Convulsive Status Epilepticus in Thai Children at Ramathibodi Hospital

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Background: *Convulsive Status Epilepticus (SE) is an emergency neurological condition with high morbidity and mortality. The outcome of this condition in children depends on the etiology and the duration of convulsion. There is no report of this condition in Thai children.*
Objective: *To study the etiology, clinical course and outcome in children with convulsive SE in a referral hospital in Thailand.*
Material and Method: *The medical records of infants and children aged between one month and 15 years with the diagnosis of SE who were admitted to the Department of Pediatrics, Ramathibodi Hospital, Bangkok from January 1st, 1981 to December 31st, 2000 were retrospectively reviewed. The demographic data, types of seizure, duration of seizure, underlying diseases, precipitating factors, laboratory results, treatment, clinical course and outcomes were collected for descriptive analysis.*
Results: *Thirty-two patients (15 boys, 17 girls) whose ages ranged from 2 months to 14.4 years (mean 6.5 years) were included. Twenty-four patients had underlying epilepsy. Twelve patients had prior diagnosis of symptomatic and idiopathic/cryptogenic epilepsy. Seven patients had acute insults to the central nervous system leading to SE. One patient with acute lymphoblastic leukemia presented with SE without association to either the underlying disease or the treatment. Fever with or without specific infection was the most common precipitating factor observed in these patients. The mean duration of SE was 64.4 minutes. The mean duration from initiation of treatment to the cessation of seizure was 41.4 minutes. Twelve patients were lost to follow up. Of the two patients who died, one had severe infection and the other had renal failure. Twelve patients had severe neurological deficits and six had mild neurological deficits. Among the thirteen patients who had ≥ 1 hour of convulsion, eleven had severe neurological deficits or died.*
Conclusion: *Infantile SE occurred more frequently in children with pre-existing epilepsy or neurological disorder. Acute febrile illness and infection were the most common precipitating causes in the present study. Early recognition and treatment of fever and infection in conjunction with prompt and appropriate termination of seizure in epileptic children may prevent the occurrence of SE and its morbidity.*

Keywords: *Status epilepticus, Etiology, Children*

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Status Epilepticus (SE) is one of the most common neurological emergencies in children and adults[1-4]. Convulsive SE poses high mortality and morbidity[2,5]. There are many acute illnesses and conditions that might be either the direct cause or the precipitator of convulsive SE such as infections of the central nervous system, febrile illness, cerebrovascular accidents, neurodegenerative diseases, metabolic derangements and intoxications[1,2,6,7]. SE may also be the first manifestation of epilepsy[1-3]. Any type of seizures may evolve to SE if it is not appropriately managed initially[2,4,8]. The morbidity and mortality in children were high and were associated with either

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inappropriate management or underlying diseases[1,2,4,5]. There are a number of reports from Western and developed countries regarding this condition in children[2,4]. There are also some reports from Asian and other developing countries[9-13]. This study reports of the condition in Thai children who were presented to the authors' institution. The underlying etiologies, the clinical courses, and the outcomes are compared to those from the previous studies.

Material and Method

A retrospective study was conducted from January 1st, 1981 to December 31st, 2000 at the Department of Pediatrics, Ramathibodi hospital, Bangkok, Thailand, which is a university and referral hospital. The medical records of infants and children, aged from one month to fifteen years with the diagnosis of SE upon admission to the hospital were reviewed. Convulsive SE was defined as a clinical seizure lasting 30 minutes or longer, or repeated seizures without recovery[2]. The data included the demographic data, types of status epilepticus, duration of the seizure, underlying neurological disorders, precipitating factors, laboratory results, treatments, clinical course and outcomes and was collected for descriptive analysis in the form of frequency and percentage distributed tables. The association between the outcomes and underlying diseases, the duration of SE and the response to treatment where deployed was analysed.

Results

Thirty-two children were included in the present study; 15 fifteen boys and 17 girls with an age range from two months to 14 years and 11 months (mean age 6.5 years).

Table 1 shows the underlying patients diseases. Previously diagnosed epilepsy in 24 patients divided equally between the symptomatic and cryptogenic/ idiopathic categories. Among those 24 patients either an infection such as upper respiratory tract infection, gastroenteritis or nonspecific cause of fever was observed prior to the onset of SE in 66.7%. Noncompliance to treatment with an antiepileptic drug was found in 12.5%. The remainder did not have any illness or precipitator of seizure. Seven children presenting with SE were previously healthy. Five of these patients had infection of the central nervous system that was either encephalitis or meningitis. The other two did not have specific cause of febrile illness. One patient was a child with newly diagnosed acute lymphoblastic leukemia. He was receiving treatment and there was no evidence indicating direct CNS involvement of leukemia, infection of the CNS or toxic effect of medication documented. Table 2 demonstrates precipitating causes of SE in the 32 patients.

Duration of SE from the onset of seizure to cessation of clinical seizure ranged from 30 minutes to 4 hours. Mean duration of seizure was 68 minutes with 56% lasting more than 60 minutes. Duration from initiation of treatment to cessation of seizure ranged

Table 1. Underlying diseases of the patients

Underlying disease	Number of patients	Percent
Idiopathic / cryptogenic epilepsy	12	37.5
Symptomatic epilepsy	15	46.9
- Anatomical defects	6	
- Static encephalopathy	4	
- Infection	2	
- Cerebrovascular disease	1	
- Metabolic encephalopathy	1	
- Malignancy	1	
No underlying diseases	5	15.6
Total	32	100.0

Table 2. Precipitating causes of status epilepticus according to underlying diseases

	Infection	Drug withdrawal	Trauma	Tumor	Unknown
Idiopathic / cryptogenicepilepsy	7	2	1	1	4
Symptomaticepilepsy	9	1	0	0	2
No underlyingdisease	5	0	0	0	0
Total	21	3	1	1	6
Per cent	65.6	9.4	3.1	3.1	18.8

from 10 minutes to 3 hours with mean duration of 41 minutes. Treatment with benzodiazepines in combination of either phenobarbital or phenytoin was able to control clinical seizure within 30 minutes in 20 children. Six patients, whose duration of seizures was longer than 30 minutes and did not respond to the combination of the above mentioned antiepileptic drugs, had their convulsions stopped within one hour with the additional treatment with one of these following drugs; lidocaine, midazolam, or paraldehyde. Therefore, these six patients needed at least three antiepileptic drugs to control their seizures. The number of antiepiletic drugs used in the regimen of treatment and the effectiveness for the termination of SE are shown in Table 3.

The outcomes of the patients are demonstrated in Table 4. During admission, two patients died from septicemia and acute renal failure respectively. Among the rest, eighteen patients had been followed with the range of duration from 1 month to 14 years. The mean duration was 45 months. Severe neurological deficits with dependency were found in 12 patients. They were mentally retarded and needed total assistance for their daily lives. Nine of these patients had a prolonged seizure lasting longer than one hour. Another six patients had abnormal neurological functions such as hemiparesis, spasticity of extremities, epilepsy and were able to function with minimal assistance. Table 5 demonstrates the clinical outcome in 20 patients according to the underlying diseases. There was no significant association between the severity and underlying diseases.

Table 3. The numbers of administered antiepileptic drugs in the regimen of treatment and their effectiveness in termination of status epilepticus

Duration	1 AED	2 AEDs	> 2 AEDs	Total
< 30 minutes	5	15	0	20
30-60 minutes	1	1	4	6
> 60 minutes	0	0	6	6
Total	6	16	10	32

* AED = Antiepileptic drug

Table 4. The outcome of the patients

Outcome	Number of patients	Percent
Dead during admission	2	10
Mild or moderate disability	6	30
Severe disability	12	60
Total	20	100

Table 5. Clinical outcomes in 20 patients according to the underlying diseases

Etiology	Outcome (No. of patients)		
	Mild/moderate disability	Severe disability	Dead
No underlying disease	2	2	1
Symptomatic epilepsy	2	4	0
Idiopathic epilepsy	2	6	1
Total	6	12	2

Discussion

SE is one of the most common neurological emergencies in children, adolescents, and young adults. Acute neurological conditions such as meningitis, encephalitis, stroke, complicated febrile seizures, degenerative diseases and intoxication might lead to SE[3,14-16]. More than 90% of children with SE were convulsive and the majority was generalized[17]. First manifestation of epilepsy presenting as SE occurred up to one-third of the children[15,18]. In Richmond County, Virginia, United States of America, the absolute incidence rate was 41 patients per 100,000 residents per year and the overall mortality rate observed in this population was 22%[2]. In developing countries, there were hospital-based studies with various clinical courses and outcomes. Children with preexisting neurological abnormalities were most susceptible[9,11,12]. Most of the patients in the present study were children with established diagnosis of epilepsy and SE included 47%. This finding was similar to previous reports in children in developing and developed countries[1-5,11-13]. The common precipitator or cause of SE observed in the present study was either infection or nonspecific febrile illness that was also in line with previous reports in Asian children[9,11-13]. Among children with established diagnosis of epilepsy; high risk was observed in those who received polyantiepileptic treatment, discontinued taking their daily antiepileptic drug, had neurological and motor retardations, and had an abnormal EEG including abnormal generalized

background[12,17]. Antiepileptic drug withdrawal or non-compliance to treatment was observed in less than 10% of the presented patients. Besides remote symptomatic cause, the young age at onset of epilepsy especially in those who were younger than 5 years of age was found to be another risk[9,15,19-21]. Because of the wide range of age of onset from 2 months to 15 years with a mean age of 6.5 years observed in the present study, it was not possible to draw any significant statistical predictor of development of status epilepticus. Nevertheless, the result obviously demonstrated that in children with pre-existing neurological disorders who had acute onset of nonspecific infection or acute pyrexia, the chance of developing SE was high.

The morbidity of SE in children ranged from 3.4 to 27 percent[4,9,19,22]. Among those who were followed in the present study, none had normal neurological function. The severe neurological disability observed in most of the participating patients reflected the serious sequalae of this condition. Although, the major neurologic sequalae were usually due to the underlying insult rather than to the prolonged seizure[22,23]. The duration of SE still possessed direct effect to the outcomes. With longer duration of SE, higher mortality rate was expected[2,4,18,24-26]. The result of the present study showed that among thirteen patients who had the duration of convulsion of > 1 hour, eleven had severe neurological deficits or died. The prompt, appropriate and effective medical therapy to provide the cessation of convulsion as well as the supportive treatment to stabilize the function of other systems were indicated in those who were having SE[27]. Diazepam, phenobarbital and phenytoin were the three main-antiepileptic drugs used in the treatment of SE. Diazepam and phenobarbital have been used as the first and the second drugs in treatment of this condition for years[3,28]. However, respiratory depression might occur if a large dose of these drugs were administered. Furthermore, in some situations such as in a child with encephalitis or cardiovascular compromised, there are risks of developing respiratory depression, hypotension and obscuration of consciousness[18]. Combination of lorazepam and phenytoin was reported to be the most effective regimen in the treatment of SE owing to the longer duration of action of lorazepam than diazepam and the reduced respiratory depression caused by phenytoin over phenobarbital[24]. Fosphenytoin, a phenytoin prodrug, represented a significant advance in the treatment of children with convulsive SE and had been used in Western countries[29]. This drug may be administered intramuscularly with similar efficacy compared to intravenous administration of phenytoin. Rapid achievement of effective concentrations was obtained after intramuscular administration. This might be suitable for treatment of SE especially in children, when intravenous access might not be possible at the time of diagnosis[29]. Intravenous lorazepam and intramuscular fosphenytoin were the two preferred drugs for the treatment of generalized convulsive SE in a survey of 106 members of the Critical Care or Epilepsy sections of the American Academy of Neurology[30]. At present, however, this might not be applicable in developing countries like Thailand where lorazepam for intravenous administration and fosphenytoin are not available. Fosphenytoin might not be the country's pharmacopeias because of its cost. Intravenous valproate loading, which was reported to be safe and effective for treating SE in children, might be another drug of choice[31,32]. However, valproate is contraindicated in those who have hepatic dysfunctions[33].

The outcomes of the children in the present study were still unfavorable despite being treated in a referral center. Obviously, the result of the present study did not represent the real situation in the community. The authors extrapolate that the magnitude of the severity and the number of children presenting with SE with poor outcomes is higher than that observed in the present study owing to the fact that, there were limitations of the first line antiepileptic drugs, the insufficiency of intensive care in the remote areas, and the lack of National Guidelines for treatment of SE in the country. The appropriate administration of prehospitalized medication including buccal administration of midazolam and rectal administration diazepam and setting up a practical guideline in managing children with convulsive SE would make it possible to lower the risk of development of SE[34]. Additional information obtained from the present study confirms the results in other reports that this condition occurred in children with pre-existing neurological abnormalities who had either acute febrile illness or non-specific infection as the precipitating factor. Early recognition and treatment of associated fever or infection, along with effective termination of seizure once it occurred with appropriate antiepileptic medication would prevent the occurrence of SE and might ultimately reduce the morbidity and mortality.

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การชักต่อเนื่องในเด็ก: รายงานการศึกษาในโรงพยาบาลรามาธิบดี

อนันต์นิตย์ วิสุทธิพันธ์, จันทร์จิรา ลิมป์หิรัณย์, สุรางค์ เจียมจรรยา, พงษ์ศักดิ์ วิสุทธิพันธ์

การชักต่อเนื่องเป็นภาวะฉุกเฉินทางระบบประสาทที่พบได้บ่อยในผู้ป่วยเด็กและจำเป็นที่จะต้องได้รับการรักษาอย่างถูกต้อง เนื่องจากอาจทำให้ผู้ป่วยถึงแก่กรรมหรือก่อให้เกิดความพิการอย่างถาวรได้ คณะผู้รายงานได้ทำการศึกษาแบบย้อนหลังในผู้ป่วยเด็กอายุ 1 เดือนถึง15 ปี ที่มีการชักต่อเนื่องที่โรงพยาบาลรามาธิบดีระหว่าง พ.ศ.2524-2543 เพื่อศึกษาสาเหตุ ผลการรักษา การดำเนินโรค และผลที่เกิดขึ้นจากการชักต่อเนื่องนี้โดยศึกษาข้อมูลดังต่อไปนี้ ได้แก่ ข้อมูลทั่วไป ชนิดของการชักต่อเนื่อง ระยะเวลาที่มีการชัก สาเหตุ ปัจจัยกระตุ้น ผลการตรวจทางห้องปฏิบัติการ การรักษา ระยะเวลาที่หยุดชักหลังให้การรักษา จำนวนวันที่อยู่โรงพยาบาล การดำเนินโรค ผลการรักษา อัตราการเสียชีวิตและความพิการ พบว่ามีผู้ป่วยจำนวน 32 คน เป็นเด็กชาย 15 คน และเป็นเด็กหญิง 17 คนโดยมีอายุตั้งแต่ 2 เดือนถึง 14 ปี 4 เดือน (อายุเฉลี่ย 6.5 ปี) มีผู้ป่วยจำนวนร้อยละ 75 ที่เป็นโรคลมชักก่อนเกิดอาการชักต่อเนื่อง จำนวนร้อยละ 21.8 ที่ไม่เป็นโรคลมชัก และจำนวนร้อยละ 3.1 ที่มีโรคประจำตัวซึ่งไม่ได้เป็นสาเหตุของการชัก ปัจจัยกระตุ้นให้เกิดการชักต่อเนื่องที่พบบ่อยที่สุดคือ ไข้สูง หรือ การติดเชื้อที่ไม่เฉพาะเจาะจง มีผู้ป่วยจำนวน 12 คนที่ไม่ได้มารับการรักษาต่อ ผู้ป่วยเสียชีวิต 2 คนจากการติดเชื้อ และไตวายตามลำดับ มีผู้ป่วยจำนวน 12 คน (ร้อยละ 37.5) ที่มีความพิการที่ระบบประสาทรุนแรง ในผู้ป่วยจำนวน 13 คน ที่มีการชักต่อเนื่องนานกว่า 1 ชั่วโมงมีผู้ป่วย 11 คนที่มีความพิการที่ระบบประสาทอย่างรุนแรงหรือเสียชีวิต จากการที่พบว่าผู้ป่วยที่มีการชักต่อเนื่องส่วนใหญ่เป็นผู้ป่วยที่เป็นโรคลมชักมาก่อนและมีปัจจัยกระตุ้นที่ทำให้เกิดอาการชักต่อเนื่องพบบ่อยที่สุดคือไข้สูงหรือการติดเชื้อ ดังนั้นการตรวจค้นหาสาเหตุของอาการไข้และการให้การรักษาเฉพาะที่เหมาะสมแก่ผู้ป่วยเด็กที่เป็นโรคลมชักอาจจะช่วยป้องกันการเกิดการชักต่อเนื่องที่อาจเกิดตามมาได้