CLINICAL SPECTRUM OF SEIZURES AND EFFICACY OF ANTICONVULSIVE TREATMENT IN CHILDREN

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ABSTRACT

Objective: To study the clinical spectrum of seizures and efficacy of anticonvulsive treatment in children.
Study Design: A descriptive study.
Place and Duration of Study: Military Hospital (MH) Rawalpindi from October 2011 to March 2012.
Material and Methods: One hundred children of either gender aged 1 month to 12 years presenting with seizures at Military Hospital Rawalpindi were evaluated and consented to participate in the study. All children with a febrile seizures were evaluated. The seizures were classified according to international league against epilepsy guidelines. Antiepileptic treatment regimen was evaluated in terms of number of drugs, correct dosage and efficacy in control of seizures.
Results: It was observed that generalized seizures were (58%) followed by focal seizures (32%) in children. Valproic acid was prescribed in (51%) cases. Epilepsy was diagnosed in (56%) followed by cerebral palsy (20%), post meningoencephalitis sequalae (11%), intracranial hemorrhage (7%) and leukodystrophies (3%) as underlying cause of seizures. Statistically significant association was seen between age groups and diagnosis (*p* value=0.001); age groups and types of seizures (*p* value=0.046); correct dosage of antiepileptics and control of seizures (*p* value=0.007); compliance to treatment and control of seizures (*p* value=0.007).
Conclusion: Generalized seizures are the commonest form followed by focal seizures. Epilepsy was the common etiology of seizures in all age groups in children. Cerebral palsy was the second leading cause of seizures in children followed by post meningoencephalitis, stroke and leukodystrophies. Valproic acid was the most commonly prescribed antiepileptic. Normal delivery with delayed cry was the major risk factor for cerebral palsy. Prescription of appropriate antiepileptics according to diagnosis in optimum dosage and compliance to treatment affect control of seizures in children.

Keywords: Cerebral palsy, Epilepsy, Intracranial hemorrhage, Meningoencephalitis, Leukodystrophies, Seizures.

INTRODUCTION

A seizure is defined as a paroxysmal, time-limited change in motor activity and / or behavior that results from abnormal electrical activity in the brain.At least 4-10% of children observe an episode of seizure during the first 16 years of life[1]. Seizures may represent aneurological illness or disease because of any systemic or biochemical disturbance[2].

The prevalence of seizures is >3 per 1000 in developed world as compared to 9 per 1000 in developing nations[3]. Christopher et al described that around 3% of all children below 15 years of age have a seizure, 50% of which are febrile seizures and epilepsy is the underlying cause in one of every hundred children with seizures[4]. Hamdy et al described the annual incidence of seizures was 153 per 100,000 for new onset seizuresand it was significantly higher in south Asians[5]. Sillanpaa et al studied to show that children with epilepsy have 7% life time risk of sudden death at 40 years and 12% in another group of patients with epilepsy[6].

Childhood seizures have many different causes which include prenatal or genetic causes (65%), perinatal causes (8%) and complications of prematurity (13%) or acquired causes (7%). Epilepsy is common in some families like (36%)

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had first- or second-degree relatives affected and mostly it is idiopathic (54% vs 30%) even without neurological sequalae (57% vs 26%)[7].

There are many types of seizures in children which include focal, generalized, unknown seizures and electroclinical syndromes according to ILAE classification[8]. Seizures not only cause physical concerns, behavioural issues and cognitive impairment but also are responsible for persistent psychosocial stress for the children and their parents[9]. Theseizures in children lead to regular follow up visits to concerned specialists, affectingtheir school performance, and their inability to take part in sports and other extracurricular activities[10]. Burton et al described that seizures cause long term cognitive impairment (64%), behaviour disorder (61%), motor difficulties (26%), burns and other previous injuries (26%) and poor school attendance (50%)[11].

The conventional antiepileptics are still the main modality of epilepsy treatment in Asian children even after the availability as well as safety of newer antiepileptics, like Valproate (about 40%). Most of the patients (62.8%) were taking only one drug[12]. Antiepileptics werebeing used in 2.23/1000 children in 2005. Valproic acid was advised mostly followed by carbamazepine and benzodiazepines. The newer antiepileptics are are increasingly being prescribed 26.9% nowadays[13].

This study is being planned to know the clinical spectrum of seizures and efficacy of anticonvulsive treatment in children. Epilepsy is a common problem in Pakistan (Prevalance 9.99 per 1000 population) especially in children of growing age[14]. The presentstudy involves indoor and outdoor patients reporting at the Military Hospital Rawalpindi and the patients referred to this hospital from other primary or secondary care hospitals for evaluation of seizures.

PATIENTS AND METHODS

This descriptive study was conducted from October 2011 to March 2012 at Department of Paediatrics, Military Hospital (MH), Rawalpindi. All children of army personnel and civilians reported for evaluation of seizures to MH Rawalpindi, either directly or referred from peripheral hospitals, were considered in study population. Sample size was calculated as 100, using World Health Organization (WHO) calculator with confidence level 95; anticipated population proportion 0.4 (40%) and absolute precision 0.10. Consecutive non probability sampling technique was used.

The Children presented with seizures without a febrile illness, one month to twelve years of age without gender discrimination, were included in the study. Children with febrile seizures were excluded from the study. Neonates were also excluded from the study as neonatal seizures have different simiology, types and etiologies.

All the patients were included after taking written informed consent from the parents. They were examined thoroughly for any neurological involvement and achievement of developmental milestones appropriate for their age groups. Parents were asked in detail about risk factors like trauma, medical or surgical history, birth history, type and number of antiepileptics prescribed, all drugs doseswere calculated according to weight, duration and compliance especially any gaps in treatment, frequency of seizures in last 3 months while on treatment and it was recorded on a performa by the researcher.

Their baseline investigations like blood complete picture, blood glucose levels, renal function tests, serum calcium, phosphate and magnesium levels were carried out. EEG, CT scan and MRI brain were performed to know the exact cause as well as type of seizures. Approval of the Military Hospital Research and Ethics Committee was obtained. The children were managed with appropriate antiepileptics and their doses were also adjusted. Parents were counseled about nature of disease and the importance of continuous drug treatment. Patients are on regular follow up visits in child OPD.

Statistical Package for Social Sciences (SPSS) version 15.0 was used for data analysis. The qualitative data frequencies and percentages were calculated. Median and interquartile range were calculated for quantitative variables. Pearson chi-square method was used to calculate associations between variables. At 95% confidence level, *p*-value less than 0.05 was taken as significant.

RESULTS

Hundred children presented with seizures, meeting the inclusion criteria, were studied and (16%) 16/100 were 1 month to 1-year-old; (43%) 43/100 were 1 to 5-year-old; and (41%) 41/100 were 5 to 12-year-old (table-I). Median age is 4.75 years with interquartile range 6.0. Male children were (64%) 64/100 and (36%) 36/100 were female children with a male to female ratio of 1.7:1.

Generalized seizures (58%) 58/100 were most common followed by (32%) 32/100 focal seizures, (4%) 4/100 absence, (4%) 4/100 unclassified, (1%) 1/100 myoclonic seizures and (1%) 1/100 infantile spasm (table-I). Of the 100 children, majority were diagnosed to have (56%) 56/100 epilepsy while (20%) 20/100 had cerebral palsy, (11%) 11/100 had post meningoencephalitis sequalae, (7%) 7/100 had intracranial hemorrhage (stroke), (3%) 3/100 had leukodystrophy, (1%) 1/100 had rickets, (1%) 1/100 had down syndromeand (1%) 1/100 leukoencephalopathy (table-II).

Of the 100 children, (68%) 68/100 had normal occipitofrontal circumference while

Table-I: Type of seizure and age groups.

Type of seizure	Age groups			Total	*p* value
	1 month to 1 year	1-5 years	5 -12 years		
Focal &multifocal	10	10	12	32	
Generalized	5	25	28	58	
Absence	0	1	3	4	
Unclassified	0	3	1	4	0.046
Myoclonic	0	1	0	1	
Infantile spasm	1	0	0	1	
	16	40	44	100	

Table-II: Diagnosis and age groups.

Diagnosis	Age groups			Total	*p* value = 0.001
	1 month to 1 year	1-5 years	5-12 years		
Epilepsy	5	20	31	56	
Cerebral palsy	1	14	5	20	
Post meningoencephalitis sequalae	3	4	4	11	
Leukodystrophy	1	2	0	3	
Intracranial haemorrhage	5	2	0	7	
Rickets	0	1	0	1	
Down syndrome	0	0	1	1	
Leukoencephalopathy	0	0	1	1	
	15	43	42	100	

Table-III: Cerebral palsy obstetric data.

Serial no.		Cerebral palsy 20/100				Total
1	Mode of delivery	SVDs 16			LSCS 4	20
		Home 8	Hospital 7	Clinic 1		
2	Delayed cry	10				10
3	Birth asphyxia	10				10

(28%)28/100had microcephaly and (4%) 4/100 had macrocephaly. All patients with cerebral palsy (20%)20/100 had microcephaly.History of aura was present only in (2%) 2/100 of patients in 5-12 year age group and that was headache. Out of cerebral palsy patients (20%) 20/100, (80%) 16/20 were SVDs (50% at home, 43% at hospital, 7% at clinic) while (20%)4/20 were LSCS; 10/16 (62%) had a history of delayed cry and birth asphyxia (table-III).

All patients were investigated and it was observed that EEG was positive in (29%) 29/100 and negative in (71%) 71/100 while CT scan brain was diagnostic in (38%) 38/100, normal in (58%) 58/100 and MRI brain was diagnostic in (4%) 4/100.

Out of 100 children, (55%)55/100 were on monotherapy, (25%) 25/100 were taking 2 drugs, (10%) 10/100 were taking 3 drugs, (6%) 6/100 were taking more than 3 drugs and (4%) 4/100 were not taking any medication for seizures. Valproic acid was most commonly prescribed antiepileptic in children (51%) 51/100. Seizureswere controlled for last 3 monthsin (83%) 83/100 children on previous treatment while (17%)17/100were still having seizures. Drug dosage as well as compliance to treatment was appropriatein (91%) 91/100 but (13%) 12/91 out of above were still having seizures in spite of good compliance. Dose adjustment was required in (9%) 9/100 as well as they required counseling to improve compliance but (0.5%) 5/9 of these were still having persistent seizures. These patients were followed up for 03 months and it was observed that they have multiple reasons for persistent seizures like missed dose or recurrent vomiting after medication (0.4%) 2/5, febrile illness (0.2%) 1/5, hypocalcemia (0.2%) 1/5 and resistant despite multiple drugs were used according to simiology (0.2%) 1/5.

Age groups and types of seizures (*p*-value=0.046) table-I; Statistically significant

Table -IV: Type of seizures and gender.

		Gender		Total	*p*-value = 0.835
		Male	Female		
Types of Seizures	Focal	3	2	5	
	Multifocal	19	8	27	
	Generalized	34	24	58	
	Absence	3	1	4	
	Myoclonic	1	0	1	
	Unclassified	3	1	4	
	Infantile spasm	1	0	1	
Total		64	36	100	

Table-V: Correct dosage of antiepileptics and control of seizures.

Correct Dosage of Antiepileptic		Seizures Controlled		Total	*p*-value = 0.007
		yes	no		
	Yes	79	12	91	
	No	4	5	9	
Total		83	17	100	

Table-VI: Compliance to treatment and control of seizures.

Compliance to Treatment		Seizures Controlled		Total	*p*-value = 0.007
		yes	No		
	yes	79	12	91	
	no	4	5	9	
Total		83	17	100	

association was seen between age groups and diagnosis (*p* value=0.001) table-II; No significant association was seen between type of seizures and gender (*p*-value=0.835) table-IV using Pearson Chi-square method.Correct dosage of antiepileptics and control of seizures (*p*-value=0.007) table-V; compliance to treatment and control of seizures (*p* value=0.007) table-VI.

DISCUSSION

Seizures are common in children and occur in approximately 10% of paediatric age group[15]. The prevalence of seizures is 45.2/1000 in under five age group which is very high and had a relation to socio-economic conditions[16]. Seizures are a common cause of emergency paediatric admissions to hospitals in developing countries and also a risk factor for long term neurological and cognitive sequalae and epilepsy. The incidence of sudden seizures was 425 per 100,000/year in children till 13 years of age and was 879 per 100,000/year in children under five[17]. There is an increased risk of seizures in children of parents with epilepsy. Seizures and epilepsy affect infants and children more than any other age group[18].

All types of seizures are more common in male gender because of the predominance of all underlying etiologies[18]. The current study also showed the same with male to female ratio of 1.7:1. The main seizure types are focal motor with secondary generalization in (65.2%) and generalized convulsive seizuresin (16.9%)[19]. The present study showed that generalized seizures (58%) were most common followed by focal (32%), absence (4%), unclassified (4%)and myoclonic seizures (1%), infantile spasm (1%) (*p* value 0.174).

Central nervous system infections are the main cause of seizuresand acquired epilepsy in the developing world. Meningoencephalitis, cerebral malaria and neurocysticercosis are common etiologies of seizures and they also cause increased mortality and morbidity including epilepsy[20]. The present study showed that epilepsy was (56%) followed by (20%) cerebral palsy, (11%) post meningoencephalitis sequalae, (7%) intracranial hemorrhage (stroke), (3%) leukodystrophy, (1%) rickets, (1%) Down syndrome and (1%) leukoencephalopathy. Baca CB et al studied and described comorbidities associated with seizures are psychiatric diagnosis 26%, neurodevelopmental spectrum disorder 39%, chronic medical illness 24% and migraine 15%[21].

The risk factors for cerebral palsy are from the antenatal, natal and postnatal period in full term neonates[22].Multiparity and cesarean section were prognostic factors for having cerebral palsy while low APGAR scores at one minute had limited prognostic value[23].The present study showed that normal delivery with delayed cry and birth asphyxia were the major risk factors for cerebral palsy.

Brain imaging study in children with seizures showed clinically significant results in 19.7% of patients and especially more than twice children without fever had a positive CT scan (*p*= 0.049)[24]. The present study showed that CT scan brain was diagnostic in (38%), normal in (58%) while MRI brain was diagnostic in (4%). MRI is essential to consider surgical treatment, allowing one to localize potential epileptogenic anatomic lesions[25]. The present study showed that EEG was positive in (29%) and negative in (71%). EEG monitoring had a role in relevant clinical management changes in 59%of children either to start or add on therapy in 43% patients or to determine whether a specific event was a seizure or not in 21%[26].

The present study showed that 55/100 (55%) were on monotherapy, 25/100(25%) were on2 drugs, 10/100(10%) were on 3 drugs, 6/100(6%) were taking more than 3 drugs and 4/100(4%) were not taking any medication for seizures. Kelemen A et al described that although 70-80% of children may be well treated with monotherapy, 15% of children require combination of 2 or more drugs causing drug interactions in resorption, distribution, metabolism and elimination[27]. The present study

showed that 51% patients were on valproic acid. Kwong et al found out that antiepileptics were being used in 2.23/1000 children in 2005. Valproic acid was advised mostly followed by carbamazepine and benzodiazepines. The newer antiepileptics areincreasingly being prescribed 26.9% nowadays[13].

Most patients become rapidly seizure free, and poor compliance or prescription of an inappropriate antiepileptic drug because of misdiagnosis are the most common causes of treatment failure in idiopathic generalized epilepsy[28]. The present study also showed that drug dosage as well as compliance to treatment was appropriate in (91%) 91/100 but (13%) 12/91 out of above were still having seizures in spite of good compliance. Dose adjustment was required in (9%) 9/100 as well as they required counseling to improve compliance but (0.5%) 5/9 of these were still having persistent seizures in our study. Efficacy of treatment was observed by the changes in frequency of seizures after 6 months in 63.75% patients while effect was absent or minimal in 29.5%[29]. The present study patients were followed up for 03 months and it was observed that they have multiple reasons for persistent seizures like missed dose or recurrent vomiting after medication (0.4%) 2/5, febrile illness (0.2%) 1/5, hypocalcemia (0.2%) 1/5 and resistant despite multiple drugs were used according to simiology (0.2%)1/5.

Mostly parents have knowledge about seizures, however, there is a continuous need to spread more information in general public about itscommon causes, clinical presentation, management, and prognosis. Regular mass campaigns and public education seminars should be carried out about epilepsy through various modalities of communication in order to reduce the morbidity and mortality associated with this disease[30]. Prognosis is based on the etiology and associated syndromes and is usually excellent in acute symptomatic epilepsy, very favorable in idiopathic epilepsy and less favorable in remote symptomatic cases[31].

CONCLUSION

Generalized seizures are most common in children followed by focal seizures. Epilepsy was the common etiology of seizures in all age groups in children. Cerebral palsy was the second leading cause of seizures in children followed by post meningoencephalitis, stroke and leukodystrophies. Valproic acid was the most commonly prescribed antiepileptic. Normal delivery with delayed cry was the major risk factor for cerebral palsy. Prescription of appropriate antiepileptics according to diagnosis in optimum dosage and compliance to treatment affect control of seizures in children.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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