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Araştırma

Risk factors for epilepsy after ischemic stroke in children

Çocuklarda iskemik inme sonrası epilepsi için risk faktörleri

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ABSTRACT

Objective: We performed this study to determine the incidence of seizures and post-stroke epilepsy and risk factors of post-stroke epilepsy after childhood ischemic stroke.
Methods: In this study, we retrospectively analyzed data from children who had ischemic stroke.
Results: Of the one hundred and two children, mean age of stroke onset was 67.32± 25.48 months (1-180 months). There were 56 (54.9%) boys and 46 (45.1%) girls in the study . Of the 102 patients, 39 (38.2%) had seizures. Twenty seven (69.2%) had early-onset post-stroke seizures, and 12 (30.8%) had late-onset post-stroke seizures. Epilepsy were detected in 17 (16.7%) of the patients. Eight of them had early-onset and nine had late-onset post-stroke seizures. We found that cortical involvement and late onset post-stroke seizure are predictors of the development of post-stroke epilepsy.
Conclusions: Post-stroke seizures and epilepsy in children are common. Therefore, further studies are needed to describe risk factors for the development of post-stroke epilepsy in this population.

Keywords: Ischemic stroke, post-stroke epilepsy, risk factors, children

ÖZ

Amaç: Bu çalışma, çocukluk çağı iskemik inme sonrasında nöbet, epilepsi ve epilepsi insidansı ile risk faktörlerinin saptanması için yapıldı.
Yöntem: Çalışmada, iskemik inme geçiren çocukların verileri retrospektif olarak analiz edildi.
Bulgular: İskemik inme geçiren 102 hastanın yaş ortalaması 67,32± 25,48 ay (1-180 ay) idi. Elli altısı (%54,9) erkek ve 46'sı ise (%45,1) kız idi. Yüz iki hastanın, 39'u (%38,2) nöbet geçirmişti. Yirmi yedi (%69,2) hastanın nöbeti erken başlangıçlı iken, 12 (%30,8) hastanın nöbeti geç başlangıçlıydı. Hastaların 17'sinde (%16,7) epilepsi gelişmişti. Bunların 8'i erken başlangıçlı nöbeti olan hastayken, 9'u ise geç başlangıçlı nöbeti olan hastalardı. Lezyonun lokalizasyonu ve nöbet başlama zamanı epilepsi için risk faktörü saptandı.
Sonuç: İnme sonrası nöbetler ve epilepsi çocuklarda sık görülür. Bu nedenle, bu populasyonda, inme sonrası epilepsi gelişme riskini saptamak için daha fazla çalışmaya gereksinim vardır.

Anahtar kelimeler: İskemik inme, epilepsi, risk faktörleri, çocuklar

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INTRODUCTION

Childhood stroke is defined as a sudden onset of neurological deficit due to a cerebrovascular disorder, which lasts for 24 hours or longer. The incidence of pediatric stroke has been estimated as 2 to 13 per 100,000 children [1,2]. Strokes are currently broadly classified as either hemorrhagic or ischemic. Ischemic stroke is more common.

Stroke is presented with various neurological complications at onset including focal signs (hemiparesis, visual field deficit, and speech deficit), diffuse signs (decreased level of consciousness, headache), and seizures [3]. Seizures and epilepsy are complications which can occur after ischemic stroke. The incidence of post-stroke seizures in children is known to be high [4,5].

There have been reports about the incidence of

seizures after stroke in adults [6], but there are few studies concerning seizures and epilepsy occurring after ischemic stroke in children [5,7-9]. Therefore, we conducted a retrospective study to identify the prevalence of seizures and epilepsy and risk factors of developing epilepsy in children with ischemic stroke.

MATERIAL and METHODS

This is a retrospective study about patients who had ischemic strokes at Çukurova University hospital between January 2004 and January 2014. Transient ischemic attack, hypoxic-ischemic encephalopathy, and neonatal stroke were not included in this study. The patients were divided into three subgroups: as patients with early-onset seizures, patients with late remote seizures, and patients without seizures. We classified seizures according to the International League Against Epilepsy (ILAE) criteria [10]. According to the guidelines of ILAE, early post-stroke seizures were defined as those occurring within 7 days and late post-stroke seizures as unprovoked seizures developing beyond 1 week after stroke [3].

Strokes were related to various etiologies as cardiovascular, infection, hematological disease (sickle cell anemia, and thalassemia major), prothrombotic state, trauma, nephrotic syndrome, and idiopatic.

We reviewed the medical records of our study population, retrospectively. Clinical and laboratory data such as age, gender, age at stroke, etiology, neurologic deficits, history of seizures, seizure type, seizure onset time, number of antiepileptic drugs (AEDs), epilepsy, neuroimaging findings, infarct areas (cortical, subcortical, cortico-subcortical), number of infarct areas, affected hemisphere (right, left, or bilateral), duration of follow-up, and EEG findings (focal and generalized abnormalities) were recorded.

The SPSS version 19.0 was used for statistical analysis. The chi-square tests were used to determine the associations between categorical data. We carried out univariate and multivariate analyses of potential predictors of recurrence risk using Cox regression analysis. The level of statistical significance was established at p- value of <0.05. Initially, we performed a univariate analysis, in order to determine which predictor would be used in multivariate analysis.

RESULTS

One hundred and two children were identified as having ischemic stroke. The mean age at stroke was 67.32±25.48 months (1-180 months). Of the 102 patients, 56 (54.9%) were boys and 46 (45.1%) were girls. The median follow-up period was almost 2 years.

Of the 102 patients, 39 (38.2%) had seizures, and 63 (61.8%) had no seizures. While 27 (69.2%) patients had early-onset, and 12 (30.8%) late-onset post-

Table 1. Summary of demographics data of patients with ischemic stroke.

Parameters		n	%
Gender	Boy	56	54.9
	Girl	46	45.1
Age at stroke	<5 years	37	36.3
	5-10 years	60	58.5
	>10 years	5	4.9
Neurologic deficits	Yes	75	73.5
	No	27	26.5
History of seizures	Yes	39	38.2
	No	63	61.8
Seizure onset time	Early onset	26	69.6
	Late onset	13	30.4
Type of seizure	Partial	26	60.9
	Generalized	13	30.4
Development of epilepsy	Yes	17	16.7
	No	85	83.3
Neurologic deficits	Yes	75	73.5
	No	27	26.5
Type of neurologic deficits	Right hemiparesis	32	42.6
	Left hemiparesis	38	50.6
	Bilateral involvement	5	6.8
Lesion location	Cortical	50	49.0
	Noncortical	38	37.3
	Both	14	13.7
Number of infarct areas	1	85	83.3
disorders	≥ 2	17	16.7
Affected hemisphere	Unilateral hemisphere	96	94.1
	Bilateral hemisphere	6	5.9
EEG findings	Focal abnormalities	27	69.2
	Generalized abnormalities	12	30.8
Etiology	Cardiac disease	30	29.4
	Infection	18	17.6
	Hemotological disease	16	15.7
	Prothrombotic state	14	13.7
	Trauma	6	5.9
	Nephrotic syndrome	3	2.9
	Idiopatic	15	14.7

EMG: Electromyelography

Table 2. Risk factors associated with epilepsy development.

Parameters		Epilepsy		No epilepsy		P value
		n	%	n	%	
Gender	Boy	6	33.3	12	66.7	0.192
	Girl	11	52.4	10	47.6	
Age at stroke	<5 years	7	41.2	10	58.8	0.956
	5-10 years	9	45	11	55	
	>10 years	1	50	1	50	
Seizure onset time	Early onset	7	26.9	19	73.1	0.004
	Late onset	10	76.9	3	23.1	
Type of seizure	Partial	13	50	13	50	0.213
	Generalized	4	30.8	8	69.2	
Neurologic deficits	Yes	15	40.5	22	59.5	
	No	2	100	0	0	
Type of neurologic deficits	Right hemiparesis	5	38.5	8	61.5	0.634
	Left hemiparesis	10	45.5	12	54.5	
	Bilateral involvement	2	50	2	50	
Lesion location	Cortical	13	56.5	10	43.5	0.040
	Noncortical	2	15.4	11	84.6	
	Both	2	66.7	1	33.3	
Number of infarct areas	1	11	37.9	18	62.1	0.199
	≥ 2	6	60	4	40	
Affected hemisphere	Unilateral hemisphere	16	45.7	19	54.3	0.407
	Bilateral hemisphere	1	25	3	75	
EEG findings	Focal abnormalities	13	48.1	14	51.9	0.307
	Generalized abnormalities	4	33.3	8	66.7	

stroke seizures. Focal and generalized seizures were identified in 26 (66.7%) and 13 patients (33.3%), respectively. Epilepsy was detected in 17 (16.7%) patients. Eight of them had early-onset and nine late-onset post-stroke seizures. Most of them (76%) used AED as monotherapy.

Focal neurological signs were the most common presentations, but these were not risk factors for the development of epilepsy. The most common risk factors for stroke were the presence of congenital/acquired heart disease (29.4%), central nervous system infection (17.6%), and hematological disease (SCD, and thalassemia major) (15.7%). In 14.7% (n=15) of children there were no identifiable risk factors.

EEG recordings were performed in all the patients who had seizures. Twenty five patients had focal, and 14 (35.9%) had generalized EEG abnormalities. The demographic details of these patients are summarized in Table 1.

There was no correlation between epilepsy and gender, age at stroke, etiology, neurologic deficits, seizure type, number of foci of infarction, affected hemisphere, and EEG findings (focal and generalized abnormalities). But, a statistically significant correlation between epilepsy and lesion location, and seizure onset time was detected (Table 2). In the multivariate analysis, seizure onset time was the only risk factor for epilepsy.

DISCUSSION

Cerebrovascular disease is the most common and well-known etiology of epileptic seizures in adults. The estimated incidence of seizures after stroke in adults ranges from 0.4% to 43%, with variation on the basis of stroke subtype [6,11]. Seizure is a consequence of stroke more often in children than in adults; it has been reported that the incidence rate of seizures within 24 hours of a stroke is 18 times higher in children than in adults [6]. In literature, there have been a few studies concerning the incidence on the post-stroke seizures and subsequent epilepsy, and risk factors for post-stroke epilepsy [7-9].

We found seizures in 38.2% of the patients who

had suffered strokes. Kopyta et al. [12] described strokes in 26% of their 78 patients. In other studies, Incecik et al. [5] and Morais et al. [13] reported seizures in 35% and 64.6% of children, respectively. In our study, post-stroke epilepsy developed in only 16.7% of the patients. Similarly, Kopyta et al. [12] reported post-stroke epilepsy rate as 13%. In contrast, the incidence of epilepsy after stroke was higher in the other group of pediatric studies. Lee et al. [3] observed seizures in 41.4%, and epilepsy in 22.3% of children with stroke. Morais et al. [5] reported that 29.2% of their patients developed post-stroke epilepsy. These discrepancies in the frequency of post-stroke epilepsy exist because different groups of children, and different populations have been investigated in each study.

We detected that the only risk factors for developing epilepsy were seizure onset time and lesion location in neuroimaging.

Lee et al. [3] reported that epilepsy was the most common sequelae in both the early post-stroke seizure (38.1%) and late post-stroke seizure group (100%). Morais et al. [5] and Yang et al. [14] found a significant association between late post-stroke seizures and epilepsy in children after ischemic stroke similar to our study. These studies agree that late post-stroke seizure was a risk factor for post-stroke epilepsy. The occurrence of early and late post-stroke seizures parallels that of post-traumatic epilepsy. These similar pathophysiologic mechanisms are cellular biochemical dysfunction for early post-stroke seizures and epileptogenic gliotic scarring for late post-stroke seizures [15]. This high risk of post-stroke epilepsy has been also observed in the cases with late post-stroke seizures investigated in other studies [3,5,14] and furthermore this risk is higher than that reported for the general population experiencing their first unprovoked seizures [16]. Therefore, Dhanuka et al. [17] also made a conclusion that early post-stroke seizures were rather common, did not recur and could not be treated with AEDs. Late post-stroke seizures were less common but they were associated with post-stroke epilepsy.

About seizure types, Horner et al. [18] described that early post-stroke seizures were more likely to be generalized. On the contrary, Gupta et al. [19] reported that early post-stroke seizures were more likely to be partial (57%), whereas late post-stroke seizures were more likely to be generalized (65%). We detected same finding as Gupta et al. [19] But, there was not significant difference between focal seizures and generalized seizures and epilepsy in our study.

Previous studies reported epilepsy to be caused more often by cortical rather than noncortical involvement [5,20,21]. However, Kotila and Waltimo [22] reported that lesion location did not play any role in the development of epilepsy. Cortical involvement was also found as a risk factor for the development of epilepsy in our study.

Some studies have shown that focal cortical dysfunction on EEG was a risk for developing epilepsy [3]. But other studies have found no significant relation [5,7,9]. We also found no association between EEG findings and development of epilepsy.

In conclusion, seizures and epilepsy may occur in children with ischemic stroke. We found that cortical involvement and late onset post-stroke seizure are predictors of the development of post-stroke epilepsy. Further studies are required to identify risk factors for the development of post-stroke epilepsy in childhood ischemic stroke.

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