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The evaluation of epilepsy and other contributing disorders in patients with cerebral palsy using the Gross Motor Function Classification System

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ABSTRACT

Objectives. Morbidity and mortality in patients with cerebral palsy are related to motor function disability, as well as other contributing disorders. The aim of this study was to evaluate the contribution of epilepsy and other disorders in cerebral palsy patients using the Gross Motor Function Classification System (GMFCS), and to determine their relationship. ***Methods.*** This study was performed in Eskişehir Osmangazi University School of Medicine, Department of Pediatric Neurology between May 2011-January 2012, with a total of 154 patients diagnosed with cerebral palsy. Epilepsy and other contributing disorders were evaluated in the patients. GMFCS was used to measure the motor function. ***Results.*** Mental retardation (89.6%), ophthalmological problems (68.2%) and epilepsy (61.0%) were the leading disorders, followed by oromotor dysfunction (48.7%), malnutrition (40.9%), orthopedic problems (38.3%), dental problems (18.8%), sleep disorders (17.5%) and hearing loss (9.1%) in cerebral palsy patients. Epilepsy, mental retardation, oromotor dysfunction and malnutrition were mostly observed in GMFCS level 5 ($p<0.001$). Sleep disorder and dental problems were mostly observed at level 5 ($p<0.05$). Epilepsy was seen more frequently in patients who had neonatal seizure history, microcephaly and mental retardation ($p<0.05$). ***Conclusions.*** There are correlations between the occurrence of disorders such as mental retardation, epilepsy, oromotor dysfunction, malnutrition, sleep disorders, dental problems and gross motor function levels. GMFCS levels were thought to be instructive for possible additional disorders.

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Keywords: Cerebral palsy, Gross Motor Function Classification System, disorders, epilepsy

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Introduction

Cerebral palsy was first described in 1862 by the Orthopedics surgeon William James Little [1]. Cerebral palsy is a non-progressive disorder caused by damage of the brain in the intrauterine period and at the first months of life; however, the disorder changes in characteristics with aging, with permanent motor function loss and limited movement, postural and movement disorders [2]. Cerebral palsy may progress due to many causes in the prenatal, natal or the early postnatal period [3]. The essential finding of the disease is loss of motor function. Auditory, visual, cognitive, perceptional and behavioral disorders, malnutrition and epilepsy mostly contribute to the disease [2, 4]. Morbidity and mortality are due to motor function disorder, as well as other contributing disorders [5].

The determination of the prognosis of cerebral palsy in the early period is difficult. The most prominent fear of the family is whether their child would be able to resume a normal life in the future and be able to walk or not. Initially, Palisiano et al. [6] developed a scale to determine the motor prognosis. The Gross Motor Function Classification System (GMFCS) consists of measuring the sitting and walking ability in children with cerebral palsy. To determine the motor prognosis, it can be a guide for possible additional disorders and for planning of the treatment [7, 8]. The aim of this study was to evaluate the contributing epilepsy and other disorders and to determine their relationship in patients with CP, using GMFCS.

Methods

This study was performed in Eskişehir Osmangazi University School of Medicine, Department of Pediatric Neurology between May 2011-January 2012, with a total of 154 patients with a diagnosis of cerebral palsy. Epilepsy and other contributing disorders were evaluated in patients. GMFCS was used to measure the motor function. The age-dependant GMFCS groups children into 1 of 5 levels based on their ability to mobilize and reflects overall gross motor skills and severity of motor impairment. Level 1 (walks and climbs stairs, without limitation) represents the highest level of gross motor function and level 5 (unable to walk, severely limited self-mobility) the lowest [6]. Patients under the age of 3 were not included in the study. Cerebral palsy was classified clinically according to the recommendations of the workshop held in Bethesda and the European Cerebral Palsy Surveillance Group [9].

The nutritional and defecation habits and the sleep disorders of the patients were evaluated. Each patient was ophthalmologically evaluated and Visual Evoked Potentials were performed. All patients were examined by the ear, nose and throat specialist and Otoacoustic Emission (OAE) was performed. Patients who failed the OAE were evaluated with electrophysiological audiometry. The seizure history was evaluated in detail. All patients underwent electroencephalography (EEG). The electroencephalography records were performed using the Nihon Kohden Neurofax 7310 F EEG device. The patients who had 2 or more seizures in the absence of any stimulating factor and with no repeated seizures in the same day were accepted as epileptic. A decrease in the seizure's frequency of more than 50% was accepted as partial response, a less than 50% frequency was accepted as refractory seizure, and absence of seizure was accepted as total response.

For children over 6 years of age, the WISC-R intelligence test, and for children under 6, the Denver developmental screening test, were performed. All patients routinely underwent urine-blood amino acid analysis and cranial MRI. MRI examinations were performed on 1.5 T MR scanner (Siemens, VisionPlus, Germany) equipped with the head coil. The motor functions were measured with GMFCS.

Statistical Analysis

SPSS (Statistical Package for Social Sciences) for Windows 16.0 (SPSS Inc., Chicago, IL) statistical pocket program was used to evaluate the data. The frequency distribution was expressed as %, and the age was expressed as “months”, and given as the average values ± standard deviation. The Student t test was used for comparison of 2 average values, and the chi-square test used for comparison of the percentages. The Spearman correlation analysis was used for the correlation analysis. A p value of <0.05 was accepted as the statistically significant level.

Results

The mean age of the total of 154 patients was

8.07±4.15 (3-18 years) and the male/female ratio was 1.3. One hundred and forty-one (91.6%) of the patients were spastic, 8 (5.2%) were dyskinetic, 3 (1.9%) were ataxic, and 2 (1.3%) had mixed type cerebral palsy. 36.4% of (56 patients) the spastic cerebral palsy patients were quadriparetic, 28.6% (44 patients) were diplegic, and 26.6% (41 patients) were hemiparetic cerebral palsy.

According to the GMFCS, 12 patients (12%) were at Level 1, 49 patients (31.8%) were at Level 2, 13 patients (8.4%) were at Level 3, 22 patients (14.3%) were at Level 4, and 58 patients (37.7%) were at Level 5. 47.5% of the patients at GMFCS Levels 4 and 5 had a birth weight of >2500 and their relationship was statistically significant (p<0.05). There was no statistical significance between the gestational age, perinatal asphyxia and MRI findings and the GMFCS levels (p>0.05). Level 5 was detected mostly in quadriplegic type cerebral palsy (p<0.001) (Table 1).

The other contributing disorders were, in particular, mental retardation (89.6%), ophthalmological problems (68.2%) and epilepsy (61%), followed by oromotor dysfunction (48.7%), malnutrition (40.9%), orthopedic problems (38.3%), dental problems (18.8%), sleep disorders (17.5%) and hearing loss (9.1%). The most common ophthalmological problems were strabismus (48%), refractive disorders (12.9%) and nystagmus (12.3%). Pes equinovarus deformity (11.7%) and scoliosis (9%) were the most common orthopedic problems. 38.9% of the patients had sialorrhea and 73 (47.4%) of them had constipation. Two (1.3%) of the patients had gastrostomy. Mental retardation, epilepsy, oromotor dysfunction and malnutrition were most commonly observed at GMFCS Level 5 (p<0.001). Sleep disorder and dental problems were most commonly observed at Level 5 (p<0.05) (Table 2).

Table 1. The distribution of patient characteristics according to the GMFCS levels

GMFCS	Level 1 n (%)	Level 2 n (%)	Level 3 n (%)	Level 4 n (%)	Level 5 n (%)
Birth weight					
<1500 gr	1 (8.3)	9 (18.4)	1 (7.7)	2 (9.1)	9 (15.5)
1500-2500 gr	1 (8.3)	11 (22.4)	9 (69.2)	8 (36.4)	23 (39.7)
≥2500 gr	10 (83.4)	29 (59.2)	3 (23.1)	12 (54.5)	26 (44.8)
Gestational age					
<32 weeks	0 (0)	16 (32.7)	6 (46.1)	3 (13.6)	14 (24.1)
32-36 weeks	2 (16.7)	7 (14.3)	3 (23.1)	6 (27.3)	12 (20.7)
≥37 weeks	10 (83.3)	26 (53)	4 (30.8)	13 (59.1)	32 (55.2)
Perinatal asphyxia					
Present	3 (25)	14 (28.6)	6 (46.2)	9 (40.9)	19 (32.8)
absent	9 (75)	35 (71.4)	7 (53.8)	13 (59.1)	39 (67.2)
Cerebral palsy type					
Spastic quadriparesis	0 (0)	0 (0)	3 (23)	6 (27.3)	47 (81)
Spastic diplegia	1 (8.3)	24 (49)	8 (61.5)	9 (40.9)	2 (3.5)
Spastic hemiparesis	11 (91.7)	25 (51)	1 (7.7)	3 (13.6)	1 (1.7)
Other	0 (0)	0 (0)	1 (7.7)	4 (18.2)	8 (13.7)
MRI finding					
Present	12 (100)	47 (95.9)	12 (92.3)	22 (100)	55 (94.8)
Absent	0	2 (4.1)	1 (7.7)	0	3 (5.2)

MRI: Magnetic resonance imaging

Ninety-four (61.0%) of the patients had epilepsy. The average starting age of the seizures in the patients was 29.31±32.21 (range; 1-180) months. The seizures had begun before 1 year of age in 44.7% of the patients. Gender, birth weight and perinatal asphyxia had no statistically significant relationship with epilepsy (p>0.05). Epilepsy was seen more frequently in patients who had a history of seizure and microcephaly at the neonatal period (p<0.05, p<0.05, respectively). Mental retardation was more common in patients who had epilepsy, compared with patients without epilepsy (p<0.05) (Table 3). Thirty-five (37.2%) of the patients with epilepsy, and 3 (5%) of the patients who did not have epilepsy demonstrated epileptiform discharges on EEG.

Table 2. Distribution of the contributing disorders according to their GMFCS levels

GMFCS	Level 1 n=12 n (%)	Level 2 n=49 n (%)	Level 3 n=13 n (%)	Level 4 n=22 n (%)	Level 5 n=58 n (%)
Mental retardation					
Present	9 (75)	38 (77.5)	12 (92.3)	22 (100)	57 (98.3)
Absent	3 (25)	11 (22.5)	1 (7.7)	-	1 (1.7)
Ophthalmological problems					
Present	5 (41.7)	31 (63.3)	10 (76.9)	16 (72.7)	43 (74.1)
Absent	7 (58.3)	18 (36.7)	3 (23.1)	6 (27.3)	15 (24.9)
Epilepsy					
Present	8 (66.7)	24 (49)	2 (15.4)	16 (72.7)	44 (75.9)
Absent	4 (33.3)	25 (51)	11 (84.6)	6 (27.3)	14(24.1)
Oromotor dysfunction					
Present	1 (8.3)	11 (22.5)	5 (38.5)	11 (50)	47 (81)
Absent	11 (91.7)	38 (77.5)	8 (61.5)	11 (50)	11 (19)
Malnutrition					
Present	3 (25)	7 (14.3)	3 (23.1)	9 (40.9)	41 (70.7)
Absent	9 (75)	42 (85.7)	10 (76.9)	13 (59.1)	17 (29.3)
Orthopedic problems					
Present	5 (41.7)	24 (49)	5 (38.5)	7 (31.8)	18 (31)
Absent	7 (58.3)	25 (51)	8 (61.5)	15 (68.2)	50 (69)
Dental problems					
Present	0 (0)	4 (8.2)	1 (7.7)	8 (36.4)	21 (36.2)
Absent	12 (100)	45 (91.8)	12 (92.3)	14 (63.6)	37 (63.8)
Sleep disorders					
Present	1 (8.3)	2 (4.1)	2 (15.4)	3 (13.6)	19 (32.8)
Absent	11 (91.7)	47 (95.9)	11 (84.6)	19 (86.4)	39 (67.2)
Hearing loss					
Present	1 (8.3)	4 (8.2)	2 (15.4)	1 (4.5)	6 (10.3)
Absent	11 (91.7)	45 (91.8)	11 (84.6)	21 (95.5)	52 (89.7)

Eighty (85.1%) patients had one type of seizure, while 14 (14.9%) had more than one type of seizure. The most common seizure types were generalized tonic-clonic (GTC) and tonic seizures. The most common type of seizure in spastic quadriparesis was GTC, generalized tonic in spastic diplegia, and complex partial in spastic hemiparesis. Thirty-two (34%) of the patients had status epilepticus history. Thirty-eight (40%) epileptic patients were using monotherapy, and 56 (60%) were using polytherapy. Eighteen (19%) patients had refractory seizures. Sixteen (17%) patients had a history of infantile spasm.

The epileptic patients demonstrated more GMFCS Levels 4 and 5 compared to the non-epileptic patients ($p<0.001$). There was no statistically significant relationship between the response to the seizure treatment and the GMFCS levels ($p>0.05$). Status epilepticus was most commonly observed in Level 5 ($p<0.05$). Cognitive and mental retardation were most common in GMFCS Level 4 and 5. A statistically significant relationship was detected between the mental retardation and GMFCS levels ($p<0.001$). The patients with mental retardation and epilepsy were most common in Level 5. This difference was statistically significant ($p<0.001$). No relationship was detected between the response to seizure treatment and cerebral palsy type ($p>0.05$).

Fifty-six (70%) of 80 patients who could sit without support before age 3, could walk before age 6, while 3 (23.1%) of 13 patients who could sit without support after age 3, could walk. The potential to walk was higher in patients who could sit without support before age 3, and this relationship was statistically significant ($p<0.001$).

Discussion

In spite of the fact that intensive care conditions have improved, the frequency of cerebral palsy has not

Table 3. The characteristics of the patients with or without epilepsy

Variable	Epilepsy			
	Present		Absent	
	n=94	%	n=60	%
Gender				
Male	55	58.5	32	53.3
Female	39	41.5	28	46.7
Birth weight				
< 2500 gr	40	42.5	34	56.7
≥2500 gr	54	57.5	26	43.3
Gestational age				
<37 weeks	36	38.3	33	55
≥37 weeks	58	61.7	27	45
Neonatal seizure				
Present	37	39.4	12	20
Absent	57	60.6	48	80
Perinatal asphyxia				
Present	30	31.9	21	35
Absent	64	68.1	39	65
Microcephaly				
Present	51	54.3	17	28.3
Absent	43	45.7	43	71.7
Cerebral palsy type				
Spastic quadriparesis	45	47.8	11	18.4
Spastic diplegia	14	14.9	30	50
Spastic hemiparesis	26	27.7	15	25
Other	9	9.6	4	6.6
Mental retardation				
Present	88	91.2	50	68.7
Absent	6	8.8	10	31.3

changed due to the effort to keep babies with very low birth weight and prematurity alive [10, 11]. With a difference due to the socioeconomic level, the frequency of cerebral palsy has been determined as 1.5-2.5 in 1000 live births [12, 13]. In this study, a total of 154 patients with a cerebral palsy diagnosis between 3-18 years of age were evaluated. Comparable with the literature, the male/female ratio was 1.3. The most common clinical cerebral palsy form is the spastic type. Dyskinetic and mixed type cerebral palsy are seen rarely [14,15]. In this study, 91.6% of the patients had spastic cerebral palsy, quadriplegic type being the most common.

There are no specific criteria for the severity of the movement disorder in patients with cerebral palsy. In previous classification systems, it had been graded generally as mild, moderate and high according to the walking ability [16]. The GMFCS, which was created by Palisano *et al.* [6] in 1997, has been stated as an available and reliable method to detect the future motor prognosis. The frequency of the contributing problems varies according to the patients' GMFCS levels. As it may be a predictive issue for the possible problems in patients, it may also lead the clinician in planning the treatment [7, 8]. In our study, a GMFCS Level of 5 was detected most commonly in spastic quadriparetic patients. Mental retardation, speech disorders, oromotor dysfunction, malnutrition, sleep disorders and dental problems were determined to be most frequent in Level 5. Although epilepsy and EEG findings were most commonly observed in Level 5, there was no relationship between the response of seizures to therapy and GMFCS levels.

Although the main problem in cerebral palsy is the motor disorder, the damage is not limited to the motor area. Epilepsy contributes with a frequency of 15-90% [17, 18]. The seizures start at 1 year of age in approximately half of the patients and a relationship has been detected with the neonatal seizures [19]. In a study held in 17 centers with 9654 cerebral palsy patients, it was reported that epilepsy was present in 35% of the patients, and this was related to neonatal seizures and microcephaly, and it was most commonly seen in dyskinetic and bilateral spastic cerebral palsy [20]. In this study, epilepsy was present in 61.0% of the patients. In the neonatal period, epilepsy was more

common in patients with a seizure history and microcephaly. Mental retardation was more common in epileptic patients. In approximately half of the patients, the seizures had begun before 1 year of age. The most common seizure type in spastic quadriparesis was GTC, generalized tonic in spastic diplegia, but complex partial in spastic hemiparesis. The most common EEG finding was spike-wave activity. In approximately one fifth of the patients, the seizures were refractory. No relationship was determined between the response to the seizure treatment and the cerebral palsy type.

Mental retardation was determined in 30-50% of cerebral palsy patients and it was related to the cerebral palsy type. In spastic diplegia, while the cognitive functions were affected mildly due to the sparing of the cortical gray matter, in spastic quadriparesis, mental retardation was observed more frequently and in a more severe form [21]. It has been reported that approximately half of the hemiparetic cerebral palsy patients have an average intelligence [22]. The frequency of mental retardation increases in epileptic patients [23]. In this study, 89.6% of the patients had mental retardation at variable degrees. Mental retardation was most commonly detected in the spastic quadriparetic cerebral palsy type. In children with cerebral palsy, sleep disorders may be observed due to the mental state levels, the treatment and the epilepsy [24]. In this study, sleep disorder was observed in 17.5%, and it was most frequent at GMFCS Level 5.

Ophthalmological problems are observed in approximately half of the patients with cerebral palsy. The most common types are refractive disorders and strabismus [25]. In this study, ophthalmological problems such as strabismus, refractive disorders and nystagmus were detected in 68.2% of the patients. No relationship was detected between the ophthalmological problems and the GMFCS levels. Hearing loss is seen in 7-15% of the cerebral palsy patients [26, 27]. In this study, this rate was 9.1%. It is crucial to perform a complete opthalmological examination and to detect and treat the ocular problems in cerebral palsy patients. With early diagnosis and treatment of opthalmological problems and hearing loss, the negative influence of the quality of life in children with cerebral palsy should be prevented and contribution to their mental, social and spiritual improvement should be promoted.

Alimentation problems and malnutrition are more frequent in children with cerebral palsy compared to the normal population. These children develop malnutrition due to oral motor disability, low calorie intake, stagnation, spasticity and difficulty in feeding. In their study, Del Giudice *et al.* [28] reported gastrointestinal system symptoms in 92% of the patients. In another study performed in Turkey with 120 cerebral palsy patients, sialorrhea, constipation, dysphagia and alimentation disorder were observed in 30.6%, 25%, 19.2%, and 21.7%, respectively. GIS problems and alimentation problems were more common in patients with severe GMFCS levels. The time spent for a meal was longer in patients with alimentation disorders [29]. In this study, oromotor dysfunction was seen in 48.7%, malnutrition in 40.9%, dental problems in 22.1%, and they were most common at GMFCS Level 5. Because the required time for a meal is longer in these children compared to normal children, it is one of the most difficult problems for the family. Furthermore, dental problems are observed in CP patients in relationship with feeding disability and excessive sialorrhea [28, 29].

The stretching of the muscles is inadequate in cerebral palsy, and contracture, muscle weakness, spasticity, and as the child grows, due to contractures, bone deformities such as equinus deformity, increased lordosis, kyphosis and scoliosis may develop [30]. In this study, orthopedic problems were detected in 38.3% of the patients. The most common types were pes equinovarus and scoliosis. The treatment of the orthopedic problems in patients with a walking potential is crucial to develop functional ambulation, and in non-ambulatory patients, to render sitting easy, to develop hygiene and to prevent pain.

The prognosis of cerebral palsy differs with the cerebral palsy type, severity, contributing mental retardation, epilepsy, presence or absence of malnutrition, and the opportunity of the patient to benefit from the rehabilitation resources. The most prominent fear of the family when their child is first diagnosed with cerebral palsy is whether their child would be able to walk or not. The patients who can sit without support by 2 years of age are most likely to be able to have the walking potential, and most of the hemiparetic cerebral palsy patients can walk independently [31]. In this study, it was detected that children who could sit without support before 3 years of age had an increased chance of walking. Beside the physical therapy and rehabilitation, detection of epilepsy and other contributing disorders and their treatment are crucial for the patient's life quality and prognosis.

Conclusions

As a result, although the main problem is the motor disability in patients with cerebral palsy, other contributing problems such as mental retardation, epilepsy, alimentation problems, audio- and visual problems also exist. There are correlations between the occurrence of disorders such as mental retardation, epilepsy, oromotor dysfunction, malnutrition, sleep disorders, dental problems, and the gross motor function levels. GMFCS, as a scale used to detect the motor prognosis, is thought to be an instructive instrument in possible additional problems. It is crucial to detect and treat the contributing problems for the quality of life and prognosis in patients with cerebral palsy.

Conflict of interest

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