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Original article

Predictors of unprovoked seizure after febrile seizure: Short-term outcomes

Gul Hwang, Hyun Sik Kang, Sin Young Park, Kyoung Hee Han, Seung Hyo Kim *

Department of Pediatrics, Jeju National University College of Medicine, Republic of Korea

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Abstract

Introduction: We performed this study to confirm the known risk factors and to identify possible new risk factors for subsequent unprovoked seizure after febrile seizure (FS) on Jeju Island, South Korea.

Methods: A population-based retrospective study of 204 children with FS, whose first FS developed between March 2003 and August 2011, and who were seen in the Pediatric Department at the Jeju National University Hospital.

Results: Two hundred four children (136 boys and 68 girls) were enrolled in this study. Simple FS was found in 107 children, and complex FS was found in 97 children. The average age at the first FS was 18.9 months. The average total number of FSs was 4.3. A family history of FS or epilepsy was found in 29.4% and 7.8% of patients, respectively. Abnormal findings of EEG were observed in 35.8%. Complex features in the first FS were noted in 28.9%. Subsequent unprovoked seizures occurred in 23.0%. Univariate analysis showed that low parental educational level was one of several variables that were significantly related to unprovoked seizure. Parental educational level was not included in the multivariate model because of an insufficient sample size. Multivariate analysis identified the following factors as significant predictors of unprovoked seizure: late onset of FS at age > 3 years, complex features in the first FS, family history of epilepsy, and abnormal findings on EEG, and FS developed at a body temperature of <39 °C.

Conclusions: We confirmed the known risk factors for subsequent unprovoked seizure and found that low parental educational status may be a new prognostic indicator. However, further investigation using larger populations and a prospective design is needed to confirm that this is a valid prognostic factor for FS.

Keywords: Febrile seizure; Unprovoked seizure; Complex febrile seizure

1. Introduction

Febrile seizure (FS) is the most common convulsive disorder of childhood and has been reported in 2–5% of all children in the United States and Western Europe, 5–10% in India, 9–10% in Japan, and 14% in Guam [1–4]. The main concern with FS is whether this benign phenomenon progresses to the development of unprovoked seizure or epilepsy. Some investigations have reported that there is a variable incidence of unprovoked seizure and epilepsy [1–8]. The variability may be attributed to differences in the patients' age, the duration of follow-up, the method of study such as population-based or hospital-based study, and the study design such as a retrospective or prospective method. Following a first FS, 2–4% of children develop at least one unprovoked seizure [3,5,6].

* Corresponding author. Address: Department of Pediatrics, Jeju National University College of Medicine, Ara-1 Dong, Jeju-si, Jeju Special Self-Governing Province, Jeju-do 690-767, Republic of Korea. Tel.: +82 10 9024 2947; fax: +82 64 717 1097.

E-mail address: shped@jejunu.ac.kr (S.H. Kim).

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Some cohort studies and retrospective investigations have confirmed the risk factors for unprovoked seizure after FS; these include complex FS, neurodevelopmental abnormalities, onset of FS at an early age, epileptiform activity shown by electroencephalography (EEG), and a family history of epilepsy [5–8]. However, these studies have not added any new risk factors. There have been few reports on the comparison of risk factors for the occurrence of unprovoked seizure after the classification of FS according to simple FS or complex FS and including EEG data.

We tried to evaluate the prognostic factors for unprovoked seizure after FS in relation to the type of FS and to identify any new prognostic factors in children living on Jeju Island, with a homogeneous population.

2. Patients and methods

The Jeju National University Hospital (JNUH) is a tertiary hospital located on Jeju Island, which is located at the southernmost part of South Korea. The population of Jeju Island was about 600,000 inhabitants in August 2013. This is the only university hospital on Jeju Island providing EEG for children or pediatric neurology consultation.

We reviewed retrospectively the computerized medical records of 323 patients whose first FS developed between 3 months and 5 years of age among the patients who visited the outpatient clinic or were admitted to the pediatric department at the JNUH because of their first FS attack between May 2003 and August 2011. The data obtained from the records included demographic variables, seizure semiology, family history, birth history, EEG findings, the family's economic status, and parental educational background.

We excluded patients with evidence of intracranial infection or afebrile seizure that had developed before the occurrence of FS. Patients with abnormal results from their neurological examination at presentation were excluded. Of this population, all neurologically normal patients with at least 2 years of follow-up and EEG data were included in this study to evaluate the prognostic indicators, especially EEG findings.

A pediatric neurologist determined the patients' developmental status by performing a neurological examination and obtaining a history of developmental milestones. The pediatric neurologist also recorded the medical history, such as seizure semiology, family history, and other variables obtained mainly from the mothers at the outpatient clinic or ward at admission. We contacted parents by phone in cases of missing information such as the mother's age at birth, monthly income, and parental educational background.

EEG studies were performed using the 10–20 international system with bipolar and referential montages. EEG was performed within 7 days after the FS for 14 patients, between 7 and 14 days after the FS for 33 patients, between 14 and 21 days for 114 patients, and more than 21 days after the FS for 43 patients. The first EEG was performed at the first FS for 96 patients, at the second FS for 32 patients, at the third FS for 28 patients, and at the time of other FSs for patients who experienced more than three attacks of FS. The duration of the recording was 20–30 min. Each EEG was interpreted by one pediatric neurologist who is certificated by the Korean Child Neurology Society. We classified spike or sharp wave discharges on EEG as abnormal findings. Imaging studies, including brain computed tomography (CT) or magnetic resonance imaging (MRI), were performed when considered necessary.

FS was defined as a provoked seizure where the acute provocation was fever (temperature $>$ 38.3 °C or 101 °F) documented in the emergency department in a patient with no evidence of an acute central nervous system infection. Prolonged ($>$15 min), focal convulsive activity or repeated occurrence within 24 h, was defined as a complex FS. FS plus was defined as FS continuing beyond 6 years of age. Nonfebrile seizure was defined as a seizure that developed after at least one episode of FS. We defined low educational level for each parent as having high school graduation as the highest level attained. We defined low economic status of the family as having a monthly income less than 2,000,000 Korean won, based on the classification suggested by the Ministry of Employment and Labor, 2013.

Statistical analysis was performed using the t test for continuous variables, and Pearson's chi-square and Fisher's exact test for dichotomous variables. Multivariate logistic regression was performed for the variables with a P value < 0.05 in the univariate analysis. Odds ratios and 95% confidence intervals were also calculated. The statistics package SPSS for Windows (version 18.0; SPSS Inc., Chicago, IL) was used.

The design of this study was approved by the institutional ethical review committee at JNUH.

3. Results

We obtained information about FS for 323 patients among the 628 patients who visited our outpatient clinic or who were admitted to the ward because of their first FS. Demographic variables such as age and sex did not differ significantly between the study population (323 patients) and patients who were not included in the study (the other 305 patients among the total population of 628 patients). The male/female ratios were 127/196 and 110/195 ($P = 0.401$), and the mean ages were 5.08 and 4.89 years ($P = 0.384$), respectively. We included patients whose first FS developed between 3 months and 5 years of age, those with at least 2 years follow-up after first FS, and those who had EEG data, resulting in 246 patients. Forty-two patients were excluded because of suspected