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Risk Factors of Poorly Controlled Childhood Epilepsy - A Study in A Tertiary Care Hospital

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Abstract

Objective: Identifying the risk factors of poor seizure control in children in a setting of tertiary care hospital.

Design: Retrospective study.

Setting: Child Development and Neurology Unit in the department of Paediatrics of Bangabandhu Sheikh Mujib Medical University (BSMMU).

Study period: January 2004 through December 2005.

Subjects: One hundred and twenty epileptic children were studied. They were grouped into controlled group (seizure free for more than six months) and poorly controlled group (having one or more seizure per month over a period of six months or more and who had experienced trials of at least two different antiepileptic drugs at optimum doses alone or in combination with adequate compliance) at the end of intervention and compared.

Results: In this study 76 (63.3%) children were male and 44 (36.7%) children were female. Out of 120 cases 79 (65.8%) were in controlled group and 41 (34.2%) cases had poorly controlled epilepsy. Mean age of the controlled group and poorly controlled group of children were 79 months and 40.3 months respectively. Focal epilepsy was found in 30 (68%) cases in controlled and in 14 (31.8%) cases of poorly controlled group and generalized epilepsy was found in 42 (72%) cases in controlled and in 19 (28.8%) cases in poorly controlled group. Idiopathic epilepsy was more common which was 37 (46%) in controlled group against 14 (34%) in poorly controlled group. But symptomatic and cryptogenic cases were more prevalent with poorly controlled group 57.5% than controlled group 53%. In poorly controlled group 48.8% had cerebral palsy in comparison to 22.8% of controlled group.

Early onset of seizure before one year was 25.3% in controlled and 78% in poorly controlled group (odds ratio=.2322, p =.0082) and one or more seizure per week 43% in controlled and 92.7% in poorly controlled group (odds ratio=.1218, p=.0032) were found as risk factors of poorly controlled epilepsy.

Conclusion: Early onset of seizure before one year, symptomatic epilepsy and one or more seizure per week at diagnosis were found as risk factors of poorly controlled epilepsy in children attending a tertiary care hospital.

Key words: *Risk factors, poorly controlled epilepsy.*

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Introduction

Childhood epilepsy is a common neurological problem[1]. In Bangladesh incidence of epilepsy was found to be 2.54 per 1000 population[2]. Children below 10 years represent a large group of individuals with epilepsy[3]. Between birth and 2 years of age incidence of epilepsy is more[4]. More than 10% of patients develop medically poor controlled epilepsy[3]. Many studies have stated that risk factors which are unfavorable for outcome include an early onset of

seizures, status epilepticus, presence of symptomatic or cryptogenic epilepsy, types of seizures, large number of seizure before treatment, complex febrile seizure, increased frequery of seizures, abnormal epileptic form activity, abnormal neuroimaging, associated disabilities like cerebral palsy and mental retardation[4,5]. The risk factors of poorly controlled epilepsy varies with etiology, clinical characteristics, investigation findings and other factors[4-7]. There is a paucity of data regarding poorly controlled epilepsy in Bangladesh, especially in children. This study was done in a tertiary care hospital to observe the risk factors of poorly controlled epilepsy as compared to controlled epilepsy in children. Early identification of risk factors of poorly controlled epilepsy would help in counseling patients and their families, selecting patients for intensive investigations and treatment and also to consider surgical treatments.

Materials and Methods

It was retrospeetive study. Duration of study was from January 2004 through December 2005. Study was done at Child Development and Neurology unit in the Department of Paediatrics of Bangabandhu Sheikh Mujib Medical University. Inclusion criteria was epileptic children of 1 month to 15 years of age. One hundred twenty patients were studied, of them 79 were in controlled group and 41 were in poorly controlled group. All of them got treatment for at least 6 months period. Study patients were collected purposfully on working days. Thorough history of every aspect related to epilepsy was taken. Neuro-developmental and other relevant examinations were done in every patient. Psychological assessment was carried out by the developmental psychologist. Hearing assessment and complete ophthalmologic assessment were done, when required. Twenty one channel EEG was done in every patient. EEG was reported by paediatric neurologist. Neuroimaging like CT scan / MRI, USG or X-ray skull were done in cases, where these were feasible and relevant. Appropriate antiepileptic drugs were given to all epileptic children under the supervision of paediatric neurologist. Conventional antiepileptic drugs (AED) were tried as the first and second AED and later in cases of partial or no response, newer AED were used. Valproic acid, carbamazepine and phenobarbitone were more commonly used drugs (with the exception in west syndrome where steroids were used) in this study.

Polytherapy (combination of AED) was given when monotherapy failed. Serum drug level was measured in some of the patients, when required. All relevant informations from history, clinical examination, investigation, and follow-up visits were also collected from medical records in pre-designed sheets.

After assessment patients were grouped in two groups as defined below:

1. Controlled group: who became seizure free for six months or more after treatment.
2. Poorly controlled group: who had one or more seizure per month over a period of six months or more and who had experienced trials of at least two different anti epileptic drugs at optimum doses alone or in combination with adequate compliance.

The predisposing risk factors between the two groups were analyzed. Working definitions of different terms are given below.

Working definition:

Epilepsy: Occurance of at least two unprovoked seizures at least 24 hours apart[7].

Controlled epilepsy: who responded to antiepileptic drug (Seizure free for 6 months or more)[4].

Poor controlled epilepsy: One or more seizure per month over a period of 6 months or more and who had experienced trials of at least two different AEDs at optimum doses alone or in combination with adequate compliance[4].

Partial seizure control: Defined as more than fifty percent reduction of frequency of seizure[4].

Complete seizure control: Defined as complete remission of seizure for six months or more[4].

Epilepsy and epileptic syndrome were classified by International League Against Epilepsy (ILAE) classification 1989[5].

Idiopathic epilepsy syndrome: A syndrome that only epilepsy with no underlying structural brain lesion or other neurologic signs or symptoms. These are presumed to be genetic and are usually age dependent[5].

Symptomatic epilepsy syndrome: A syndrome in which the epileptic seizure are the result of more identifiable structural lesion of the brain[5].

Probably Symptomatic epilepsy syndrome: Synonymous with but preferred to the term cryptogenic, used to define syndromes that are believed to be symptomatic, but no etiology has been identified[5].

Early onset of seizure : Onset of seizure before one year[7].

Abnormal EEG: It is either the background abnormality or epileptogenic discharge[8].

Data were processed and analysed using soft-ware SPSS (Statistical Package for Social Sciences) version 11.5. The test statistics used to analyse the data were descriptive statistics, Chi-square (χ^2) test, Fisher's

exact probability test and odds ratio. The level of significance was 0.05 and p <0.05 was considered significant. Finally all the variables who showed significant association with outcome were entered into logistic regression model to determine independent predictors of poorly controlled epilepsy. The analysed data were then presented in the form of tables.

Results

One hundred and twenty children with epilepsy were studied, 76 were male and 44 were female with a male-female ratio of 1.73 : 1. There were 79 (65.8%) children in the controlled group and 41(34.2%) children in the poorly controlled group. Mean age of the controlled group and poorly controlled group of children were 79 months and 40.3 months respectively. Mean age of controlled group was almost double than that of poorly controlled group and mean weight was 20.3 and 12.6 kg in controlled and poorly controlled group respectively. Focal epilepsy was found in 30 (68%) cases in controlled and 14 (31.8%) cases in poorly controlled group; generalized epilepsy was found in

Table-I

Classification of Epilepsies, Epileptic Syndromes (as per ILAE, 1989) among studied patients

	Controlled group	Poorly controlled group	Total
Localization-related (focal, local, partial) epilepsies and syndromes	**30**	**14**	**44**
Idiopathic:	11	7	18
Benign childhood epilepsy with centro-temporal spikes	2	0	2
Childhood epilepsy with occipital paroxysms	1	0	1
Others	8	7	15
Symptomatic:	17	4	21
Secondary generalised seizures	13	2	15
Others with seizures	4	2	6
Cryptogenic	2	3	5
Generalized epilepsies and syndromes	**49**	**27**	**76**
Idiopathic:	26	7	33
Benign myoclonic epilepsy in infancy	2	0	2
Childhood absence epilepsy	3	0	3
Juvenile myoclonic epilepsy	0	1	1
Gneralized idiopathic epilepsies	21	6	27
Cryptogenic :	4	8	12
West syndrome (infantile spasms)	2	5	7
Lennox-Gastaut syndrome	0	1	1
Epilepsy with myoclonic-astatic seizures	1	1	2
Epilepsy with myoclonic absence	1	1	2
Symptomatic:	17	4	21
Early myoclonic encephalopathy	1	2	3
Specific syndromes (included those diseases in which seizures are presenting or predominant feature)	3	0	3
Others	13	2	15
Epilepsies and syndromes with both generalized and focal seizure:	1	5	6
Severe myoclonic epilepsy in infancy	0	2	2
Acquired epileptic aphasia	1	3	4
Special syndromes:			4
Situation-related seizures	1	3	4

49 (72%) cases in controlled and in 19 (28.8%) cases in poorly controlled group. Idiopathic epilepsy was in 37 (72.5%) cases in controlled and 14(27.5%) cases in poorly controlled group and symptomatic and cryptogenic epilepsy were in 19 (57.5%) cases in poorly controlled and 42 (53%) cases in controlled group (Table-I). Onset of epilepsy was before 1 year of age among 78% cases in poorly controlled group, compared to 25.3% cases in controlled group (Table-II).

Univariate comparison between controlled group and poorly controlled group of patients revealed that there was significant association between poorly controlled epilepsy and onset of seizure before 1 year of age (p<.001). Initial seizure frequency before treatment (1 or more seizure per week) revealed a strong positive association with poorly controlled epilepsy (p=.0032) Table-III.

In multivariate analysis by stepwise logistic regression, age at onset of seizure less than 1 year, symptomatic epilepsy and initial seizure frequency before treatment (1 or more seizure per week) demonstrated to be independent predictors of poorly controlled epilepsy.

Associated disabilities were found more in poorly controlled cases. Poorly controlled seizures (48.8%) were more than controlled seizures (22.8%) in CP patients. Most of the different form of the cerebral palsy (CP) occur in higher frequency in poorly controlled group (Table-IV). Behavioral problems were also more in poorly controlled group (Table-I). Intelligence level was also found affected in both group, more on intractable group with (66%) having moderate to severe mental retardation (Table-V).

EEG was abnormal in 53 (67.7%) cases of controlled group and 34 (88.9%) cases of poorly controlled group. Relation between abnormal EEG and poorly controlled epilepsy was significant (P <.001).

Sixty four (81%) patients of controlled group responded completely and 19% responded partially to first anti-epileptic drug (AED); on the other hand in the poorly controlled group, there was absence of complete response and 73% responded partially with first AED (Table-VI). Fifteen (19%) patients of controlled group who had partial controll with first AED, responded completely to second AED, but there was no complete response even to second AED in the poorly controlled group.

Table-II

Comparison between controlled group and poor controlled group for onset of seizure before 1 year of age

Age of onset of seizure	Controlled group		Poorly controlled group		P
(years)	n	%	n	%	value
<1 year	20	25.3	32	78.0	
>1 year	59	74.7	9	22.0	< 0.001
Total	79	100.0	41	100.0	

Table-III

Univariate comparison of age of onset and seizure frequency before treatment between controlled group and poorly controlled group of patients

Variable	Controlled group n (%)	Poorly controlled group n(%)	Odds ratio	95% confidence interval	P value
Age at onset of seizure (< 1 year)	20 (25.03)	32 (78.0)	.2322	.0787 - .6849	<0.001
Frequency of seizure before treatment (1 or more per week)	34 (43.0)	38 (92.7)	.1218	.0300 - .495	.0032

Table-IV

Distribution of types of associated disabilities among the controlled group and poorly controlled group of the patients

Types of Associated disabilities	Controlled group		Poorly controlled group		Total	
	n	%	n	%	n	%
Cerebral palsy (CP)	18	22.8	22	53*	40	75.8
Spastic tetraplegia	5	6.3	10	24.4	15	12.5
Mixed CP	1	1.3	1	2.4	2	1.7
Spastic diplegia	3	3.8	1	2.4	4	3.3
Spastic hemiplegia	9	11.4	7	17.1	16	13.3
Hypotonic CP	0	0	3	7.3	3	2.5
Attention deficit Hyperactive disorder	2	2.5	6	14.6	8	6.7
Autism	0	0	2	4.9	2	1.7
Neurocutaneous syndrome	3	3.8	0	0	3	2.5

*P<.001

Table-V

Intelligence level among the controlled and poorly controlled group of the patients

IQ level	Controlled group		poorly controlled group		Total	
	n	%	n	%	n	%
115-85 (Normal intelligence)	47	59.5	6	14.6	53	44.2
84-70 (Borderline intelligence)	3	3.8	5	12.2	8	6.7
69-50 (Mild mental retardation)	11	13.9	3	7.3	14	11.7
49-35 (Moderate mental retardation)	14	17.7	15	36.6	29	24.2
34-20 (Severe mental retardation)	2	2.5	12	29.3	14	11.7
<20 (profound mental retardation)	2	2.5	0	0	2	1.7
Total	79	100	41	100	120	100

Table-VI

Response to first AED among the controlled group and poorly controlled group of the patients

Response to first AED	Controlled group		Poor controlled group		Total	
	n	%	n	%	n	%
Complete	64	81	0	0	64	53.3
Partial	15	19	30	73.2	45	37.5
No control	0	0	11	26.8	11	9.2
Total	79	100	41	100	120	100

Discussion

Poorly controlled epilepsy is a burning concern for both patients and personnel dealing with epilepsy. This study was done to search the factors that are associated with poorly controlled epilepsy. Early identification of these factors would help in planning early intervention.

One hundred twenty patients with epilepsy were enrolled in this study. Mean age of controlled group was 79 months and that of poorly controlled group

was 40.3 months. The mean age of poorly controlled group was almost half of controlled group, which might be due to the fact that poor controlled epilepsy present in the early life[6].

Among the total 120 patients 76 (63%) were male and 44 (37%) were female. Male and female ratio was 1.7 : 1. This finding was consistent to another study[6], which was 1.85 : 1. Berg et. al. found equal ratio of both male and female[8]. Most studies reported a slightly higher incidence in boys than girls[9]. The high ratio of male might be due to the fact that boys get preference in the family in seeking healthcare.

Out of 120 cases 79 (63.3%) were in controlled group and 41(34.2%) cases were poorly controlled epilepsy. In a meta-analysis they showed that 40-70% childhood epilepsy were poorly controlled[10].

In this study 44 (36.7%) patients had focal seizure, 68 (56.7%) patients had generalized seizure and 8 (6.7%) had unclassified seizure. These figures have got similarity with most of the other studies[8,9]. Incidence of primary generalized seizure disorder was higher than that of partial seizure, 39-44 vs 21-32 / 100,000[11].

Age of onset of seizure before one year was present in 78.1% children of poorly controlled group in comparison to 25.4% of controlled group. Poorly controlled epilepsy was found significantly associated with early age of onset of seizure (P <.001). By multivariate stepwise logistic regression it was found that early age of onset of seizure was an independent predictor of poorly controlled epilepsy. In other studies it was also found as an independent predictor[3,4,8,11-13].

Epilepsy due to structural malformation, neuronal migration disorder and other congenital structural defects manifest early in the life. These types of epilepsy are usually poorly controlled. Epilepsy due to severe brain damage caused by severe perinatal insult manifest early in the life. A significant number of which also become poorly controlled [3-5,8-12] .

Symptomatic epilepsy was found more in poorly controlled group 19 (57.5%) than in case of controlled group 42 (53%). Association between symptomatic epilepsy and poorly controlled was found statistically significant (P<.001). Symptomatic epilepsy was found as an independent predictor of poorly controlled epilepsy by multivariate stepwise logistic regression (P=.0004). In other studies similar result was found[4,8,14-17].

Cerebral palsy was present in 38 (31.7%) patients. More common varieties were spastic tetraplegia and spastic hemiplegia. Aneja S in India found almost same picture in cerebral palsy with epilepsy[18]. In poor controlled group 53% of patients had cerebral palsy (P <.001), in comparison to 22.8% of controlled group. These figures also reflect significant association of symptomatic epilepsy with poorly controlled group.

Association of seizure frequency before treatment was compared between two groups. One or more seizures every week were found significantly associated with poorly controlled epilepsy (P<.001) by multivariate stepwise logistic regression analysis. So, it was found as an independent predictor of poorly controlled epilepsy. Sillanpaa in 1993 found similar result[5]. EEG was abnormal in 53 cases of controlled group out of 79 and 34 cases of poor controlled group out of 41. Relation between abnormal EEG and poorly controlled group was significant (P<.001). Tae-Sung K and Holmes in 1999 found same result[15].

Attention deficit hyperactivity disorder and autism were more in poorly controlled epilepsy like other studies[17]. Increase incidence of severe mental retardation in poorly controlled epilepsy (29.3%) than controlled epilepsy (2.5%) reflects the effects of both seizures and drugs[18]. Only 2 cases of profound mental retardation in controlled group but not in poorly controlled group might be an incidetal finding. Large sample study is required to comment on this finding. Valproic acid, carbamazepine and phenobarbitone were more commonly used drugs in this study (82.6%). This study has focused on the facts and figures of childhood poorly controlled epilepsy in our perspective.

Conclusion

Early age of onset of seizure, symptomatic epilepsy, frequency of seizure (one or more seizure per week) were found significantly associated with poorly controlled epilepsy in children. Early identification of risk factors of poorly controlled epilepsy in children will help in reducing the incidence and severity of poorly controlled epilepsy and thus the quality of life of epileptic children.

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