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Adult tonic-clonic convulsive status epilepticus over the last 11 years in a resource-poor country: a tertiary referral centre study from southern Thailand

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ABSTRACT – Status epilepticus is a common condition in patients admitted to hospital in resource-poor countries and reports indicate that aetiology, factors of poor outcome, and treatment strategies are variable. To date, there is no report of a prospective study in Thai adults. Herein, we investigated the aetiology, clinical features, factors of predicted poor outcome, and treatment strategies in Thai adult patients who presented with convulsive status epilepticus. A total of 180 patients, whose ages ranged from 15 to 106 years, were included. Of these, 121 patients (67.2%) had acute symptomatic aetiology. The most common aetiology of status epilepticus was encephalitis (36.1%), followed by scarring of the cerebral hemisphere (15%). The median duration of status epilepticus before treatment was three hours. The rate of mortality in the study was 26.7%. Poor outcome was identified in 112 (62.2%) patients. For referral patients, all received only intravenous drugs before referral. The variables that correlated with poor outcome were aetiology and duration of status epilepticus. An approach to incorporate improved prevention of encephalitis, a more effective transportation system, and provision of the essential intravenous antiepileptic drugs would effectively increase the response to treatment.

Key words: adult, convulsive status epilepticus, Thailand, resource-poor, encephalitis

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Convulsive status epilepticus (SE) is one of the most common neurological emergencies and is not unusual in patients admitted to hospital in resource-poor countries. Although there are few reported data, there appear to be differences in epidemiology, aetiology, and outcome of SE within such regions, countries. compared to

high-income countries. Data on SE from developing countries are sparse and based mostly on retrospective studies (Maharaj *et al*., 1992; Kwong *et al*., 1995; Mhodj *et al*., 2000; Hui *et al*., 2003). Furthermore, as with epilepsy, several factors may interfere with correct diagnosis and management: poor health facilities, including a lack of appropriately trained personnel and a limited number of intensive care units; long distances and difficulties in transportation (Quet *et al*., 2008); and an inadequate use of appropriate treatment due to a lack of antiepileptic drugs. In previous studies, an earlier definition of SE was used (Murthy *et al*., 2007; Chen *et al*., 2009). Today, convulsive status epilepticus is defined as two or more convulsive seizures, without full recovery of consciousness between a seizure of continuous convulsions, lasting for more than five minutes (Alldredge *et al*., 2001; Sibergleit *et al*., 2012). In recent years, research into SE in Thailand has focused on its treatment using retrospective methods, however, sample sizes were small and these studies did not reflect current SE in southern Thailand. In this prospective, consecutive case series, we aimed to describe the age and sex of patients with SE, aetiology of SE, duration of SE before adequate treatment, antiepileptic drug treatment, and factors correlated with poor outcome in adults, 15 years and older, from a resource-poor country who presented with generalised convulsive SE in a tertiary care hospital in southern Thailand.

Methods

The study was divided into two parts. In the first part, we performed a retrospective search of patients from January 2000 to December 2004, based on the hospital computerised information system in order to access the admission/discharge records of the Emergency Department and Medicine Department and Intensive Care Unit (International Classification of Disease (ICD)-9 code 345.2, 345.3, 345.7 and 780.39.). In the second part, from 2005 to December 2011, we prospectively collected data on all demographic characteristics. The following information was recorded using a data sheet: demographic information including age, history of pre-existing medical disease, history of epilepsy and antiepileptic drugs used, aetiology of SE, clinical features, results of physical and auxiliary examinations, treatment methods, and complications and condition at time of discharge. In total, 180 patients with generalised tonic-clonic SE were admitted to the inpatient unit at the Songklanagarind Hospital from 2000 to 2011. The hospital is located in southern Thailand. The clinical characteristics of patients is summarised in *table 1*.

Definitions

The definition used to define generalized tonic-clonic SE is the new definition, which has been commonly used in recent research. SE is defined as two or more convulsive seizures, without full recovery of consciousness between a seizure of continuous convulsions, lasting for more than five minutes (Alldredge *et al*., 2001; Sibergleit *et al*., 2012). Encephalitis is defined as a condition characterised by an alteration of consciousness, with or without other neurological symptoms, in which pleocytosis and a high protein level is demonstrated in cerebrospinal fluid. Scarring is defined as a condition characterised by a chronic, non-progressive, abnormal structural brain lesion.

Aetiology

Aetiology of SE was classified as:
1) acute symptomatic: SE occurs within a week of acute central nervous system (CNS) or systemic insult (*i.e*. stroke, meningitis, encephalitis or alcohol intoxication or withdrawal);
2) remote symptomatic: SE with a history of CNS insult presumed to result in a static condition associated with an increased risk for epilepsy;
3) progressive symptomatic: SE during the occurrence of non-static conditions, *i.e*. CNS tumours, multiple sclerosis, or neurodegenerative disease;
4) unknown: SE owing to conditions presumed to be symptomatic, but the cause is unclear; and
5) poor compliance: SE in known cases of epilepsy with non-compliance (Commission on Epidemiology and Prognosis, International League Against Epilepsy, 1993).

Antiepileptic drug (AED) treatment

The standard treatment of SE in our hospital is intravenous diazepam (10-20 mg), followed by intravenous phenytoin (18-20 mg/kg), which are the first-line drugs for treatment. If the patients have a contraindication to phenytoin (*i.e*. phenytoin allergy or severe heart disease), intravenous valproate, at 15-20 mg/kg, is used as an alternative therapy. The second-line drugs consist of an intravenous loading dose of phenobarbital, intravenous valproate, a continuous infusion of midazolam or, more rarely, intravenous levetiracetam and topiramate, intravenous phenobarbital, intravenous propofol or intravenous ketamine. Patients are given mechanical ventilator support whenever necessary. In addition, patients receive appropriate treatment for the aetiology of SE. Response to AED treatment is defined as

Table 1. Clinical characteristic features in subjects with status epilepticus.

Characteristic Features	Total (*n*=180)	Good outcome (*n*=68)	Poor outcome (*n*=112)
Age at inclusion (years)			
median (IQR)	54.5 (39.0, 69.7)	50.5 (32, 70)	58 (44, 68.5)
Gender			
male *n* (%)	105 (58.3)	39 (37.1)	66 (62.9)
female *n* (%)	75 (41.7)	29 (38.7)	46 (61.3)
Aetiology			
acute symptomatic *n* (%)	121 (67.2)	40 (33.1)	81 (66.9)
remote symptomatic *n* (%)	26 (14.4)	17 (65.4)	9 (34.6)
progressive symptomatic *n* (%)	16 (8.9)	1 (6.3)	15 (93.7)
non-compliance antiepileptic drugs *n* (%)	10 (5.6)	9 (90.0)	1 (10.0)
unknown *n* (%)	7 (3.9)	1 (14.3)	6 (85.7)
Duration of status epilepticus before treatment (hours)			
<1 *n* (%)	72 (40)	35 (48.6)	37 (51.4)
1-5 *n* (%)	83 (46.1)	31 (37.3)	52 (62.7)
>5 *n* (%)	25 (13.9)	2 (8)	23 (92)
Duration of hospitalisation (days)			
median (IQR)	16 (7,23.8)	9 (5,20)	18 (9.25,28)

IQR: interquartile range.

the clinical cessation of SE for at least 12 hours without recurrent seizure after the completion of AED administration.

Procedures

All subjects underwent complete blood count or electrolyte, blood sugar, and metabolic work-up. Brain imaging (computed tomography and/or magnetic resonance imaging) was performed for all patients. Lumbar puncture and analysis of cerebrospinal fluid were performed if necessary. Initial standard electroencephalography (EEG) was performed for 79% patients and the EEG was postponed until the next follow-up visit for 19% patients. Continuous EEG monitoring was performed for 20% patients. Follow-up studies were performed as clinically required.

Outcome

Outcome, measured by the Glasgow Outcome Score (GOS), was recorded for all patients at the time of discharge and three months after discharge (Jennett and Bond, 1975). Poor outcome was defined as death or functional deterioration corresponding to one or more points of the GOS among survivors at three months, relative to the pre-admission period.

Statistical analysis

The characteristics of patients were described in terms of median and interquartile range for continuous variables and number and percentage for categorical variables. Comparisons of continuous variables between the two subgroups of subjects were made using the rank sum (Mann-Whitney) test. Statistical analyses were performed using Stata version 7.0 (Stata Statistical Software: version 7.0 College Station, TX. USA).

Results

We diagnosed 180 SE episodes occurring in 180 patients during the study. Twenty-six patients were referred from neighbouring primary local hospitals (within 70 kilometres). The median (IQR) age was 54.5 (39.0, 69.7) years (range: 15 to 106 years) and 34.4% were elderly (≥65 years). The male to female ratio was 1.4:1 (58.3% were male, 41.7% were female). Aetiology was acute symptomatic in 67.2%, remote symptomatic in 14.4%, progressive symptomatic in 8.9%, unknown in 3.9%, and 5.6% were non-compliant. CNS infections (39.6%) were the most common cause (encephalitis [36.1%], cerebral cysticercosis [1.1%], cryptococcal meningitis [0.6%], tuberculous meningitis [0.6%], bacterial meningitis [0.6%], and brain abscess [0.6%]), followed by scarring of the cerebral hemisphere

Table 2. Aetiologies of convulsive Status Epilepticus.

Aetiology	Total 180 (%)	Good outcome 68 (%)	Poor outcome 112 (%)
Encephalitis	65 (36.1)	20 (30.8)	45 (69.2)
Hypoxic ischaemic encephalopathy	11 (6.1)	2 (18.2)	9 (81.8)
Metabolic disturbance	4 (2.2)	4 (100)	0 (0)
Cysticercosis	2 (1.1)	2 (100)	0 (0)
Systemic lupus erythrematosus	7 (3.8)	3 (42.9)	4 (57.1)
Head injury	1 (0.6)	0 (0)	1 (100)
Ischaemic stroke	8 (4.4)	4 (50)	4 (50)
HIV	1 (0.6)	1(100)	0 (0)
Cerebral venous sinus thrombosis	1 (0.6)	1 (100)	0 (0)
TTP	1 (0.6)	0 (0)	1 (100)
Intoxication	3 (1.6)	0 (0)	3 (100)
Cryptococcal meningitis	1 (0.6)	0 (0)	1 (100)
Intracranial bleeding	2 (1.1)	1 (50)	1 (50)
Bacterial meningitis	1 (0.6)	0 (0)	1 (100)
Brain abscess	1 (0.6)	0 (0)	1 (100)
Sepsis	10 (5.5)	1(10)	9 (90)
Posterior leukoencephalopathy	1 (0.6)	1 (100)	0(0)
Tuberculous meningitis	1 (0.6)	0 (0)	1 (100)
Scar	27 (15)	17 (62.9)	10 (37.1)
Neurodegenerative disease	2 (1.1)	0 (0)	2 (100)
Primary brain tumour	1 (0.6)	0 (0)	1 (100)
Brain metastasis	12 (6.7)	1 (8.3)	11 (91.7)
Non-compliance AEDs	10 (5.5)	9 (90)	1 (10)
Unknown	7 (3.8)	1 (14.3)	6 (85.7)

TTP = Thrombotic Thrombocytopenic Purpura; AED: antiepileptic drug.

(15%), cerebrovascular disease, which accounted for 6.1% (ischaemic stroke [4.4%], intracranial bleeding [1.1%], and cerebral venous sinus thrombosis [0.6%]), and hypoxic ischaemic encephalopathy (6.1%). The less common aetiologies were primary brain tumour (0.6%), head injury (0.6%), and HIV (0.6%) (*table 2*). The median disease duration between the onset of SE and hospital treatment was three hours (range: 1 to 24 hours). In 102 (56.7%) patients, the disease duration was less than five hours at the time of presentation to the emergency room (ER). The median (IQR) duration of hospitalisation was 16 (7, 23.8) days. For referral patients, all of the patients received only intravenous diazepam as the first-line AED for treatment of SE before referral to our hospital. In contrast, patients with SE who were initially admitted to our hospital were treated with intravenous diazepam followed by intravenous phenytoin; they received the first-line drug treatment. If patients had a contraindication to phenytoin, they were treated with intravenous valproate or intravenous phenobarbital as alternative first-line therapy. One hundred patients (55.6%) required admission to the ICU.

Of the 180 patients with SE, 68 (37.8%) had good outcomes and 112 (62.2%) patients had poor outcomes. For refractory SE patients, 39 received intravenous valproate with a response rate of 46.2%, 55 received intravenous midazolam with a response rate of 49.1%, eight received intravenous propofol with a response rate of 62.5%, four received pentobarbital with a response rate of 50%, three received intravenous midazolam and intravenous ketamine with a response rate of 33.3%, and three received levetiracetam with a response rate of 33.3%. The mortality rate of our study was 26.7%. All patients received supportive treatment, including oxygenation, rehydration, electrolyte and other symptom relief treatments, as indicated.

Based on the multivariate model, the factors associated with poor outcome were duration of SE ($p<0.01$) and aetiology ($p<0.01$) (*table 3*).

Discussion

Most research into SE conducted in resource-poor countries has been retrospective (Maharaj *et al*., 1992;

Table 3. Multivariate model for predictors of poor outcome.

Variable	Odds ratio	95% Confidence interval	*p* value
Aetiology			<0.01
Acute symptomatic	1	1	
Remote symptomatic	0.32	0.13-0.80	
Unknown	4	0.46-34.84	
Poor compliance	0.05	0.00-0.44	
Progressive symptomatic	7.12	0.89-57.17	
Duration of status epilepticus (hours)			<0.01
<1	1	1	
1-5	1.64	0.81-3.30	
>5	11.15	2.04-60.81	

Mah and Mah, 1999; Kwong *et al*., 1995; Hui *et al*., 2003) and there are very few reported prospective studies (Murthy *et al*., 2007; Chen *et al*., 2009). Moreover, there are no previous studies which focus on SE in tropical Southeast Asian countries. In this study, patient data was collated prospectively in order to ascertain the clinical characteristics, aetiology, treatment response, outcome, and predictors of poor outcome.

The time window of pre-hospital emergency treatment of SE in Europe and the United States is set at 10 minutes. A long latency between the onset of SE and initiation of appropriate treatment with AEDs was noted in previous studies (Murthy *et al*., 2007; Chen *et al*., 2009). We found that, contrary to the experiences of Murthy *et al*. (2007) who studied SE in India, the time periods reported from seizure onset to ER arrival were quite variable and prolonged due to transportation problems, including the limited availability of ER service. In our study, times of SE length prior to ER arrival varied greatly (1 to 24 hours). Only 40% of patients arrived at the hospital within 30 minutes of onset of symptoms. Compared to developed countries, for patients with overt convulsive SE, the median duration at enrolment was 2.8 hours (Treiman *et al*., 1998). The time from patients' arrival at the ER to treatment with a first-line AED ranged from 20 minutes to 10 hours. In contrast to the studies of Skinner *et al*. (2010), from the developing country of Honduras, the time from seizure onset to treatment at ER ranged from 5 to 420 minutes. The most common reason for delayed treatment was a transportation issue. A growing body of basic science (Walton and Treiman DM, 1988) and clinical observation (Rowan and Scott, 1970) supports the concept that SE becomes more difficult to control as its duration increases. Also, duration of SE was an independent predictor of poor short-term outcome (Murthy *et al*., 2007).

In our study, 154 patients with SE came to the ER with their family. Therefore, seizure patients did not receive any AED before arriving at the ER. One of the most important types of inappropriate treatment of SE, especially in referral patients, is treatment with intravenous diazepam, which is a short-acting AED. Surprisingly, 26 patients who had been referred from neighbouring primary local hospitals had received only intravenous diazepam before arriving at our hospital. In this study, 96.2% of patients had breakthrough seizures during transportation, 92.3% of referral patients had refractory SE, and 80.8% had poor outcomes. The reason for inadequate treatment with AEDs is because essential intravenous AEDs are not available at primary care hospitals. Moreover, in southern Thailand, it is not possible to treat SE in ambulances with first-line AEDs, with the exception of diazepam. Improving the transportation system and providing the essential intravenous AEDs may improve treatment outcome in our setting.

The aetiology of SE in developing countries is distinct from that in developed countries. In previous studies, based on hospital-based series in developing countries, acute symptomatic aetiology accounted for the most common aetiology (Maharaj *et al*., 1992; Hui *et al*., 2003; Murthy *et al*., 2007). The main cause of acute symptomatic aetiology of SE was CNS infection (39.6%), which is consistent with previous reports from other developing countries (Murthy *et al*., 2007; Chen *et al*., 2009). In 2010, Tiamkao *et al*. also reported that the predominant aetiology of SE was acute symptomatic (52.5%) in northeast Thailand (Tiamkao *et al*., 2010). Among acute symptomatic cases, encephalitis is the most common aetiology. This finding, supported by our study, indicates that acute symptomatic aetiology accounted for 67.2% of the aetiology. Encephalitis is the most common aetiology in southern Thailand. Regarding acute symptomatic aetiology, cerebrovascular disease is the predominant cause in

developed countries (Lowenstein and Alldredge, 1993; Fountain, 2000; Vignatelli *et al*., 2003), whereas the predominant cause in developing countries is CNS infections. Surprisingly, AED withdrawal was uncommon in our study. Tiamkao *et al*. (2010) reported that AED withdrawal was found in 25% of cases. A study conducted in the developing country of Honduras found that non-adherence to AEDs was the most common aetiology; identified in 75% patients (Skinner *et al*., 2010). In this study, we found that non-adherence was uncommon, in only 5.6% total patients with SE. Several factors might contribute to this, including a good education, non-negative attitudes regarding epilepsy, as well as the good socioeconomic status of southern Thailand. Surprisingly, our study showed a low prevalence of SE caused by head injury compared with other studies on convulsive SE (Li *et al*., 2009). This finding may be due to referral policy. Our hospital is a tertiary care provider and only severely injured patients are transferred. For more than half of the patients with moderate-to-severe head injuries, the seizures were non-convulsive and were diagnosed on the basis of continuous EEG studies alone (Vespa *et al*. 1999). Our study therefore focused on convulsive SE and the low prevalence of head trauma could therefore be the result of referral bias.

The management of SE with AEDs in our hospital is not different from that in Europe. Currently, based on the European Federation of Neurological Societies guideline on the management of SE in adults, intravenous administration of lorazepam or diazepam, directly followed by fosphenytoin or phenytoin, as the first-line therapy, is preferred. Due to the limited availability of medication in hospitals in southern Thailand, diazepam was used instead of lorazepam, and phenytoin instead of fosphenytoin. In our study, the intravenous administration of diazepam followed by phenytoin was used as first-line treatment in 75% patients. About 25% of our patients were treated with intravenous valproate in the setting of contraindication to phenytoin. In the case of failure to respond to first-line treatment, refractory SE was diagnosed and an anaesthetic agent was introduced. The most common anaesthetic agent is midazolam. The reason why midazolam is commonly used may be due to the fact that midazolam is routinely used in the medical ICU at Songklanagarind Hospital. All of the refractory SE patients were transferred to the medical ICU. Critical care physicians prefer to use midazolam as routine treatment if the patient has suffered any agitation or there is any difficulty in controlling the mechanical ventilators.

The short-term mortality rate in this study was 26.7% (*n*=48). We also observed significantly increased mortality in patients with acute symptomatic epilepsy rather than remote symptomatic, cryptogenic, or established epilepsy. This study demonstrates that the short-term mortality rate of SE in our hospital is higher than that of developed countries, but appears to be similar to that of some other developing countries (Chen *et al*., 2009). In a recent systematic review of data from developed countries, short-term mortality (<30 days) was 7.6 to 22% (Chin *et al*., 2004). The reported short-term mortality in SE in series from developing countries varied from 16 to 19% (<30 days) (Mhodj *et al*., 2000; Hui *et al*., 2003; Garzon *et al*., 2003). The differences may be a result of differences in methodology and the definition of SE in the studies (Logroscino and Hesdorffer, 2005). On the other hand, the aetiology of SE in different studies was also different and this may have again influenced the reported mortality rate. We found that alcohol withdrawal, non-adherence to AEDs, and metabolic abnormalities were conditions not frequently associated with death with regards to short-term mortality (<30 days). This finding is in agreement with previous studies (Lowenstein and Alldredge, 1993; Towne *et al*., 1994; Rossetti *et al*., 2006). Aetiologies associated with poor outcome were encephalitis and hypoxic ischaemic encephalopathy (Treiman *et al*., 1998; Rossetti *et al*., 2006). In our study, 69.2% of patients with SE who had encephalitis had a poor outcome. However, a previous study has shown that age, gender, and the cause and duration of SE may affect mortality (Rossetti *et al*., 2006). This study used multivariate analysis to confirm that the duration and aetiology of SE influences prognosis. Furthermore, we showed that a longer duration of SE is associated with poor outcome. Unfortunately, an issue that can critically add minutes, even hours, to the time of initiation and effectiveness of treatment in developing countries, is the delay in transportation.

In our study, none of the patients had either standard EEG or continuous EEG monitoring before the initiation of appropriate treatment, as a continuous EEG monitoring facility was not available. After 2010, we performed continuous EEG monitoring on some of the patients whose convulsions had ceased due to first-line AEDs but who were still comatose. Among those, 7 of a total of 36 (19.4%) had an electrographic seizure and 12 were dead within 30 days. In an earlier study, cEEG monitoring demonstrated electrographic seizures in 48% of patients and in 14% subtle SE was manifested (DeLorenzo *et al*., 1999). In the VA Study, it was found that 20% of patients with overt convulsive SE, who were believed to have received adequate treatment, continued to have non-convulsive SE (Treiman *et al*., 1998).

In conclusion, the majority of aetiologies of SE in our study of adult patients at the Songklanagarind Hospital were acute symptomatic (67.2%). Of these, encephalitis was the most common aetiology. The predictors of poor outcome were identified as aetiology, particularly

encephalitis, and duration of SE. Improving the transportation system and providing essential intravenous AEDs may improve the treatment outcome in our setting. □

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References

Alldredge BK, Gelb AM, Isaacs SM. A comparison of lorazepam, diazepam, and placebo for the treatment of out-of-hospital status epilepticus. *N Engl J Med* 2001; 345: 631-7.

Chen L, Zhou B, Li JM. Clinical features of convulsive status epilepticus: a study of 220 cases in western China. *Eur J Neurol* 2009; 16: 444-9.

Chin RFM, Neville BGR, Scott RC. A systematic review of the epidemiology of status epilepticus. *Eur J Neurol* 2004; 11: 800-10.

DeLorenzo RJ, Garnett LK, Towne AR. Comparison of status epilepticus with prolonged seizure episodes lasting from 10 to 29 minutes. *Epilepsia* 1999; 40: 164-9.

Fountain NB. Status epilepticus: risk factors and complications. *Epilepsia* 2000; 41(S2): S23-30.

Garzon E, Fernandes RM, Sakamoto AC. Analysis of clinical characteristics and risk factors for mortality in human status epilepticus. *Seizure* 2003; 12: 237-45.

Commission on Epidemiology and Prognosis, International League Against Epilepsy. Guidelines for epidemiologic studies on epilepsy. *Epilepsia* 1993; 34: 592-6.

Hui AC, Joynt GM, Li H, Wong KS. Status epilepticus in Hong Kong Chinese: etiology, outcome and predictors of death and morbidity. *Seizure* 2003; 12: 478-82.

Jennett B, Bond M. Assessment of outcome after severe brain damage. A practical scale. *Lancet* 1975; 1: 480-4.

Kwong KL, Lee SL, Yung VC. Status epilepticus in 37 Chinese children: etiology and outcome. *J Paediatr Child Health* 1995; 31: 395-8.

Li JM, Chen L, Zhou B, Zhu Y, Zhou D. Convulsive status epilepticus in adults and adolescents of southwest China: mortality, etiology, and predictors of death. *Epilepsy Behav* 2009; 14: 146-9.

Logroscino G, Hesdorffer DC. Methodology issues in studies of mortality followed epilepsy: measures, types of studies, sources of cases, cohort effects, and competing risks. *Epilepsia* 2005; 46: 3-7.

Lowenstein DH, Alldredge BH. Status epilepticus at an urban public hospital in the 1980s. *Neurology* 1993; 143: 483-388.

Mah JK, Mah MW. Pediatric status epilepticus: a perspective from Saudi Arabia. *Pediatr Neurol* 1999; 20: 364-9.

Maharaj M, Henry D, Alik K, Mohammed PD. Status epilepticus: recent experience at the Port-of-Spain General Hospital, Trinidad. *West Indian Med J* 1992; 41: 19-22.

Mhodj I, Nadiaye M, Sence F. Treatment of status epilepticus in a developing country. *Neurophysiol Clin* 2000; 30: 165-9.

Murthy JM, Jayalaxmi SS, Kanikannan MA. Convulsive status epilepticus: clinical profile in a developing country. *Epilepsia* 2007; 48: 2217-23.

Quet F, Odermatt P, Preux PM. Challenges of epidemiological research on epilepsy in resource-poor countries. *Neuroepidemiology* 2008; 30: 3-5.

Rossetti AO, Hurwitz S, Logroscino G, Bromfield EB. Prognosis of status epilepticus: role of etiology, age, and consciousness impairment at presentation. *J Neurol Neurosurg Psychiatry* 2006; 77: 611-5.

Rowan AJ, Scott DF. Major status epilepticus: a series of 42 patients. *Acta Neurol Scand* 1970; 46: 573-84.

Skinner HJ, Dubon-Murcia SA, Thompson AR, *et al*. Adult convulsive status epilepticus in the developing country of Honduras. *Seizure* 2010; 19: 363-7.

Sibergleit R, Durkalski V, Lowenstein D, *et al*. Intramuscular versus intravenous therapy for prehospital status epilepticus. *New Engl J Med* 2012; 366: 591-600.

Tiamkao S, Suko P, Mayurasakorn N, Srinagarind Epilepsy Research Group N. Outcome of status epilepticus in Srinagarind Hospital. *J Med Assoc Thai* 2010; 93: 420-3.

Towne AR, Pellock JM, Ko D, DeLorenzo RJ. Determinants of mortality in status epilepticus. *Epilepsia* 1994; 35: 27-34.

Treiman DM, Meyers PD, Walton NY. A comparison of four treatments for generalized convulsive status epilepticus. Veterans Affairs Status epilepticus Cooperative Study Group. *N Engl J Med* 1998; 339: 792-3.

Vespa PM, Nuwer MR, Nenov V, *et al*. Increased incidence and impact of nonconvulsive and convulsive seizure after traumatic brain injury as detected by continuous electroencephalographic monitoring. *J Neurosurg* 1999; 91: 750-60.

Vignatelli L, Tonon C, D'Alessandro R. Bologna Group for the Study of Status Epilepticus. Incidence and short-term prognosis of status epilepticus in adults in Bologna, Italy. *Epilepsia* 2003; 44: 964-968.

Walton NY, Treiman DM. Response of status epilepticus induced by lithium and pilocarpine to treatment with diazepam. *Exp Neurol* 1988; 101: 267-75.