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EPILEPSY AND MENTAL RETARDATION IN CHILDREN WITH CEREBRAL PALSY – BULGARIAN STUDY

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Abstract

Epilepsy is common in children with cerebral palsy (CP). In a group of 521 children with cerebral palsy it was found that 58% ($n = 303$) of the affected had epilepsy and 74.5% ($n = 388$) had mental retardation. We found a higher percentage of symptomatic epilepsy in a combination of CP with mental retardation – 84.2% ($n = 255$), while only 15.8% ($n = 48$) of children with normal intellect had epilepsy. In our CP patients, the focal seizures were the most common – 34.7% ($n = 181$), followed by the secondary generalized 29.6% ($n = 154$) and the generalized seizures (tonic, clonic and generalized tonic-clonic) 25.3% ($n = 132$), most often with early onset, with 43.5% ($n = 132$) of them with onset in the first year of life. The earlier onset of the epileptic seizures correlated with a more severe mental retardation. We found that symptomatic epilepsy and severe mental retardation are most common in children with spastic quadriparesis.

Key words: cerebral palsy, epilepsy, mental retardation

Introduction. Cerebral palsy (CP) combines a group of non-progressive, residual motor syndromes (paresis, muscle tone disorders, impairment of coordination, posture changes and involuntary movements) often combined with mental retardation, speech pathology, and symptomatic epilepsy due to non-development or disability of the brain in the prenatal, perinatal and postnatal period [1,2]. CP

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as a clinical syndrome was described by William John Little in 1840. There are numerous CP descriptions from other authors, with one of the most detailed definitions and classifications being the result of the work of Rosenbaum et al. [2]. Freud first reported a high risk of epilepsy in children with CP, and then other authors evaluated epilepsy as an unfavourable factor for cognitive function in children with CP. The average incidence of epilepsy in children is 3–6/1000, but in children with CP the incidence of symptomatic epilepsy is much higher, varying between 15 to 60% [3,4].

The purpose of our study is to evaluate the frequency of the accompanying syndromes, such as symptomatic epilepsy and intellectual deficiency in various forms of CP.

Materials and methods. A retrospective analysis of 521 children with different forms of CP (spastic quadriparesis – 30.1%, spastic diparesis – 15.7%, spastic hemiparesis – 27.4%, dyskinetic – 3.6%, ataxic – 8.3%, mixed – 14.8%) diagnosed at the University Hospital for Neurology and Psychiatry "Sveti Naum" for the period 2008–2018 was carried out, encompassing: 1. The incidence and type of symptomatic epilepsy according to the type of CP. 2. Types of epileptic seizures conforming to the International League Against Epilepsy (ILAE) classification, depending on the forms of CP and the most common EEG findings in children with concomitant Epilepsy. 3. Frequency and severity of intellectual deficit in different forms of CP. 4. Statistical correlations were sought between epilepsy and mental retardation in children with CP, as well as the significance of the period of epileptic seizures with regards to mental retardation.

The methods used for the analysis of epilepsy and mental retardation were: detailed history of epileptic seizures and their type according to the ILAE classification; neurological and somatic examination; video-electroencephalography (EEG) conducted on a 64-channel device Deltamed with Coherence software 5.1.2; the arrangement of the EEG electrodes is according to the standards of the international system 10–20 and bipolar longitudinal installation is used. Neuropsychological battery included tests for intelligence quotient (IQ) such as Wechsler Intelligence Scale for Children, Binet Terman Test, Raven Progressive Matrices. The statistical analysis was performed using SPSS (Statistical Package for Social Sciences) version 13. The statistical analysis used are Chi-square test and Fisher's exact test.

Results. From the 521 children with cerebral palsy included in the study, 303 (58%) had epilepsy and 388 children were mentally retarded (74.5%). A statistically significant dependence between epilepsy and CP forms was established ($p < 0.001$): spastic quadriparesis had the highest epilepsy rate – 37.0% ($n = 112$), followed by spastic hemiparesis – 27.4% ($n = 83$), and mixed form – 19.5% ($n = 59$) (Table 1).

A statistically significant correlation was found between the presence of epilepsy and the type of CP on focal, secondary generalized, generalized (tonic, clonic

Table 1

Frequency of epilepsy in various forms of cerebral palsy

CP forms	Statistics	Epilepsy		Total	χ^2	Df	p
		No	Yes				
Spastic quadriparesis	N	45	112	157	69.82	5	< 0.001
	%	20.6	37.0	30.1			
Spastic diparesis	N	64	18	82			
	%	29.4	5.9	15.7			
Spastic hemiparesis	N	60	83	143			
	%	27.5	27.4	27.4			
Dyskinetic	N	7	12	19			
	%	3.2	4.0	3.6			
Ataxic	N	24	19	43			
	%	11.0	6.3	8.3			
Mixed	N	18	59	77			
	%	8.3	19.5	14.8			
Total	N	218	303	521			
	%	100.0	100.0	100.0			

and tonic-clonic), myoclonical, atonic, neonatal epileptic seizures and epileptic spasms. Statistical dependence has not been proven for atypical absences in relation to CP, $p = 0.075$. In epileptic encephalopathies (West syndrome and Lennox–Gastaut syndrome), there was also a statistically significant correlation depending on the form of CP, $p < 0.001$.

For all EEG findings (background activity, hypsarrhythmia, focal epileptic changes, generalized paroxysms, multifocal changes and electrical status epilepticus during sleep (ESES), a statistically significant correlation was found with the form of CP. Focal epileptic changes were the predominant EEG findings compared to other epileptic changes, most common in the mixed form (69.0%), followed by the quadiparetic and hemiparetic form of CP.

Statistical correlation between the severity of mental retardation and the forms of CP was established ($p < 0.001$) (Table 2).

Statistically significant correlations were found between epilepsy and neuropsychological development – children with normal mentality, $p = 0.001$ and with different degrees of mental retardation, $p < 0.001$. A high percentage of epilepsy was present in children with severe mental retardation – 33.0%, whereas only 15.8% of the children with normal intellect had epilepsy (Table 3).

Statistical significance also occurred when comparing the period of seizures onset (neonatal seizures and those occurring before one year of age) and the severity of mental retardation ($p < 0.001$), with neonatal seizures and those before one year of age being the dominant factor for severe mental retardation.

Statistically significant correlation was found between severe epileptic encephalopathies (West syndrome and Lennox–Gastaut syndrome) which were 11.5%

T a b l e 2

Degrees of mental retardation in different forms of CP

CP forms	Statistics	Mental retardation					Total
		No	Mild	Moderate	Severe	Profound	
Spastic quadriparesis	N	6	31	34	64	22	157
	%	4.4	23.8	35.1	51.2	64.7	30.1
Spastic diparesis	N	37	23	16	6	0	82
	%	27.4	17.7	16.5	4.8	0.0	15.7
Spastic hemiparesis	N	78	48	13	4	0	143
	%	57.8	36.9	13.4	3.2	0.0	27.4
Dyskinetic	N	3	4	5	7	0	19
	%	2.2	3.1	5.2	5.6	0.0	3.6
Atactic	N	7	13	9	11	3	43
	%	5.2	10.0	9.3	8.8	8.8	8.3
Mixed	N	4	11	20	33	9	77
	%	3.0	8.5	20.6	26.4	26.5	14.8
Total	N	135	130	97	125	34	521
	%	100.0	100.0	100.0	100.0	100.0	100.0

T a b l e 3

Correlation between epilepsy, normal intellect and degrees of mental retardation

Indicator			Epilepsy		Total	χ^2	Df	p
			No	Yes				
Mental retardation	Mild	N	60	70	130	58.33	4	< 0.001
		%	27.5	23.1	25.0			
	Moderate	N	40	57	97			
		%	18.3	18.8	18.6			
	Severe	N	25	100	125			
		%	11.5	33.0	24.0			
	Profound	N	7	27	34			
		%	3.2	8.9	6.5			
Normal intellect	No	N	134	255	389	34.51	1	< 0.001
		%	61.5	84.2	74.7			
	Yes	N	84	48	132			
		%	38.5	15.8	25.3			

($n = 60$) and mental retardation, $p < 0.001$. It has been confirmed that epileptic encephalopathies are more common in severe mental retardation.

Discussion. Our results showed the high incidence of concomitant CP syndromes such as epilepsy and mental retardation. We confirm a greater incidence of epilepsy and severe mental retardation in the quadriparetic form, as evidenced by other meta-analyses [3,5,6]. In our study, 58% ($n = 303$) of children with cerebral palsy had epilepsy, which is consistent with previous studies [5,7,8].

The incidence of epilepsy varies in different forms of CP, and is the highest in quadiparetic form (37.0%), proven in other meta-analyses [3,5,6,8], followed by

the spastic form of CP (27.4%). In other reports [10] the rate of epilepsy was higher in spastic hemiplegia, and in the dyskinetic form of CP [8], possibly due to overlap of hyperkinesias and epileptic seizures. The correlation between the initial age of occurrence of epileptic seizures of the type of CP was presented in previous studies. CARLSSON et al. [3] reported that the mean age of occurrence of seizures in the quadriparetic form of CP was 6 months, in the spastic diparesis – 12 months, and in spastic hemiparesis – 2.5 years. According to some researchers, about 49% to 79% of epileptic seizures begin within the first year of life [5,6], considering that neonatal seizures are associated with a very high risk of developing epilepsy [7]. In our study in 303 children with epilepsy the epileptic seizures occurred prior to one year of age in 43.5% ($n = 132$) of the affected, of which 19.8% ($n = 60$) were with epilepsy in the neonatal period. In our CP patients, the focal seizures were the most common – 34.7% ($n = 181$), followed by the secondary generalized 29.6% ($n = 154$), and the generalized seizures (tonic, clonic and generalized tonic-clonic) 25.3% ($n = 132$), which is similar to previous reports [5,7]. In other studies, generalized seizures prevail [9,10]. With regards to forms of CP, we found that focal seizures were most common in the mixed form of CP (44.2%), followed by spastic hemiparesis (42.0%), whereas generalized seizures were more common in spastic quadriparesis (36.9%) and in mixed form (35.1%). We also demonstrated a correlation between the CP forms and presence of severe epileptic encephalopathy ($p < 0.001$). A total of 11.5% ($n = 60$) of our patients had severe epileptic encephalopathies (West syndrome, Lennox–Gastaut syndrome), which prevailed in spastic quadriparesis (25.6%), followed by the mixed form of CP (18.2%). Several other studies also found a high incidence of patients with West syndrome and Lennox–Gastaut syndrome in spastic quadripapresis and the mixed form of CP [7,11].

We found focal epileptic changes in the EEG of 54.3% of patients ($n = 259$), generalized paroxysms in 15.87% ($n = 75$), followed by multifocal changes – 11.9% ($n = 57$). Similar results of dominance of focal changes have been demonstrated in other studies [7,12]. Focal manifestations are most prominent in the mixed form – 69.0%, spastic quadraparesis – 65.3%, and spastic hemiparesis – 60.3%. We demonstrated that normal background activity predominated in spastic diparesis – 78.3%, while abnormal background activity predominated in spastic quadriparesis – 72.1%, i.e. there is a link between the severity of motor abnormalities with abnormal background activity [13].

Mental retardation severity varies in different forms of CP, with the percentage of normal intellect being highest in the hemiparetic form (57.8%), followed by the spastic diparesis (27.4%), and the lowest percentage of normal intellect found in mixed form – 3.0% and spastic quadraparesis – 4.4%, with a severe degree of mental retardation dominating in the latter two forms. In our study we found that 84.2% of children with CP and mental retardation had epilepsy, while in those with normal intellect, epilepsy is significantly less frequent (15.8%). The relative

share of epilepsy in our research is highest in children with cerebral palsy and severe mental retardation. Similar to our results, another researcher [3] reported that, in children with CP and normal mentality, only 15% had epilepsy, while in children with CP and mental retardation, the rate of epilepsy is increased above 61%. Other researchers also confirm that in children with CP and epilepsy there is a tendency for lower IQ and poor rhythmic and logical abilities compared to other children with similar motor abnormalities but without epilepsy. In a number of studies, the link between mental retardation, epilepsy and motor deficiency in various forms of CP has been established [13, 14].

We have shown that the IQ correlates positively with the age of onset of seizures ($p < 0.001$), i.e., the earlier epileptic seizures begin, the more pronounced the degree of mental retardation [13]. Only 8.3% of children with neonatal seizures have normal intellect, while 43.3% have severe mental retardation. We also found similar statistics for epileptic seizures before one year of age, where normal intellect was about 7.6% and severe mental retardation was 43.9%.

We confirm that severe epileptic encephalopathies (West syndrome and Lennox–Gastaut syndrome) lead to severe and profound mental retardation, as 51.7% of our patients with epileptic encephalopathy had severe mental retardation.

Conclusion. Our study identifies the high incidence of epilepsy and severe mental retardation in the quadriparetic form of CP, which correlates with the severity of motor impairment. In children with CP, epilepsy was recorded in 84.2% of mentally retarded children, with the percentage of epilepsy being highest in severe mental retardation.

REFERENCES

[1] Bojinova V., I. Chavdarov, I. Milanov (2019) Consensus for diagnosis, rehabilitation, treatment and administration of children with cerebral palsy, Bulg. Neurol., **20**(5), 1–10.

[2] Rosenbaum P., N. Paneth, A. Leviton et al. (2007) A report: the definition and classification of cerebral palsy April 2006, Dev. Med. Child Neurol. Suppl., **109**, 8–14.

[3] Carlsson M., G. Hagberg, I. Olsson (2003) Clinical and aetiological aspects of epilepsy in children with cerebral palsy, Dev. Med. Child Neurol., **45**(6), 371–376.

[4] Wallence S. J. (2001) Epilepsy in cerebral palsy, Dev. Med. Child Neurol., **43**, 713–717.

[5] Gururaj A. K., L. Sztriha, A. Bener, A. Dawadou, V. Eapen (2003) Epilepsy in children with cerebral palsy, Seisure, **12**(2), 110–114.

[6] Zelnik N., M. Konopnicki, O. Benett-Back, T. Castel-Deutsch, E. Tirosh (2010) Risk factors for epilepsy in children with cerebral palsy, Eur. J. Paediatr. Neurol., **14**(1), 67–72.

[7] Kulak W., W. Sobaniec (2003) Risk factors and prognosis of epilepsy in children with cerebral palsy in north-easten Poland, Brain Dev., **25**(7), 499–506.
[8] Sellier E., P. Uldall, E. Calado, S. Sigurdardottir, M. G. Tirrioli et al. (2012) Epilepsy and cerebral palsy: characteristics and trends in children born in 1976–1998, Eur. J. Paediatr. Neurol., **16**(1), 48–55.
[9] Salam O., A. Esmael, M. El-Sherif (2016) Epilepsy among cerebral palsy children: clinical predictors and frequency, Int. Neuropsychiatr. Dis. J., **6**(2), 1–8.
[10] Singhi P., S. Jagirdar, N. Khandelwal, P. Malhi (2003) Epilepsy in children with cerebral palsy, J. Child Neurol., **18**(3), 174–179.
[11] Gürkan F., S. Gökben, H. Serin, S. Yilmaz, G. Aktan et al. (2018) Determining risk factors of epilepsy in children with cerebral palsy: a retrospective study, J. Pediatr. Res., **5**(2), 76–81.
[12] Mert G. G., F. Incecik, S. Altunbasak et al. (2011) Factors affecting epilepsy development and epilepsy prognosis in cerebral palsy, Pediatr. Neurol., **45**(2), 89–94.
[13] Bojinova V., I. Aleksandrova, V. Stoyanova (2014) Child cerebral palsy, epilepsy and intellectual deficiency – etiology, diagnosis and therapy, Pediatrics, **2**, 35–41.
[14] Todoran A., A. Sin, C. Micheu, K. Scep, S. Voldazan et al. (2015) Predictive factors in the onset of epilepsy in children with cerebral palsy, Acta Marisiensis – Seria Medica , **61**(3), 200–205.

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