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Original Article

Epilepsy, a common sequelae in Children with Cerebral Palsy — A Study in a Tertiary Care Hospital in Bangladesh

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ABSTRACT

Introduction: *Cerebral palsy (CP) is the most ordinary motor disability in childhood. It is defined as non-progressive and changing disorders of movement and posture. Basically, cerebral palsy (CP) is a group of disorders that affect a person's ability to move, balance and posture. On the other hand, epilepsy is a frequent association that affects the brain and causes recurrent seizures.* ***Aim of the study:*** *The aim of the study was to assess the types and nature of epilepsy among children with cerebral palsy.* ***Methods and materials:*** *This case-control study was conducted in the Department of Pediatric Neurology, National Institute of Neurosciences and Hospital, Dhaka, Bangladesh from January 2020 to December 2020. This study was screening by definitive assessment of history, clinical, GMFCS level, MACS level, and CT scan of head.* ***Results:*** *In this study, in analyzing the types of CP of the participants we observed that, 8 (16%) had spastic hemiplegia, 6 (12%) had spastic diplegia, 27 (54%) had spastic quadriplegia, 3 (6%) had dyskinetic and mixed events were found in 6 (12%). On the other hand, among CP without epilepsy cases 21(21%), 36(36%), 15(15%), 1(11%) and 17(17%) were with hemiplegia, spastic diplegia, quadriplegia, dyskinetic and mixed respectively. 56.0% had age at onset of epileptic*

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seizure less than 12 months. ***Conclusion:*** *Among CP cases epilepsy is most common in spastic quadriplegic CP. Generalized and syndromic epilepsy is a more common type of epilepsy in spastic quadriplegic CP. Focal epilepsy is more common in spastic hemiplegia CP. Epilepsy is earlier age of onset.*

Keywords: *Cerebral palsy, CP, Epilepsy, Children, Seizures*

INTRODUCTION

Cerebral palsy (CP) is the result of unprogressive damage to the developing brain and consists of a number of clinical neurological syndromes of heterogeneous aetiology [1]. Epilepsy is familiar to have a higher association with cerebral palsy. More then 15–60% of children with cerebral palsy have been reported to have epilepsy [2]. It has been noticed that, seizures in these children tend to have an earlier onset, require the use of more than one anti-epileptic drug (AED) with the risk of seizure relapse after AED discontinuation [3, 4]. CP (cerebral palsy) is a term that defines a heterogeneous group of early-onset, unprogressive, neuro developmental disorders secondary to injury to the developing brain [5]. Studies showed that, among children with CP epilepsy is associated with greater impairment of cognitive function, poorer motor outcomes, more profound behavioral and psychological problems, and poorer quality of life, all of which collectively contribute to a greater burden of disability and care [6]. To centers controlling such posture and movement as documented by findings related to pyramidal, extra pyramidal and cerebellar system. Epilepsy is considered to be present when two or more unprovoked seizures occur in a time frame of longer than 24 hours. In comparison to children with epilepsy only, children with CP and epilepsy tend to have early onset of seizures which can often be difficult to control [7]. Bangladesh is a densely populated country, of which 31% are children. Epilepsy is common in children about 8.6/1000 population. In a current nation-wide epilepsy survey it was found that, focal epilepsy is more common about 11.5/1000 population in children. Which is about 30.6% of total epilepsy in children, according to National epilepsy survey in Bangladesh by NINS in collaboration with WHO (unpublished). CP can be classified in various ways. Traditionally, it has been classified using a combination of the motor type and the topographical distribution, as well as subjective severity level. Motor types include terms like spastic, hypotonic, ataxic, dyskinetic or mixed. The topographic classifications include the limbs that are affected, namely diplegia, hemiplegia or quadriplegia. Cerebral palsy severity is classified subjectively in terms of mild, moderate or severe [8, 9].

METHODS & MATERIALS

This case-control study was conducted in the Department of Pediatric Neurology, National Institute of Neurosciences and Hospital, Dhaka, Bangladesh from January 2020 to December 2020. This study was approved by the ethical committee of the mentioned hospital. In total 150 children with cerebral palsy were enrolled in this study who were divided in to two groups. In 'CP with epilepsy' group, there were 50 patients and in CP without epilepsy group, there were 100 age-sex matched CP

patients without epilepsy patients. As per the inclusion criteria of this study, patients of cerebral palsy with epilepsy and without epilepsy between the ages of 18 month and 12 years were included. Nonspecific motor delay patients, cases with provoked seizure (eg. febrile seizure), suspected cases of neuro metabolic disease and neuro degenerative disorder were excluded. Every morning first case of CP with epilepsy was enrolled as case group. Age (±2 months) and sex matched next two cases of CP without epilepsy were enrolled as control group sequentially. Diagnosis of cerebral palsy was clinical, based on disorder of posture and movement of cerebral origin with improving developmental trend and findings related to centers controlling such posture and movement as documented by findings related to pyramidal, extra pyramidal and cerebellar system. Epilepsy was considered to be present when two or more unprovoked seizures occurred in a time frame of longer than 24 hours. Diagnosis of epilepsy was based on history from a reliable eyewitness or video documentation if available and EEG. All the diagnoses were made by the pediatric neurologist(s) based on the study definition. The motor disorders were evaluated and classified according to the Gross Motor Function Classification System (GMFCS) into five levels [10, 19]. Levels I, II, and III were named as mild-moderate GMCFS level and levels IV and IV were named as severe GMCFS level. Fine motor disorders were classified according to Manual Ability Classification System (MACS) [11,12, 20, 21]. It was developed to evaluate each hand function separately and it has five levels. Levels I, II, and III were named as mild-moderate MACS level and levels IV and IV were named as severe MACS level. CT scan of the head was done at the Neuroradiology Department of the National Institute of Neurosciences and Hospital (NINS&H) by HitachiEclos (Japan) with 16-mm axial slices, skilled professionals and expert opinions were taken from neuroradiologists and carefully reviewed by the pediatric neurologist. Along with data regarding demographic characteristics, natal events, post-natal complication, family history of epilepsy, onset of seizure, GMFCS, MACS and CT scan findings of head were recorded and analyzed. A predesigned questioner was used in data collection. All statistical tests of hypotheses were two sided. Besides standard descriptive statistical methods (mean ± standard deviation), an unpaired t-test was used in the comparison of groups, and the chi-square test was performed during the evaluation of qualitative data. P values of less than 0.05 for associations were considered to indicate statistical significance. The main analyses were performed with the use of SPSS software, version 22.0 (IBM).

RESULT

In this study, most of the patients were from 24-48 months' age groups which was CP with epilepsy 18 (36.0%) and CP without epilepsy 42 (42.0%) (P value=0.820). Male sexes were more 31 (62.0%) in case of CP with epilepsy 59 (59.0%) in case of CP without epilepsy (P value = 0.724) (Table I). Comparison Regarding postnatal complication neonatal seizure was significantly higher in CP with epilepsy 24 (48.0%) than CP without epilepsy 12 (12.0%) (p=<0.001) when compared between two groups (Table II). As per the distribution of the CP patients

according to family history of epilepsy we observed that, it was significantly higher in CP with epilepsy cases, 10 (20%) than CP without epilepsy cases, 2 (2%) (P value < 0.001) (Table III). First seizure during 1st year of life was observed significantly higher in CP with epilepsy 35 (70%) than CP without epilepsy 23 (23%) (P= < 0.001). Distribution of severity of functional dysfunction of CP patient by GMFCS was significantly different when compared between groups (p<0.001). Severe disability was higher in CP with epilepsy 32 (64.0%) and mild to moderate disability was higher in CP without epilepsy 69 (69.0%). Significant difference was also observed when CP functional level by MACS was compared between groups (p<0.001). Severe disability was higher in CP with epilepsy 26 (52.0%) and mild to moderate disability was higher in CP without epilepsy 78 (78.0%) (Table IV). In analysing the types of CP of the participants we observed that, 8 (16%) had spastic hemiplegia, 6 (12%) had spastic diplegia, 27 (54%) had spastic quadriplegia, 3 (6%) had dyskinetic and mixed events were found in 6 (12%). On the other hand, among CP without epilepsy cases 21(21%), 36(36%), 15(15%), 1(11%) and 17(17%) were with hemiplegia, spastic diplegia, quadriplegia, dyskinetic and mixed respectively. Spastic quadriplegia was higher in number in CP with epilepsy cases which was found in 27 (54%) cases. On the other hand, spastic diplegia was higher in number in CP without epilepsy cases which was found in 36 (36%) cases (p value < 0.001) (Table V).Abnormal CT scan findings of head were significantly higher in CP with epilepsy 42 (84.0%) than CP without epilepsy 46 (46.0%) (p=<0.001) (Table VI). In this study distribution of CP patients with epilepsy by EEG findings, it was found that 28 patients (56.0%) had focal origin (focal epileptiform activity 38.0%, multifocal epileptiform activity 14.0%, focal epileptiform activity with 2nd generalization 4.0%), 9 patients (18.0%) had epileptic encephalopathy and 2 patients (4.0%) had generalized epileptiform activity (Table VII).In distributing the patients according to age at onset of epileptic seizure, it was found that, 56% had onset less than 12 month, 36% had onset between 12 months to 24 months and 8% had onset between 25 months to 72 months. No patient was found between 72 months to 144 months (Figure 1). Clinically Focal epilepsy was found in 18 patients (36.0%), generalized epilepsy in 16 patients (32.0%), unknown epilepsy in 2 patients (4.0%) and syndromic epilepsy in 14 patients (28.0%) (Figure-2). Focal epilepsy is more common in spastic hemiplegia CP. Generalized and syndromic epilepsy is more common spastic quadriplegic CP (Table VIII).The mean age at onset of epilepsy was 8.30 ± 3.34 months. The onset of epileptic seizure was earlier in spastic quadriplegic patient and later in spastic hemiplegic patients (Figure-3).

Table I: Demographic status of patients (N=150)

Characteristics	CP with epilepsy (n=50)	CP without epilepsy (n=100)	P-value
Age Distribution (in months)			
<24	8 (16.0%)	12 (12.0%)	0.802
24 - 48	18 (36.0%)	42 (42.0%)	
48 - 72	9 (18.0%)	18 (18.0%)	
72 - 144	15 (30.0%)	28 (28.0%)	
Gender Distribution			
Male	31 (62.0%)	59 (59.0%)	0.724
Female	19 (38.0%)	41 (41.0%)	

Table II: Distribution of the CP patients according History of postnatal complication (n=150).

Parameters	CP with epilepsy (n=50)	CP without epilepsy (n=100)	p-value
Perinatal asphyxia	44 (88.0%)	86 (86.0%)	0.734
Neonatal seizure	24 (48.0%)	12 (12.0%)	<0.001
Neonatal jaundice	12 (24.0%)	32 (32.0%)	0.31

Table III: Distribution of the CP patients according to family history of epilepsy (N=150)

Family history	CP with epilepsy (n=50)	CP without epilepsy (n=100)	p-value
Yes	10 (20.0%)	2 (2.0%)	<0.001
No	40 (80.0%)	98 (98.0%)	

Table IV: Clinical feature of CP patients with epilepsy and CP patients without epilepsy (n=150).

Clinical features	CP with epilepsy (n=50)	CP without epilepsy (n=100)	p-value
1st Seizure during 1st year of life			<0.001
Yes	35 (70.0%)	23 (23.0%)	
No	15 (30.0%)	77 (77.0%)	
GMFCS			<0.001
Mild to moderate	18 (36.0%)	69 (69.0%)	
Severe	32 (64.0%)	31 (31.0%)	

MACS			<0.001
Mild to moderate	24 (48.0%)	78 (78.0%)	
Severe	26 (52.0%)	22 (22.0%)	

Table V: Distribution of the CP patients according to type of CP (N=150)

Type of CP	CP with epilepsy (n=50)	CP without epilepsy (n=100)	p-value
Spastic hemiplegia	8 (16.0%)	21 (21.0%)	<0.001
Spastic diplegia	6 (12.0%)	36 (36.0%)	
Spastic quadriplegia	27 (54.0%)	15 (15.0%)	
Dyskinetic	3 (6.0%)	11 (11.0%)	
Mixed	6 (12.0%)	17 (17.0%)	

Table VI: Distribution of the CP patients according to CT scan findings of head (n=150).

CT scan of head	CP with epilepsy (n=50)	CP without epilepsy (n=100)	p-value
Abnormal findings	42 (84.0%)	46 (46.0%)	<0.001
Non-specific cerebral atrophy	14 (28.0%)	13 (13.0%)	
Encephalomalacia	10 (20.0%)	09 (9.0%)	
Hydrocephalus	4 (8.0%)	7 (7.0%)	
Calcification	0 (0.0%)	1 (1.0%)	
Infarction	5 (10.0%)	8 (8.0%)	
Cystic lesion	3 (6.0%)	4 (4.0%)	
Cerebral malformation	2 (4.0%)	2 (2.0%)	
Periventricular Hypodensity	4 (8.0%)	2 (2.0%)	

Table VII: EEG findings of CP patients with epilepsy (n=50)

EEG findings	Frequency (n)	Percentage (%)
Normal findings	4	8
Generalized epileptiform activity	2	4
Focal origin		
Focal epileptiform activity	19	38
Multifocal epileptiform activity	7	14
Focal epileptiform activity with secondary generation	2	4
Epileptic encephalopathy	9	18
Hypoarrythmia	4	8
Burst suppression	2	4
Electrical status epilepticus	1	2

Table VIII: Epilepsy type (clinical) in different type of cerebral palsy (n=50).

Clinical epilepsy type	Spastic Hemiplegia	Spastic Diplegia	Spastic Quadriplegia	Dyskinetic	Mixed
Focal	7 (87.5%)	1(16.7%)	6 (22.2%)	2 (66.7%)	2(33.3%)
Generalized	0 (0.0%)	5(83.3%)	7 (25.9%)	1 (33.3%)	3(50.0%)
Unknown	0 (0. %)	0 (0.0%)	2 (7.4%)	0 (0.0%)	0 (0.0%)
Combined generalized and focal	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
West syndrome	0 (0.0%)	0 (0.0%)	8(29.6%)	0 (0.0%)	1(6.7%)
Lennox Gastaut syndrome	1 (12.5%)	0 (0.0%)	4(14.8%)	0 (0.0%)	1(16.7%)

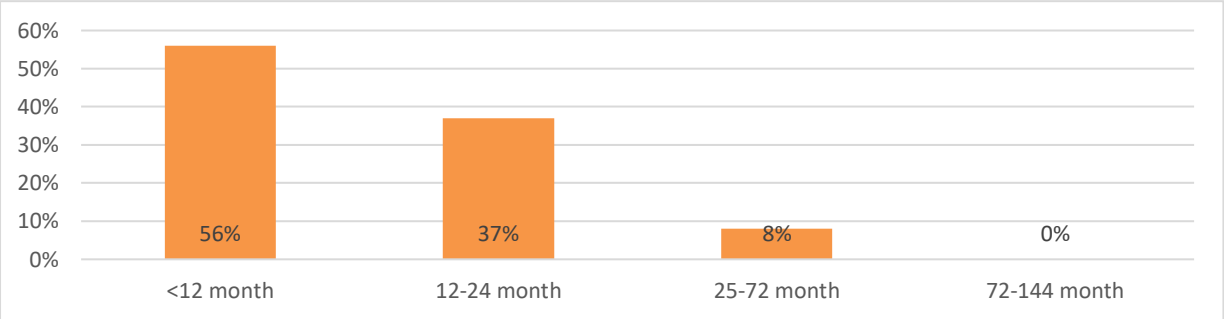

Figure 1: Distribution of the patients according to age at onset of epileptic seizure (n=50)

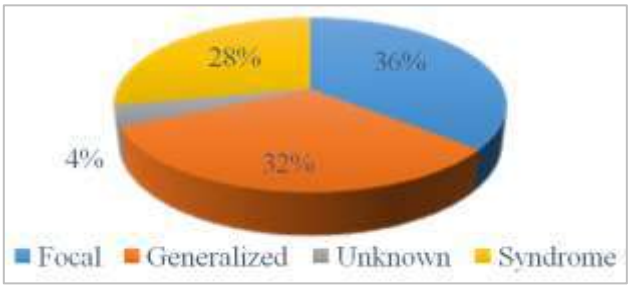

Figure 2: Clinical epilepsy type of CP patients (n=50).

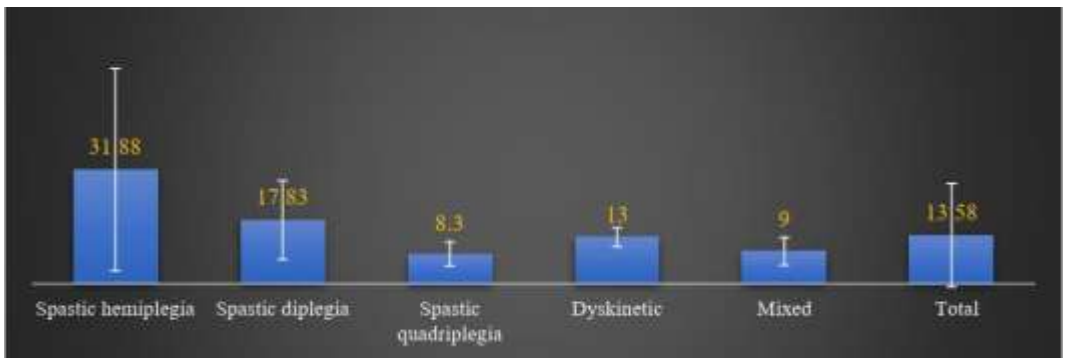

Figure 3. Mean age (in month) at onset of epileptic seizure in children with different type of cerebral palsy (n=50).

DISCUSSION

This study was conducted on 150 children with CP (age-sex matched 50 patients CP with epilepsy and 100 patients CP without epilepsy) in National Institute of Neurosciences and Hospital Dhaka, Bangladesh. The aim of the study was to explore the relationship between cerebral palsy and epilepsy and to determine the associated factors, occurrence and nature of epilepsy in children with cerebral palsy. Children age range between 18 months to 12 years were included in our study and found the age range between two to less than four years were commonest in both CP with epilepsy group 18 (36.0%) and CP without epilepsy group 42 (42.0%). In this study 90 patients (60%) were male. A similar observation was found by Pratibha Singhi et al. [7]. In their study they found 65 patient (62%) out of 105 Cerebral Palsy cases were male. Male cases were more, 31 (62.0%) in CP with epilepsy and 59 (59.0%) in CP without epilepsy. There was no significant difference in terms of age and sex between CP patients with epilepsy and CP patients without epilepsy. Karatoprak E et al. also did not found any relation between age-sex and risk for epilepsy development [13]. Bruck I et al. reported that 30 out of 62 (48.4%) children with a history of neonatal seizure subsequently developed epilepsy [14]. Similar to the literature, in our study during the analysis of postnatal events neonatal seizure was significantly higher in CP with epilepsy 24 out of 50 (48.0%) than in CP without epilepsy (12.0%) (p=<0.001). In contrast to our finding Kulak et al., and Kwong et al. noted neonatal seizure in 17% and 19% of children with CP and epilepsy respectively [15, 2].

In our study, a family history of epilepsy was significantly higher in CP with epilepsy 10 (20.0%) than CP without epilepsy 2 (2.0%) (P= < 0.001). Kulak et al. and Bruck I et al. found 10.9%, and 29% epileptic children with cerebral palsy had a family history of epilepsy [14,15]. In our study 1st seizure during 1st year of life was significantly higher in CP with epilepsy 35 (70%) than in CP without epilepsy 23 (23%) (P= < 0.001) which is in accordance with Zafeiriou et al. they found that first seizures occurred during the first year of life in 69.7% [16]. In this study distribution of severity of functional dysfunction of CP patients by GMFCS severe disability was significantly higher in CP with epilepsy 32 patients (64.0%) than in CP without epilepsy 31 patients (31.0%) (p=<0.001) and by MACS severe disability was also significantly higher in CP with epilepsy 26 patients (52.0%) than CP without epilepsy 22 patients (22.0%) (p=<0.001). Karatoprak et al. also found severe functional disability in CP with epilepsy by GMFCS was 57.1% and by MACS was 46.8% respectively [13]. Bruck et al. also found the degree of CP severity was associated with a higher incidence of epilepsy [14]. Spastic quadriplegia was higher in CP with epilepsy 27 (54.0%) and Spastic diplegia was higher in CP without epilepsy 36 (36.0%). Karatoprak et al. [13] also found in CP with epilepsy spastic quadriplegia was 66.1% and in CP without epilepsy spastic diplegia was 40.6%. In contrast Singhi et al. reported that the rate of epilepsy was the highest in spastic hemiplegic patients (65.9%) [17]. We demonstrated a higher proportion of CT abnormalities in children with CP with epilepsy 42 patients (84.0%) compared with the CP without epilepsy in 49 patients (49.0%) and their differences were

statistically significant (p=<0.001). Kulak et al. also found CT abnormalities in CP with epilepsy was 68 patients (82.9%) compared with the CP without epilepsy 56 patients (48.2%) [10]. Regarding the abnormal findings cerebral atrophy was most often associated with epileptics, a finding consistent with data found in the literature [18, 19, 20]. In our study it was found that 28 patients (56.0%) had age at onset of epileptic seizure less than 12 months. Zaferiou et al. also found that 69% of patients with CP had their first epileptic attack before they were a year old [16]. This indicates the severity of underlying brain injury. In our study we found the mean age of onset of epilepsy was 31.88 ± 28.27 months in spastic hemiplegia patients, 17.83 ± 11.03 months in spastic diplegia patients and 8.30 ± 3.34 months in spastic quadriplegia patients respectively. Smililar to our study Carlsson et al. reported that the mean age of epilepsy onset 2.5 years in hemiparetic cerebral palsy, 12 months in diparetic cerebral palsy and 6 months in quadriparetic cerebral palsy [21]. In this current study we found that the total mean age at onset of epilepsy was 13.58 ± 14.47 months. These findings were consistent with the previous study by Bruck I et al. they found the average age at onset of epilepsy was 12.59 months [14]. In contrast to our study Delgado et al. found mean age at onset of epilepsy 2.5 years (range, 1 month to 11 years) [4]. EEG is essential in the work-up of children with CP and suspected seizures. It can lend support to the diagnosis of epilepsy and assist in seizure/epilepsy classification to better guide the choice of antiseizure drugs. In our study regarding EEG findings, we found epilepsy of focal origin was more common 28 patients (54.0%) in CP patients with epilepsy. Similar to our study focal epileptiform activity was the common EEG findings observed by Şenbil et al. (48.39%) [22]. In contrast to our study generalized epileptiform abnormality was detected in a large proportion of patients with cerebral palsy and epilepsy 50 patients (41.4%) by Hanci et al. [23]. In our study clinical focal epilepsy (18 patients 36.0%) were more common in CP. Similarly focal epilepsy was more commonly observed by Gururaj et al. (39.3%), Kwong et al. (37.5%), Aksu et al. (93.1%), Delgado et al. (71%), in CP with epilepsy [14, 2-4]. In contrast to our study Hadjipanayis et al. reported generalized epilepsy (36.8%) followed by focal epilepsy (33%) in cerebral palsy with epilepsy [1]. Classification of the type of epilepsy is difficult in children with CP for the following reasons. First, partial seizure onset that rapidly becomes generalized may not be witnessed or reported reliably. Second, impairment of consciousness during an episode may be impossible to clarify in patients with multiple handicaps. Third, the differentiation between myoclonic, tonic, and atonic seizures occasionally could be extremely difficult without ictal EEG or video EEG. In this current study we found focal epilepsy was more common in the hemiplegic variety of CP representing a unilateral, focal lesion, such as infarct or a porencephaly and epilepsy was less common in dyskinetic CP. Other studies have found a similar high incidence of focal epilepsy in this variety of CP ranging from 69 to 73% [24]. In the dyskinetic type of CP, epilepsy is believed to be uncommon [25].

Limitation of the study:

This was a single centered study with small sized samples. Moreover, the study

was conducted at a very short period of time. So, the findings of this study may not reflect the exact scenario of the whole country.

CONCLUSION & RECOMMENDATION

Cerebral palsy is associated with a higher incidence of epilepsy, which in a majority has earlier age of onset. Spastic quadriplegia is the most common types of cerebral palsy among children with epilepsy. Generalized and syndromic epilepsy is a more common type of epilepsy in spastic quadriplegic CP. Focal epilepsy is more common in spastic hemiplegia CP. In clinical assessment focal types of epilepsy is most common type of epilepsy, may take more attention from the health professionals of epilepsy as well as cerebral palsy.

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Conflict of interest: None declared.

Ethical approval: The study was approved by the institutional ethics committee.

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