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Evaluation of risk factors associated with first episode febrile seizure

A. GÜNEŞ, S. FIDAN, R. DULKADIR, E. ÜNLÜ

Department of Pediatrics, Medical School, Ahi Evran University, Kırşehir, Turkey

Abstract. – OBJECTIVE: Febrile convulsion (FC) is one of the most common neurological findings in children. This study was aimed to investigate the difference in laboratory parameters between Febrile Seizure and control groups.

PATIENTS AND METHODS: In this study, 169 children admitted to the pediatric emergency department with their first episode of FS and 189 control groups were retrospectively analyzed. The demographic characteristics and laboratory parameters of children were obtained from their files.

RESULTS: Upper respiratory tract infection (URTI) was determined the most common disease (81.6%) in the FC group followed by acute gastroenteritis (AGE) (15.4%) and urinary tract infection (UTI) (3%), respectively. Similarly, URTI was detected as the most common disease (81.8%) in control groups. It was determined that there was no statistically significant difference between the two groups in terms of diseases. The leukocyte and neutrophil counts of the children with FC were significantly higher but the mean corpuscular volume of lenfosit and lenfosit/neutrophil ratio was significantly lower than the control groups (p= 0.009, <0.001, 0.001, <0.001, <0.001, respectively). Children with FC had significantly higher blood glucose, urea, creatinine, creatine kinase, alkaline phosphatase and albumin levels compared with the control groups (p<0.001, in all parameters). On the other hand, the potassium, sodium and chlorine levels of the Children with FCs were significantly lower than control groups (p=0.017, <0.001, p <0.001, respectively).

CONCLUSIONS: To conclude, febrile patients with high leukocyte counts, high neutrophil counts, and several biochemical parameters should be carefully monitored for FCs due to the increasing seizure risk.

Key Words:
First febrile convulsion, Laboratory parameters, Children.

Introduction

Febrile convulsion (FC) is a type of convulsion that occurs in children aged between 6 months and 5 years due to fever in the absence of central nervous system infections. It is one of the most common neurological findings in children. Even though it has been stated that simple febrile seizures do not cause any mortality in children[1], the risk of recurrence and developing epilepsy following seizures is important in terms of traumatizing parents seriously and occupying an important place among the admissions to pediatric emergency departments. FC occurs in 2-4% of children[2,3]. Although the mechanism of FC has not been fully elucidated, it is assumed that genetic and environmental factors play important roles[4]. Upper respiratory tract infections [URTI), acute gastroenteritis (AGE) and urinary tract infections (UTI)] are among the most common etiologies[5].

It is noteworthy that some children have febrile seizures, while some others have fever without seizures. Moreover, some children with previous history of febrile seizures do not have seizures in other febrile illnesses, and this fact supports the opinion that there may be other underlying causes. This study was planned to determine the risk factors for convulsion by comparing the findings of patients with febrile seizures and control groups.

Patients and Methods

The medical records of patients who were admitted to the Pediatric Emergency Department with fever between 2017 and 2020 were examined. One hundred and sixty-nine (169) children between age 6 months to 6 years with their first episode of FS and one hundred and eighty-nine (189) children between the age 6 months to 6 years with fever but without seizures were included in this study. The control groups consisted of children (applied at almost the same age, on the same day and time) with fever as a complaint, without history of seizures in the present or past. The patients' records were retrospectively

Corresponding Author: Ali Güneş, MD; e-mail: draligunes@gmail.com

analyzed. The age, gender, causes of admission, demographic characteristics, and laboratory parameters of children were obtained from their files. Patients were excluded from the study if any of the following criteria applied: children with central nervous system infection and neurological deficits, with more than one convulsion, younger than 6 months and older than 6 years. This study was approved by the Clinical Research Ethics Committee of Kırşehir Ahi Evran University Faculty of Medicine with the date of 03.11.2020 and the decision number of 2020-16/117. Written consents were obtained from the parents for the children participating in the study.

Statistical Analysis

The data were analyzed using SPSS (Statistics Package for Social Sciences; 18.0 software; Chicago, IL, USA). Normality of data distribution was determined using Kolmogorov Smirnov or Shapiro-Wilk tests. Numerical values consistent with normal distribution were compared using the *t*-test or One-way ANOVA test. Abnormally distributed data were compared using the non-parametric Mann-Whitney U test or the Kruskal-Wallis test. Numerical data were expressed as mean ± standard deviation. Categorical values were compared using the Chi-square test. Although a minimum value of $p \leq 0.05$ was taken for statistical significance, $p<0.001$ was set for highest degree of statistical significance.

Results

In this study, 57.4% of the children with febrile convulsion were boys and 42.6% were girls, 56.2% of children in control groups were boys and 43.8% were girls. It was determined that there was no statistically significant difference between the groups in terms of gender ($p> 0.05$).

The mean of age of the FS were 30.5± 15.3 months (6-72 months) and the mean age of the controls were 31.7 ± 19.4 months (6-72 months). It was determined that there was no statistically significant difference between the groups in terms of age ($p> 0.05$). Twenty-nine patients (17.2%) had a family history of febrile convulsion.

URTI (81.6%) was determined the most common diseases in children with FC and AGE (15.4%), UTI (3%), respectively. The similar results were found in the control group. It has been determined that URTI, AGE and UTI were as 81.8, 8.3 and 9.9%, respectively. There was no statistically significant difference between the two groups in terms of diseases.

High fever above 38°C was present in both groups and 17% of children with FC also had a family history of febrile seizures. All patients had seizures for the first time and all seizures were generalized tonic-clonic seizures.

The laboratory parameter has shown that, while the leukocyte and neutrophil counts of children with FC were significantly higher, the mean corpuscular volume of lymphocyte and lymphocyte/neutrophil ratio were lower than the control groups ($p= 0.009$, $p <0.001$, $p= 0.001$, $p <0.001$, $p <0.001$, respectively). It was determined that there was no significant difference between the groups in terms of hemoglobin levels, platelet count, monocyte and mean platelet volume (MPV) ($p> 0.05$) (Table I).

The biochemical parameters of children with FC have shown that the levels of blood glucose, urea, creatinine, creatine kinase, albumin and alkaline phosphatase were significantly

Table I. Comparison of biochemical parameters of children with febrile seizures and control groups.

	Febril seizures (n: 169)	Control groups (n: 189)	p
CRP (mg/L)	1.833 ± 2.584	2.45 ± 1.42	0.001
Glucose (mg/dL)	124.6 ± 33.1	92.1 ± 20.22	< 0.001
Urea (mg/dL)	23.54 ± 7.79	20.14 ± 11.17	< 0.001
Creatinine (mg/dL	0.38 ± 0.12	0.34 ± 0.13	< 0.001
CK (U/L)	139.5 ± 117.2	108.5 ± 76.7	< 0.001
ALP (U/L)	227.6 ± 69.0	195.3 ± 70.3	< 0.001
Albumin (g/dL)	4.53 ± 0.30	4.37 ± 0.50	< 0.001
Na (mmol/L)	135.7 ± 2.9	137.6 ± 3.3	< 0.001
K (mmol/L)	4.45 ± 0.5	4.56 ± 0.49	0.017
Cl (mmol/L)	100.93 ± 3.27	102.8 ± 3.34	< 0.001
Ca (mmol/L)	9.67 ± 0.51	9.76 ± 0.59	0.215

CRP: C reactive protein; CK: creatine kinase; ALP: alkaline phosphatase; Na: sodium; K: potassium; Cl: chlorine; Ca: calcium.

higher than control groups (p<0.001, p<0.001, p=0.001, p<0.001, p<0.001, p<0.001, respectively). On the other hand, the levels of CRP, potassium (K), sodium (Na) and chlorine (Cl) of children with FC were significantly lower than control groups (p=0.017, p= 0.001, p <0.001, p <0.001, respectively) (Table II). It was determined that there was no significant difference between the groups in terms of calcium (Ca) levels (p> 0.05). While the levels of glucose of one hundred children (59.2%) with FC were determined over 102 mg/dl, the levels of sodium of 65 (38%) and the levels of chlorine of 24 (14.2%) were determined below 135 mmol/L and 98 mmol/L, respectively.

Discussion

Febrile convulsion is one of the most common neurological disorders in the pediatric age group and is not associated with mortality[5]. Due to the frightening nature of the clinic and the concerns of the families, various laboratory tests are usually ordered for these patients in emergency rooms. Serum electrolytes, biochemical parameters and complete blood count are the most important tests requested.

In this study, the levels of urea, creatine phosphokinase (CK) and alkaline phosphokinase (ALP) were significantly found higher in children with FCs compared to the control groups. In febrile patients, kidney function tests may temporarily give high results due to fever, nausea, vomiting, dehydration, and hypoxia at the time of convulsion[6]. Differences of urea levels between children with FC and control groups can be explained by this situation. Gunes et al[7] reported that the levels of early markers in kidney injury increases in patients with FCs. We think that the increased CK and ALP levels during convulsion may be due to convulsion itself and therefore the increase is not clinically significant.

We observed that while the sodium and chlorine levels were significantly lower in children with FCs compared to control groups, the calcium and potassium levels were normal. Arginine vasopressin (AVP) is secreted from the pituitary gland to control fever in acute febrile illnesses. AVP is also responsible for maintaining the homeostasis of body fluids during fever. It has been stated that hyponatremia can often accompany acute febrile illnesses due to inappropriate secretions of AVP[6]. In addition, studies[8,9] have shown the role of genetic predisposition in children with febrile seizures. It has been reported[8] that mutations of the voltage-gated ion channels such as sodium, potassium and chlorine channels are associated with some types of seizures. Genetic predisposition and immature brain functions along with serum electrolyte imbalances may have triggered seizures. Another study[9] has reported that serum Na and Ca levels in patients with febrile seizures were low. These electrolyte imbalances may increase the risk of seizures and recurrence during a febrile period in patients with a tendency to seizures. Imbalances in serum electrolytes and trace elements, such as calcium, sodium, and magnesium have also been detected in patients with febrile seizures[2, 7-10]. Ladan et al[6] have shown that the level of serum sodium, potassium and calcium were abnormal in 32, 4 and 16 cases, respectively. Karimzadeh et al[1] have shown that of 289 patients with FC, nine had hyponatremia, one had hypokalemia, and one had hypocalcemia[1]. On the contrary, Nikavar et al[9] have reported that there was no significant difference between serum sodium and calcium levels in children with simple and recurrent FCs and they did not recommend routine serum electrolyte screening

Table II. Comparison of hematological parameters of childrenwith febrile seizures and control groups.

	Febril seizures (n: 169)	Control groups (n: 189)	p
WBC (10^3/uL)	12088.3 ± 5535.8	10577.9 ± 5070.1	0.009
HGB (g/dL)	11.901 ± 1.023	12.026 ± 1.656	0.727
MCV (fL)	76.35 ± 6,54	78.71 ± 6.72	0.001
PLT (10^3/uL)	307.8 ± 109.0	327.8 ± 115.1	0.073
NEU (%)	6.793 ± 4.348	5.302 ± 4.279	< 0.001
LYM (%)	3.952 ± 2.397	4,.05 ± 2.46	< 0.001
Monocyte (%)	1.24 ± 1.26	0.96 ± 0.47	0.704
MPV (fL)	9.31 ± 0.69	9.49 ± 0.79	0.074
LYM/NEU	0.90 ± 1.16	1.60 ± 2.26	< 0.001

WBC: leukocyte; HBG: hemoglobin; PLT: platelet count; NEU: neutrophil; LYM: lymphocyte; MPV: mean platelet volume.

for febrile seizures. However, these studies have only compared patients with simple and complex FCs. Children without FC as a control group was not included in these studies. In our study, the sodium level was below 135 mmol/L in 65 (38.5%) of the patients, and the chlorine level was below 98 mmol/L in 24 (14.2%) of the patients.

Serum glucose levels were found to be higher in 59.2% of patients with FS than those with seizure-free fever. This increase may be due to the stress in patients with FC as well as due to the severity of the infection. As a consequence, the leukocyte and neutrophil counts of the children with FCs were significantly higher than the control groups in this study.

A previous study[10] has reported that patients with FC did not have significant hematological parameters. Unlike our study, Mohebbi et al[11] have not found any relationship between FCs and leukocyte count. In contrast to these studies, we found that the leukocyte and neutrophil counts were significantly higher in children with FC compared to control groups. Also, platelet count was not significant.

The etiology of FC may be directly related to URTI or pharyngitis, acute otitis media (AOM) pneumonia, UTI and roseola infantum[12,13]. A study performed by Abuekteish et al[13] and involving 203 children have shown that URTI was the most common cause of fever in 53% of patients with FC. Consistent with the literature, URTI was found to be the most common cause of fever in our study (75.8% of patients).

The limitations of our study are the retrospective nature of our study, the inability to question whether the control group patients have a family history of epilepsy or febrile convulsions, and the inability to determine on which day the febrile patients applied to the hospital with their symptoms.

Conclusions

To conclude, febrile patients with high leukocyte counts, high neutrophil counts, low sodium levels, low chlorine levels and high biochemical parameters including blood glucose, urea, creatinine, creatine kinase, albumin and alkaline phosphatase levelsshould be carefully monitored for FCs. We considered that although glucose level may be increased due to seizure stress, other biochemical data may contribute to the to the increasing seizure risk.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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