Original paper

Clinical Evaluation of Seizures in Pediatric Intensive Care Unit in Babylon Teaching Hospital - A Retrospective Study

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Abstract

Background: A seizure is a paroxysmal time limited change in motor activity and /or behavior that results from abnormal electrical activity in the brain and most common seizures in children are provoked by somatic disorders or originating outside the brain. The aim of our study was to retrospectively evaluate all the patients with seizure required admission to Pediatric Intensive Care Unit to determine the etiologies of seizure and their clinical outcome.

Materials and Methods: A total of 378 children were admitted to PICU from January 2019 to January 2020, 40 patients were eligible, Age ranged above one month to 16 years. Seizures were organized as epileptic or acute symptomatic, pediatric risk factors, classification of diagnosis, description and duration of convulsion, medications given to the patients with duration of admission to Intensive Care Unit and immediate outcome.

Results: The numbers of males equal to the females, mean age was 14.6 months, the most common causes of seizures were acute symptomatic, most frequent coexistent diagnosis was infectious diseases and 70% progress to status epilepticus.

Seizures were generalized in (28) 70% patients, (12) 30% had focal. Intravenous phenytoin and phenobarbiton was second line of therapy in 57.5%.

Acute symptomatic seizures were usually new onset, and duration was shorter. Epileptic seizures tended to be recurrent and were likely to progress to SE.

However type of seizures didn't change severity of the disease, also laboratory test results, requirement for mechanical ventilation, duration of admission and mortality were not significant between epileptic/ acute symptomatic patients.

Conclusion: Seizure in critically ill children, which may evolve in to status epilepticus is an important condition that require attention regardless of cause. Intensified educational programs for Pediatric Intensive Care Unit physicians and international guidelines are necessary for a more efficient approach to children with seizures.

Keyword: pediatric intensive care unit (PICU), status epilepticus (SE).

Introduction

A seizure or convulsion is a paroxysmal; time limited change in motor activity and/or behavior that results from abnormal electrical activity in the brain. Seizures are common in pediatric age group and occur in nearly 10% of children. Most seizures in children are provoked by somatic disorders originating outside the brain, such as high fever, infection, syncope, head trauma, hypoxia, toxins, or cardiac arrhythmia. [(1)]

In recent years seizure duration of 5-10 min have been considered sufficient for diagnosis of status epilepticus.

Because all self-limited seizures stop within 5 min. The Working Group of Status Epilepticus and Epilepsy Foundation of American recommends that any patient with seizure duration more

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than 10 min, or in another words any child presented to the emergency department actively seizing should be considered to be in status epilepticus (SE) at that point and managed accordingly for the initiation of treatment [2].

Seizures are the most common medical problem for emergency medical services transport in children, accounting for approximately 15% of all patients calls in the USA [3]. In addition, an improvement in seizure control and a decrease in morbidity and mortality were confirmed by early and effective treatment [4,5,6]. Accordingly, that recognizing the frequent seizure etiologies admitted to a PICU will guide for a more efficient approach to critically ill patients and more successful treatment strategies will reduce morbidity and mortality.

Therefore; the study aimed to analyze the information data of the patients with seizure admitted to PICU regarding etiologies and their outcome.

Materials and Methods

Three hundred seventy-eight patients were admitted as a total to PICU of Babylon Teaching Hospital of Gynecology and Children consecutively from Jan. 2019 to Jan. 2020; forty patients who had clinical seizure were observed by the PICU physician, and they were included in the study. Information's was obtained from parents / caregiver of the patients.

Study setting:

The PICU is 14 beds, tertiary referral center with general pediatrician, intensivest, neurologist, urologist, cardiologist and well-trained staff; in which nearly 600 patients are followed up in each year.

The seizures occurring only outside of the unit; those presenting to the emergency department with seizure and not stopped by first line medicine which need further treatment in PICU and patients with duration of internalization in the PICU less than 48 hours were excluded from this study. Their ages ranged from 1 month to 16 years. The pediatric risk of mortality score Glasgow Coma Scale (GCS) were used for the estimation of the severity of the disease [7, 8].

Distribution of seizures was organized as epileptic (including patients with a known history of seizures and epilepsy or proved to be epileptic) or acute symptomatic (seizure that do not meet the diagnosis of epilepsy such as cranial infection like meningitis or encephalitis or hydrocephalous with shunt infection, sepsis, metabolic, intracranial hemorrhage or brain tumor.

Status epilepticus was defined as seizure lasting more than 10 min. or two or more seizures without a return of consciousness between seizures. [9] Beside seizures, patients were classified according to coexistent diagnosis at admission to the PICU.

Demographic data such as age, gender, Glasgow Coma Scale, risk factor (prenatal asphyxia, admission to neonatal intensive care unit, chronic disease or medications taken preadmission to the PICU or history of diagnosed epilepsy), type and duration of seizure, drugs used to control the convulsion, requirement to mechanical ventilation and length of stay in PICU and fate of the patients were collected and documented retrospectively for statistical evaluation. All patients included in the study were subjected to history taking, physical examination and routine laboratory investigations such as complete blood count, biochemical tests and blood gas analysis, results were determined as low, normal or high according to the age in the reference lists [10].

According to our hospital protocol, in seizure lasting more than 5 min. an intravenous bolus dose of midazolam

0.1_0.2 mg /kg (maximum 5 mg.) was initiated and repeated if necessary. If seizure control was not achieved despite three doses of midazolam, the loading of 20 mg. / kg phenytoin was initiated followed by 5 mg. / kg maintenance per 24 hours given after 12 hours from the loading dose, sometimes we used phenobarbitone loading dose of 20 mg. / kg if indicated also followed after 12 hours by 5mg. / kg / day maintenance.

If seizure control not achieved an intravenous infusion of midazolam was initiated at a dose of 0.1mg./ kg / h. and increased by 0.1mg./ kg / h. every 5 min. until seizure control was achieved. In the case of patients unresponsive to these drugs, the maximum dose of midazolam included 1mg. / kg / h. after seizure free period of 24 h the infusion of midazolam was decreased to 0.05_0.1mg. / kg / h and discontinued. Patients unresponsive to maximum dose of midazolam infusion were initiated an initial loading dose of 10 mg/kg intravenous thiopental followed by a continuous intravenous infusion of 3-5 mg /kg/h after controlling on the seizure further evaluation need by lumber puncture, EEG or cranial neuro-imaging methods like cranial computer tomography(CT) or magnetic resonance imaging (MRI).

Statistical Analysis

Statistical analysis describe were summarized as counts and percentages for categorical variables and as medians. None of the variables were normally distributed, therefore the data were analyzed by using Mann-Whiteny U-test to compare continuous variables.

All the data were analyzed using statistical software SPSS (Statistical Package for Social Sciences) for window 20. A level of *p* value less than 0.05 was considered statistically significant.

Results

Forty children were eligible for one-year study period, the male to female ratio nearly one. Demographic characteristics of the patients are listed in table (1), Mean age was 14.6 mo.- + 13.4(median =7.5 mo.)

The most common causes of seizures in our PICU setting were acute symptomatic in 28 (70%) and epileptic in 12 (30%).

Most frequent coexistent diagnosis at admission was infectious disease encephalitis 17 (42.5%), meningitis 6 (15%), sepsis 1(2.5%) (Table 2)

Seizure were generalized in 28 (70%) patients, focal in 12 (30%) and 28 (70%) of them develop status epilepticus. Duration of seizure was < 5 min in 12 (30%) patients.

Laboratory tests results are summarized in table (3).

Twenty-six patients were indicated for lumber puncture and three of them get normal result while 23 patients have infectious marker either viral or bacterial type although culture showed no growth.

Metabolic screening was indicated in 4 (10%) patients and 2 (5%) of them were diagnosed with a metabolic disease (organic acideamia), (galactosceamia).

EEG were performed in 19 patients, one of them had normal whereas 18 (94.7%) has diffuse background slowing.

Brain CT scan was indicated in 35 patients; 26 (82.8%) were pathological and 9 (25.7%) normal finding.

Anatomical, developmental and other neuro imaging abnormalities were as summarized in table 4.

Cranial MRI was performed to 15 patients of whom 14 (93.3%) had pathological finding; 5 had cerebral atrophy, 4 partial agenesis, 2 hydrocephallous, 2 brain tumor and one had leukodystrophy.

Intravenous midazolam control the seizure actively in 4 (10%) patients as first

line therapy,23 (57,5%) was received second line of therapy while 13 (32.5%) on need to third line of anticonvulsant to control the seizure by midazolam infusion and for thiopental.

The study demonstrate that acute symptomatic seizures were usually new onset (70%) and may become prolonged >5 min (56.5%) while epileptic seizure (100%) prolonged so *p* value < 0.05.

Table 1. Demographic characteristics of the patients

variables	N=40
Gender Male n. (%) Female n. (%)	 19 (47.5 %) 21 (52.5 %)
Age (months) Mean - + SD (median)	 14.6+- 13.4 (7.5 mo.)
Glasgow coma scale Mean +- SD (median)	 8.5+-4.6 (8)
History (risk factors) n (%) Normal previously Prenatal asphyxia Epilepsy Chronic disease	 21 (52.5 %) 6 (15%) 3 (7.5 %) 10 (25 %)
Mechanical ventilation n (%)	28 (70 %)
Length of stay in PICU (days) Mean +- SD (median)	 10.5+- 10.4 (14)

Table 2. Coexistent diagnosis at admission

Diagnosis	N (%)
Encephalitis	17(42.5%)
Meningitis	6 (15%)
Hydrocephalus with infected shunt	5 (12.5%)
Epilepsy	5 (12.5%)
Brain tumor	2 (5%)
Intracranial heamorrage	2 (5%)
Metabolic disease	2 (5%)
Sepsis	1 (2.5%)
Total	40

Table 3. laboratory results

Laboratory test	Low n(%)	Normal n (%)	High n (%)
White blood cell count	2 (5%)	10 (25%)	28 (70%)
hemoglobin	20 (50%)	10 (25%)	0
Renal function	0	28 (70%)	12 (30%) more than normal value
SPGT, SGOT	0	32 (80%)	8 (20%)
Blood gas analysis pH	16 (40%)	19 (47.5%)	5 (8.5%)
Serum calisium	17 (42.5%)	23 (57,5%)	0
Serum sodium	4 (10%)	36 (90%)	0
Serum potasium	4 (10%)	33 (82.5%)	3 (7.5%)

Table 4. Brain CT finding to 35 patients explained as n (%)

Brain CT finding	N (%)
Brain atrophy	8 (22.8%)
Brain edema	10 (28.5%)
hydrocephlous	4 (11.4%)
Intracranial hemorrhage	2 (5.7%)
Brain tumor	2 (5.7%)
Normal CT finding	9(25.7%)

However; type of seizure and GCS do not change with the severity of the disease, also laboratory test results, requirement to mechanical ventilation, duration of staying in PICU and mortality were not statistically significant between epileptic and acute symptomatic seizure patients ($p > 0.05$ %).

Discussion

The most common causes of seizures in the PICU setting were acute symptomatic seizures which contrast with finding of Valencia et al ;were symptomatic epilepsy and seizures after post-operative craniotomy were the most common underlying etiology [(11)], this might be because of cross sectional nature of the study, and no post-operative cases received at time of the study.

The most common causes of symptomatic seizures was infectious (57.5%) of patients like one study done by Priyanka Amonkar et al; were record (64%) of their cases had infectious cause [(12)].

The seizure was the first (new onset) seizure in 21 (52.5%) patients, whereas 19(47.5%) had prior history of epilepsy consistent with the literature [(13)]. We observed that epileptic seizure tended to be recurrent and may progress to status epilepticus like other studies [(13,14).]

In our study (100%) of epileptic cases develop prolonged seizure while 56.5% of acute symptomatic convulsion had seizure of > 5 min whereas an Indian study conducted in Bihar [(15)] showed 38.5% of cases of status epilepticus had infectious cause this was explained by that this PICU tertiary unit and received complicated types of epilepsy at time of study.

Intravenous midazolam was administered to 10 % of the patients as first line therapy in contrast with literature by Sasidaran et al were record 48%; because this PICU received patients who are referred from the emergency department where the first line therapy given already to the patients and when failed they refer to PICU. while 57.5% was received second line of therapy, 32.5% was on need to the third line.

Various rate of seizures controlled by midazolam infusion ranging from (75_90%) as reported previously [(17,18)].

In this study 28 (70%) of patients had high white blood cell count because most causes of acute symptomatic seizure was due to infectious cause. also theres 4(10%) patients had hyponatraemia, 4(10%) had hypokalaemia,16(40%) had hypoglyceamia, and 17(42.5%) had hypocalcaemia. This condition may not be associated directly with the development of seizure; but our opinion is that these are mentioned because they might precipitate seizures, and those patients administration of supportive treatment was required.

In previous study to children presenting to the emergency room with unprovoked seizures; the authors stated that hyponatreamia was a rare cause of seizures unless suggested by the history [(19)].

In a study conducted in PICU none of the children had recognizable metabolic abnormalities attributed to be responsible for the development of seizure [(20)].

EEG was performed in 19 patients, one had normal finding, whereas 18(94.7%) had diffuse background slowing and this result in agree with many studies which consider EEG evaluation of patients in the PICU and neurological consultation were of the highest importance to help ruling out epileptic disorders in emergency situation [(21)].

In this study the limitations include; it is single centered design and restriction of available data in the hospital, so should be planned to include not only the outcomes of the patients but also the degree of affection and morbidity rates wishing to address the neurologic fate

in detail. Also exact timing of EEG might be one of the other limitations.
In this study 35 patients were indicated for cranial CT resulting 26 (82.5%) patients had pathological imaging finding. Cranial MRI was performed in 15 patients of whom 14 (93.3%) had pathological finding. In recent study; regarding the rule of head CT scan in the evaluation of children admitted to the PICU with new onset seizure and aged < 2 years were recommended to have immediate CT or MRI scanning [(22)].

Conclusion

Seizures in critically ill children, which may evolve into status epilepticus, is a serious concern for PICU clinicians. The study show that the type of seizure did not change the severity of the disease. In addition, laboratory test results, requirement of mechanical ventilation, duration of admission and mortality was not significant between epileptic and acute symptomatic seizures.
Based on these results, should be consider that seizing is an important condition that requires attention regardless of the cause.
Intensified educational programs for PICU physicians and international guidelines are necessary for more efficient approach to critically ill children with seizures.

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