confounder.

The hourly air pollution data were obtained from fixed monitoring stations in Edmonton. These data were also supplied by Environment Canada. For every ambient air pollutant, we have 24 measurements provided by a monitor station at hourly intervals. These include gaseous data: carbon monoxide (CO), nitrogen oxide (NO_2), sulfur dioxide (SO_2), and ozone (O_3), and particulate matter data: respirable particles, particles with median aerodynamic diameter of 2.5 μm or less ($PM_{2.5}$), and inhalable particles, particles with median aerodynamic diameter of 10 μm or less (PM_{10}). The daily average exposures of the population were expressed as mean values among stations.

To relate short-term effects of air pollution and weather factors to the number of daily ED visits for migraine and headache, we applied a generalized linear mixed models

Table 2 Number of days, mean, SD, median, IRQ (the 75th-25th percentile values) of daily average concentrations of the ambient air pollutants, and meteorological factors

Variable (unit)	Days	Mean	SD	Median	IQR
CO (ppm)	3652	0.7	0.4	0.6	0.4
NO_2 (ppb)	3652	21.9	9.4	19.7	12.8
SO_2 (ppb)	3616	2.6	1.8	2.2	2.3
O_3 (ppb)	3652	18.6	9.3	17.8	14.0
PM_{10} (μg/m^3)	2813	22.6	13.1	19.4	15.0
$PM_{2.5}$ (μg/m^3)	1444	8.5	6.2	7.2	6.2
Temperature (°C)	3652	3.9	11.9	5.4	17.9
Relative humidity (%)	3652	66.0	13.6	66.1	18.5

Data were gathered in Edmonton from April 1, 1992, to March 31, 2002.

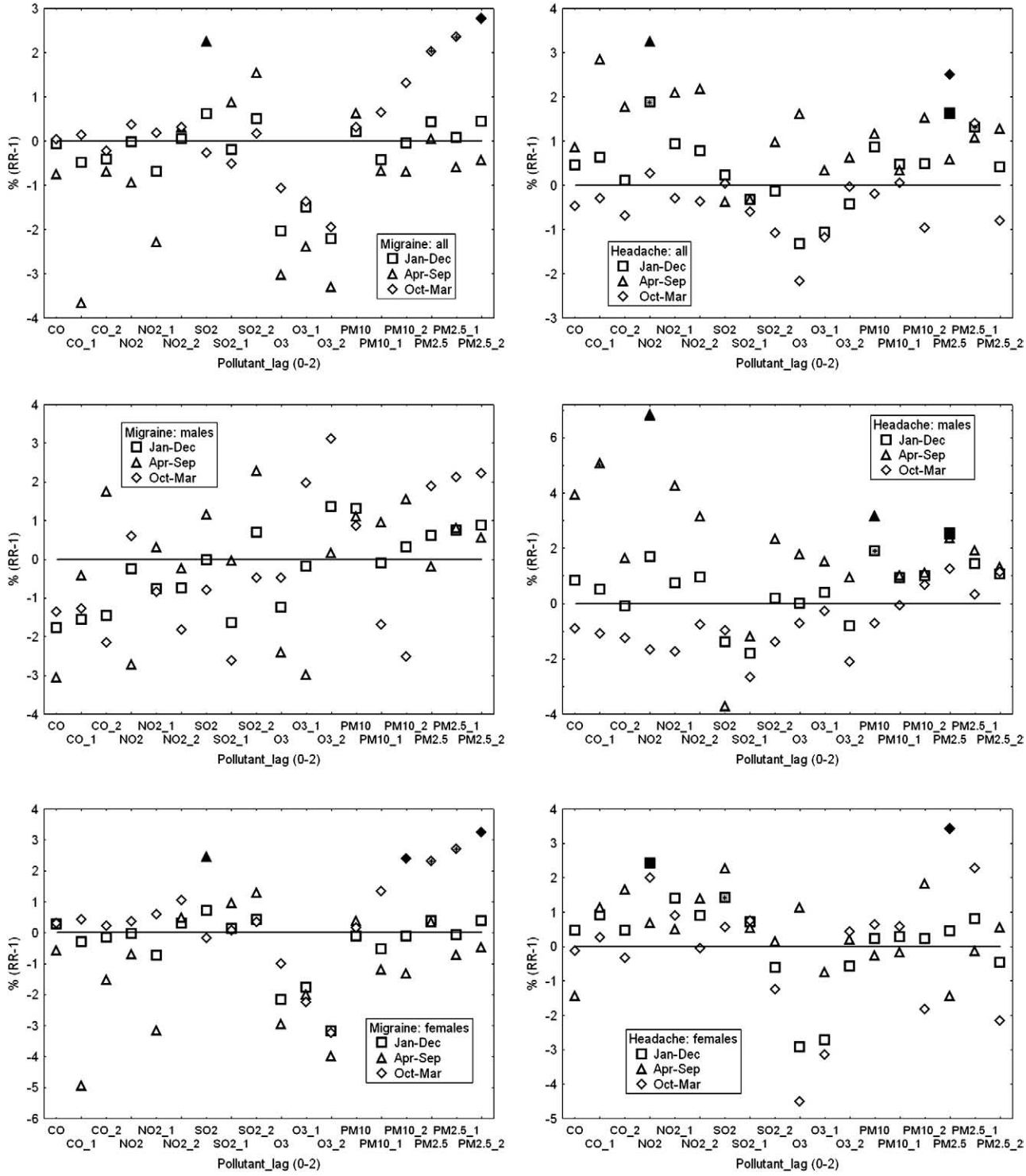

Fig. 1 The excess risk [%(RR-1)] by pollutants (lagged by 0-2 days), sex, and season. The bolded symbols indicate positive results, where $P \leq .05$ (black) and $.05 \leq P \leq .1$ (gray).

(GLMM) methodology [11,12]. We first defined clusters based on the following triplet {year, month, day of week}. Our clusters may have 4 or 5 observations (days). The clusters have a hierarchical structure: days are nested in days of the week, which are nested in months, and months are nested in years. The days of the same day of the week, in the same month, and in the same year are grouped in 1 cluster. We applied a Poisson model to clustered counts. We assumed fixed slope and random intercept on the constructed clusters. As a sensitivity analysis, we used 2 alternative adjustments for temperature and relative humidity: (a) linear and (b) nonlinear (natural cubic splines with 3 degrees of freedom).

Table 3 The percentage change in risk [%(RR-1)] for ED visits for migraine, in relation to an increase in the IQR of ambient air pollutants in Edmonton, adjusted for relative humidity and temperature

Adjusted form			Linear		Spline	
Pollutant_lag	Season	Gender	% (RR-1)	95% CI	% (RR-1)	95% CI
SO2	Warm	All	2.3	0.4, 4.2	2.2	0.2, 4.1
SO2	Warm	Female	2.5	0.3, 4.6	2.3	0.1, 4.5
PM10_2	Cold	Female	2.2	0.2, 4.6	2.4	0.2, 4.6
PM2.5	Cold	All	2.0	−0.3, 3.3	2.1	−0.2, 4.6
PM2.5_1	Cold	All	2.4	0.0, 4.8	2.4	0.0, 4.8
PM2.5_2	Cold	All	2.8	0.5, 5.2	3.0	0.6, 5.4
PM2.5	Cold	Female	2.3	−0.4, 5.1	2.2	−0.5, 5.1
PM2.5_1	Cold	Female	2.7	0.0, 5.5	2.5	−0.2, 5.4
PM2.5_2	Cold	Female	3.3	0.6, 6.0	3.2	0.5, 6.1

The results are presented for all period (January-December), warm period (April-September), and cold period (October-March) by sex.

Among existing software that realizes the GLMM technique, we have chosen the *glmmPQL* function from the R statistical package [13].

Relative risk (RR) of ED visits for migraine and headache attributable to each single pollutant and weather factors using current day exposure level, as well as 1- and 2-day lagged exposure levels, was estimated for an increase in pollutant concentration equal to the interquartile range (IQR). Results are expressed as excess risk: percentage changes in daily visits associated with the pollutant (RR-1) after adjusting for the effects of temperature and relative humidity. The 95% confidence intervals (CI) were also calculated.

2. Results

Table 1 contains the number of ED visits for migraine and headache by age and sex. *Migraine*: Of the 56 241 total visits for migraine in the study, 78.5% (n = 44 132) occurred among females. Between 1992 and 2002, the percentage of the number of visits to ED for migraine, by month, ranged from 7.5% in December to 9.0% in August. Percentage of total visits by days of the week ranged from 13.3% on Fridays to 15.7% on Sundays (14.0% on Saturdays). *Headache*: The table also contains the number of ED visits for headache by age and sex. Of the 48 022 total visits in the study, 56.3% (n = 27 031) occurred among females. Between 1992 and 2002, the percentage of the number of ED visits for headache, by month, ranged from 7.8% in July to 8.7% in October. Percentage of total visits by days of the week ranged from 14.0% on Saturdays to 14.7% on Sundays.

Table 2 provides a summary of ambient air pollutants and weather variables, including the number of days for which the values were available. Fig. 1 illustrates the results, by sex (both sexes, males, females) and season (all: January-December, warm: April-September, cold: October-March) for all the considered pollutants and their lagged values (none, 1-day, 2-day). The values of the excess risk [%(RR-1)] are shown. Tables

Table 4 The percentage change in risk [%(RR-1)] for ED visits for headache, in relation to an increase in the IQR of ambient air pollutants in Edmonton, adjusted for relative humidity and temperature

Adjusted form			Linear		Spline	
Pollutant_lag	Period	Gender	%(RR-1)	95% CI	%(RR-1)	95% CI
CO_1	Warm	Male	5.1	−0.5, 11.0	5.3	−0.2, 11.2
NO2	All	All	1.9	0.3, 3.5	1.6	−0.1, 3.3
NO2	All	Female	2.4	0.4, 4.6	2.3	0.1, 4.5
NO2	Warm	All	3.3	−0.1, 6.7	3.6	0.2, 4.8
NO2	Warm	Male	6.8	1.5, 12.5	7.0	1.7, 12.7
SO2	All	Female	1.4	−0.3, 3.1	1.4	−0.3, 3.1
PM10	All	Male	1.9	−0.2, 4.1	1.8	−0.4, 4.7
PM10	Warm	Male	3.2	0.2, 6.3	3.1	0.1, 6.2
PM2.5	All	All	1.6	0.2, 3.1	2.0	0.4, 3.5
PM2.5_1	All	All	1.3	−0.2, 2.8	1.7	0.2, 3.3
PM2.5	All	Male	2.5	0.3, 4.8	2.5	0.2, 4.8
PM2.5	Cold	All	2.5	0.2, 4.9	2.7	0.3, 5.1
PM2.5	Cold	Female	3.4	0.3, 6.6	4.1	0.9, 7.3

The results are presented for all period (January-December), warm period (April-September), and cold period (October-March) by sex.

3 and 4 present selected results from Fig. 1 that are positive and statistically significant ($P \leq .1$). For migraine visits, $PM_{2.5}$ exhibited the most consistent association over multiple lags in the cold season, for both females alone and together with males. Associations with SO_2 were also observed, but only at lag 0 in the warm season. With respect to headache visits, the largest effects were associated with CO and NO_2 at lag 0, for visits by males in the warm season. Effects of $PM_{2.5}$ were observed at lags 0 and 1 for females and males combined and for males alone at lag 0. Results for both migraine and headache were generally insensitive to the treatment of weather variables as linear vs nonlinear.

3. Discussion

In this study, the short-term effects of outdoor air pollution on daily ED visits for migraine and headache in a Western Canadian regional health authority were examined. Females between the age of 20 and 50 accounted for the majority of visits for migraine, which is consistent with published data on the epidemiology of migraine [14], whereas visits for headache were more evenly distributed by sex and age. Our observation of positive, statistically significant associations of air pollution with migraine visits for females but not males and with headache visits for both males and females may therefore be a function of statistical power.

Particulate matter exhibited the most consistent association over multiple lags with both migraine and headache, despite fewer available observations for this pollutant. Particulate matter is known to be associated with a variety of acute and chronic respiratory and cardiovascular effects through diverse pathophysiological mechanisms including inflammation (oxidative stress and neurogenic mechanisms), translocation of particles outside the respiratory system, and effects on coagulation, endothelial function, and autonomic function [15]. An association between exposure to SO_2 and ED visits for migraine, for females, was also observed. The association of reduced sulfur compounds with headache has been previously reported in the literature; based on a cross-sectional survey, headache was more common in a neighborhood with a pulp mill compared with one without [16]. For ED visits for headache, a significant association was found for males, for exposure to NO_2 as well as a slightly weaker association with CO, both of which are vehicle-related pollutants. CO and NO_2 were associated with ED visits for stroke in a previous analysis of data from Edmonton [17]. In previous studies of ED visits in Ottawa, CO, NO_2, and SO_2 exhibited associations with headache [18], whereas no associations were observed between migraine visits and weather [19]. Associations with particulate matter were not examined.

A recent clinical practice guideline concluded that in the minority of episodes in which specific triggers of migraine are identified, the most common are stress or relaxation after stress, change of habit, dietary factors (certain alcoholic drinks or cheeses), light, noise, and menstruation [4]. Persons who have migraine commonly also identify weather, odors, smoke, and heat [20]. Importantly, there is increasing evidence of the role of inflammation in migraine headache, evident from randomized controlled trials of treatment with corticosteroids such as dexamethasone [21-23]. Whether air pollution or other environmental factors potentially act as nonspecific stressors or through specific pathophysiological mechanisms remains to be determined.

Limitations of this study are typical of this type of research. They include the adequacy of the statistical model and impact of measurement error in the exposure to pollutants and weather factors and outcome variables (particularly the complexity of the diagnosis of headache syndromes). Fixed-site monitors provide daily pollution exposures of ambient air pollution and are applied to represent average population exposure. Edmonton is a large city geographically, and thus, fixed-site monitors will not fully reflect variation in exposure between individuals. Similarly, individual data on potentially important effect modifiers such as medication use, socioeconomic status, race, and comorbidity were not available. At the same time, the presented results are based on methodology consistent with time-series and case-crossover analysis, which are widely accepted. The proposition to use the GLMM technique based on the triplet {year, month, day of week} was previously presented [9]. We have conducted numerous hypothesis tests, increasing the risk of false-positive results, but have attempted to highlight those exhibiting greatest consistency over multiple lags. Pollutants exhibit correlations with one another to the extent that they originate from common sources, making it difficult to singularly attribute observed associations to individual pollutants. Many episodes of migraine or headache do not result in an ED visit; thus, our findings are not generalizable to all such episodes. Finally, because few studies have examined the association between migraine or headache and air pollution, our findings should be replicated in other settings before a causal association can be established and appropriately translated into recommendations for clinical management of these conditions.

Acknowledgments

The authors acknowledge Environment Canada for providing the air pollution data from the National Air Pollution Surveillance network. They appreciate the efforts of Ms Chris Houston from Information Services, Capital Health, and Ms Virginia Willis, from the Emergency Medicine Research Group (EMeRG), for securing these data and to Health Canada for funding data acquisition. Ms Lela Gary suggested the hypothesis.

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