

The effect of weather and air pollution on the prevalence of headaches

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Abstract

Background: Some epidemiological studies have indicated that weather and air pollution can cause adverse health conditions and that these effects can exhibit regional variation. The prevalence of headache is so high and it is a common cause of morbidity. Therefore, this study evaluated whether weather and air pollution were associated with the prevalence of headaches. **Methods:** A symmetric bidirectional case-crossover design was applied, using conditional logistic regression models to determine the association between headaches and weather and air pollution. From January 2006 to August 2007, a total of 245 patients with headaches were recruited. Headache subtypes were classified as migraine, tension-type headaches, and others. Meteorological data (average temperature and relative humidity) and values related to air pollutants (CO, NO₂, O₃, SO₂, and particulate matter with an aerodynamic diameter of less than 10 μm) were obtained. **Results:** Higher average temperatures were associated with the total number of headaches (hazard ratio 1.124-1.130; P<0.001). With regard to headache subtype, O₃ seems to provoke headaches, especially those related to tension and those listed as other headache varieties. Conversely, other pollutants, especially CO and SO₂, showed the opposite association. **Conclusions:** These findings indicated that temperature and some air pollutants are able to affect headaches, suggesting that weather and air pollution levels seem to have an effect on the risk of headache.

INTRODUCTION

Headaches are painful symptoms that virtually everyone experiences at one time or other, and they represent an enormous source of morbidity.¹⁻³ An epidemiologic study in South Korea reported the prevalence of headache was as much as 68%.² There is increasing evidence that weather and air pollution are associated with adverse health effects.⁴⁻⁷ Therefore, it is important for us to know how much weather and air pollution affect highly prevalent conditions such as headaches.

However, it remains controversial whether weather and air pollution are associated with headache.⁸⁻¹⁹ Furthermore, most previous studies have been predominantly conducted in Western cities and therefore, their findings might not necessarily apply to Asia including Korea, where both weather and environment pollutants are different.

To investigate the nature of this relationship, we evaluated patients with headaches who had visited an out-patient clinic and had given us exact information regarding the onset of headache among individuals residing in South Korea.

METHODS

Consecutive patients with headaches, who had provided daily headache calendars, were prospectively recruited from the out-patient headache clinic in the Department of Neurology at Korea University Ansan Hospital, from January 1st, 2006 to August 31st, 2007. All patients underwent a standardized interview using a structured questionnaire as well as clinical neurological and psychiatric examinations by neurologists, as previously described.²⁰ All patients filled in headache diaries in which they documented for each day whether or not they had experienced a headache. Those who were not living in Ansan city at the time they filled in their diaries were excluded.

The diagnosis of headache was made according to the International Classification of Headache Disorders 2nd edition²¹ and was categorized into migraine with or without aura as Migraine, tension-type headache as TTHA, and all the other primary headaches including cluster headaches and headaches attributed to somatization disorder as Others.³ Among 245 headache patients, there

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were 33 Migraines, 143 TTHAs, and 69 Others. Among the total, 145 patients (59.2%) were women. The mean age of all patients was 45.9 ± 14.2 years and the mean frequency of headache was 1.9 ± 3.2 attacks per month. All patients were informed of the procedure, and informed consent was obtained from all subjects in accordance with the guidelines of the institutional review board at Korea University Medical Center.

Exposure assessment

Ansan, located in the southern part of Gyeonggi-do province, South Korea, comprises rural and urban areas and is now included as a part of the Seoul metropolitan area. Ansan has a 4-season climate and an annual temperature range of -15.1°C to 35.8°C . Meteorologic data (mean temperature, maximum temperature, minimum temperature, and relative humidity) were obtained from the daily surface observations at meteorological monitoring stations in South Korea.²² Further, hourly measures of carbon monoxide (CO, 0.1 ppm), nitrogen dioxide (NO₂, ppb), ozone (O₃, ppb), sulfur dioxide (SO₂, ppb), and fine particulate matter with an aerodynamic diameter of less than 10 μm (PM₁₀, $\mu\text{g}/\text{m}^3$) were obtained at stationary ambient monitoring sites in South Korea.²³ For each day, weather and air pollution data were extracted from all monitoring stations, data which were provided by the National Institute of Environmental Research of Korea and the Korea Meteorological Administration.

Statistical analysis

The data were analyzed using the case-crossover technique.²⁴⁻²⁶ This design is an alternative to Poisson time-series regression models for studying the short-term effects attributed to air pollutants.²⁷ It is generally suitable for studying relations with a short time interval of individual exposure, a disease with abrupt onset and short latency for detections, and a short induction period. Because cases serve as their own controls, the design eliminates confounding by stable individual characteristics and bidirectional selection of control periods allows individual adjustment for seasonal or secular trends. Moreover, the symmetric bidirectional case-crossover design can substantially control for confounding by linear long-term trends and/or seasonality of an exposure variables by design. In this study, a bidirectional case-crossover design with conditional logistic regression model^{24,28} was used to determine the relationship between weather or air pollutants

and headaches recorded in the patients' diaries. Control periods were chosen using a bidirectional paired matching technique 7, 14, and 21 days before and after the first case periods. Hence, we present hazard ratios (HR) and 95% confidence intervals (95%CI) associated with an increment of 1 ppb in the case of O₃, SO₂ and NO₂, with an increment of 0.1 ppm in the case of CO, or with an increment of 1 $\mu\text{g}/\text{m}^3$ in the case of PM₁₀ in 24-hour mean levels of exposure. HR and 95%CI were obtained using SAS 9.1 though the PHREG procedure. We used the first headaches as the primary outcome of interest. In all cases, we employed distributed lag models, in which we examined the associations of exposure in the 24-48 hour (lag 1 day), 48-72 hour (lag 2 day), and 72-96 hour (lag 3 day) periods preceding the first headache. The 24hr mean values, 24hr maximum values, and 8hr mean values of five pollutants were analyzed using one- and two- pollutant models with adjustment for daily average temperature and relative humidity. As such, in the one pollutant model, we analyzed three variables (average temperature, relative humidity, and one pollutant), whereas four variables with two pollutants were used in the two pollutant model.

RESULTS

Table 1 summarizes ambient levels of meteorologic variables (average temperature and relative humidity) as well as pollutant variables (CO, NO₂, O₃, SO₂, and PM₁₀) during the time period of the study. Table 2 indicates the pair-wise Pearson correlation coefficients among these variables. Average temperature was moderately correlated with relative humidity ($r=0.458$, $P<0.001$) and levels of pollutants tended to be at least moderately correlated with each other, particularly for the pairs of NO₂ with SO₂, SO₂ with CO, and CO with NO₂. However, O₃ was negatively correlated with NO₂ ($r=-0.506$, $P<0.001$) and levels of CO and NO₂ were also negatively correlated with average ambient temperature ($r=-0.526$, $P<0.001$ and $r=-0.326$, $P<0.001$, respectively).

With respect to the relationship with headaches, temperature was the most powerful predictor (HR 1.124-1.130; $P<0.001$), in both the one- and two-pollutant models. For the subtypes of headache, temperature was associated with TTHAs and Others, but it was not statistically associated with Migraines. Table 3 shows an example of the one pollutant model involving three variables (average temperature, relative humidity, and 24hr mean O₃) indicating that average temperature as well

Table 1: Distribution of air pollutants and meteorological data

	Mean (SD)	Min	25 th Percentile	Median	75 th Percentile	Max
Temperature (°C)	13.1 (9.3)	-11.2	5.0	14.2	21.3	28.5
Relative humidity (%)	68.4 (14.5)	25.8	57.1	69.9	80.0	97.5
CO (ppb)	6.54 (3.00)	2.13	4.48	5.76	7.48	18.86
NO ₂ (ppb)	27.90 (12.30)	6.57	18.42	25.62	34.90	72.50
O ₃ (ppb)	21.51 (11.25)	3.52	12.86	20.16	28.83	72.38
PM ₁₀ (µg/m ³)	71.41 (44.91)	14.93	44.71	65.10	89.82	628.33
SO ₂ (ppµb)	6.90 (2.83)	1.90	4.88	6.50	8.29	20.13

as 24hr mean O₃ concentration were associated with the occurrence of headaches.

Figure 1 demonstrates the risk of headache with 24hr mean values of each pollutant for an increment of 1µg/m³ for PM₁₀, 0.1 ppm for CO, and an increment of 1 ppb for the other pollutants (SO₂, O₃, and NO₂), using one pollutant models and lag 1 to 3 models. Figure 2 demonstrates the risk of five pollutants with respect to headaches. The higher 24hr mean value of O₃ increased the risk of headache (HR for an increment of 1 ppb calculated from all groups in ‘lag 1’ – ‘one pollutant’ model, 1.014; 95%CI, 1.003-1.025). In particular, O₃ was associated with TTHAs and Others. Conversely, other pollutants such as CO or SO₂, showed some opposite effects to some degree.

DISCUSSION

This study represents one of few studies on the effects of weather and air pollution on headaches as indicated by out-patient headache clinic

visits in Asia. Data showed that higher ambient temperature increased the risk of headache. There was also the association of TTHAs and Others with ozone. However, we did not find a clear association between any other air pollutants and headache.

In this study, a bidirectional case-crossover design with conditional logistic regression model was used to determine the relationship between weather and air pollutants, and headaches. With regard to methodology, a case crossover design has been suggested because of the transient effect of brief exposure on the occurrence of an acute-onset disease.²⁴ There have been a few studies which used this method and evaluated air pollution and subjects with headaches. These focused only on those who visited emergency departments and these individuals were recruited without determining the timing of actual symptom onset.¹³

Several triggering factors for headache have been identified, which include environmental

Table 2: Pearson correlation coefficients for 24hr means of weather and air pollutants

	CO	NO ₂	O ₃	PM ₁₀	SO ₂	Temperature	Humidity
CO	1.000	0.712*	-0.395*	0.478*	0.687*	-0.526*	-0.146*
NO ₂		1.000	-0.506*	0.298*	0.618*	-0.326*	-0.285*
O ₃			1.000	0.066	-0.169*	0.395*	0.100*
PM ₁₀				1.000	0.477*	-0.150*	0.001
SO ₂					1.000	-0.350*	-0.134*
Temperature						1.000	0.458*
Humidity							1.000

*P<0.05

Table 3: An example of a one pollutant model, using the mean value of ozone (O₃) during a single day

	Total (lag1/lag2/lag3)	Migraine (lag1/lag2/lag3)	TTHA (lag1/lag2/lag3)	Others (lag1/lag2/lag3)
Temperature	1.124(1.086-1.163)* /1.127(1.089-1.166)* /1.130(1.092-1.170)*	0.978(0.886-1.080) /0.905(0.816-1.004) /0.931(0.843-1.028)	1.086(1.034-1.141)* /1.056(1.006-1.108)* /1.043(0.995-1.094)	1.187(1.104-1.277)* /1.107(1.029-1.190)* /1.087(1.018-1.161)*
Humidity	1.000(0.992-1.008) /0.999(0.991-1.007) /1.000(0.992-1.007)	0.984(0.959-1.010) /1.008(0.981-1.036) /1.003(0.976-1.030)	0.997(0.986-1.008) /0.997(0.986-1.009) /1.006(0.995-1.017)	0.984(0.968-0.999) /0.985(0.970-1.000) /0.988(0.974-1.002)
O ₃	1.014(1.003-1.025)* /1.010(0.997-1.022) /1.004(0.992-1.016)	1.010(0.974-1.047) /1.004(0.968-1.041) /1.012(0.976-1.049)	1.039(1.023-1.056)* /1.018(1.001-1.035)* /1.022(1.005-1.040)*	1.008(0.986-1.030) /1.035(1.009-1.061)* /1.015(0.993-1.038)

*P<0.05. The value is expressed as hazard ratio with 95% confidence interval in parenthesis.

factors such as weather conditions and temperature, physical activity and psychological factors, sleep disturbance, and some food items.²⁹ Among the environmental factors, weather has been mentioned most often^{15, 16}; however, results regarding the relationship between weather and headache have been controversial.¹³⁻¹⁹ Some have shown that headaches were not related to weather conditions^{9,14}, while others have suggested an association, such as the finding of higher rates of migraines in warmer seasons¹⁷⁻¹⁹ more headaches requiring emergency department evaluation during period of higher temperature¹³, or the association of weather conditions and diagnostic symptoms with headache.¹⁵ In this study, higher ambient temperature was linked to the risk of headache and the potential is there for it to be used as a marker for headache risk. It is possible that previous inconsistent results may have stemmed from the issue as to whether headaches were directly caused by high ambient temperature or just whether this represented an epiphenomenon. For example, one study found that some patients were sensitive to high temperature with high humidity, while others were sensitive to low temperature with low humidity.³⁰

With regard to headache subtypes, we initially hypothesized that migraines might be the one with the closest association to weather and air pollution because they have been known to be associated with hyperexcitability.³¹ The interictal migraine brain seems to be hyperexcitable in regards to general sensory processing.³² Moreover, thermal pain threshold, especially in the forehead area during pre-attack period, is shown to be decreased in migraineurs.³³ Therefore, hot environment or weather might influence occurrences of headache

attacks in migraineurs. This is further supported by a recent study³⁴, which suggests that the brainstem nucleus cuneiformis is hypofunctional in interictal migraine patients and that a non-noxious thermal stimulus activates a brainstem modulatory region like nucleus cuneiformis. Hence, a non-noxious hot environment should activate the brainstem nucleus cuneiformis, but a hypofunctional nucleus cuneiformis in migraineurs seems to contribute to central sensitization during attacks through partial loss of inhibition and/or enhanced facilitation of ascending nociceptive pathways. However, this study demonstrated that weather and air pollution were actually associated with the other two types of headaches and not migraines. Because migraines may be associated with many other precipitating factors which were not controlled for in this study¹⁵, it is possible that the effects of weather and air pollution may have been blurred. With regard to tension-type headaches, the pathophysiological hypothesis has been put forth which states that increased myofascial pain sensitivity could be the result of the release of inflammatory mediators which result in excitation and sensitization of peripheral sensory afferents.³⁵ However, temperature can potentially act on headache through nonspecific inflammatory mediators or specific pathways through pain sensitivity mechanisms which remain to be determined.^{13,14}

There has been growing interest in the effects of air pollution on health conditions, due to the possibility that air pollution can be reduced or controlled using various methods. Air pollution represents a complex mix of pollutants, including both coarse and fine particles and gaseous constituents.¹³ Previous contradictory results

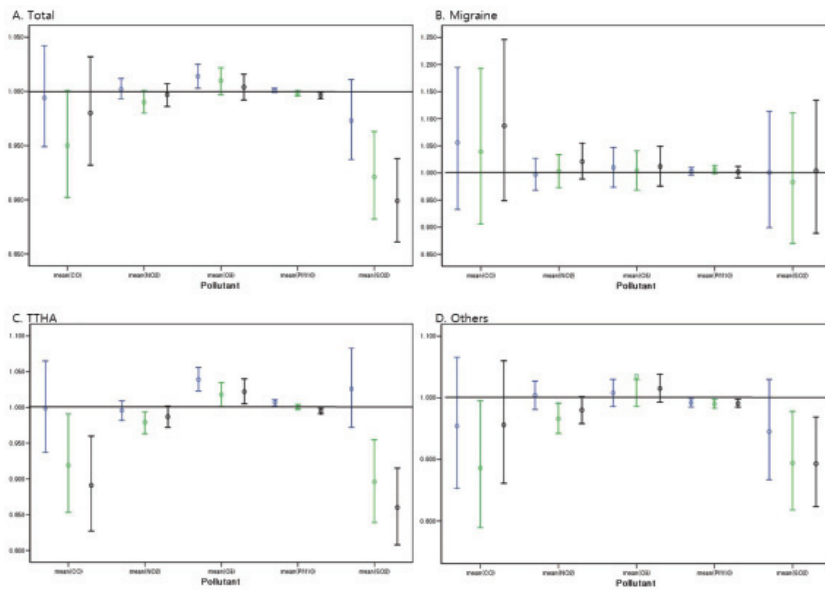


Figure 1: Hazard ratios of each headache with respect to pollutants.

Error bars indicate HR (hollow circles) and 95%CI (bars). Meteorological variables were included simultaneously as covariates in all models. Blue, green, and black represent for lags of 1, 2, and 3 days, respectively.

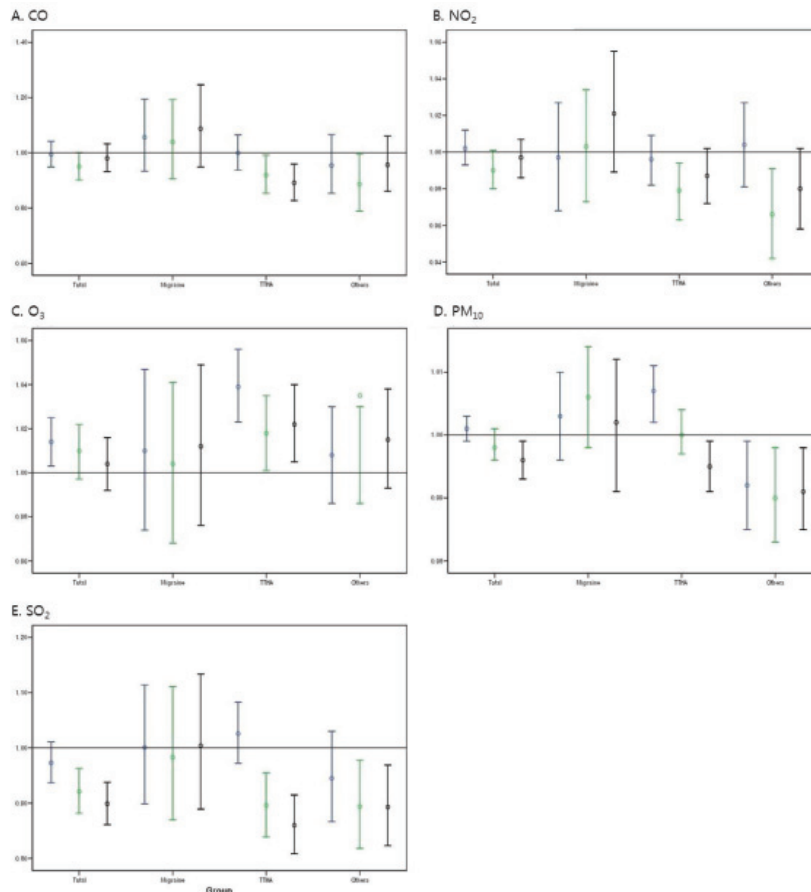


Figure 2: Hazard ratios of each pollutant with respect to headaches

Error bars indicate HR (hollow circles) and 95%CI (bars). Meteorological variables were included simultaneously as covariates in all models. Blue, green, and black represent for lags of 1, 2, and 3 days, respectively.

regarding the association of air pollution with the occurrence of headaches are perplexing. One study showed no association between air pollution and headaches¹³, whereas others reported that headaches could be caused by various pollutants.⁸⁻¹² The current study showed that ozone was associated with headaches. Ozone is a strong oxidizing agent formed in the troposphere through a complex series of reactions involving the action of sunlight on nitrogen dioxide and hydrocarbons. It has been known that ozone entrained into buildings from the outdoor air plays an important role in air quality and ambient ozone concentrations, and that health effects including headache have been identified.³⁶ However, the results of this study seem to be unusual with respect to other pollutants (CO, SO₂) which even though were previously known to provoke headache, correlated negatively here. We thought this opposite correlation may have been due to the levels of CO and SO₂ in opposition to observed temperature and ozone in this study. Another consideration is that most people would likely have been inside their homes or other buildings when the air pollution was worse, a consideration which was not assessed in this study.

The results of this study must be interpreted with caution. First, there were some methodological problems as well as important biological considerations in this type of study. Fixed-site monitors provided daily pollution exposures of ambient air pollution and were applied to represent average population exposure. Weather and air pollutants exhibited correlations with one another to the extent that they originated from common sources, making it difficult to singularly attribute observed associations to individual factors.¹² Further, Ansan is a large city geographically, and thus, fixed-site monitors may not have fully reflected variation in exposure between individuals. However, this kind of measurement error is known to cause a bias toward the null hypothesis and underestimates weather or air pollution effects.³⁷ Second, this study only evaluated those who came to our hospital, a sample which could differ from that of the general population of headache sufferers. However, compared to most previous studies for patients with headaches, in which subjects were selected from those who had visited emergency departments⁹⁻¹², this study should be more similar to the general population. Third, this study had a relatively small sample size. Although statistically significant, the association between headaches and weather or air pollution should be considered in

understanding the biological characteristics of headache. On the other hand, it is also important to recognize the expected magnitude of an effect when considering the lack of statistical association between weather or air pollutants and headache.¹³ Because the association between air pollution and risk was relative small, the precision of these estimates was generally insufficient to exclude an effect of that magnitude.^{13,38} Fourth, this study also did not control for many other factors, which have been known to be associated with headaches.³⁹ Individual data on the potentially important effects of modifiers such as medication use, socio-economic status, and co-morbidity were not available in this study. These limitations indicate that additional studies employing larger sample sizes and including other ethnic or environmental communities are needed to determine in detail the role of weather and air pollution in the occurrence of headaches.

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REFERENCES

1. Lipton RB. Prevalence of migraine and of headache. *Headache* 1996; 36:465.
2. Roh JK, Kim JS, Ahn YO. Epidemiologic and clinical characteristics of migraine and tension-type headache in Korea. *Headache* 1998; 38:356-65.
3. Park MH, Koh SB, Park MK, et al. A study on headache in an island area of Korea. *J Korean Neurol Assoc* 2003; 22:40-5.
4. Katsouyanni K, Touloumi G, Spix C, et al. Short-term effects of ambient sulphur dioxide and particulate matter on mortality in 12 European cities: results from time series data from the APHEA project. *Air Pollution and Health: a European Approach. BMJ* 1997; 314:1658-63.
5. Roberts S. A new model for investigating the mortality effects of multiple air pollutants in air pollution mortality time-series studies. *J Toxicol Environ Health A* 2006; 69:417-35.
6. Schwartz J. Air pollution and daily mortality: a review and meta analysis. *Environ Res* 1994; 64:36-52.
7. Samet J, Krewski D. Health effects associated with exposure to ambient air pollution. *J Toxicol Environ Health A* 2007; 70:227-42.
8. Nattero G, Enrico A. Outdoor pollution and headache. *Headache* 1996; 36:243-5.
9. Szyszkowicz M. Air pollution and daily emergency department visits for headache in Montreal, Canada. *Headache* 2008; 48:417-23.
10. Szyszkowicz M. Ambient air pollution and daily emergency department visits for headache in Ottawa, Canada. *Headache* 2008; 48:1076-81.
11. Szyszkowicz M, Rowe BH, Kaplan GG. Ambient

- sulphur dioxide exposure and emergency department visits for migraine in Vancouver, Canada. *Int J Occup Med Environ Health* 2009; 22:7-12.
12. Szyszkowicz M, Stieb DM, Rowe BH. Air pollution and daily ED visits for migraine and headache in Edmonton, Canada. *Am J Emerg Med* 2009; 27:391-6.
 13. Mukamal KJ, Wellenius GA, Suh HH, *et al.* Weather and air pollution as triggers of severe headaches. *Neurology* 2009; 72:922-7.
 14. Villeneuve PJ, Szyszkowicz M, Stieb D, *et al.* Weather and emergency room visits for migraine headaches in Ottawa, Canada. *Headache* 2006; 46:64-72.
 15. Spierings EL, Ranke AH, Honkoop PC. Precipitating and aggravating factors of migraine versus tension-type headache. *Headache* 2001; 41:554-8.
 16. Wober C, Holzhammer J, Zeitlhofer J, *et al.* Trigger factors of migraine and tension-type headache: experience and knowledge of the patients. *J Headache Pain* 2006; 7:188-95.
 17. Brewerton TD, George MS. A study of the seasonal variation of migraine. *Headache* 1990; 30:511-3.
 18. Salvesen R, Bekkelund SI. Migraine, as compared to other headaches, is worse during midnight-sun summer than during polar night. A questionnaire study in an Arctic population. *Headache* 2000; 40:824-9.
 19. Alstadhaug KB, Salvesen R, Bekkelund SI. Seasonal variation in migraine. *Cephalalgia* 2005; 25:811-6.
 20. Seo W, Lee JB, Koh SB, *et al.* Headache epidemiologic study in Ansan city, Kyunggi-do, Korea. *J Korean Neurol Assoc* 2002; 20:479-85.
 21. The International Classification of Headache Disorders: 2nd edition. *Cephalalgia* 2004; 24 Suppl 1:9-160.
 22. Annual climatological report. Seoul, Korea: Korea meteorological administration; 2007.
 23. Annual report of air quality in Korea. Seoul, Korea: Ministry of environment & National institute of environmental research; 2007.
 24. Maclure M. The case-crossover design: a method for studying transient effects on the risk of acute events. *Am J Epidemiol* 1991; 133:144-53.
 25. Mittleman MA, Maclure M, Robins JM. Control sampling strategies for case-crossover studies: an assessment of relative efficiency. *Am J Epidemiol* 1995; 142:91-8.
 26. Yang CY. Air pollution and hospital admissions for congestive heart failure in a subtropical city: Taipei, Taiwan. *J Toxicol Environ Health A* 2008; 71:1085-90.
 27. Levy D, Lumley T, Sheppard L, *et al.* Referent selection in case-crossover analyses of acute health effects of air pollution. *Epidemiology* 2001; 12:186-92.
 28. Navidi W. Bidirectional case-crossover designs for exposures with time trends. *Biometrics* 1998; 54:596-605.
 29. Rasmussen BK. Migraine and tension-type headache in a general population: precipitating factors, female hormones, sleep pattern and relation to lifestyle. *Pain* 1993; 53:65-72.
 30. Prince PB, Rapoport AM, Sheftell FD, *et al.* The effect of weather on headache. *Headache* 2004; 44:596-602.
 31. Aurora SK, Wilkinson F. The brain is hyperexcitable in migraine. *Cephalalgia* 2007; 27:1442-53.
 32. Schoenen J. Neurophysiological features of the migrainous brain. *Neurol Sci* 2006; 27 Suppl 2: S77-81.
 33. Sand T, Zhitniy N, Nilsen KB, *et al.* Thermal pain thresholds are decreased in the migraine preattack phase. *Eur J Neurol* 2008; 15:1199-205.
 34. Moulton EA, Burstein R, Tully S, *et al.* Interictal dysfunction of a brainstem descending modulatory center in migraine patients. *PLoS One* 2008; 3:e3799.
 35. Bendtsen L. Central sensitization in tension-type headache--possible pathophysiological mechanisms. *Cephalalgia* 2000; 20:486-508.
 36. Apte MG, Buchanan IS, Mendell MJ. Outdoor ozone and building-related symptoms in the BASE study. *Indoor Air* 2008; 18:156-70.
 37. Zeiger SL, Thomas D, Dominici F, *et al.* Exposure measurement error in time-series studies of air pollution: concepts and consequences. *Environ Health Perspect* 2000; 108:419-26.
 38. Wellenius GA, Schwartz J, Mittleman MA. Particulate air pollution and hospital admissions for congestive heart failure in seven United States cities. *Am J Cardiol* 2006; 97:404-8.
 39. Spencer B. The effect of weather on headache. *Headache* 2005; 45:960; author reply 960.