RESEARCH ARTICLE

ASSESSMENT OF COGNITIVE AND MOTOR DEVELOPMENT IN 150 CHILDREN WITH REFRACTORY EPILEPSY

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Abstract

Objective

Neuropsychological impairment is an important co-morbidity of chronic epilepsy. The aim of this study was to determine the state of the cognitive and motor development of patients with refractory epilepsy.

Materials & Methods

We studied 150 consecutive children with epilepsy who were referred to Mofid Children Hospital, a third level public referral University Hospital in Tehran, Iran, from October 2007 to October 2008. Refractory epilepsy was defined as therapeutic failure of three antiepileptic drugs which were used appropriately. Data regarding sex, age, age at which the first seizure occurred, microcphaly, muscle tonicity, EEG findings, kind of treatment for controlling seizures and cognitive and motor development delay were collected from medical records. Development delay was defined as delay in acquiring cognitive ability and motor skills for age according to the Denver Scale II.

Results

Of 150 patients 72% were younger than 2 years old and 56.7% were male. About 35.3% were microcephalic while 76% had normal muscular tonicity. Only 2.7% had normal EEGs. About 37.3% showed a good response to anticonvulsive drugs and became seizure free, 13.3% showed a relative response to anticonvulsants but 49.3% did not respond. In the present study, 68% had cognitive developmental delay and 60.7% suffering motor delay. There was a significant difference in response to treatment between patients with cognitive and motor development delay

Conclusion

Cognitive developmental delay was more frequent in patients with refractory epilepsy, suggesting that early cognitive screening and introduvtion of rehabilitation programs are necessary for patients with refractory epilepsy.

Keywords: Refractory epilepsy, cognition, motor development, children

Introduction

Antiepileptic drug therapy is the mainstay of treatment for most patients with epilepsy (1). Despite the introduction of several novel antiepileptic drugs (AEDs) in the past decades (2), over 30% of people with epilepsy never achieve remission with antiepileptic drug (AED) therapy (3-5). Refractory epilepsy, in addition, represents a significant drain on health care resources (6).

Cognition can be defined as the capacity of the brain to process information accurately and to program adaptive behaviour. Cognition involves the ability to solve problems, to memorize information, or to focus attention. On a higher level, it involves dealing with complex situations creatively by transcending from the immediate circumstances to anticipate future acting (7). Neuropsychological impairment is an important co-morbidity of chronic epilepsy. A long and rich history of research has characterized the relationships between impaired cognition and a variety of factors related to clinical epilepsy including aetiology, age of onset, seizure type and severity, duration, anti-epilepsy medications and other factors. In addition, modal cognitive profiles have been derived for several syndromes of epilepsy, and efforts have been undertaken to identify the shared versus unique cognitive abnormalities evident across epilepsy syndromes (8). The epileptic child has three times more risk of presenting cognitive disorders than other children with no neurological pathology, in accordance with three essential facts: 1. the effect exerted by the actual epilepsy. 2. any associated preexisting neuropsychosocial deficits. 3. the side effects of the AEDs (9). The motor developmental delay in children with refractory epilepsy has a total sensorimotor impairment pattern, including balance, co-ordination, and perceptual capacity (10). Van Mil et al. reported that motor functioning was abnormal in children with cryptogenic localization related epilepsy (11) and Thomas et al. showed that motor developmental in infants of mothers with epilepsy was impaired (12). However, the state of cognitive and motor development of patients with refractory epilepsy was not clear in our patients. Therefore, the aim of this study was to determine the cognitive and motor development of patients with refractory epilepsy in Mofid Children's Hospital.

Materials & Methods

In this cross-sectional study, we studied 150 consecutive children with refractory epilepsy who had returned to the Mofid children Hospital, a third level public referral University Hospital in Tehran, Iran, from October 2007 to October 2008. Refractory was defined as therapeutic failure of three antiepileptic drugs (13-16). Exclusion criteria were febrile seizures. Data regarding sex, age, age at which the first seizure occurred, microcphaly, muscle tonisity, EEG finding, kind of treatment for the control of seizure and their cognitive and motor developmental state were collected from medical records or interview from parents. Cognitive development delay was defined as a delay in cognitive ability for age according to the Denver Scale. Patients who had no seizure in the past year in fallow up were defined as seizure-free (complete response) and more than 50% reduction in time and number of seizure was defined as a relative response (5). Data was analyzed using SPSS 12 and chi-square test, and $p<0.05$ was considered as a significant level.

Results

Of 150 children, 65 (43.3%) were female and 85 (56.7%) were male. One hundred and eight patients (72%) were younger than 2 years old. the mean age at which seizures began was 20.97±26.34 months. Our results showed that 53 patients (35.3%) were microcephalic while 114 patients (76%) had normal muscular tonicity. At the time of assessment, 10 patients (6.7%) had hypotonicity and 25 patients (6.7%) had hypertonicity. Only 4 patients (2.7%) had normal EEGs, but 64 patients (42.7%) had non-specific abnormality in EEG and 82 patients (54.6%) had abnormal EEGs as convulsive waves like spike, diffuse or focal paroxismal discharge. Fifty six patients (37.3%) responded well to anticonvulsive drugs and became seizure free. Twenty patients (13.3%) responded relatively to anticonvulsants while 74 patients (49.3%) did not respond at all.

In the present study, 102 patients (68%) had cognitive developmental delay. The relationship between cognitive state and response to treatment was indicative of a significant difference between the three different groups of response to treatment and this state ($p=0.004$), with treatment response being 28.4% in patients with cognitive development delay and 56.3% in normal patients (Table 1).

Motor development delay was observed in 91 patients (60.7%), and there was a significant difference between treatment response and motor development status such that 26.4% of the patients with motor development delay and 54.2% of the patients without this disorder responded to anticonvulsants ($p=0.002$) (Table 1).

Table 1: Cognitive and motor development in patients with refractory epilepsy according to response totreatment

Development \ Response to treatment		Uncontrolled	Relatively controlled	Seizure free	p-value (chi-square)
		Frequency (%)	Frequency (%)	Frequency (%)	
Cognitive development	Normal	17 (35.4)	4 (8.3)	27 (56.3)	0.004
	Delay	57 (55.9)	16 (15.7)	29 (28.4)	
Motor development	Normal	20 (33.9)	7 (11.9)	32 (54.2)	0.002
	Delay	54 (59.3)	13 (14.3)	24 (26.4)	

Discussion

Cognitive behavioral problems were recognized in patients with epilepsy in ancient times and documented in the 19th century neurologic literature. Gowers found that although most patients demonstrated a normal intellect and pattern of behavior, some had interictal abnormalities. He recognized that the etiology of this change was multifactorial but hypothesized that epilepsy was the most important cause. Lennox expanded on Gower's work, identifying five potential factors in the cognitive and behavioral decline associated with epilepsy: heredity, brain injury prior to seizure onset, epilepsy itself, medications for epilepsy, and psychological handicaps (17). In the present study, 68% of patients had cognitive developmental delay. Some studies have shown that in newly diagnosed and untreated epileptic patients, cognitive problems are already present in more than 50% of the patients (18-20).

In the present study, there was a significant difference between treatment and cognitive state such that treatment response was lower in patients with cognitive development delay as compared to normal state patients. In other words, patients with a poor treatment response and a high frequency of seizures had a low cognitive state. Several studies have found that seizure frequency is negatively correlated with cognitive outcome (17,21,22).

Motor development delay was observed in 60.7% of our patients and there was a significant difference between treatment response and motor development status. In a study by Van Mil et al., 33-55% of the children with cryptogenic localization related epilepsy had abnormal motor function (11) and in another study, 33.5% of the infants who had exposure to antiepileptic drugs had motor developmental delay (12). Therefore, provision of rehabilitation services is nessessary for these children.

In the present study, 72% of the patients were younger than 2 years old. There are several studies which indicate that early age of onset of seizures correlates with a poor cognitive function in epilepsy (17,23,24). Some studies emphasize that age of onset is, in fact, the most important predictor of cognitive outcome in patients with epilepsy (7,25).

EEG findings are one of the principal aspects of the definition of an epileptic syndrome and may have a specific influence on cognition (7). In our study, 42.7% had non-specific abnormality and 54.6% had abnormal EEG patterns such as convulsive waves like spike, diffuse or focal waves.

In conclusion, we noticed that cognitive and motor developmental delay was more frequent in patients with refractory epilepsy, suggesting that early cognitive screening and rehabilitation programs are necessary for patients with refractory epilepsy.

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