

AMBIENT SULPHUR DIOXIDE EXPOSURE AND EMERGENCY DEPARTMENT VISITS FOR MIGRAINE IN VANCOUVER, CANADA

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Abstract

Objectives: Ambient exposure to sulphur dioxide (SO₂) has been previously associated with emergency department (ED) visits for migraine headaches. In the present study, the objective was to examine the relationship between ED visits for migraine and ambient sulphur dioxide concentrations. **Design and Methods:** This was a time-series study of 1 059 ED visits for migraine (ICD-9: 346) recorded at a Vancouver hospital between 1999 and 2003 (1 520 days). Air pollution levels of SO₂ were measured by fixed-site monitoring stations. The generalized linear mixed models technique was applied to regress daily counts of ED visits for migraine on the levels of the pollutant after adjusting for meteorological conditions: temperature and relative humidity. The analysis was stratified by season and gender. **Results:** Positive and statistically significant correlations were observed for SO₂ exposure and ED visits for migraine for females during colder months (October–March). The percentage increase in daily visits was 16.8% (95% CI: 1.2–34.8) for a 4-day average (of daily mean concentrations) SO₂ level, for an interquartile range (IQR) increase of 1.9 ppb. **Conclusions:** Our findings provide additional support for a consistent correlation between migraine headache and air pollution (SO₂).

Key words:

Air pollution, Urban, Migraine, Mixed models, Emergency department visit, Sulphur dioxide

INTRODUCTION

Migraine headache is a common clinical problem, an important cause of morbidity in our society, and its treatment consumes considerable health care and personal resources. Migraine triggers include weather [1], fatigue, stress, food, menstruation, and infections [2]. Air quality in the home [3], office environment [4,5], and occupational setting may play a role in the exacerbations of migraine headache [6]. A daily diary study of 32 headache sufferers in Italy revealed that the severity and frequency of headaches correlated with days when elevated concentrations

of carbon monoxide and nitrogen dioxide were recorded [7]. In another study, the headache reported was more common in a neighborhood with a pulp mill, compared to one without [8]. In general, the evidence would suggest that air quality may play an important role as a trigger for exacerbations in patients suffering from chronic migraine headache.

The purpose of the present study was to assess the relationship between urban outdoor air pollution and emergency visits for migraine headaches in Vancouver, Canada. The study was based on data on ED visits for migraine

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recorded over a period of four years and two months. The goal was to examine the hypothesis that ambient air pollution exposure to sulphur dioxide (SO₂) may trigger migraine attacks.

MATERIALS AND METHODS

Study Population

The study population consisted of the population serviced by St. Paul's hospital, Vancouver, British Columbia, between January 1, 1999 and February 28, 2003. During that period of time, St. Paul's hospital serviced approximately 53 000 patients per year, with an admission rate of 15%. The hospital was staffed by full-time emergency physicians. They coded ED charts applying a pick list of accepted discharges, including migraine headache, based on the International Classification of Diseases, 9th revision (ICD-9) code 346.X [9]. In total, the analysis was based on 1 059 ED visits for migraine over a span of 1 520 days. This represented approximately 0.5% of all the recorded ED visits to this hospital during the study period.

Meteorological Data

Environment Canada supplied hourly data for relative humidity, temperature (dry bulb) and atmospheric pressure (at sea level) for the city of Vancouver. We used the daily mean of these weather parameters.

Air Pollution Data

Hourly air pollution data (SO₂) were obtained from 11 fixed continuous monitoring stations in Vancouver. These data were supplied by Environment Canada. During the study period (4 years and 2 months) the number of monitoring stations that reported air pollution data ranged from 4 to 11. The distance of the stations from the hospital varied between 3 and 43 kilometres. The configuration of the monitoring stations was carefully determined in the past for a larger study related to ED visits for cardio-pulmonary problems. The daily shared exposures of the population were expressed as mean values among the stations.

Statistical Methods

To relate the short-term effects of air pollution to the number of daily ED visits for migraine, we applied the time-series methodology. We first removed the smoothed seasonal cycles, secular trends, and day of the week effects to produce the time-series of logarithm of ED admissions. Bartlett's test was used to qualify the best fitted model [10]. Natural splines were applied to smooth the effect of all the continuous covariates. We built models with a single pollutant and different combinations of continuous weather covariates. The model with the lowest Akaike's Information Criterion (AIC) value was selected [11]. The analysis was performed using S-Plus software [12]. The generalized linear model (GLM) techniques were implemented using the *gam* function in the S-plus package. The *gam* function was used with natural splines and with a very conservative convergence criterion [12]. This statistical approach was only used to investigate and confirm a pattern in the potential correlations between exposures and ED visits.

In addition, in the second stage of our analysis, another statistical method was used. The generalized linear mixed models (GLMM) technique was applied to the defined clusters. The clusters grouped the days according to the triplet {year, month, day of week} with a hierarchical nested structure. The final calculations were performed using this methodology, based on hierarchical cluster modeling [13]. The calculations on clusters were executed using the R statistical software [14]. The use of two different statistical methods was justified by the sample size. We had a relatively small number of counts of ED visits for migraine. Therefore, we felt more confident when two different methods showed similar correlations. In the reported results (Table 3), the meteorological components, namely temperature and relative humidity, were incorporated into the models in the form of a natural spline with three degrees of freedom.

Air pollutant concentrations were expressed in several ways: current-day exposure level (lag = 0), lagged exposures (lag = 1–10 days, separately), and average (0-n)-day lagged air pollutants for n = 1, 2, ..., 10, respectively. We calculated the percentage increase (%RR) in ED visits for migraine for an interquartile range (IQR) increase in SO₂ concentration. Our analysis was also stratified by age, gender, and season.

RESULTS

Sub-group analyses

Table 1 displays the number of migraine-related ED visits by age and sex. Of the 1 059 total visits considered in the study, 691 (65%) referred to females. Between 1999 and 2003, the mean number of ED visits for migraine, by month, ranged from 26.1 in July to 16.0 in June. The percentage of total visits by the days of the week changed from 16.4% on Sundays (15.5% on Saturdays) to 11.9% on Thursdays.

The mean values and standard deviations (SD) for the variables included in the study are presented in Table 2. The mean frequency of ED visits for migraine was 0.7 per day (SD = 0.9).

Table 1. Frequency of ED visits for migraine by age group and gender, St. Paul's Hospital in Vancouver, January 1, 1999 to February 28, 2003

Age	No. visits	%Visits	Female	Male
0-19	34	3.2	26	8
20-29	294	27.8	201	93
30-39	326	30.8	193	133
40-49	252	23.8	162	90
50-59	130	12.3	89	41
60-69	14	1.3	12	2
70-79	4	0.4	3	1
80-80+	5	0.5	5	0
Total	1,059	100	691	368

Table 2. Mean, standard deviation (SD), and interquartile range (75th-25th, IQR) of daily average concentration of air pollutants (SO₂), weather variables, and ED visits for migraine. Vancouver, January 1, 1999 to February 28, 2003

Variable (unit)	Mean	SD	IQR
Migraine (N = 1.059)	0.7	0.9	
Air pollutants			
SO ₂ (ppb)	6.1	4.8	1.9
Weather parameters			
Temperature (°C)	7.7	11.4	8.6
Relative Humidity (%)	70.7	12.5	13.4
Pressure (kPa)	101.1	0.8	0.8

Environmental Correlations

Figure 1 shows the results from the time-series approach (GLM) applied to all visits for all periods (January-December). In the figure, the x-axis is labelled as follows: SO21 means SO₂ lagged by 1 day, etc.; SO2a1 means the average of the same day and 1-day lagged SO₂, etc., respectively. Although none of the daily lags or averages were significant, the time-series analysis indicated that the current-day exposure (lag = 0) and the 4-day average

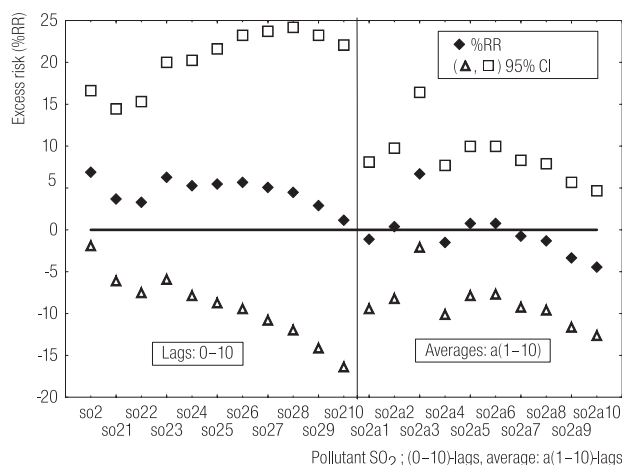


Fig. 1. The excess risks (%RR) and their 95% CIs for exposures expressed as lagged values (0-10 — day) and cumulative averages (a1-a10).

Table 3. The excess risks (%RR) and their 95% CIs for ED visits for migraine, in relation to an increase in the IQR of ambient SO₂ in Vancouver. The results are presented for all periods (January-December), warm periods (April-September) and cold periods (October-March) by gender (All, Male, Female)

Period	Gender					
	All		Male		Female	
	%RR	95% CI	%RR	95% CI	%RR	95% CI
All						
SO2	6.9	-1.2-15.6	7.4	-5.2-21.6	8.5	-1.3-19.3
SO2a3	6.9	-3.3-18.1	4.7	-10.4-22.4	10.4	-1.7-24.0
Warm						
SO2	6.2	-5.9-19.9	<S>	<S>	6.7	-7.7-23.4
SO2a3	4.2	-11.1-22.3	8.7	-14.5-38.2	5.7	-12.6-27.9
Cold						
SO2	<S>	<S>	10.0	-7.2-30.3	13.0	-0.2-28.0
SO2a3	11.2	-2.7-27.1	7.8	-11.8-31.9	16.8	1.2-34.8

<S> — problem with calculations (singularity).

SO2a3 — average of (0-3)-day concentrations.

(0 to 3) had the highest risk estimates. Thus, these exposures were chosen for evaluation in our hierarchical models. Table 3 demonstrates the results generated by the GLMM technique realized on the hierarchical clusters. Table 3 shows that the concentration levels of the 4-day average of SO₂ led to significantly higher rates of ED visits for migraine headache in women during the colder season (%RR = 16.8; 95% CI: 1.2–34.8).

Sensitivity Analyses

We used the daily maximum value of SO₂ among the monitoring stations to represent exposure (IQR = 10.0 ppb) in the sensitivity analysis. From the time-series analysis (GLM), we obtained 5.6% (95% CI: –1.3–13.0) for the same-day average, and 11.0% (95% CI: 0.2–23.0) for the 4-day average. We also restricted our monitors for the distance from the hospital and included data only if the distance was less than 13 km. In this case, we obtained the estimates of 5.9% (95% CI: –1.0–13.2) and 11.8% (95% CI: 0.9–23.9), respectively.

DISCUSSION AND CONCLUSIONS

We detected significant correlations between ambient SO₂ concentrations and ED visits for migraine headache for females during the cold period (October–March). The SO₂ correlation was identified using the 4-day average of the mean values. Although not statistically significant, the majority of correlations between SO₂ and ED visits for migraine were positive. In addition, our sensitivity analysis, employing daily maximum values for SO₂, provides further evidence that the relationship is valid. The correlation between SO₂ and ED visits for women with migraine headaches was consistent with prior studies that demonstrated a relationship between SO₂ and ED visits for migraines in Edmonton, Canada [15].

The advantages of this study design included control of temporal trends, which may have confounded the results such as season, day of the week, measures of relative humidity, and temperature. Moreover, we used two independent statistical approaches: the time-series (GLM) and hierarchical clusters (GLMM) [16,17]. The time-

series analysis suggested a trend towards the 4-day average of SO₂, which was substantiated in the hierarchical models when the data were stratified by gender and season.

The mechanism by which air pollution may trigger migraine headaches is not completely clear. Migraine headaches may be mediated by neurogenic inflammation which can be initiated by air pollutants [18]. Furthermore, air pollutants have been shown to impair the endothelial-dependent vasodilation [19], which may contribute to the onset of migraine headaches. Migraine headaches occur more commonly in women [20,21].

The gender difference observed for migraine headaches is in part due to estrogen, which is an important hormonal modulator of endothelial vasodilation and is believed to contribute to the occurrence of migraine headaches [22]. Air pollution has also been shown to have estrogenic effects [23], which may explain why this and other studies demonstrated significant findings primarily in women [14]. Alternatively, 2/3 of our study population were women and thus the study may not have been powered to detect the effects in men. For example, in both men and women, the higher concentrations of the 4-day average of SO₂ were correlated with a greater than 10% excess risk of migraine headaches, but this was only significant in women.

There are several limitations of this study. First, the fixed-site monitoring stations provide daily pollution exposures of ambient air pollutants and are applied to represent average population exposure. Vancouver is a large city geographically and thus the fixed-site monitors will not fully reflect the variation in exposure between individuals. Second, individual data on the potentially important effect modifiers such as medication use, socio-economic status, race and co-morbidity were not available from this database. Third, we have conducted numerous hypothesis tests, which increased the risk of false positive results; however, we have attempted to highlight those exhibiting the highest consistency with other research findings. Fourth, air pollutants exhibit correlations with one another to the extent that they originate from common sources, making it difficult to singularly attribute the observed correlations to individual pollutants. Fifth,

many episodes of migraine and/or general headache do not result in an ED visit, thus our findings cannot be generalized to all such episodes. Finally, because few studies have examined the correlation between migraine or headache and air pollution, our findings should be replicated in other settings before a causal association can be established.

In our study, ambient SO₂ concentrations strongly correlated with ED visits for migraine headache, especially for females during the cold months of the year (October–March) in one Canadian urban emergency department.

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