

EPILEPSY IN CHILDREN WITH CEREBRAL PALSY

**S.Pour Ahmadi MD¹,
M.Jafarzadeh MD²,
M. Abbas MD³,
J.Akhondian MD⁴**

1. Assistant Professor of Pediatrics, Mashad University of Medical Sciences

2. Associate Professor of Pediatrics, Mashad University of Medical Sciences

3. General practitioner

4. Associate Professor, Pediatric Neurologist, Department of Pediatric Neurology & Neonatal Research Center, Mashad University of Medical Sciences

Corresponding Author:

J.Akhondian MD

Fax: +98 511 8417451

e-mail: J-Akhondian@mums.ac.ir

Abstract:

Objective

Epilepsy occurs in 12 % to 90 % of children with cerebral palsy (CP). However its clinical course is not well defined. This investigation was undertaken to study and determine the characteristics and prevalence of epilepsy in children with cerebral palsy.

Materials & Methods

Of 133 children with cerebral palsy, seen between 1998 and 2001, in the pediatric neurology clinic of the Imam Reza hospital, fifty-three had epilepsy. During the same period, a group of 70 epileptic children with normal neurodevelopmental status was studied as the controls.

Results

Patients with spastic quadriplegia were the most commonly affected with epilepsy. When compared with the control group, children with CP had a higher incidence of epilepsy with onset within the first year of age (52.8% vs. 18.5%), history of neonatal seizures (20.7% vs. 4.2%), and poly therapy (73.6% vs. 29.1%) respectively.

Conclusion

Epilepsy is common in children with CP and can be predicted if seizures occur in the first year of life, in the neonatal period and based on the need for polytherapy.

Keywords: Epilepsy, Cerebral palsy, Polytherapy

Introduction

Cerebral palsy (CP) is the result of non-progressive damage to the developing brain and consists of a number of clinical neurological syndromes of heterogeneous etiology (1). The significance of epilepsy in patients with cerebral palsy (CP) is a controversial subject in present day literature. Studies show that the prevalence of epilepsy varies from 12 to 90% in children with CP (2,3,4), being maximum in patients with the quadriplegic type and minimum in those having the diplegic and athetoid types (5). However the clinical features of epilepsy in children with CP have not been well defined. Mental retardation and epilepsy are more common in children with CP (6). Early prediction of intractable epilepsy would be valuable because rapid identification of the patients at highest risk would allow physicians to initiate their treatment earlier with recently approved medications and to consider, if necessary, other surgical and nonsurgical treatments (7,8). The aim of this study was to determine and assess the characteristics and prevalence of epilepsy in children with CP.

Patients and Methods

In this retrospective investigation, the records of the children with CP, referred between 1998 to 2001, to the pediatric neurology clinic of Imam Reza Hospital in, Mashad, Iran, were studied and the data obtained was compared to that of a control group.

The main factors studied were type of CP, type of epilepsy, history of neonatal seizure existence, status epilepticus, brain CT scan, EEG (electroencephalogram), antiepileptic drugs usage and epilepsy prognosis. Data obtained for children with cerebral palsy and epilepsy was compared to that of a group of controls.

Children with febrile convulsion and neonatal epilepsy were excluded from this study. CP was defined as motor disabilities caused by non-progressive damage to the developing brain (9) and was classified into spastic hemiplegia, spastic diplegia, spastic tetraplegia, extrapyramidal, and mixed types (10).

Epilepsy was defined as separate occurrence of two or more apparently unprovoked seizures. (11) Seizure outcome was defined as "good" if the patient remained seizure free for more than 1 year, "slightly controlled" if seizures occurred once a month or less, and "poor" if the patient suffered from daily or weekly seizures (12).

Differences between groups were assessed by nonparametric statistical tests, i.e. Fisher's Exact Test and chi-Square Test.

Results

Of 133 patients (69 male, 64 female) with CP, 86 had spastic CP, 18 had hemiplegic CP; (13.5%), 12 had quadriplegia (9%), 55 had diplegia (41.3%), one had monoparesia (0.7%), 21 had hypotonic CP (15.8%), 20 patients had athetoid CP (15%) and 6 patients had mixed CP (4.5%).

Fifty-three children (39.8%) with CP had epilepsy, its prevalence being most common in the quadriplegic type. Frequency of epilepsy differs according to the types of CP (table 1). Some other factors related to CP were:

1. Mental disorders in children with CP and epilepsy were seen more often than in those with CP but without epilepsy (75.5% vs. 48.7% $p < 0.05$).
2. Neonatal seizures in children with CP and epilepsy (20.75%) was 4 times that observed in children with CP but without epilepsy (20.75% vs. 5% $p < 0.05$).

3. Abnormal brain CT scan in children with CP and epilepsy was observed more than in children but without epilepsy (50.9% vs. 27.5%, $p < 0.05$).

Other factors such as sex and family history showed no statistically significant effect on the incidence of epilepsy (table 2).

Fifty-three children (26 girls and 27 boys) with CP had epilepsy; their age range was between 4 months to 11 years, the age average being 5.8 years. The control group was 70 epileptic cases (29 girls and 41 boys) without CP, with an age range between 6 months to 16 years, average age 8.3 years. Epilepsy in children with CP occurs sooner than in epileptic children with normal brain development. Of the children with CP, 28 (52.8%), developed epilepsy within their first year of age, compared to 18.5% of controls ($p < 0.05$).

Of patients with hypotonic CP, 88% (8 of 9 cases) developed epilepsy within their first year of life ($p < 0.05$).

Eight patients (72.7%) with neonatal seizures and 16 patients (51.8%) with abnormal brain CT scan developed epileptic attacks before they were a year old (table 3).

In CP children with epilepsy, 31 cases (58.4%) had generalized epilepsy, 4 cases (7.6%) had Lennox syndrome, 2 cases (3.8%) had infantile spasms, 6 cases (11.3%) had partial epilepsy and 10 cases (19%) had polymorph epilepsy. Lennox syndrome and polymorphic seizures were more common in the CP group and partial epilepsy was more common in controls ($p < 0.05$) (table 4).

Histories of neonatal seizures was found in 11 children (20.7%) of the study group and 3 children (4.28%) in the control group ($p < 0.05$).

Status epilepticus was found in 2 cases (3.7%) of the study group, whereas no case was seen among controls.

Assessing seizure outcome in 43 cases (CP & epilepsy) and in 63 controls (epilepsy per se) 23 (48.8%) of the former and 46 (76%) of the latter had suitable responses to treatment ($p < 0.05$).

In study group, patients with athetoid CP and diplegic spastic CP showed the best outcomes, while the worst outcomes were seen in the patients with the hypotonic and quadriplegic types (57.14%) ($p < 0.05$) (table 5).

Polytherapy was used more commonly in the study group than in the control group (54.7% vs. 34.2% $p < 0.05$).

EPILEPSY IN CHILDREN WITH CEREBRAL PALSY

Other factors, like mental disorders and EEG changes and history of neonatal seizures had no statistically significant effect on epilepsy outcomes (table 6).

Table 1: Frequency of epilepsy according to types of cerebral palsy

| Type of CP | Seizure frequency | Total |
|---------------------|-------------------|-------|
| Spastic hemiplegic | 10 (55.5%) | 18 |
| Spastic tetraplegic | 9 (75%) * | 12 |
| Hypotonic | 9 (42.85%) | 21 |
| Athetoid | 3 (15.78%) | 20 |
| Spastic diplegic | 19 (34.54%) | 55 |
| Mixed | 3(50%) | 6 |
| Monoparesis | 0 | 1 |

*P<0.05.

Table 2: Factors affecting the development of epilepsy in patients with cerebral palsy(CP)

| | Cerebral palsy without epilepsy n- 80 | Cerebral palsy with epilepsy n- 53 | P value |
|-------------------------|--|---------------------------------------|---------|
| Male/ female | 38.42 | 26.27 | NS |
| Neonatal seizure * | 4 | 11 | 0.011 |
| Abnormal CT scan * | 22 | 27 | 0.016 |
| Positive family history | 1 | 2 | NS |
| Mental retardation * | 39 | 39 | 0.04 |

NS=Not significant

Table 3: Distribution of patients according to age at seizure onset

| Age (years) | Diplegia | Mixed | Athetoid | Hypotonic | Hemiplegic | Tetraplegia | Total | Control |
|-------------|----------|-------|----------|-----------|------------|-------------|-------------|-----------|
| <1 year | 7 | 2 | 1 | * 8 | 5 | 5 | 28 (52/8%)* | 13(18/5%) |
| 1-6years | 12 | 1 | 1 | 1 | 5 | 4 | 24(45/3%) | 33(47%) |
| >6 years | 0 | 0 | 1 | 0 | 0 | 0 | 1(1/9%) | 24(34/5%) |

* P <0.05

Table 4:Epilepsy type in patients with cerebral palsy compared to the control group

| Epilepsy type | Cerebral palsy(n=53) | Control (n=70) |
|-----------------------|----------------------|----------------|
| Generalized | 31 (58.4%) | 35 (50%) |
| Partial | 4 (7.6%) | 30 (42.8%) |
| infantile spasms | 2 (3.8%) | 1 |
| * Lennox syndrome | 6 (11.3%) | 1 |
| Polymorphic seizures* | 10 (19%) | 3 (4.2%) |

* P<0.05

Table 5 :Seizure outcome in patients with CP comparing with control group

EPILEPSY IN CHILDREN WITH CEREBRAL PALSY

| | Mixed | Athetoid | Hypotonic | Hemiplegic | Tetraplegic | Diplegic | Total | Control |
|----------------|-------|----------|-----------|------------|-------------|----------|------------|-----------|
| Good | 0 | 3 | 3 | 3 | 2 | 10 | 21 (40%)* | 46(65%) * |
| Slight control | 1 | 0 | 0 | 3 | 1 | 7 | 12 (23%) | 13(19%) |
| Bad | 0 | 0 | 4 | 1 | 4 | 1 | 10(18/5%)* | 4 (6%)* |
| Unknown | 2 | 0 | 2 | 3 | 2 | 1 | 10(18/5%) | 7(10%) |

* P<0.05

Table 6: Factors effective in good seizure outcomes

| Variable | Good seizure outcome | p |
|---|----------------------|-------|
| Athetoid vs other CP types | 45% VS 100% | NS |
| Diplegia vs other CP types | 44% VS 55.55% | NS |
| Normal IQ vs mental retardation | 40.62%VS 62.5% | NS |
| No neonatal seizure vs neonatal seizure | 28.57% VS 56.25% | NS |
| Mono therapy vs polytherapy * | 29.16% VS 73.68% | 0.009 |
| Normal EEG vs abnormal EEG | 41.93% VS 33.33% | NS |

NS=Not significant

Discussion

In this study, 39.8% of patients with CP had epilepsy. The frequency of epilepsy varied with different forms of CP, being 75% for spastic tetraplegia and 15% for athetoid. In a similar study done by Kwong et al, quadriplegic CP had the highest prevalence, whereas spastic diplegia had the least; we also found that spastic diplegics that were term at birth time, suffered from epilepsy more than did those that were preterm when born (13).

Several studies have documented various prevalence for seizures, in different types of CP (1, 2, 5). In the present study, generalized tonic clonic seizure (GTCS) was more common than focal seizures. In the Hadjipanayis et al study, focal seizures were more common in spastic hemiplegics, whereas generalized seizures were more common in the other types (1). In other studies done by Aksu and Delgado, focal seizures or secondary generalized seizures were more common in patients with CP(4,14).

In Kwong et al's study, generalized epilepsies had the least prevalence, while polymorph seizures were the most common; also, they added that classification of epileptic disorders in patients with CP was difficult because focal seizures soon become generalized. Again, the impairment

of consciousness is not completely distinguishable in patients with various infirmities, whereas differentiation between various forms such as myoclonic, tonic and atonic by EEG, during the attack, or by video EEG is possible (13). The reasons given in the results of the studies mentioned may explain the differences between their findings and those of our study.

In this study, mental retardation was more common in children with CP and epilepsy than in epileptic patients without CP (73.5% vs. 15.7%). Kwong et al reported similar findings.(13) Zaferiou et al in their study showed that epilepsy is the main predisposing factor for mental retardation and motor developmental delay (15).

In this study, epilepsy in children with CP was associated with an earlier onset of seizures than in controls; in our investigation, 28 (53%) children with CP had epilepsy in their first year of life, compared to 13 children (18.5%) without motor-neurological disorder. Zaferiou et al found that 69% of patients with CP had their first epileptic attack before they were a year old (15).

In the Kwong and Aksu studies, 47% and 38.5% children with CP developed epilepsy respectively (13, 4).

Sixteen cases (52%), whose brain CT scans showed structural disorders, had seizures within their first year of

age. The correlation of neuroradiologic findings between age and seizure onset has been described by Aksu et al (4). In the present study, neonatal seizures were found to be more common than in the controls; it is not however clear, whether short-acting anticonvulsant therapy is useful for prevention of seizures.

The presence of neonatal seizure was considered to be a risk factor for subsequent development of neurologic disabilities, such as mental retardation, CP, or epilepsy (13,16,17).

Kwong et al noted neonatal seizures in 19% of children with CP and epilepsy, similar to the percentage noted in the patients with CP per se (13).

Levene reported that neonatal seizures had an adverse effect on neurodevelopmental progression and may predispose to cognitive, behavioral, or epileptic complications later in life (18).

Mellitits et al showed that the incidence of the probability of mental retardation, CP or epilepsy following neonatal seizures ranges between 64% to 83% (19).

EEG was documented as being the most useful method for the prognosis of neonatal seizures; (17,19) in our study however no such association was observed.

Status epilepticus is more common in patients with CP (20). In one study, 88% of status epilepsies were reported in children with a neurological disorder (13). In our study 2 cases with status epilepticus had CP, whereas no case of status epilepticus was found in the control group.

Controlling seizures in children with CP is more difficult than in patients with normal brain development, and which is the reason for polytherapy or second-line drug usage. In this study, polytherapy was used for over half the patients with CP, while just 34% of the controls needed polytherapy. Percentages of polytherapy usage in the Kwong (13), Aksu (4) and Wojciech (16) studies were 30%, 82% and 45% respectively.

Of the cases, 48% showed good outcomes in just over one year, as compared to 76% of the controls. Patients with athetoid and diplegic CP had the best outcome. Of patients with CP, 23.3% had poor outcomes with regard to epilepsy, i.e. they suffered from daily or weekly seizures; this was in comparison to 6.3% of the controls. The worst outcomes were observed in the hypotonic and quadriplegic types.

In Kwong's study, 37% of the study group, as compared

to 90% of the controls had good outcomes; Of the cases, 34% had bad outcomes, in comparison to 3% of controls group. In this study diplegic spastics had the best outcomes, while quadriplegics had the worst outcome, findings that were in agreement with the Delgado and Guraraj studies (14, 21).

It seems that more extensive studies are required to identify, differentiate and confirm the outcomes in children suffering from epilepsy.

To conclude, epilepsy is more common in children with CP, the prevalence being related to the severity and its associated disabilities. The treatment of these children is more difficult and usually there is a need for poly therapy. The outcome depends on the types of cerebral palsy. New antiepileptic drugs and advances in surgical interventions are promising; they offer improved care of epileptic children with mental retardation and cerebral palsy, and a better quality of life, facilitating the integration of these patients and their families into society.

References

1. Hadjipanaysi A, Hadjichristodoulou C, Youroukas S. Epilepsy in patients with cerebral palsy. *Dev Med Neurol* 1997; 39(10):659-63.
2. Aicardi J, Epilepsy in brain-injured children. *Dev Med Child Neurol* 1990; 32 : 192-202.
3. Aicardi j. epilepsy as a presenting manifestation of brain tumors and of other selected brain disorders. In: Aicardi J, ed. *Epilepsy in children (The international review of child neurology)*, 2nd ed. New York: Raven Press;1994. P. 350-1.
4. Aksu F. Nature and prognosis of seizures in patients with cerebral palsy. *Dev Med Child Neurol* 1990; 32:661-668.
5. Hagberg B, Hagberg G, Olow I. The changing panorama of CP in Sweden 1954-70; II. Analysis of the various syndromes. *Acta peditar scand* 1975; 64: 193-200.
6. Uvebrandt P. Hemiplegic cerebral palsy: etiology and outcome. *Acta peditar Scand* 1988;345 Suppl:5-100.
7. Berg A.T, Shinnar S, Levy S R and Testa F M. Status epilepticus in children with newly diagnosed epilepsy. *Ann Neurol* 1999; 45: 618- 623.
8. Brorson L.O. and Wranne L. Long-term prognosis in childhood epilepsy: survival and seizure prognosis. *Epilepsia* 1987; 28 : 324-330.
9. Bruck I, Antoniuk S.A, Spessatto A, et al. Epilepsy in children with cerebral palsy. *Arq Neuropsiquiatr* 2001;

- 59: 35–39.
10. Nelson KB, Swaiman KF, Russman BS. Cerebral palsy. In: Swaiman KF(ed). *Pediatric neurology: Principles and practice*. 2th ed. St. Luis: Mosby; 1994. P.471-82.
 11. International League Against Epilepsy Commission on Classification and Terminology of the International League Against Epilepsy, Proposal for revised classification of epilepsies and epileptic syndromes. *Epilepsia* 1989; 30: 389–399.
 12. Webb DW, Fryer AE, Osborne JP. Morbidity associated with tuberculosis sclerosis: A population study. *Dev Med Child Neurol* 1996; 38: 146-55.
 13. Kwong KL, Wong SN, So KT. Epilepsy in children with cerebral palsy. *Pediatr neurol* 1998;19: 31-36.
 14. Delgado MR, Riela AR, Mills J, et al. Discontinuation of antiepileptic drug treatment after two seizure-free years in children with cerebral palsy. *Pediatrics* 1996; 97(2): 192-7.
 15. Zaferiou DI, Kontopoulos EE, Tsikoulas I. Characteristics and prognosis of epilepsy in children with CP. *J child Neurol* 1999;14(5): 289-94.
 16. Wojciech K, Wojciech S. Risk factors and prognosis of epilepsy in children with cerebral palsy in north-eastern Poland. *Brain and Development* 2003; 25 :499-506.
 17. Ellenberg J.H., Hirtz D.G. and Nelson K.B. Age at onset of seizures in young children. *Ann Neurol* 1984;15: 127–134.
 18. Levene M. The clinical conundrum of neonatal seizures. *Arch Dis Child Fetal Neonatal Ed* 1984;86 : F75–F77.
 19. Mellitis ED, Holden KR, Freeman JM. Neonatal seizures II :A multivariate analysis of factors associated with outcome. *Pediatrics* 1982;70: 177- 85.
 20. Shinnar S, Berg AT, Moshe SL et al. Discontinuing antiepileptic drugs in children with epilepsy: A prospective study. *Ann Neurol* 1994; 35: 534-45.
 21. Guraraj AK, Sztriha L, Bener A, et al. Epilepsy in children with cerebral palsy. *Seizure* 2003;12:110 -114.