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Araştırma / *Research Article*

Psychosocial And Behavioral Functioning of Cognitively Normal Children with History of Neonatal Seizure: Case Control Study

Yenidoğan Döneminde Nöbet Geçiren Mental Düzeyleri Normal Çocukların Psikososyal ve Davranışsal İşlevleri: Olgu-Kontrol Çalışması

Edibe Pembegül Yıldız
Gonca Bektaş
Uğur Tekin
Melis Ulak Özkan
Mine Çalışkan
Nur Aydınlı
Meral Özmen

ABSTRACT

Objective: *Neurological sequelae associated with the neonatal seizures (NSs) are known in the long-term as epilepsy, neurodevelopmental retardation, and cerebral palsy. This study reports the psychosocial and behavioral problems among children whose neurodevelopmental status was not affected in the long-term.*
Method: *Patients who were diagnosed with and treated for NSs between January 2006 and December 2008 were included in this case-control study. Children with physical inabilities, epilepsy, continuous medication use, concomitant chronic diseases and mental retardation (intelligence quantity <70) were excluded from the study. Children matched with patient group for age, sex, and socioeconomic status were recruited as the control group. All participants were screened for their intelligence and psychosocial and behavioral functioning using standardized tests and questionnaires. The Wechsler Intelligence Scale for Children IV (WISC-IV) were used to evaluate intellectual performence. Psychosocial and behavioral functioning were assessed using a set of standardized questionnaires including Strengths and Difficulties Questionnaire (SDQ).*
Results: *Seventeen patients (9 women) with NS and 18 healthy controls (10 women), aged 9-12 years, participated in the study. There was no statistically significant difference between children with neonatal seizures and controls as for their intelligence levels (p>0.05). The total scores and subscala SDQ scores were not statistically different between children with neonatal seizures and controls (p>0.05).*
Conclusion: *Psychosocial monitorization and referral of risky children who were exposed to seizures during active stages of brain development to psychiatric evaluation may be a reasonable approach.*

Keywords: *neonatal seizure, behavioral problems, epilepsy, psychiatric evaluation*

ÖZ

Amaç: *Yenidoğan nöbetleri (YN) ile ilişkili nörolojik sekeller uzun dönemde epilepsi, nörogelişimsel gerilik ve serebral palsi olarak bilinir. Bu çalışma, YN geçirmiş, nörobilişsel açıdan uzun dönemde etkilenmeyen çocukların psikososyal ve davranışsal sorunları araştırmayı amaçlamaktadır.*
Yöntem: *Ocak 2006 ile Aralık 2008 tarihleri arasında YN tanısı alan ve tedavi edilen hastalar olgu-kontrol çalışmasına dâhil edildi. Epilepsi, eşlik eden kronik hastalık, düzenli ilaç kullanımı öyküsü olan ve nöromotor gelişim basamaklarında gecikme olan hastalar çalışamaya dâhil edilmedi. Yaş, cinsiyet ve sosyoekonomik düzeyi hasta grubuna benzer olan çocuklar kontrol grubu olarak seçilmiştir. Davranış ve psikososyal değerlendirme için tüm katılımcılara standardize edilmiş sorular ve testler uygulandı. Çocuklar için Wechsler Zeka Ölçeği (WISC-IV) zihinsel performansı değerlendirmek için kullanıldı. Psikososyal ve davranışsal işlevsellik, Güçler ve Güçlükler Anketi (GGA) kullanılarak değerlendirilmiştir.*
Bulgular: *YN olan 17 hasta (9 kız) ve yaşları 9-12 olan 18 sağlıklı kontrol (10 kız) çalışmaya dâhil edildi. YN olan çocuklar ile kontrol grubu arasında zekâ düzeylerinde istatistiksel olarak anlamlı bir fark bulunmadı (p>0,05). YN ve kontrol grubu arasında toplam puanlar ve alt ölçek SDQ puanları istatistiksel olarak farklı değildi (p>0,05).*
Sonuç: *Beynin gelişim aşamasında nöbetlere maruz kalan riskli çocukların okul çağına geldiklerinde psikososyal açıdan izlenmesi, psikiyatrik değerlendirmeye yönlendirilmesi doğru bir yaklaşım olacaktır.*

Anahtar kelimeler: *yenidoğan, nöbet, epilepsi, davranış*

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Edibe Pembegül Yıldız
SBÜ. Kanuni Sultan Süleyman EAH
Çocuk Nöroloji Kliniği
34303 İstanbul - Türkiye
✉ edibepembegul@hotmail.com
ORCİD: 0000-0002-8016-0404

G. Bektaş 0000-0002-6725-3964
İ. Ü. İstanbul Tıp Fakültesi
Çocuk Sağlığı ve Hastalıkları ABD
Çocuk Nörolojisi Bilim Dalı
İstanbul - Türkiye

U. Tekin 0000-0003-0008-1333
Ege Üniversitesi Tıp Fakültesi
Çocuk ve Adolesan Psikiyatri ABD
İzmir - Türkiye

M. Ulak Özkan 0000-0002-8226-3941
M. Çalışkan 0000-0002-6869-3937
N. Aydınlı 0000-0003-0492-3411
M. Özmen 0000-0003-4316-1499
İ. Ü. İstanbul Tıp Fakültesi
Çocuk Sağlığı ve Hastalıkları ABD
Çocuk Nörolojisi Bilim Dalı
İstanbul - Türkiye

INTRODUCTION

Epilepsy, a group of central nervous system disorder, is characterized by seizures generated by abnormal, excessive or hypersynchronous neuronal activity in the brain [1]. Neonatal period conveys a high risk for seizures, linked to higher seizure susceptibility and lower seizure threshold compared to other ages. The short-term prognosis of neonatal seizures (NS) is considered to be improved by perinatal and neonatal care. However, the long-term neurologic prognosis has not improved especially in terms of intellectual disability and learning disabilities [2-5].

Psychosocial and behavioral problems including mood, anxiety, attention deficit/ hyperactivity disorders and autism suggestively arise from the delayed brain maturation [3]. NSs can contribute to delay in brain maturation and may increase the likelihood of psychosocial and behavioral problems.

It may be noteworthy to investigate the psychosocial and behavioral problems that may potentially develop in cognitively normal children with neonatal seizures to clarify direct relationship between neonatal seizures and psychosocial and behavioral problems. In this study, we evaluated the influence of neonatal seizures on psychosocial and behavioral functioning.

MATERIALS and METHODS

Participants

The participants consisted of children presented with NS between January 2006 and December 2008. Review of the medical records revealed a total of 80 patients with NS. The seizures of the neonates were diagnosed by a neonatologist based on clinical observations, and then the patients were referred to our center for consultations. The final diagnoses of the neonatal seizures were confirmed by the pediatric neurologists, based either on the direct observation of the clinical manifestations, and/or electroencephalography (EEG) events.

Children aged 6-16 years who regularly attended school and had an intelligence level of >70 were included in the study . Children with epilepsy, continuous medication use, concomitant chronic disease and delay in neurodevelopmental milestones were excluded from the study. All of the children with neonatal seizures were contacted by phone and invited to participate into the study. Healthy children matched with patients as for age, sex, and socioeconomic status were recruited as the control group.

The study was reviewed and approved by the Institutional Ethics Committee of Istanbul Faculty of Medicine. All participants and/or their legal representatives provided their written informed consent.

Clinical Data

Data on demographics, prenatal and perinatal history consisted of gestational age; type of delivery, birth weight, APGAR score, requirement for neonatal resuscitation, timing and type of seizures, etiology of neonatal seizure, the presence of status epilepticus, response to antiepileptic medication, treatment duration as derived from medical records. Electroencephalography and brain imaging findings were also recorded.

Psychosocial and Behavioral Evaluation

All participants were screened for their intelligence level, psychosocial and behavioral functioning using standardized tests and questionnaire forms. The Wechsler Intelligence Scale for Children IV (WISC-IV) was used to evaluate verbal, performance and general intelligence status and administered by an experienced and certified psychologist. Psychosocial and behavioral functioning including emotional symptoms, conduct problems, hyperactivity and concentration difficulties, peer relationship problems and prosocial properties were assessed using the Turkish version of Parent Form of Strengths and Difficulties Questionnaire (SDQ-Tur) forms which were filled out by parents. The SDQ consists of 5 subscales, each with 5 items, is defined as a reliable and valid screening tool for assessing psychosocial and behavioral problems [6-8]. SDQ survey is performed and evaluated by a child and adolescent psychiatrist (UT).

Statistical analysis

Statistical analysis was performed using the SPSS for Windows version 21.0 software (IBM Corp., Armonk, NY, USA). Demographic variables were expressed in mean and standard deviation (SD), median and percentage. The Shapiro-Wilk test was used to assess the normality for demographic variables and ques-

tionnaire scores. Intergroup differences in terms of the scores and subscores of questionnaire forms were assessed using the Mann-Whitney U test. A p value of <0.05 was considered statistically significant.

RESULTS

Demographics and clinical data

A total of 35 children, 17 patients (9 female) with neonatal seizures and 18 healthy controls (10 female) participated in the study. Demographic and clinical characteristics of participants are listed in Table 1.

Table 1. Demographic and clinical characteristics of participants.

	Neonatal Seizure	Healty Group
n	17	18
Mean age at participation (years) (SD)	9.8 (0.8)	9.6 (1.2)
Gender (% female)	9 (53%)	10 (55%)
Etiology		
Structural	7	-
Metabolic	6	-
Genetics	1	-
Unknown	3	-
Status Epilepticus (%)	2 (11.7)	-
Full-scale IQ (SD)	106.2 (17.9)	110.5 (11.14)
SDQ total scores (SD)	10.53 (7.5)	10 (6.2)

Abbreviations: IQ = intelligence quantity; SD = standard deviation.

There were no significant differences observed as for demographic characteristics, gestational age, type of delivery, birth weight, Apgar score, requirement for neonatal resuscitation between 2 groups (p>0.05). Seizures manifested within the first 24 hours in 6 (35.2%) within 24 to 72 hours in 7 (41%) and after 72 hours in 4 (23.6%) patients. Status epilepticus developed in 2 (11.7%) patients. Based on the data obtained from patient files, tonic (n=6: 35.2%), clonic (n=6: 35.2%), subtle (n=4: 23.5 %) and myoclonic in= 1: 5%) seizures were detected in respective number of patients. The etiology of neonatal seizures was structural in 7 (41%), metabolic in 6 (35%), genetic in 1 (5%) and unknown in 3 (17.6%) patients. The median time elapsed from the last observed clinical seizure was 10.2 months (range: 8 days to 46 months). The median duration of antiepileptic treatment was 24.7 months (range: 1 month- 6 years). Four patients received no antiepileptic medication.

Psychosocial and Behavioral Evaluation

Any statistically significant difference was not observed in general, verbal and performance intelligence quotient (p>0.05) between children with neonatal seizures and the control group. The SDQ total scores and subscale scores relevant to emotional symptoms, conduct problems, hyperactivity and concentration difficulties, peer relationship problems and prosocial properties were not statistically different between children with neonatal seizures and controls (p>0.05).

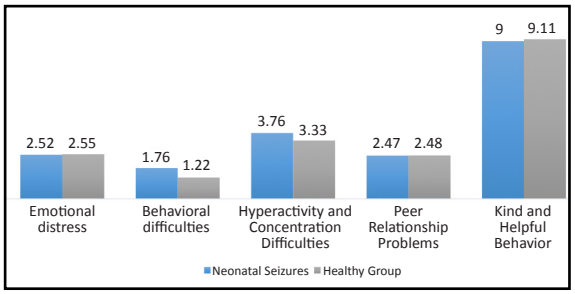

Figure 1. The means of SDQ subscale scores.

DISCUSSION

Although the negative influence of NS on a developing brain is still a matter of debate, to the best of our knowledge, this is the first study to report the psychosocial and behavioral problems among children whose neurodevelopmental was not affected in the long-term.

In the present study, school-age children who experienced NS without epilepsy or continuous drug use were compared to the healthy controls in terms of psychosocial and behavioral functioning. Clinical studies investigating the impact of NS on long-term outcome have addressed neurological outcomes, although psychosocial and behavioral influences were not previously addressed in any study. Different from previous studies, we investigated whether these children develop potential psychosocial and behavioral problems compared to healthy controls using the SDQ-Tur-parents scale. Based on the parent reports, there was no statistically significant difference between the two groups in terms of the total and sub-scale scores of the SDQ-Tur scale.

The impact of seizures experienced in early stages of life on social behavior was previously investigated in several animal studies, and these seizures were

found to be associated with negative effects in the long-term [9-11]. The changes induced by the NS, particularly in the functions of the hippocampus, were considered as the potential causes of such behavioral problems [12,13]. In the literature, we were unable to find any study investigating the impact of NS on the long-term psychosocial and behavioral development of children. On the other hand, previous reports indicated that the frequency of psychosocial and behavioral problems increased in patients diagnosed with childhood epilepsy, and the severity of these psychosocial and behavioral problems considerably increased with increasing frequency of seizures, their intensity as well as the number of anti-epileptics used and their side effects [14,15]. In the present study, we evaluated the permanent negative effects of NS in the clinical practice, which were experienced, when the rate of brain development was still high, on an individual's behaviors in the long-term, irrespective of the effects of still active seizures or anti-epileptics used. Therefore, we excluded patients with conditions including intellectual disability, chronic disease, diagnosis of epilepsy or concomitant medication use, which might affect psychosocial and cognitive functioning. Based on the parent reports, there was no significant difference between the SDQ scores of healthy controls who did not experience a NS and the patients who were neurodevelopmentally healthy and developed intellectual capabilities. In terms of neonatal patient history, our patient population represented a heterogeneous group with low Apgar scores, refractory seizures, history of status epilepticus and neonatal resuscitation. It is evident that further clinical studies including larger patient groups that are more homogeneous in terms of clinical history with data collected from various resources such as the parents, schools, psychiatric examinations and observations, are needed to explore this subject. Epidemiological studies have consistently shown that children with epilepsy have higher rates of behavior problems than children with other chronic physical conditions, but our results were contradictory to those findings.

This study has some limitations. First of all, our patient sample was not classified in terms of the etiologies of their seizures and represented a heterogeneous, and small study population. Secondly, psychosocial and behavioral problems were assessed by a scale based on parents' report, whereas psychiatric examinations were not performed and no data were collected from the schools or teachers. Considering these factors, future studies investigating psychosocial and behavioral problems in NS more objectively by the use of neuropsychiatric testing tools in larger patient populations would be informative and may improve our understanding.

CONCLUSION

In conclusion, the presence of comorbid psychiatric disorders has a significant impact on the quality of life and, thus, recognition of these disorders is of utmost importance to initiate treatment in children with neurological disorders. Our study results showed that the frequency of psychosocial and behavioral problems did not increase among patients who had a history of NS in the absence of epilepsy or an intellectual disability, compared to the healthy controls. Still, as these children were exposed to seizures during active stages of brain development, it may be reasonable to monitor them with respect to psychosocial and behavioral problems, when they reach school-age and ensure that problematic high-risk children are referred to psychiatric evaluation.

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