소아의 열성경련에 날씨가 미치는 영향

고려대학교 의과대학 소아과학교실

우정희·오석빈·임정혁·변정혜·은백린

Impact of Weather on Prevalence of Febrile Seizures in Children

Purpose: Febrile seizure (FS) is the most common type of seizure in children between 6 months to 5 years of age. A family history of febrile seizures can increase the risk a child will have a FS. Yet, prevalence of FS regarding external environment has not been clearly proved. This study attempts to determine the association between prevalence of FS and weather.

Methods: This study included medical records from the Korea National Health Insurance Review and Assessment Service. Data were collected from 29,240 children, born after 2004, diagnosed with FS who were admitted to one of the hospitals in Seoul, Korea, between January 2009 and December 2013. During the corresponding time period, data from the Korea Meteorological Administration on daily monitoring of four meteorological factors (sea-level pressure, amount of precipitation, humidity and temperature) were collected. The relationships of FS prevalence and each meteorological factor will be designed using *Poisson* generalized additive model (GAM). Also, the contributory effect of viral infections on FS prevalence and weather will be discussed.

Results: The amount of precipitation was divided into two groups for comparison: one with less than 5 mm and the other with equal to or more than 5 mm. As a result of *Poisson* GAM, higher prevalence of FS showed a correlation with smaller amount of precipitation. Smoothing function was used to classify the relationships between three variables (sea-level pressure, humidity, and temperature) and prevalence of FS. FS prevalence was correlated with lower sea-level pressure and lower humidity. FS prevalence was high in two temperature ranges (-7 to -1°C and 18 – 21°C).

Conclusion: Low sea-level pressure, small amount of precipitation, and low relative air humidity may increase FS prevalence risk.

Key Words: Seizures, Fever, Weather, Humidity, Temperature

Jung Hee Woo, MD, Seok Bin Oh, MD, Chung Hyuk Yim, MD, Jung Hye Byeon, MD, PhD, Baik-Lin Eun, MD, PhD

Department of Pediatrics, Korea University
College of Medicine, Seoul, Korea

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Correspondence to Jung Hye Byeon, MD, PhD
Department of Pediatrics, Korea University College of Medicine, 73, Incheon-ro, Seongbuk-gu, Seoul 02841, Korea

Tel: +82-2-920-5090, Fax: +82-2-922-7476

E-mail: pedbyeon@naver.com

Introduction

Febrile seizure (FS) is the most common type of seizure seen in children between 6 months to 5 years of age¹⁾. The average prevalence of FS in children younger than 5 years based on hospital visit rates in Korea was 6.92% between 2009 and 2013²⁾. Although FS is benign and self-limited, it can frighten parents by the unusual appearance of their child. For this reason, the pathogenesis of FS has been studied many times. FS has genetic susceptibility. An analysis of 2,109 FS

patients reported in 12 publications demonstrated a mean familial incidence of 17%³. Hereditary factor plays a pivotal role in the etiology of febrile seizures, but the direct cause is still unclear. Some people believe that FS can be influenced by certain weather conditions. A number of studies have reported an association between incidence of seizure and weather. Yet, none of the studies clearly proved their relation.

The main cause of FS is recent upper respiratory infection⁴. The etiology of pediatric infections has seasonality. There were studies that described correlation between meteorological factors and viral infections. One study concluded that air temperature and relative humidity were major influencing meteorological factors for respiratory tract infections⁵. Since respiratory viral infections are one of the triggering factors of FS, there would be an association between weather and incidence of FS. In this study, we discuss the prevalence of FS in Seoul, Korea, depending on four meteorological factors.

Materials and Methods

1. Study population

This retrospective observational study included medical records from the Korea National Health Insurance Review and Assessment Service (HIRA) between January 2009 and December 2013. Patients born after 2004 were included. Every clinic and hospital in Korea gives patient diagnostic and medical cost data to the HIRA. This indicates that nearly complete information about the volume and burden of disease in Korea can be obtained from this centralized database. Patients in Seoul, Korea, with a main diagnosis of FS (International Classification of Diseases, 10th Revision [ICD-10] codes: R56.0) with or without status epilepticus (G41) or convulsions (R56.8) were reviewed. We excluded patients diagnosed with epilepsy. Because even though epilepsy can be occurred with fever, it has a different mechanism from the febrile seizures, which are relatively considered benign and self-limiting. FS is considered as benign usually when it happens before age of five. So, we collected data of children younger than five years old. The information about the first event of FS of each patient was collected: the age of children at the first event of FS, the date of FS occurrence, and gender of the patients. We only counted the first event of the FS, which is the prevalence of the FS. If the patient visited hospital more than once in the same month, we only counted once.

2. Meteorological factors

During the corresponding time period, data from the Korea

Meteorological Administration on daily monitoring of meteorological factors were collected from Seoul, Korea. We were curious about seasonal variation of FS prevalence. So, we chose daily mean temperature as a variable. We were also curious when it rains, whether the FS prevalence is affected. Daily mean temperature, humidity, sea-level pressure, and amount of precipitation were included. Sea-level pressure is the pressure typically given in weather reports. When weather forecasting, sea-level pressure is considered for rain prediction. When the pressure is low, there is likely to be rain because in low-pressure areas, the air is free to rise into the atmosphere where it condenses and can form clouds made of water vapor that falls as rain. Sea-level pressure in Korea is low in the summer. We examine if the prevalence of FS differs when the mean temperature of the day increases or decreases. We study when the prevalence of FS increases depending on humidity, sea-level pressure, and amount of precipitation of the day. The average of the amount of precipitation and humidity are high in the summer because of monsoons in Korea. Accordingly, we also evaluate if there is a seasonal variation in FS prevalence.

3. Statistical analysis

Data of four meteorological factors were obtained from the Korea Meteorological Administration. These data were remodeled to the mean value of three consecutive days, because the weather condition of one day could be influenced by the condition of the day before and after. Also, it is difficult to consider a day as an independent variable. The relationships between weather and first hospital visits for FS were analyzed by the *Poisson* generalized additive model (GAM) using the MGCV, R package version 1.8–9. *Poisson* model is often used when analyzing correlation of variables and prevalence of event that occur very rarely. The following equation was formed using *Poisson* GAM. *Poisson* function with all natural causes as the dependent variables.

$$\begin{aligned} \log(\mu_i) = & 293.5 - 0.14 \text{year}_i - 0.034(\text{less than } 5 \text{ mm precipitation}_i) \\ & - 0.044(\text{equal or more than } 5 \text{ mm precipitation}_i) \\ & + s(\text{pressure}_i) + s(\text{humidity}_i) + s(\text{temperature}_i) \\ & \text{FS prevalence}_i - \text{Poisson}(\mu_i) \end{aligned}$$

μ_i indicates number of hospital visits in Seoul due to the 1st event of FS. When all variables are zero, the prevalence of FS on Seoul is 293.5. The study was approved by the Center Institutional Review Board (2016GR0052) of the Korea Centers for Disease Control and Prevention.

Results

A total of 29,240 children diagnosed with FS were admitted to the hospitals in Seoul, Korea, between January 2009 and December 2013. Each of four meteorological factors (sea-level pressure, amount of precipitation, humidity and temperature) from the Korea Meteorological Administration was remodeled to an average value of three consecutive days. Then, *Poisson* GAM was used to analyze the correlation between FS prevalence and four meteorological factors.

First of all, the amount of precipitation was examined. The amount of precipitation was divided into two groups for comparison: one with less than 5 mm and the other with equal to or more than 5 mm (Table 1). When precipitation was less than 5 mm, the estimate value was calculated as -0.034 while the estimate value of precipitation equal to or more than 5 mm was -0.044 . The values of estimate in table 1 explains the association between the variable and prevalence of FS. When the value is negative, this means negative correlation. So, when it rains it is less likely have a first attack of FS. The absolute value of estimate of precipitation equal to or more than 5 mm is higher than the absolute value of precipitation less than 5 mm. This explains the amount of precipitation also matters. Importantly, P value of both variables are less than 0.05 which explains the statistical significance of the test. Therefore, higher prevalence of FS showed correlation with smaller amount of precipitation.

To identify the relationships between three variables (sea-level pressure, humidity, and temperature) and prevalence of FS, smoothing function was used to make the correlation linear (Table 2). Each value of estimate was inserted in smoothing function and the result was concluded. As a result, FS prevalence and sea-level pressure presented a negative correlation (Fig. 1). When sea-level pressure was low at 997–1,010 hPa, FS prevalence was higher than the result of sea-level pressure higher than 1,010 hPa.

Table 1. Relation of Febrile Seizure Prevalence and Precipitation using *Poisson* Model

	Estimate	Standard error	z value	P value
Precipitation (<5 mm)	-0.034	0.015	-2.245	0.025
Precipitation ($\geq$ 5 mm)	-0.044	0.022	-2.023	0.043

*P values <0.05 were considered statistically significant.

Table 2. Relation of Febrile Seizure Prevalence and Sea-level Pressure, Humidity, and Temperature using *Poisson* Model

	Estimate	Standard error	z value	P value
s (sea-level pressure)	6.274	7.470	376.68	<2e-16
s (humidity)	7.814	8.648	404.64	<2e-16
s (temperature)	7.596	8.514	93.95	2.51e-16

*P values <0.05 were considered statistically significant.

Humidity also showed a negative correlation with FS prevalence (Fig. 2). FS prevalence was high when humidity was 20–45% and was low when humidity was as high as 90%. Thus, when the weather is humid, the possibility of FS prevalence decreases. This outcome connects with the result of FS prevalence and precipitation. When it rains, the weather will be humid and in this environment, a chance to have a 1st attack of FS would be lower than the other situation. FS prevalence did not show a linear correlation with mean temperature, but it was high in two temperature

Fig. 1. Febrile seizure (FS) and sea-level pressure. Prevalence of FS increased when sea-level pressure was low at 997–1,010 hPa.

Fig. 2. Febrile seizure (FS) and humidity. Prevalence of FS increased when the weather was dry. FS prevalence was high when humidity was 20–45% and was low when humidity was as high as 90%.

ranges (-7 to -1°C and 18 – 21°C ; Fig. 3). When the temperature is between -7 to -1°C or 18 – 21°C , it is more likely have a 1st attack of FS. All the results are statistically significant since all three of P values are less than 0.05 (Table 2).

Discussion

Respiratory viral infection has been hypothesized to be one of the important causes for febrile seizures and weather conditions are a significant driver of respiratory infections⁶. Air temperature and relative humidity were major influencing meteorological factors for hospital admissions in children due to lower respiratory tract infections⁵. A previous study in Buenos Aires found an increase in lower respiratory infections in children under 5 years old during wintertime⁷. Correspondingly, the other study found a decrease in respiratory morbidity under hot and dry weather conditions⁸. Many social and biological factors contribute to the increased incidence of these diseases during the winter months⁹. Indoor activities in crowds promote the transmission of pathogens, and low temperature favors the survival of pathogens⁹. Furthermore, breathing cold air causes cooling of the nasal epithelium, and this reduction in nasal temperature is enough to inhibit respiratory defense against infection¹⁰. Thus, it is easy to obtain respiratory viral infections in cold weather.

Viral infections play a significant role in the etiology of FS by causing a fever and producing an elevated cytokine level or abnormal immune response to infection³. Viruses most commonly

associated with FS in the last decade are human herpesvirus-6, identified as a cause of exanthema subitum, influenza, and adenovirus^{3,11}. Respiratory syncytial virus (RSV) is also important when in FS. RSV usually occurs in annual epidemics during the winter and early spring³. It infects almost all children during the first 3 years of life, the time of greatest susceptibility to FS³. Thus, RSV may be one of the diseases that can cause FS. Although acute gastroenteritis is not the major cause of FS, and is not as common as respiratory viral infections, some children with FS were admitted to the hospital due to acute gastroenteritis. Rotavirus is the most frequent cause of acute gastroenteritis in young children worldwide¹². It is well known that infections with rotavirus and RSV peak in the winter months¹³. According to a study in Washington, D.C., hospitalization of children for rotavirus gastroenteritis tended to be more common after 1 month of cold or dry weather¹⁴. There also were 45% more rotavirus hospitalizations after the set of months with the least precipitation compared with the greatest precipitation¹⁴. Dry conditions tend to encourage the formation of virus-laden dust from fecally contaminated diapers and clothing¹⁴. In addition, small particles tend to stay suspended in the air and thus reach a susceptible individual¹⁴. With increased humidity, the particles would generally be larger and thus would drop more rapidly to the floor¹⁴. In the winter-time, an increased prevalence of viral infections such as RSV and rotavirus can contribute to an increased prevalence of FS.

Similar study was demonstrated between 2005 and 2015 in Changwon, Korea¹⁵. A single-center retrospective study observing the effects of weather on pediatric seizure was done in Samsung Changwon Hospital. This study investigated whether emergency department visits due to pediatric seizure were affected by weather. Any type of seizures were included in this study. Data of maximum temperature of the day, minimum temperature of the day, diurnal temperature range, cloud cover, wind speed, humidity, sunshine, atmospheric pressure, and rainfall were collected. Also, air pollutants such as PM_{10} , O_3 , NO_2 , CO and SO_2 were controlled for as potential confounding variables. This paper concluded that low mean temperature affected to increase the occurrence of pediatric seizures and vice versa.

In this study, we investigated the association between FS prevalence and weather using reliable meteorological data. Low sea-level pressure, small amount of precipitation, and low relative air humidity may increase FS prevalence risk. When temperatures were between -7 to -1°C and 18 – 21°C , FS prevalence increased. Thus, FS is one of the illnesses affected by weather changes. Based on this thought, there would be a seasonal variations in pediatric viral infections. According to previous literature, viral infections were more easily transmitted in cold and dry conditions.

Fig. 3. Febrile seizure (FS) and temperature. FS prevalence did not show a linear correlation with mean temperature, but it was high through two temperature ranges (-7 – -1°C and 18 – 21°C).

Our result does not completely correlate with this explanation. FS prevalence does increase in dry and cold conditions such as between -7 to -1°C , but FS prevalence also increased in warm conditions such as $18-21^{\circ}\text{C}$. This explains that weather indeed is a one of the influencing factors that cause FS, but other causes also exist.

Limitations of this study include the following. First of all, our findings cannot be compared with those in countries where the climate is different from Korea. However, the results do demonstrate a relationship between FS prevalence and weather. Secondly, data of further variables could have been included such as wind speed and air pollutants. Nowadays, one of the major threats to human health in urban environments is airborne particles⁹⁾. Numerous studies have been published on the risk of airborne particles on many diseases. Since more and more attentions are on this issue, it would be important to include airborne particles or other air pollutants in the study. Lastly, this study describes the contributory effect of viral infections on febrile seizure prevalence. However, detailed data about viral infection was missing. Monthly data of viral infection should have been included for accurate comparison. This is the first review on weather and FS prevalence that has performed a multi-centered meta-analysis using big data. This paper attempts to verify the relationship between FS prevalence and weather using four meteorological factors.

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요약

목적: 열성 경련은 생후 6개월부터 만 5세 사이 발생하는 가장 흔한 유형의 경련으로 직계 가족에서 가족력이 존재할 때 더 발생률이 높다. 열성 경련의 발생률과 외부 환경과의 영향에 대하여 아직 정확히 알려진 바가 없다. 본 연구는 열성 경련의 발생과 날씨의 연관성을 파악하기 위해 시행되었다.

방법: 본 연구는 건강보험심사평가원 자료를 바탕으로 진행되었다. 2009년 1월부터 2013년 12월까지 서울 소재 병원에서 첫 번째 열성 경련으로 내원하여 진단받은 29,240명의 환아들을 대상으로 시행하였다. 동일기간 동안 기상청에서 수집한 4개의 기상인자(해면기압, 강수량, 습도, 기온)들과의 연관성을 알아보았다. 포아송 일반화 부가모

형(Poisson Generalized Addictive Model)을 이용하였다. 바이러스 감염이 열성 경련의 발생률에 기여하는 영향도 논의되었다.

결과: 강수량은 두 가지 그룹(5 mm 미만과 5 mm 이상)으로 나누어 분석되었다. 포아송 분석 결과 열성경련의 발생률은 강수량이 적을수록 증가하였다. 해면기압, 습도, 기온 등 3가지 변수들을 분석하는데 있어서 평활 함수가 사용되었고 그 결과 열성 경련 발생률은 해면기압이 낮을수록, 습도가 낮을수록 증가하였고, 기온이 -7 ~ -1°C 와 18 ~ 21°C 일 때 높았다.

결론: 본 연구는 열성경련과 날씨와의 연관성을 파악하기 위하여 시행되었고, 그 결과 강수량이 적을수록, 해면기압이 낮을수록, 습도가 낮을수록 열성경련의 발생률이 증가하였다. 그러므로, 날씨는 열성 경련 발생에 영향을 주는 요인 중 하나이다.

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