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Clinical profile and neurodevelopmental outcome of new-onset acute symptomatic seizures in children

Vimlesh Soni[a], Pratibha Singhi[b], Arushi Gahlot Saini[a], Prabhjot Malhi[a], Radha K. Ratho[c], Baijayantimala Mishra[c], Sunit C. Singhi[d,*]

[a] Department of Pediatrics, Postgraduate Institute of Medical Education & Research, Chandigarh, 160012, India
[b] Pediatric Neurology and Neurodevelopment, Post Graduate Institute of Medical Education and Research, Chandigarh 160012 India
[c] Department of Virology, Post Graduate Institute of Medical Education and Research, Chandigarh 160012 India
[d] Department of Pediatrics and Chief Pediatric Emergency and Critical Care, Post graduate Institute of Medical Education and Research, Chandigarh 160012, India

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ABSTRACT

Purpose: To study clinical profile, neurodevelopmental outcome and its predictors in children with acute symptomatic seizures (ASS).
Methods: Short-term neurodevelopmental outcome and predictors of poor outcomes were prospectively assessed in 105 consecutive children with ASS aged 3 months-12 years
Results: Mean age was 51.2 + 42.2 months (3–144 months); 67.2% were males. Central nervous system (CNS) infection in 82%, status epilepticus in 15.2%, abnormal neuroimaging in 62.8% and abnormal electroencephalography in 22.3% were noted. At discharge, 27.6% had poor outcome including death (13%); CNS infections were significantly associated with poor outcome compared to ASS of other aetiologies (32.6% vs 5.2%, p = 0.02). Low GCS (OR 4.9, 95%CI 1.2–20.7), abnormal electroencephalograph (OR 4.3, 95%CI 1–16.9) and neuroimaging (OR 12.1, 95%CI 1.4–105.2) were independent predictors of poor outcome.
After 6 months, 16% children had delayed neurodevelopment and cognition; 6% had seizure recurrences. Abnormal electroencephalograph (p = 0.002; OR 6.8, 95%CI 2.0–23.1), abnormal neuroimaging (p = 0.015; OR 9.47, 95%CI 1.18–75.8), > 1 anti-epileptic (p = 0.00; OR 9.9, 95%CI 2.88–33.9), intubation (p = 0.004; OR 6.25, 95%CI 1.79–21.7) and poor outcome at discharge (p = 0.02; OR 4.44, 95%CI1.38–14.2) predicted abnormal neurodevelopment.
Conclusions: CNS infections are the most common cause of ASS in children from developing countries. Abnormal neurodevelopment and seizure recurrences on short-term follow-up are seen in a minority of children.

1. Introduction

An acute symptomatic seizure is defined as a clinical seizure occurring in close temporal relationship with an acute central nervous system (CNS) insult, which may be metabolic, toxic, structural, infectious, or inflammatory [1]. Overall acute symptomatic seizures represent nearly 40% of total seizures [2], 40% of all cases of afebrile seizures [3] and 50–70% of status epilepticus episodes [4]. The overall life-time risk of developing an acute symptomatic seizure is 3.6% which approaches that of developing epilepsy [2,3]. The prevalence of acute symptomatic seizures among medical admissions varies from 2 to 5% in developing countries and is reported to be 3.5% among medical intensive care unit patients in the USA [5–7].

The etiological spectrum of acute symptomatic seizures in developing countries is distinctly different from that of developed countries where cerebrovascular disease and traumatic brain injury are reported as the major aetiology in the adult population [2,8] and acute gastroenteritis in children [9]. On the other hand, CNS infections are reportedly the most common cause of acute symptomatic seizures in developing countries in adults [5,6]. The

* Corresponding author at: Department of Pediatrics, MM Institute of Medical Science and Research, Mullana/World Federation of Pediatric Intensive & Critical Care Societies/Department Of Pediatrics & Advanced Pediatrics Centre, Post graduate Institute of Medical Education and Research,Chandigarh 160012, India.
E-mail addresses: drvsoni.pgi@gmail.com (V. Soni), doctorpratibhasinghi@gmail.com (P. Singhi), doc.arushi@gmail.com (A.G. Saini), pmalhi18@hotmail.com (P. Malhi), ratho.pgi@yahoo.com (R.K. Ratho), bm_mishra@hotmail.com (B. Mishra), sunit.singhi@gmail.com (S.C. Singhi).

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final outcome of acute symptomatic seizures depends upon the underlying aetiology [10]. Robust clinical data on the prognosis of acute symptomatic seizures in children is lacking and the available studies are largely retrospective in nature [11,12].

Acute symptomatic seizures have been identified as a major risk factor for neurological and cognitive impairment as well as development of epilepsy in children from developing countries [13]. In a study of 900 children with acute seizures admitted to a rural Kenyan district hospital, 3.1% patients died in the hospital while 1.3% had major neurological deficits on discharge [14]. Nearly 14% of children who survive acute symptomatic seizures develop subsequent unprovoked seizures by 5 years of age [15]. Nearly one-third of children admitted for status epilepticus have been shown to develop behavioural, emotional problems and other neurodevelopmental problems 7 years after discharge from the hospital [16]. Even in adults, the risk of 1-month mortality has been shown to be 8.9 times higher in individuals with first acute symptomatic seizure as compared to individuals with first unprovoked seizure although the risk of 10-year mortality is same and the risk of a subsequent unprovoked seizure is 80% less likely [11]. Evidently, there is paucity of studies on the clinical profile and neurodevelopmental outcomes of acute symptomatic seizures in children from developing countries. Hence, the current study was planned to (1) describe the clinical and etiological profile of acute symptomatic seizures in children (2) to describe the neurodevelopmental outcomes and (3) to identify predictors of poor outcomes in these children presenting to the paediatric emergency. Early prediction of neurological outcome may help in planning the frequency and duration of follow-up and long-term antiepileptic drug (AED) use.

2. Methodology

2.1. Methods

The study was conducted for a period of 1-year at the Post Graduate Institute of Medical Education and Research, Chandigarh, India which is a premier tertiary care centre of Northern India. A written, informed consent from the parents and assent from the child wherever applicable, was obtained.

2.2. Inclusion criteria

All consecutive children presenting to the paediatric emergency in the Department of Paediatrics with seizure were screened. Of these, children aged 3 months to 12 years with normal pre-morbid development and first acute symptomatic seizures were enrolled.

2.3. Exclusion criteria

Children with pre-existing developmental delay (based on history given by parents in the emergency room), febrile seizure, seizure disorder, systemic illness and non-convulsive status epilepticus were excluded. As children with pre-existing developmental delay and seizure disorder are commonly associated with epilepsy or have an underlying predisposition to unprovoked seizures as well as neurodevelopmental comorbidities such as learning difficulties and intellectual disabilities, hence they were excluded from the study.

2.4. Definitions

Acute symptomatic seizure was defined as a clinical seizure occurring in close temporal relationship with an acute CNS insult, which may be metabolic, toxic, structural, infectious, or inflammatory [1]. Seizure recurrence was defined as any seizure after 24 h of the first seizure [1]. Status epilepticus was defined as an epileptic seizure of >30 min duration or intermittent seizures without an intervening period of recovery of consciousness of >30 min duration [1]. Any child who continued to convulse when brought to the paediatric emergency was considered to be in status epilepticus (SE).

2.5. Measures

Seizures in the presence of active CNS infection such as meningitis, meningoencephalitis, neurotuberculosis, neurocysticercosis or brain abscess were grouped into 'acute symptomatic seizures due to CNS infections'. Diagnosis of meningitis was considered based on clinical features such as presence of seizures with or without impaired consciousness and/or signs of meningeal irritation in a febrile child and suggestive cerebrospinal fluid (CSF) features including polymorphonuclear cell count $\geq$20/mm [3], protein >40 mg%, CSF glucose $<$40 mg% or a CSF:blood glucose ratio $<$0.2 in the presence of positive gram stain or culture from CSF and/or a positive blood culture [17,18]. Diagnosis of meningoencephalitis was based on clinical features such as fever and altered sensorium in addition to CSF lymphocytic pleocytosis, elevated protein level, neuroimaging evidence of cortical involvement, and/or identification of an organism with enzyme linked immunosorbent assay or polymerase chain reaction (PCR) for common viral illnesses in our setting such as herpes simplex, enterovirus or Japanese encephalitis virus.

Clinical and etiological profile was compared between infants (3 months to 1 year) and children (1 year to 12 years). Socioeconomic status of family was classified according to Kuppuswamy Scale [19]. This scale has 3 components: family education, occupation and family income per month. Each component has 7 sub-components and socioeconomic status has been defined according to the total of each component score and a total score of $\leq$10 is defined as low socioeconomic status. All relevant investigations such as serum biochemistry, metabolic and toxic screen, neuroimaging and lumbar puncture were done to establish aetiology according to the standard unit protocol. Electroencephalography (EEG) was done in all patients at admission. Acute seizures were managed according to the standard unit protocol [20]. Treatment details including number of AEDS used for controlling seizure, neuroimaging features and EEG characteristics were noted on a pre-structured proforma. Children who had recurrent seizures, status epilepticus (SE), and persistent abnormal neurological examination at discharge and/or who had a structural lesion on neuroimaging were discharged on AED prophylaxis.

2.6. Outcome

Outcome was defined as good if the patient was discharged with minor or no sequelae and as poor when the patient died or was discharged with major sequelae (vegetative state, motor deficits, language deficits, behavioural problems disrupting daily activities, vision or hearing impairment etc). Follow-up of all patients was done at 3 and 6 months after discharge. Seizure recurrences and neurological examination details were noted. Developmental profile-3 (DP3) was used to assess neurodevelopment overall as well as in the individual domains of physical, adaptive, social development, cognition and communication [21]. Each of these domains has 34 to 38 test items. Scores in each of the five individual sector were calculated and a general development score (GDS) was derived. GDS value $<$70 was used as cut-off for 'delayed development'. Cognitive profile was used as surrogate marker of intelligent quotient. Scores $<$70 were considered as delay, whereas scores between 70 and 84 as below average, scores between 85 and 115 as average and scores between 116 and 130