Use of First Line AEDS For the Control of Acute Seizures in Pediatric Emergency Department- An Experience of Tertiary Care Hospital

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ABSTRACT

Objective: To determine the use of first line drugs after the use of Diazepam for the control of seizures in children presenting to Pediatric Emergency Department.

Study Design: Cross-sectional study.

Place and Duration of Study: Pediatric Emergency Department, Aga Khan University Hospital, Karachi, from Jan to Dec 2018.

Methodology: All the patients from one month to 18 years of age who presented with the seizures at the Pediatric Emergency Department were included in the study. Patients with intractable epilepsy, taking multiple anti-epileptic drugs, patients on ketogenic diet and metabolic seizures were excluded. Demographic information along with the duration of seizure, type of seizure, use of anti-epileptic drugs (AEDs) and response in the form of cessation of seizure to anti-epileptic drugs were recorded.

Results: A total of 105 patients with seizures were included in this study. Mean age of the patients was 73.87 ± 54.7 months. Generalized seizures were observed in 78 (74.3%) patients. In 48 (45.7%) patients, seizures were <5 minutes of duration, while 65 (62%) patients were diagnosed cases of epilepsy. Loading dose of Levetiracetam 20 mg/kg was used as first line AED in 66 (62.9%) patients. Out of 66 patients who were given Levetiracetam, 41 (39%) did not require second drug.

Conclusion: Levetiracetam was the most commonly used first line long-acting drug at our institute in all the seizure types and controlled seizures in two-thirds of the patients.

Keywords: Antiepileptic drugs, Seizures, Status epilepticus.

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INTRODUCTION

Seizures are one of the common reasons for Pediatric Emergency visits. It accounts for 2% of the emergency visits.[1] Acute seizures and status epilepticus (SE) are the most common neurological emergencies in children associated with high morbidity and mortality rates and poor long-term outcomes.[2] Status epilepticus is defined as the continuous seizure lasting for more than 5 minutes or recurrent seizures of less than 5 minute duration without gaining consciousness. Thus, seizures lasting more than 5 minutes are likely to convert into status epilepticus and the seizures that persist for 30 minutes are defined as refractory status epilepticus.[3]

Although epilepsy is common but the majority of Emergency Department (ED) visits for seizures involve patients without known epilepsy.[4] Seizures lasting for more than 10 minutes are common in children. However, once a seizure lasts for more than 5 minutes, it is unlikely to stop spontaneously and intervention is therefore indicated.[5]

Traditionally, Benzodiazepines administered via the rectal and intravenous routes have been relied upon as the first line of treatment in emergency. When intravenous Benzodiazepines, fail to terminate a seizure, a long-acting anti-epileptic drugs (AED) should be administered. Such long-acting AEDs include Phenytoin or Phenobarbital. In most of the developing countries, Phenobarbital and Phenytoin are the most commonly used second-line AED for controlling status epilepticus and acute seizures.[6] These medications have several potentially serious adverse effects especially when the patient has previously received intravenous Benzodiazepine as the first-line treatment. With Phenytoin, cardiac dysrhythmias and hypotension have frequently been reported. Local irritation, phlebitis and dizziness are other commonly observed adverse effects.[7] For the management of seizures, AEDs should be effective, rapid acting and should not be associated with any serious adverse effects.[6]

Benzodiazepines, Phenobarbital, and Phenytoin are the most commonly used anticonvulsants for controlling seizures, but studies in both adults and children have shown the better efficacy and safety of rapid

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infusion of Sodium Valproic acid with better safety profile.[8] Intravenous Levetiracetam is comparatively a newer drug and has also shown good efficacy in seizure control and safety profile in children.[9,10]

The purpose of our study was to understand the clinical practice of AEDs at our institution. Subsequently, we would use this information to support us in developing protocols and algorithms to ensure a standard of care in the management of seizures.

METHODOLOGY

This was a cross-sectional study carried out at the Pediatric Emergency department (ED) of Aga Khan University Hospital from January 2018 to December 2018.

Inclusion Criteria: All the patients from one month to 18 years of age who presented with the seizures at the Pediatric Emergency Department were included in the study.

Exclusion Criteria: Patients with intractable epilepsy taking multiple anti-epileptic drugs, on ketogenic diet, patients with metabolic seizure, movement disorder and pseudo-seizure were excluded from the study.

Ethical approval was obtained from the Ethical Review Committee of Aga Khan University Hospital (Ref. no: 2019-1763-4812). All the participant information was kept confidential with the use of serial number in place of medical record number. Demographic information along with the duration of seizure, type of seizure, use of anti-epileptic drugs (AEDS) and response in the form of cessation of seizure to AEDS was recorded on the structured proforma. The mechanism of data reporting was in the form of electronic records through health information medical system (HIMS).

Statistical Package for Social Sciences (SPSS) version 22 was used for the data analysis. Frequency and percentages were computed for qualitative variables like gender, primary diagnosis and type of seizures. Mean and standard deviation were computed for quantitative variable like age. Effect of drug in the seizure control was measured.

RESULTS

Total 105 patients with seizures were included in this study. Levetiracetam was used as the first line medication in 66 (62.9%) patients, Sodium Valproic acid was used in 27 (25.7%) patients, Phenobarbital in 10 (9.5%) patients, and Phenytoin was used as the first line medication in 2 (1.9%) patients as shown in the Table-I. Out of 66 patients who were given Levetiracetam, 41 (39%) patients did not require second AEDs. In those patients who received sodium Valproic acid as the first line drug, 17 (16%) did not require a second medication. Out of 9 (8.6%) patients were given Levetiracetam as the second drug. In patients who received Phenobarbital as the first drug, 4 (3.8) patients did not require a second drug (Table-II).

Table-I: Demographic features and description of seizure.

Characteristic	n (%)
Mean Age in months	73.87 ± 54.17
Gender	
Male	67 (64%)
Female	38(36%)
Type of Seizure	
Generalized Seizure	84 (80%)
Focal Seizure	21 (20%)
Duration of seizure	
Less than 5 min	48 (45.7%)
5-10 min	34 (32.4%)
More than 10 mins	23 (21.9%)
Known case of epilepsy	65 (62%)
Etiology	
Break through seizure	65 (61.9%)
New onset epilepsy	28 (26.6%)
Infection (meningitis, encephalitis, sepsis)	8 (7.6%)
Autoimmune encephalitis	(1%)
Stroke	3(2.9%)

Table-II: Spectrum of anti-epileptic drugs used for seizure control.

Drug of Drugs	First Drug	Second Drug	Third Drug	Fourth Drug
Levetiracetam	66 (62.9%)	16 (15.2%)	-	-
Sodium Valproic acid	27 (25.7%)	12 (11.4%)	5 (4.8%)	2 (1.9%)
Phenobarbital	10 (9.5%	8 (7.6%)	2 (1.9%)	Not used
Phenytoin	2 (1.9%)	3 (2.9%)	4 (3.8%)	1 (1%)
Lacosamide	-	3 (2.9%)	-	-

The diagnosis of epilepsy, etiology and the type of seizure did not show any association with the duration of seizure (p>0.05). We did not observe any association between etiology with type of seizure (p>0.05).

DISCUSSION

Seizure is one of the major medical emergencies. Any child who is brought in ED with seizure, should be treated as status epilepticus, with the focus on stabilization of airway, circulation and aborting seizure activity.[11,12] Heath care providers should be careful of hypocalcaemia, hypoglycemia and electrolyte imbalance while managing convulsion.[13] Benzodiazepines are the first line drugs for seizure control. If seizures do not respond to Benzodiazepines, then long acting drugs are needed.[14] Phenobarbital and Phenytoin are most commonly used second line AEDs for seizure control in ED. They are associated with several poten-

tially serious adverse effects.[15] Studies on the use of Sodium Valproic acid and Levetiracetam in ED have also shown good efficacy in seizure termination with minimum side effects.[2,7,11] We aimed to see the current clinical practice in the use of AEDs at our institute to standardize the clinical practice and developing protocols.

In our study, we found that the most commonly used AED was Levetiracetam, followed by Sodium Valproic acid. Levetiracetam was effective in controlling all types of seizures. Around two thirds of patients with seizures who were given Levetiracetam showed seizure control irrespective of age of the patient, etiology and duration of seizure. Goraya *et al*, showed that intravenous Levetiracetam was effective in seizure control in all the age group and in various clinical diagnosis including acute exacerbation of seizures and status epilepticus.[12] A study by Koukkari *et al*, on Levetiracetam as monotherapy in childhood epilepsy has shown reduction in seizure by 50% and few patients became seizure free.[13] Barr *et al*, showed Levetiracetam as monotherapy in acute and chronic seizure control.[14]

Sodium Valproic acid was the second most common drug used at our institute. Sodium Valproic acid was also effective in all the seizure types. In a clinical trial by Malamiri *et al*, use of Sodium Valproic acid was compared with Phenobarbital for controlling seizures.[2] They showed better outcome with rapid loading of Sodium Valproic acid resulting in seizure termination in 90% patients while 77% patients had seizure control with Phenobarbital. A study by Khajeh *et al*, on comparison between Phenobarbital and Sodium Valproic acid showed early response of seizure control with Phenobarbital than sodium valproate but they did not study the side effect profile of both the medications.[15]

In our study, Phenobarbital was used as the first line medication in 10% patients. Phenytoin was used in status epilepticus when the seizure was not controlled by two AEDs. Yang *et al*, compared Levetiracetam with Phenytoin in seizure control in traumatic brain injury and found that Levetiracetam was not superior to Phenytoin in seizure prophylaxis.[16] Another study by Singh *et al*, on intravenous Phenytoin versus Levetiracetam in the prevention of seizures in children showed same efficacy.[9] A study by Akter *et al*, on the use of Phenobarbital and Levetiracetam in childhood epilepsy showed good seizure controlled and lesser side effect of Levetiracetam as compared to phenobarbital.[17]

IV Lacosamide was used for focal seizures when the first AED were not effective at our institute. Strzelczyk *et al*, in their study on Lacosamide, showed good efficacy in focal motor seizure as compared to other types of seizure with fewer side effects and no drug interaction.[18]

Levetiracetam was the most commonly used first line medication in our institute in all the seizure types. Use of Levetiracetam resulted in seizure control in two -thirds of patient population. The second most common drug was Sodium valproic acid that also showed effectiveness in seizure control in all the types of seizures. Phenobarbital and Phenytoin were used in refractory status epilepticus.

CONCLUSION

Levetiracetam was the most commonly used first line long-acting drug at our institute in all the seizure types and controlled seizures in two-thirds of the patients.

Conflict of Interest: None.

Authors' Contribution

SB: Literature search article writing and collected sample size, PC: Edited the article proof reading.

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