Weather and headache onset: A large-scale study of headache medicine purchases

Weather and headache onset: A large-scale study of headache medicine purchases

Kayoko Ozeki, Tatsuya Noda, Mieko Nakamura, and Toshiyuki Ojima

Department of Community Health and Preventive Medicine, Hamamatsu University School of Medicine,

1-20-1 Handayama, Higashiku, Hamamatsu, Shizuoka 431-3192, JAPAN

Corresponding author: Kayoko Ozeki

Tel.: +81-53-435-2333

Fax: +81-53-435-2341

E-mail: kayo-oze@umin.ac.jp

Abstract

Background

It is widely recognized that weather changes can trigger headache onset. Most people who develop headaches choose to self-medicate rather than visit a hospital or clinic. We investigated the association between weather and headache onset using large-sample sales of the headache medicine, loxoprofen.

Methods

We collected daily sales figures of loxoprofen and over-the-counter drugs over a 1-year period from a drug store chain in western Shizuoka prefecture, Japan. To adjust for changes in daily sales of loxoprofen due to social environmental factors, we calculated a proportion of loxoprofen daily sales to over-the-counter drug daily sales. At the same time, we obtained weather data for the study region from the website of the Japan Meteorological Agency. We performed linear regression analysis to ascertain the association between weather conditions and the loxoprofen daily sales proportion. We also conducted a separate questionnaire survey at the same drug stores to determine the reason why people purchased loxoprofen.

Results

Over the study period, we surveyed the sale of hundreds of thousands of loxoprofen tablets. Most people purchased loxoprofen because they had a headache. We found that the sales proportion of loxoprofen increased when average barometric pressure decreased, and that precipitation, average

humidity, and minimum humidity increased on loxoprofen purchase days compared to the previous day of purchases.

Conclusions

This study, performed using a large dataset that was easy-to-collect and representative of the general population, revealed that sales of loxoprofen, which can represent the onset and aggravation of headache, significantly increased with worsening weather conditions.

Keywords: headache onset; weather; low pressure; medicine sales; loxoprofen; self-medication

Introduction

Headache onset has long been linked to adverse weather conditions such as rain and typhoon. In fact, studies have suggested greater frequency of headache onset after the approach of a low-pressure system (Hossino et al. 2005; Mukamal et al. 2009). Another study found that weather occasionally triggered migraines in 53% of people with migraine and very frequently in 11% of people with migraine (Kelman 2007). Headache is one of the most common symptoms of illnesses treated by self-medication. Previous studies indicated that most people who develop headache do not visit hospitals or clinics (Sakai and Igarashi 1997; Takeshima et al. 2004; Mehuys et al. 2012). A study in the United States on healthcare-seeking behavior reported that two-thirds of people who had at least one symptom did not visit a doctor (White et al. 1961). Ecological studies conducted in Japan obtained similar results (Tonai et al. 1989; Fukui et al. 2005). Therefore, it would appear that more people choose to self-treat with medication than seek medical attention.

Therapeutic medicine is generally classified into two groups: drugs prescribed by qualified doctors and over-the-counter (OTC) drugs used for self-medication. In Japan, OTC drugs are classified into three categories (i.e., Types 1, 2, and 3) according to magnitude of risk. Type 1 OTC drugs have special regulatory requirements because they have the largest effects and highest risk next to prescription drugs. In contrast, Type 2 and 3 OTC drugs are comparatively easy to buy. In Japan, loxoprofen sodium hydrate (LOX) is the most frequently used antipyretic analgesic: Its market share of prescribed antipyretic

analgesics is around 40% based on number of tablets sold (J-CAST News 2011). In January 2011, LOX was designated as a Type 1 OTC drug for the first time among antipyretic analgesics, and it continues to be a Type 1 OTC drug. Only drugstores with resident pharmacists can sell LOX (and other Type 1 OTC drugs); therefore, we can know the exact number of LOX tablets sold.

Presuming that LOX sales figures can act as a proxy of incidence of headache onset and aggravation of headache, in this study we examined the relationship between various weather conditions and the changes in LOX sales in stores of a large drug chain. We aimed to determine the association between the onset and aggravation of headache and weather variables by using big data of annual sales figures of LOX and other OTC medicines.

Materials and methods

Between April 1, 2011 and March 31, 2012, we collected daily sales figures of both LOX and other OTC drugs from all 52 drugstores of the biggest drug chain in western Shizuoka prefecture in Japan (approximately 600,000 customer members). Because our contract with the drug chain precluded us from publishing actual sales figures, we transformed total daily sales figures of LOX and all OTC drugs into a LOX daily sales index and an OTC daily sales index. The index for each annual average sales figure was set to 100. We also expected LOX sales to move in tandem with total OTC drugs sales under the influence of holidays, special sales, store promotions, and precipitation. To adjust for the changes in LOX daily sales due to social environmental factors, we calculated the proportion of daily sales of LOX to daily

sales of OTC drugs. We adopted the LOX daily sales proportion (LDSP) as the main outcome in this study.

We obtained the following weather data from the website of the Japan Meteorological Agency (measured at the same time each day in Shizuoka prefecture): average barometric pressure, precipitation, average humidity, minimum humidity, average temperature, minimum temperature, maximum temperature, and sunshine duration. Among three weather observation stations in Shizuoka prefecture, we chose weather data from the western Shizuoka area, the main study area.

To determine purchasers' motives for buying LOX, we analyzed other research data gathered from the same drugstores during a 1-week in December 2012. Pharmacists gave all LOX purchasers a questionnaire that asked for the reason for their LOX purchase (e.g., the customer's symptom(s) at the point of purchase).

We performed simple linear regression analysis that adopted LDSP as the dependent variable. In Model 1, independent variables were the absolute value of weather variables on LOX purchase days. In Model 2, independent variables were gradient changes from the previous day's weather variables to those on the purchase days, using the previous day of purchases as a reference. In Model 3, we performed multiple linear regression analysis adjusted by seasonal effects based on a prior study that found headache was affected by seasonality (Brewerton and George 1990), and as a covariate to each independent variable, we added a simple moving average of both average temperature and precipitation occurring 14

days before the purchase and 14 days after it.

We used JMP 10.0.2 statistical software (SAS Institute, Inc., NC). Statistical significance for all two-tailed tests was set at a *p*-value of less than 0.05.

Results

Over the 1-year study period, we surveyed the sale of several hundreds of thousands of LOX tablets and a cumulative study population in the tens of thousands. Table 1 summarizes the basic characteristics of each index (i.e., LOX daily sales index, OTC daily sales index, and LDSP). Statistical dispersion of the LOX daily sales index and OTC daily sales index by holiday and precipitation came close to the mean value of 100 and became vanishingly small for the LDSP.

Tables 2 and 3 present the results of the questionnaire survey of LOX purchases. The survey collection rate was around 75% (662, n = 891). Table 2 shows purchasers' reasons for buying LOX. Purchasers who had symptoms, including a warning sign, at the time of purchase accounted for 65.3% of the total collected sample, and purchasers who had no symptoms at the time of purchase but believed a headache would occur within a few days accounted for 13.8%; thus 79.1% of purchasers bought LOX in association upon symptom onset. Only 19.2% had no symptoms whatsoever at the time of purchase and bought LOX as a backup. Table 3 shows all symptoms reported by LOX purchasers. Headache accounted for over half (55.5%) of all reported symptoms, whereas menstrual cramps (26.3%) and toothache (13.0%) accounted for relatively few.

Model 1 of Table 4 shows the results of simple linear regression analysis using LDSP as the dependent variable and weather variables on LOX purchase days as predictors. Weather variables on LOX purchase days that showed a significant positive association with LDSP were precipitation (β: standard regression coefficient, β = 0.166, p = 0.002), and maximum temperature (β = -0.123, p = 0.018). Sunshine duration (β = -0.114, p = 0.030) and average temperature (β = -0.104, p = 0.047) were significantly negatively associated; in other words, LDSP was high in cases of rain or low temperature. In Model 2 (i.e., using weather variables of the gradient change from the previous day to the purchase day as predictors), decreased average barometric pressure (β = -0.115, p = 0.027) and increased precipitation (β = 0.158, p = 0.002), increased average humidity (β = 0.152, p = 0.004) and increased minimum humidity (β = 0.111, p = 0.034) were significantly associated with higher scores of LDSP by simple linear regression. Similarly, in Model 3 (i.e., adjusted by season), significantly higher LDSP scores were associated with lower barometric pressure (β = -0.114, p = 0.029), heavy rainfall (β = 0.158, p = 0.002), increased average humidity (β = 0.151, p = 0.004) and increased minimum humidity (β = 0.111, p = 0.034).

Discussion

To our knowledge, this is the first large study to clarify the relationship between weather and the onset and aggravation of headache using self-medication data. In Japan, few people with headaches visit a doctor, and many choose self-medication to treat headache symptoms (Hossino 2005). An

epidemiologic study in Japan found that 69.4% of people with migraine were undocumented in medical records, and 56.9% of migraine sufferers used only OTC drugs to treat headaches (Sakai and Igarashi 1997). Therefore, in this study we focused on people who at headache onset self-medicated with OTC drugs rather than consult a doctor. We also focused on LOX, the only Type 1 analgesic OTC drug among many antipyretic analgesics available for purchase. In Japan, LOX is a commonly used analgesic for headaches. Compared with other analgesics, LOX sales figures are accurate and easily accessible, face-to-face sales of LOX are controlled by on-site pharmacists, and LOX can only be sold at a fixed price. Moreover, the customer members of the drug chain (i.e. those with a loyalty card) are approximately 600,000, accounting for 28% of the population of western Shizuoka prefecture. Therefore, the regional representation of our data is considerably high.

This study clearly demonstrated that LOX purchases increased when average barometric pressure decreased, and that precipitation, average humidity, and minimum humidity increased on LOX purchase days compared to the previous day of purchases. Earlier studies have reported various results on the relationship between headache and weather (Gomersall and Stuart 1973; Schulman et al. 1980; Cull 1981; Osterman et al. 1981; Jamison et al. 1995; Spierings et al. 2001; Mukamal et al. 2009; Prince et al. 2004; Alstadhaug et al. 2005; Hossino et al. 2005; Villeneuve et al. 2006; Kelman 2007; Lilleng and Bekkelund 2009; Connelly et al. 2010; Yang et al. 2011). However, some did report an association between headache incidence and low barometric pressure and humidity (Jamison et al. 1995; Lilleng and

Bekkelund 2009; Mukamal et al. 2009; Hoffmann et al. 2011), findings that are consistent with those of the present study.

As for the relationship between weather variables and pain, the mechanism underlying how low pressure aggravates pain has been reported. A study using rats revealed that low pressure stimulated the sympathetic nervous system and directly or indirectly excited pain fibers, which worsened symptoms. A decrease in barometric pressure increases sympathetic nervous tone and adrenal medullary hormones. These hormones and sympathetic nerve stimulation work to constrict the peripheral vessels, leading to tissue ischemia, lowering of blood oxygen levels, and decreasing pH (Sato 2003). These local pathological changes increase the sensitivity of pain fibers at the time of pain (Mizumura and Kumazawa 2001), and therefore these changes stimulate the pain fibers more easily. Recent studies have shown that chronic inflammation initiates conditions in which sympathetic activity excites certain nocicepters (Sato and Perl 1991; Sato et al. 1993). Furthermore, changes in weather might contribute to headache onset through stimulation of specific neurons in the trigeminal nucleus caudalis in response to decreased atmospheric pressure (Messlinger et al. 2010).

The results of most studies on the relationship between headache and weather were based on frequency of doctor visits or survey interviews of headache patients who had hospital visit records (Gomersall and Stuart 1973; Schulman et al. 1980; Cull 1981; Osterman et al. 1981; Jamison et al. 1995; Spierings et al. 2001; Mukamal et al. 2009; Prince et al. 2004; Alstadhaug et al. 2005; Hossino et al.

2005; Villeneuve et al. 2006; Kelman 2007; Lilleng and Bekkelund 2009; Connelly et al. 2010; Yang et al. 2011), and these studies were relatively small. Our intent in this study was to discover the relationship between headache onset and weather conditions by means of analgesic sales data, rather than medical diagnosis, given that few people visit a doctor to treat a headache and few people purchase headache medicine only as a backup. Moreover, headache is a symptom that people can easily recognize. Therefore, we considered sales of headache medicine would provide a relatively accurate reflection of headache onset. Furthermore, using medicine sales to represent headache onset facilitated our investigation because it obviated the need for patient involvement. This study also took advantage of big data from the sale of hundreds of thousands of tablets.

This study had four main limitations. First, we could not determine the reasons for the LOX purchases from the sales data alone, so we examined research data on reasons for taking LOX conducted by the same drugstores in the same year. We found that headache was the reason for 55.5% of LOX purchases. These data suggest that LOX purchases were related not only with headache but also other types of pain; however, pain presumed to be associated with weather, such as arthralgia and neuralgia, accounted for only a small percentage of purchases. Most reasons for purchasing LOX other than headache had little to do with weather conditions. Although the majority of LOX purchases took place immediately before or after headache onset, the data also showed that pain occurred with worsening weather conditions not only on the day of purchase of but also for a couple of days before adverse

weather. Second, adjusting purchase behaviors to compensate for social environmental reasons was difficult. Purchasing behavior is affected by symptom development as well as social environmental factors such as holidays, rainfall, and sales promotions (Geurts and Kelly 1986). In this study, we ascertained the proportion of LOX sales to OTC drug sales to adjust for these influences. Third, we did not consider sales of analgesics other than LOX. Although people can use other analgesics for self-medication, analgesics that are not Type 1 OTC drugs like LOX can be sold at lower prices (e.g., during sales promotions), and thus are more prone to purchase for economic reasons (e.g., bulk buying) rather than for headache onset. Although LOX sales do not account for an overwhelming share of the OTC analgesics market, statistical accuracy is likely high based on the characteristics of Type 1 OTC drugs. The buying motive for LOX is likely linked to headache incidence, and LOX sales are insulated from the influence of other factors. For these reasons, we chose to study only LOX among all available analgesics. Fourth, we conducted this study in western Shizuoka prefecture, Japan. Although the drug store chain that we investigated is dominant in the study region, further investigation will be required to provide a more complete picture of the purchasing of analgesics for headache.

This study aimed to clarify the relationship between weather conditions and onset and aggravation of headache by using big data that can grasp the behaviors of headache sufferers who do not visit a doctor. Headache is a conventional disease, and its influence on a person’s daily life can lead to big social costs (Jackson et al. 2012; Mehuys et al. 2012). If the relationship between weather variables and onset and

aggravation of headache can be verified, attention to weather conditions by individuals themselves may help to alleviate pain. Alerting people to changes in weather conditions such as barometric pressure and humidity might then have a considerable positive impact.

Acknowledgments

We thank the drugstores and individuals that provided the data for this study.

Ethical standards

The Ethics Committee of Hamamatsu University School of Medicine waived the need for ethical approval because of the anonymous nature of the data used (No. 25-89). We utilized anonymized datasets before beginning data analysis. All experiments complied with the current laws of Japan.

Conflict of interest

The first author (KO) is employed by one of the drug stores from which data were collected, but no financial support was received from the drug chain. All other authors declare that no competing interests exist. The drug chain will not receive any benefits explicitly or implicitly from the publication of this research.

References

Alstadhaug KB, Salvesen R, Bekkelund S (2005) Seasonal variation in migraine. Cephalalgia 25:811-816.

Brewerton TD, George MS (1990) A study of the seasonal variation of migraine. Headache 30:511-513.

Connelly M, Miller T, Gerry G, Bickel J (2010) Electronic momentary assessment of weather changes as a trigger of headaches in children. Headache 50:779-789.

Cull RE (1981) Barometric pressure and other factors in migraine. Headache 21:102-104.

Fukui T, Rhaman M, Takahashi O, Saito M, Shimbo T, Endo H, Misao H, Fukuhara S, Hinohara S (2005) The ecology of medical care in Japan. Japan Med Assoc J 48:163-167.

Geurts MD, Kelly JP (1986) Forecasting retail sales using alternative models. Int J Forecast 2:261-272.

Gomersall JD, Stuart A (1973) Variations in migraine attacks with changes in weather conditions. Int J Biometeorol 17: 285-299.

Hoffmann J, Lo H, Neeb L, Martus P, Reuter U (2011) Weather sensitivity in migraineurs. J Neurol 258:596-602.

Hossino A, Tamura J, Ito K, Moridaira K, Kurabayashi H, Kubota K (2005) Effect of weather on chief complaints and disorders of outpatients. J Jpn Soc Balneol Climatol Phys Med 68:150-154.

Jackson JL, Kuriyama A, Hayashino Y (2012) Botulinum toxin A for prophylactic treatment of migraine and tension headaches in adults. JAMA 307:1736-1745.

Jamison RN, Anderson KO, Slater MA (1995) Weather changes and pain-perceived influence of local

climate on pain complaint in chronic pain patients. Pain 61:309-315.

J-CAST News (2011) Zutsū, seiritsūyaku ni “ōgata shinjin” iryōyō kara “kasen shijyō” ni sannyū. J-CAST News http://www.j-cast.com/2011/01/18085710.html Accessed 14 October 2013 (in Japanese)

Kelman L (2007) The triggers or precipitants of the acute migraine attack. Cephalalgia 27:394-402.

Lilleng H, Bekkelund S (2009) Seasonal variation in migraine in an Arctic population. Headache 49:721-725.

Mehuys E, Paemeleire K, Van Hees T, Christiaens T, Van Bortel LM, Van Tongelen I, De Bolle L, Remon J-P, Boussery K (2012) Self-medication of regular headache: a community pharmacy-based survey. Eur J Neurol 19:1093-1099.

Messlinger K, Funakubo M, Sato J, Misumura K (2010) Increases in neuronal activity in rat spinal trigeminal nucleus following changes in barometric pressure—relevance for weather-associated headaches? Headache 50:1449-63.

Mizumura K, Kumazawa T (2001) Thermonociception: sensory and modulatory mechanisms in pathological conditions. In: M Kosaka, T Sugahara, KL Schmidt, E Simon (eds) Thermotherapy for neoplasia, inflammation, and pain. Springer Japan: Tokyo, pp 504-513

Mukamal KJ, Wellenius GA, Suh HH, Mittleman MA (2009) Weather and air pollution as triggers of severe headaches. Neurol 72:922-927.

Osterman PO, Lovstrand KG, Lundberg PO, Lundquist S, Muhr C (1981) Weekly periodicity of headache

and the effect of changes in weather on headache. Int J Biometeorol 25:39-45.

Prince PB, Rapoport AM, Sheftell FD, Tepper SJ, Bigal ME (2004) The effect of weather on headache. Headache 44:596-602.

Sakai F, Igarashi H (1997) Prevalence of migraine in Japan: a nationwide survey. Cephalalgia 17:15-22.

Sato J (2003) Possible mechanism of weather related pain. Jpn J Biometeorol 40:219-224.

Sato J, Perl ER (1991) Adrenergic excitation of cutaneous pain receptors induced by peripheral nerve injury. Science 29:1608-1610.

Sato J, Suzuki S, Iseki T, Kumazawa T (1993) Adrenergic excitation of cutaneous nociceptors in chronically inflamed rats. Neurosci Lett 164:225-228.

Schulman J, Leviton A, Slack W, Porter D, Graham JR (1980) The relationship of headache occurrence to barometric pressure. Int J Biometeorol 24: 263-269.

Spierings EL, Ranke AH, Honkoop PC (2001) Precipitating and aggravating factors of migraine versus tension-type headache. Headache 41:554-558.

Takeshima T, Ishizaki K, Fukuhara Y, Ijiri T, Kusumi M, Wakutani Y, Mori M, Kawashima M, Kowa H, Adachi Y, Urakami K, Nakashima K (2004) Population-based door-to-door survey of migraine in Japan: The Daisen Study. Headache 44:8-19.

Tonai S, Maezawa M, Kamei M, Satoh T, Fukui T (1989) Illness behavior of housewives in a rural area in Japan: a health diary study. Cult Med Psychiatry 13:405-417.

Villeneuve PJ, Szyszkowicz M, Stieb D, Bourque DA (2006) Weather and emergency room visits for migraine headaches in Ottawa, Canada. Headache 46:64-72.

White KL, Williams TF, Greenberg BG (1961) The ecology of medical care. New Eng J Med 265:885-892.

Yang AC, Fuh J-L, Huang NE, Shia B-C, Peng C-K, Wang S-J (2011) Temporal associations between weather and headache: analysis by empirical mode decomposition. PLoS ONE 6:e14612. doi: 10.371/journal.pone.0014612.

Table 1. Basic characteristics of LOX, OTC drugs, and LOX/OTC drug daily sales indices

	LOX[a] daily sales index	OTC[b] daily sales index	LOX daily sales proportion index
Average	100	100	100
Standard deviation	21.5	19.4	16.2
Median	96.2	95.2	98.6
Maximum	178.7	181.4	162.3
Minimum	42.5	26.9	54.9
Holiday (average)	126.1	127.1	**100.0**
Weekday (average)	94.2	93.3	**100.1**
Nonprecipitation day (average)	102.2	102.2	**99.6**
Precipitation day (average)	94.8	94.7	**100.9**

[a]loxoprofen, [b]over-the-counter

Table 2. Reasons for LOX purchases

	n	%
Currently having symptoms (including warning signs)	432	65.3
Not having symptoms but believe a headache will occur in a few days	91	13.8
None of the above and purchase as backup only	127	19.2
Other	12	1.8

Table 3. Symptoms reported for LOX purchases (multiple answers possible)

	n	%
Headache	372	55.5
Menstrual cramps	176	26.3
Toothache	87	13.0
Backache	67	10.0
Stiff shoulder(s)	44	6.6
Arthralgia	32	4.8
Chills/fever	31	4.6
Muscle aches	26	3.9
Neuralgia	14	2.1
Bruise/bone fracture/sprain/pain from another injury	12	1.8
Sore throat	11	1.6
Ear pain	2	0.3
Other	17	2.5

Table 4. Three models of the LOX daily sales proportion and weather variables

	Model 1 (univariate) Weather variables on purchase day		Model 2 (univariate) Weather variables of gradient change from previous day		Model 3 (multivariate)[a] Weather variables of gradient change from previous day	
	β[*]	*p*	β	*p*	β	*p*
Precipitation	0.166	**0.002**	0.158	**0.002**	0.158	**0.002**
Maximum temperature	-0.123	**0.018**	0.022	0.676	0.022	0.679
Sunshine duration	-0.114	**0.030**	0.019	0.712	0.020	0.708
Average temperature	-0.104	**0.047**	0.064	0.220	0.064	0.221
Minimum temperature	-0.085	0.103	0.074	0.156	0.075	0.152
Average barometric pressure	0.085	0.103	-0.115	**0.027**	-0.114	**0.029**
Minimum humidity	0.064	0.219	0.111	**0.034**	0.111	**0.034**
Average humidity	0.039	0.462	0.152	**0.004**	0.151	**0.004**

[a]Model 3 adjusted for simple moving average of both average temperature and precipitation occurring 14 days before purchase and 14 days after purchase as a covariate to each independent variable.

[*]standard regression coefficient