

Study Protocol

A Study of Clinical Profile and Outcome of Status Epilepticus in Children Aged 1 Month To 18 Years.

Abstract:

Background: A common neurological emergency in children is Status epilepticus which, if not treated immediately, may trigger marked neuro morbidity and mortality and hence will need immediate and aggressive management. The neurological outcome worsens in a child as the time taken to control seizures increases and it becomes harder to terminate the seizures. This attempts to explain clinical profile and development of children with convulsive status epilepticus coming to rural hospital in central India and assess the effect of drugs used for treatment of status epilepticus.

Methodology: This Prospective Cross-sectional Study will be conducted in the paediatric intensive care unit Department of Paediatrics, PICU, AVBRH, Wardha. Parameters like clinical presentations, clinical signs, duration and types of status epilepticus, investigations used to diagnose status epilepticus, drugs (anti-epileptic drugs), immediate outcome, effect of drugs used to control seizures will be recorded. Data will be analysed using Chi-square test and independent t-test as applicable. Univariate analysis will be used for testing the influence of different variables in the outcome of present study.

Expected Results: Many factors like age, type and time period of status epilepticus, cause, treatment and corresponding comorbidities determine the end result in status epilepticus. From this study, we expect to get significant evidences to explain profile of cases of convulsive status epilepticus.

Conclusion: Outcomes of status epilepticus are determined by factors like age, time period, cause, treatment and associated comorbidities.

Keywords: Status Epilepticus, Children, PICU, Profile, Emergency.

INTRODUCTION:

A common neurological emergency in children is Status epilepticus which, if not treated immediately, may trigger marked neuro morbidity and mortality and hence will need immediate and aggressive management.¹ The neurological outcome worsens in a child as the time taken to control seizures increases and it becomes harder to terminate the seizures.² International league against epilepsy (ILAE) defined status epilepsy as an abrupt neurological discharge leading to epileptic seizure which is prolonged or repeated³. For all practical purposes definition of status epilepticus mentioned previously was seizures that would last for more than 30 minutes, irrespective of duration without the gain of consciousness. A common life threatening condition in a child is Status epilepticus which need immediate identification, management and care.^{4,5,6,7}. An operational definition of status epilepticus came into force as most of the cases were missed and not managed in paediatric population because of inherent presentation of seizures. The classical motor movements are not usually found in small children. The new definition states a seizure

activity lasting for more than 5min with or without loss of consciousness. This definition makes early treatment assessment and intervention before the seizure becomes refractory to the anti-epileptic drugs^{8,9}.

Status epilepticus is a complex disorder often requires prolonged anti-epileptic drug therapy. Even though multiple causes have been mentioned many cases remain undiagnosed. The refractory status epilepticus is difficult to control with multiple anti-epileptic therapy and is associated with major neurological deficits in the form of intellectual disability, developmental delay, visual defects, hearing abnormalities and cranial nerve palsies. In a developing country like India, education and help seeking behaviour plus prolonged therapy makes compliance difficult. The surgical correction of seizures is in infantile stage in India. There is prolongation and extension in duration of seizures and delay in starting management in developing countries Due to poor approach to facilities in the healthcare system. There is shortage of information with respect to the cause and treatment results of SE in children in India.^{4,8,9}

If status epilepticus not controlled can lead to various complications such as cardiac dysrhythmias, metabolic derangements, autonomic dysfunctions, hyperthermia, pulmonary aspiration and permanent neurological damage.

Among the children less than 16 years of age as much as 4-10% of children experience at least one episode convulsions. While around 30% of cases present as a first time. Different studies have proven that the death due to status epilepticus ranges from 3-50%. The most common age group for Status epilepticus is less than 5 years of age in children with an incidence of more 100 per 100,000 children.¹⁰ non convulsive status epilepticus accounts for around 10% of all status epilepticus in children¹¹. The types of status epilepticus vary according to age and cause. During the childhood phase, status epilepticus is related with febrile episodes and acute pathological diseases like fever triggered seizures, encephalopathies, viral encephalitis and bacterial meningitis. Whereas in older children the causes are well defined. The cryptogenic¹⁰ and chronic symptomatic diseases like severe acute malnutrition, chronic kidney disease and hypocalcemia are associated with status epilepticus¹². This study was taken up as an attempt to explain clinical profile and development of children with convulsive status epilepticus coming to rural hospital in central India.

Importance- If status epilepticus not controlled can lead to various complications such as cardiac dysrhythmias ,metabolic derangements, autonomic dysfunctions , hyperthermia, pulmonary aspiration and permanent neurological damage.¹³ Using operational definition allows early treatment before the seizure becomes refractory to antiepileptic drugs.¹⁴

Background/rationale: - If status epilepticus not controlled can lead to various complications such as cardiac dysrhythmias, metabolic derangements, autonomic dysfunctions, hyperthermia, pulmonary aspiration and permanent neurological damage.

Objectives:

- To study clinical profile of status epilepticus in children.
- To study the immediate outcome of children with status epilepticus.
- To assess effect of drugs used for control status epilepticus.

Methods:

Study design: Prospective Cross-sectional Study

Setting: - A prospective study will be conducted in the paediatric intensive care unit Department of Paediatrics, PICU, AVBRH Sawangi (MEGHE) Wardha

Participants:

Inclusion criteria: Patients diagnosed with status epilepticus All the patients between one month to 18 years with SE admitted in PICU at the time of study will be taken into consideration

Exclusion criteria: Those patients in whom information regarding seizure duration is incomplete or uncertain.

Variables: clinical presentations, clinical signs, duration and types of status epilepticus, investigations used to diagnose status epilepticus, drugs (anti-epileptic drugs), immediate outcome, effect of drugs used to control seizures.

Modified status epilepticus protocol:

On arrival, of the convulsing child, a focused history was elicited while addressing the airway and breathing. Duration of seizure activity was computed based on the time of onset and distance travelled to reach the hospital. We hypothesized that risk of ARF/CD was high if seizures lasted for more than 30 min, or if altered level of consciousness (ALOC) was noted between precipitating events (fever, focus of infection, breathlessness, or diarrhea) and generalized tonic-clonic seizures (GTCS). ALOC between the precipitating event and GTCS was presumed as secondary to severe hypoxia or shock carrying increased risk of ARF and CD. SE that occurred suddenly was less prone to ARF/CD. Developmental status, history of epilepsy, antiepileptic drugs, and nature of prehospital management were also reviewed. The second responder, concurrently, performed the rapid cardiopulmonary cerebral assessment. Clinical signs of ARF and cardiac dysfunction and signs of subtle SE (SSE) were incorporated into the modified pediatric assessment triangle (PAT) to enable decision-making.¹⁵

Intravenous or intraosseous access was established simultaneously. Blood and tissue fluids were collected for appropriate testing. An initial bolus of 10 mL/kg normal saline was administered if shock was recognized. Hypoglycemia and dyselectrolytemia were corrected. Antipyretic was administered if needed. The rapid cardiopulmonary cerebral assessment was repeated after each intervention and incorporated into the PAT, thereby guiding therapy until therapeutic goals were achieved.¹⁵ Fluid boluses were interrupted, inotrope infusion was initiated, and intubation was performed if signs of ARF or CD were unmasked during shock correction.¹⁶ SE requiring phenobarbitone or raised intracranial pressure was other indications for intubation. Shock was managed appropriately with inotropes. Following inotrope infusion and intubation, if shock persisted, further fluids were given based on etiology. If septic, hypovolemic, or anaphylactic shock was identified, large volumes (>60 mL/kg) of fluid boluses were planned.¹⁵ If severe traumatic brain injury, submersion injury, envenomation, or toxin ingestion had preceded SE, the total volume of fluids needed to correct shock was restricted to 20–30 mL/kg.¹⁵

Study size: the study will be conducted on cases of status epilepticus assuming alpha error

of 0.05 on two sided test considering power of 90% with an alternative p of 0.26, the estimated required sample size is 52.

SAMPLE SIZE: 52

STATISTICAL ANALYSIS

Statistical analysis is done by entering data into Microsoft Excel sheet. Relationship of various demographic, clinical characteristics and etiology with outcome will be evaluated employing Chi- square test and for continuous data with normal distribution independent t test are used

Further, univariate analysis will be used for testing the influence of different variables in the outcome of present study. p value will be considered significant if less than 0.05.

Expected Results:

Many factors like age, type and time period of status epilepticus, cause, treatment and corresponding comorbidities determine the end result in status epilepticus. This study was taken up as an attempt to explain profile of cases of convulsive status epilepticus admitted in PICU in rural hospitals in central India.

Discussion:

The identification, intervention and reassessment of status epilepticus is continuous and fast as the electrical activity is ongoing. With each passing time, there is progressive brain damage during status, the treatment becomes eminent intervention to halt the seizure activity of the neurons. If the duration of status epilepticus is increased, the refractoriness of anti-epileptic drug increases leading to the development of refractory status epilepticus^{17,18}. Refractory status epilepticus don't respond to first and second line anti-epileptic drugs and usually requires general anaesthesia is known as Refractory SE (RSE)¹⁸. The days without seizures are also included in the total duration of stay in the hospital.

Status epilepticus is a common paediatric emergency where quick identification and proper management is needed. Understanding the clinical profile and factors predicting morbidity and mortality with convulsive status epilepticus helps in modifying and adjusting the treatment and improve prognosis.¹⁹

The causes of status epilepticus in children is distributed according to age in children; in children below 2 years the commonest cause is febrile illness or any other acute symptomatic causes like low blood sugar, drug withdrawal or brain concussion; whereas in children above 2 years remote symptomatic causes are the commonest.^{2,20} neurological deficit and past history of convulsions is highly common in children > 2 years than those less than 2 years of age with status epilepticus²⁰.

Status epilepticus can have devastating effect on the developing brain. A child less than 3 years is more prone for sequelae of status epilepticus in the form of neuromotor deficits and behavioural issues affecting as many as 30% of cases as compared to 6 % in older children²¹. Majority of the cases of status epilepticus are terminated within first hour of onset of anti-epileptic therapy. Status epilepticus is unmanageable with Anti-Epileptic Drugs, hence named as refractory status epilepticus (RSE)²². In the studies conducted in children in the western population which included all kinds of status epilepticus, nationality, frequency

of seizures, the previously used anti-epileptic drugs and family history were formerly associated with refractory status epilepticus.²²

Of all the cases in the paediatric emergency department Seizure is the more common problem²³. Epilepsy is a condition of brain that is indicated by an ongoing susceptibility and tendency to cause seizure activity. The effects of such epileptic form activity are not limited to seizure threshold but have a long term impact on child's neurobiological, mental and social profile. Epilepsy is diagnosed clinically as an incident of at least one epileptic seizure that is unprovoked with or without second episode of such seizure or adequate EEG and clinical details to explain an undergoing susceptibility to develop recurrences. Maximum number of cases of epilepsy (more than half) occur usually in the early childhood. Between 1-16 years of age, at least one seizure will be experienced in roughly 4 to 10% of children. The incidence of epilepsy in a lifetime has increased to 3%, among which more than 50% of the cases start in childhood. The prevalence of epilepsy in one year is 0.5 to 1%.

Usually in non-febrile patients, CT scan is considered to be the initial investigation.²⁵ however according to few studies, CT scan is not always needed in these patients.²⁶ When a child presents with the 1st episode of seizure, the paediatrician in emergency has to make a decision about the investigations required which include working up for infections and metabolic disorders, CSF examination and EEG. Factors like price and exposure to radiation are taken into consideration in developing countries like India.²⁷

We need to have a good knowledge about seizures like how the patient presents clinically and the etiology for the better management of acute attack and also in cases of long term control of seizures. Possible precautionary and inhibitory measures are to be taken at the level of community level itself so as to reduce the burden of epilepsy in the region. Keeping this in mind, we carry this study so that the clinical and etiological profile of seizures is understood in the paediatric patients.

The most common neurological disorder in children is seizures which occurs in approximately 10% of the children.²⁴ Among these 2/3rd of the seizures cases are evoked due to somatic disorders developing from outside of the brain like high grade fever, hypoxia, trauma to the brain, infections etc. Remaining 1/3rd of the seizures is due to epilepsy where seizures are evoked continuously from inside the brain. There are many conditions mimicking seizure activity like cyanotic spells, gastro oesophageal reflux diseases, jitteriness, night terrors etc²⁸. Few of the related studies were reviewed²⁹⁻⁴¹.

Limitations: Those patients in whom information regarding seizure duration is incomplete or uncertain

Conclusion: Several determinants like age, quality and time period of status epilepticus, cause, treatment and associated comorbidities determine the end result of Status epilepticus.

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