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Do Febrile Seizures Influence Neurodevelopment?

Febril Konvülsiyonlar Nörogelişimi Etkiler Mi?

Hatice Güneş[1*], İrfan Oğuz Şahin[2], Aslıhan Zarasız[2], Mesut Arslan[2], Füsun Dilara İçağasıoğlu[3]

[1]Sütçü İmam Üniversitesi Tıp Fakültesi, Çocuk Sağlığı ve Hastalıkları Ana Bilim Dalı, Kahramanmaraş
[2]Cumhuriyet Üniversitesi Tıp Fakültesi, Çocuk Sağlığı ve Hastalıkları Ana Bilim Dalı, Sivas
[3]Cumhuriyet Üniversitesi Tıp Fakültesi, Çocuk Nöroloji Bilim Dalı, Sivas

ABSTRACT

Objective: Families are often concerned that febrile seizures may have negative effects on the neurodevelopment of their children. The aim of our study was to demonstrate the effects of febrile seizure on the neurodevelopment in children using the Denver Developmental Screening Test II (DDST).
Materials and Methods: This cross-sectional and prospective study included 28 patients hospitalized for febrile seizures during a six-month period. The children's age, sex, number of seizures, number of recurrences, and family history of seizure were recorded. The DDST was performed at admission (1st DDST) and one year later (2nd DDST). The results were evaluated in three categories as 'normal,' 'suspicious,' and 'abnormal.'
Results: The 1st DDSTs were found as normal, suspicious, and abnormal at the rates of 53.6%, 39.3%, and 7.1%, respectively. The 2nd DDST's were normal, suspicious, and abnormal at the rates of 67.9%, 28.6%, and 3.6%, respectively. Fourteen of the 15 found as normal were normal, but 1 was suspicious. Six of the 11 found as suspicious remained suspicious, 4 were normal, and 1 was abnormal. One of the 2 patients found as abnormal was normal, the other was suspicious. There were no significant differences between the scores of the 1st and 2nd DDSTs (p=0.423).
Conclusion: We found that febrile seizures were not associated with neurodevelopmental delay when using the DDST II. According to the results of this study, it may be possible to reassure parents about the normal neurodevelopment expectations for their children despite having febrile seizures.

Key Words: Febrile Seizure, Denver Developmental Screening Test, Neuromotor Development

ÖZET

Giriş: Aileler genellikle ateşli nöbetlerin çocuklarının nörogelişiminde olumsuz etkileri olabileceği konusunda endişe duymaktadırlar. Çalışmamızın amacı; febril konvülsiyonların çocukların nörogelişimindeki etkilerini Denver Gelişimsel Tarama Testi II(DGTT II) kullanarak ortaya koymaktır.
Gereç ve Yöntem: Bu kesitsel ve prospektif çalışma, 6 aylık dönem içinde febril konvülsiyon nedeniyle yatış verilen 28 hastayı kapsamaktadır. Hastaların yaşı, cinsiyeti, nöbet sayısı, tekrarı ve aile öyküsünde nöbet varlığı kaydedildi. DGTT II testi hastaların kabulünde (DGTT II-1) ve 1 yıl sonra (DGTT II-2) yapıldı. Sonuçlar 'normal', 'anormal' ve 'şüpheli' olarak kaydedildi.
Bulgular: DGTT II-1 testinin sonuçları sırasıyla normal (%53,6), şüpheli (%39,3), anormal (%7,1) geldi. DGTT II-2 sonuçları ise normal (%67,9), şüpheli (%28,6), anormal (%3,6) olarak geldi. Normal bulunan 15 hastanın 14'ü yine normal iken, diğeri şüpheli bulundu. Şüpheli olarak bulunan 11 hastanın 6 tanesi yine şüpheli iken, kalan 4'ü normal, 1 tanesi ise anormal bulundu. Anormal bulunan 2 hastanın 1 tanesi normal, diğeri ise şüpheli olarak bulundu. DGTT II-1 ile DGTT II-2 skorları arasında anlamlı bir farklılık bulunmadı (p=0,423).
Sonuç: Febril konvülsiyonların nörogelişim bozukluğuyla ilişkili olmadığını DGTT II kullanarak bulduk. Çalışmamızın sonuçlarına göre, ateşli nöbetlere rağmen normal nörogelişim beklentileri konusunda ebeveynleri rahatlatmak mümkün olabilir.

Anahtar Kelimeler: Konvülsiyon, Denver Gelişimsel Tarama Testi, Nöromotor gelişim

Introduction

Febrile seizure (FS) is a common neurologic problem in children aged 3 months to-5 years that is associated with fever, although there is no evidence of intracranial infection or a definite cause such as metabolic problems, electrolyte imbalance, intoxication, trauma, and prior seizures without fever (1). FS is considered as a benign form of seizure, but it has been shown to be related with damage in the hippocampus, influenced mental function, and increased risk of temporary and/or permanent neurologic squeals (2). Moreover, febrile status epilepticus may result in a deterioration of language development (3). The Denver Developmental Screening Test II

***Sorumlu Yazar:** Hatice Güneş, Sütçü İmam Üniversitesi Tıp Fakültesi, Pediatri Anabilim Dalı, Kahramanmaraş/Onikişubat, Türkiye
E-mail: drhaticegunes82@gmail.com, Ofis: +90 (344) 300 35 87, Fax: +90 (344) 300 34 09
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(DDST II) is used to detect healthy children's potential neurodevelopmental problems, to detect neurodevelopmental delays in children and infants who are suspected of having perinatal problems such as prematurity, low birth weight, and family history of developmental delay (4). In a review of the English literature, we found no studies that assessed neurodevelopment in children with FS using DDST II. The aim of our study was to demonstrate the effects of FS on neurodevelopment of children using the DDST II.

Materials and Methods

The study was approved by the Ethics Research Committee (protocol number: 2013-05/09). This cross-sectional study was performed in the pediatric neurology clinic over a six-month period between January 1st and July 1st 2013.

Thirty patients aged between 6 months and 42 months who were hospitalized for FS were included in the study. The patients was diagnosed and hospitalized by the same pediatric neurologist. FS was defined as seizure associated with fever (>38°C) in the absence of intracranial infection, metabolic problems, electrolyte imbalance, intoxication, and trauma in children aged 6 to 60 months (1). No distrinction was made between simple or complex FS, because all of our study group was consisted of complex FS. Patients with simple FS were not included in the study. Complex FS is defined as seizures that are characterized by episodes that have a focal onset (eg, shaking limited to one limb or one side of the body), last longer than 15 minutes, or occur more than once in 24 hours (5). Hospitalization criteria were lasting lethargy, unstable clinical condition, and febrile status epilepticus and low socio-cultural level (6-8). Patients with epilepsy, cerebral palsy or motor/mental retardation were excluded. Two patients were excluded from study because their families couldn't be contacted for follow-up after one year due to changes in their address and phone number.

The patients' age, sex, number of seizures, medications, family history, (especially in terms of seizures), and number of seizures were recorded. Medication was started in the event that first seizures occurred before the age of one year, FS was present in the family history, in the presence of complex FS, and repeated FS that occurred more than three times (3,9). The DDST II test was performed to measure the patients' personal-social, fine motor adaptive, language, and gross motor skills at admission (1st DDST). After 1 year of their seizure, each patient was called to the hospital and the second DDST was performed (2nd DDST). According to the tests results, patients were divided into 3 groups as 'normal,' 'suspicious,' and 'abnormal.' Those who could make the items in the whole test considered normal, 2 and / or more delayed were considered to be suspicious, if they received abnormal, only 1 delay, or one or more warnings in addition to 1 delay with 2 or more warning areas (10).

Statistical Analysis: In the statistical evaluation of the data, the appropriateness of the normal distribution of the age variable was examined by the Shapiro-Wilk test. The statistical parameters of the variables with no normal distribution are expressed by Median (Min-Max). The qualitative variables were analyzed by the McNemar-Bowker test for the relationship between frequency distribution between the first and second measurements. The statistical parameters in qualitative variables are expressed in terms of frequency (%) n (%). Statistical significance was accepted as $p<0.05$. The data were evaluated in the IBM SPSS 22 package program.

Results

Of the 28 patients included in the study, 18 (64.3%) were male and 10 (35.7%) were female. The mean age was 16,50 (6-42) months. Four of the patients in the study group were prescribed phenobarbital and 2 patients were prescribed valproic acid. Ten of the patients had a family history of seizures. At the end of 1 year, 6 of these patients were found to have a seizure recurrence (Table 1).

The 1st DDSTs were found as normal, suspicious, and abnormal at the rates of 53.6%, 39.3%, and 7.1%, respectively. The 2nd DDSTs were normal, suspicious, and abnormal at the rates of 67.9%, 28.6%, and 3.6%, respectively.

Fifteen patients had normal scores in the 1st DDST, 14 of these remained normal and 1 was suspicious in the 2nd DDST. Eleven patients had suspicious scores in the 1st DDST, 6 remained suspicious, 4 were normal, and 1 was abnormal in the 2nd DDST. One of two patients with an abnormal score in the 1st DDST was found suspicious in the 2nd DDST and the other was abnormal. T
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(Table 2).

It was determined that both of the patients with abnormal test results had delayed gross-motor functions. The patient whose 1st DDST result was suspicious was found that there was a regression in

Table 1. Socio-demographic statistics

Age, months		Median (Min-Max)	16,50 (6-42)	
Gender	male	n(%)	18	(64,3)
	female	n(%)	10	(35,7)
Medication	non	n(%)	22	(78,6)
	Phenobarbital	n(%)	4	(14,3)
	valproic acid	n(%)	2	(7,1)
Presence of seizure history in family	no	n(%)	10	(35,7)
	yes	n(%)	18	(64,3)
Seizure recurrence	no	n(%)	22	(78,6)
	yes	n(%)	6	(21,4)

Table 2. Change in DDST results in follow-up

		2nd DDST score**							
		normal		Suspicious		abnormal			
		n	%	n	%	n	%	Test Value [a]	p
1stDDST score*	Normal	14	93,3	1	6,7	0	0,0		
	suspicious	4	36,4	6	54,5	1	9,1		
	abnormal	1	50,0	1	50,0	0	0,0		
Total		19	67,9	8	28,6	1	3,6	2,800	0,423

[a]McNemar-Bowker Test;α:0,05, *DDST II test score at admission,**DDST II test score one year after admission

the areas of language and gross-motor with an abnormal score in the 2nd DDST. Of the 6 patients with both suspicious DDST scores was found that 3 of them had delayed motor and language areas and, the remaining 3 had delayed in fine-motor and language areas.

All patients had seizures in generalized tonic-clonic form and, none had postictal problems, but all had multiple seizures in the first 24 hours.

Discussion

The parents of children with FS are generally concerned about the health of their children in the future. The majority of concerns are about the risks of mental retardation (48%), paralysis (31%), disability (30%), learning difficulty (22%) and recurrence (66%) (11,12). Some other concerns (33%) are hearing, sight, and memory loss, brain damage, walking disruption, drug adverse effects, coma, and death.

The aim of our study was to demonstrate the neurodevelopment of children with FS using the DDST II. Febrile seizures are believed to be benign, but some studies showed that they could result in temporary or permanent neurologic sequel, epilepsy, and mental dysfunction (13,14). Neuroradiologic imaging has shown that prolonged FSs cause damage in the hippocampus (15). Animal studies have shown that seizures triggered by hyperthermia lead to long-term changes in the hippocampus, neuron synapses, and cause convulsions due to permanent dysfunction of neurons (16). It has also been shown that prolonged FSs can cause chronic hippocampal injury, mesial temporal sclerosis, and epilepsy of the mesial temporal lobe, and decreased memory functions (2,17-23).

The incidence of mental retardation is reported as 8-22% among patients with FS admitted to hospital (24). In a large community-based prospective study, (National Collaborative Perinatal Project (NCPP), neither intelligence quotient (IQ) scores nor academic performance of children with FS were significantly different from the control group (25). In another population study in the United Kingdom, (the Child Health and Education Study (CHES), 381 children with FS aged 10 years were compared with healthy peers in terms of academic, intellectual, and behavioral acts, and no significant differences were found (26). However, a study showed that 5% of patients with FS who were admitted to hospital had new neurologic abnormalities (24). In a study of 14 monozygotic twins, it was found that there was a minimal effect on the intellectual

capacity of twin partner who had febrile convulsions compared with the twin with no convulsions (27).

In recent studies, children with FS were compared with other healthy groups at admission in terms of IQ levels, neurologic problems, and intellectual and behavioral acts. In our study it was found that the patients with abnormal DDST score had a delay in gross-motor area. The recurrence of these patients' seizures within 1 year can be related to this, but more studies are needed to claim this. According to our English literature review, this is the first study to compare the neurodevelopment of children with FS with themselves after a 1 year period using DDST II.

According to the non-significant difference in the scores of the 1st and 2nd DDSTs, it may be concluded that febrile convulsions may not result in an effect on the neurodevelopment of patients.

The limitations of this study are the absence of a healthy control group, the small size of the study group, and the short follow-up period. Other limitations of the study are that the patients were not evaluated in simple-complex FS groups, or in groups with and without medication. However, further studies with more subjects can be performed comparing simple and complex febrile seizures on this issue.

In conclusion, FS was not found associated with neuromotor developmental delay using the DDST II. According to the results of this study, it may be possible to reassure parents about the normal neurodevelopment expectation for their children despite FS to reduce their anxiety about future. Further studies are needed to define long-term neurodevelopment of children with FS.

Conflict of Interest: All authors declare that they have no conflicts of interest.

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