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Factors associated with poor discharge status in patients with status epilepticus at Khon Kaen Hospital

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Background: Status epilepticus (SE) is a serious neurological condition and has high a mortality rate. Data on importance of factors associated with poor outcomes in Asian or Thai populations are limited.

Methods: Adult patients diagnosed as SE at Khon Kaen Hospital, Thailand from October 1, 2010 to September 30, 2012 were enrolled. Patients were categorized as good or poor outcomes at discharge. Good outcomes were defined by improvement at discharge and absence of neurological deficits, while poor outcomes were defined by: not being improved at discharge; being discharged against advice; death; or presence of a neurological deficit. Clinical factors were compared between both groups.

Results: During the study period, there were 211 patients diagnosed as SE. Of those, 130 patients were male (61.61%). The mean age of all patients was 53.28 years. Acute stroke was the most common cause of SE in 33 patients (15.64%). At discharge, there were 91 patients (43.13%) who had poor outcomes. Only initial plasma glucose levels were significantly associated with poor outcomes with an adjusted odds ratio of 1.012 (95% confidence interval of 1.003 and 1.021).

Conclusion: Initial plasma glucose is associated with poor discharge status in patients with SE.

Keywords: hyperglycemia, outcomes, prognosis, risk factors

Introduction

Status epilepticus (SE) is an emergency neurological condition defined as a continuous seizure of more than 5 minutes.[1] Its prevalence varies between 10 and 41 cases per 100,000 population outside of Thailand.[2] In Thailand, SE occurred in 5.10 cases per 100,000 population with a mortality rate of 0.6 per 100,000 population.[3] Causes of SE are different between countries. A report from Taiwan showed that central nervous system infection and previous strokes are the two most common causes of SE,[4] while antiepileptic drug (AED) withdrawal and alcohol-related causes were leading causes of SE in Western countries.[5]

Factors associated with poor outcomes of SE were related to comorbid complications such as metabolic disorders, cerebrovascular disease, and hypoxemia as shown in systematic reviews.[6,7] A report from Thailand did not find any significant predictors for SE.[2] Unlike in Western countries, there are limited data on predictors of SE outcomes in Thailand and other Asian countries. Here, the study was aimed to determine whether any factors associated with initial laboratory findings or treatment of SE had influences on outcomes at discharge.

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Materials and methods

This study retrospectively reviewed charts of adult patients who were at least 15 years old and diagnosed as SE at Khon Kaen Hospital from October 1, 2010 to September 30, 2012. SE patients were identified by using the International Classification of Diseases code G41. Khon Kaen Hospital is the tertiary care hospital located in the northeastern part of Thailand.

Baseline characteristics, initial laboratory findings, treatment, and treatment outcomes were recorded. Patients were categorized into two groups by type of discharge status and neurological outcomes; good or poor outcomes. Good outcomes were defined by improvement at discharge and absence of neurological deficits, while poor outcomes were defined by: not being improved at discharge; being discharged against advice; death; or presence of a neurological deficit.

Statistical analysis

Descriptive statistics were used to detect significant differences between patients with good and poor outcomes. Univariate logistic regression analysis was applied to calculate the crude odds ratios (ORs) of individual variables for having poor outcomes. All variables with $P<0.20$ in univariate analysis were included in subsequent multivariate logistic regression analysis. The final model was composed of factors associated with poor outcomes. Analytical results are presented as adjusted ORs, and 95% confidence intervals.

The study protocol was approved by an institutional review committee, Khon Kaen University (HE 561217).

Results

During the study period, there were 211 patients diagnosed as SE. Of those, 130 patients were male (61.61%). The mean age (standard deviation [SD]) of all patients was 53.28 years (15.92). Epilepsy (24.64%) and hypertension (23.22%) were the two most common comorbid diseases. Generalized tonic–clonic seizure was the most common type of SE (179 patients; 94.71%). Acute stroke was the most common cause of SE in 33 patients (15.64%). Other common causes of SE are shown in Table 1. The mean (SD) numbers of AEDs used were 2.05 (1.56) and the mean (SD) length of stay was 5.12 days (6.75). There were 104 patients (49.29%) who developed complications after SE and the most common complication was aspiration pneumonia (53 patients; 25.12%).

At discharge, there were 120 patients (56.87%) who had good outcomes, while 91 patients (43.13%) had poor outcomes categorized by: death (29 patients; 13.74%); not improved or discharged against advice (55 patients; 26.07%); and presence of neurological deficits (7 patients; 3.32%). Most clinical factors at initial presentation were comparable between those who had good and poor outcomes at discharge (Tables 2 and 3). Those who had poor outcomes had more SE occurrences in hospital (30.77% versus 3.33%), a lower Glasgow coma scale (7.97 versus 9.78), higher plasma glucose (203.11 versus 159.26 mg/dL), lower serum albumin (2.73 versus 3.52 g/dL), higher serum aspartate aminotransferase (171.36 versus 82.78 U/L), and higher total bilirubin (1.84 versus 1.04 mg/dL) than those with good outcomes. The serum electrolytes, except for potassium and phosphate levels, were also statistically different between those who had good and poor outcomes (Table 3). In the final model of multivariate analysis, only plasma glucose was significantly associated with poor outcomes with an adjusted OR of 1.012 (95% confidence interval of 1.003 and 1.021).

Regarding treatment and treatment outcomes, those with poor outcomes had a higher proportion of recurrent SE (42.86% versus 10.83%) and longer duration of respirator use (4.18 versus 1.83 days) as shown in Table 4.

Table 1 Causes of status epilepticus in the present study

Causes	Number (%)
Acute stroke	33 (15.64)
Alcohol related (withdrawal/toxicity)	30 (14.22)
Sepsis	24 (11.37)
Central nervous system infection	19 (9.00)
AED withdrawal	19 (9.00)
Cardiac arrest	18 (8.53)
Post-stroke	11 (5.21)
Subtherapeutic AED level	11 (5.21)
Hyponatremia	7 (3.32)
Hyper-/hypoglycemia	5 (2.37)
Acute subdural hematoma	4 (1.90)
Uremia	4 (1.90)
Acute febrile illness	4 (1.90)
Hypertensive encephalopathy	4 (1.90)
Sleep deprivation	4 (1.90)
Venous sinus thrombosis	3 (1.42)
Others	11 (5.21)

Notes: "Others" were autoimmune encephalitis, brain abscess, hydrocephalus, central nervous system vasculitis, hypocalcemia, intracerebral hemorrhage, posterior reversible encephalopathy syndrome, subarachnoid hemorrhage, and subdural hygroma.
Abbreviation: AED, antiepileptic drug.

Discussion

This study showed two important findings: poor discharge status of SE in a tertiary care hospital was 43.13% and the discharge status of SE patients was associated with initial

Table 2 Clinical factors at initial presentation of patients with SE categorized by type of hospital discharge

Factors	Good outcome N=120	Poor outcome N=91	*P*-value
Male	76 (63.33)	54 (59.39)	0.555
Mean age (SD), years	52.71 (18.71)	54.04 (19.58)	0.655
Comorbid diseases			
Hypertension	28 (23.33)	21 (23.08)	0.965
Diabetes mellitus	23 (19.17)	16 (17.58)	0.769
Alcoholism	13 (10.83)	7 (7.69)	0.445
Stroke	27 (22.50)	20 (21.98)	0.928
Epilepsy	31 (25.83)	21 (23.08)	0.645
Causes of SE			
Acute stroke	22 (18.33)	11 (12.09)	0.432
AED withdrawal	9 (7.50)	10 (10.99)	0.381
Alcohol related	14 (11.67)	16 (17.58)	0.223
Cardiac arrest	11 (9.17)	7 (7.68)	0.704
CNS infection	7 (5.83)	12 (13.19)	0.065
Septic encephalopathy	12 (10.00)	12 (13.19)	0.470
Type of SE			
Generalized tonic–clonic	103 (95.37)	76 (93.83)	0.703
Nonconvulsive	1 (0.93)	2 (2.47)	0.703
Epilepsia partialis continua	4 (3.70)	3 (3.70)	0.703
Place of SE occurrence			
Home	106 (88.33)	55 (60.44)	<0.001
Primary Hospital	10 (8.33)	8 (8.79)	<0.001
Khon Kaen hospital	4 (3.33)	28 (30.77)	<0.001
History of previous SE	10 (8.33)	2 (2.20)	0.057

Notes: Poor outcome: discharge by death, not improved, or discharged against advice. Khon Kaen Hospital is a tertiary care hospital. Data presented as number (percentage) unless indicated.
Abbreviations: AED, antiepileptic drug; CNS, central nervous system; SD, standard deviation; SE, status epilepticus.

Table 3 Physical signs and laboratory findings at initial presentation of patients with status epilepticus categorized by type of hospital discharge

Factors	Good outcome N=120	Poor outcome N=91	*P*-value
Body temperature, °C	37.22 (1.01)	37.42 (1.26)	0.219
Systolic blood pressure, mmHg	138.22 (28.41)	138.24 (32.72)	0.996
Pulse rate, bpm	98.42 (23.40)	102.44 (24.75)	0.249
Glasgow coma scale	9.78 (3.51)	7.97 (4.01)	<0.001
Endotracheal intubation, n (%)	67 (58.26)	58 (65.17)	0.315
Laboratory results			
Hematocrit, %	26.04 (17.53)	23.83 (17.76)	0.367
White blood cell count, cells/mm^3	8,492.60 (6,724.24)	8,411.43 (7,789.93)	0.936
Plasma glucose, mg/dL	159.26 (84.18)	203.11 (121.93)	0.006
Blood urea nitrogen, mg/dL	13.32 (10.69)	31.09 (36.64)	<0.001
Creatinine, mg/dL	1.18 (1.26)	2.01 (1.88)	<0.001
Serum sodium, mEq/L	135.49 (8.03)	138.03 (6.57)	0.034
Serum potassium, mEq/L	3.57 (0.89)	3.70 (0.77)	0.318
Serum chloride, mEq/L	99.27 (9.09)	103.30 (7.27)	0.006
Serum bicarbonate, mEq/L	22.37 (4.81)	20.03 (5.82)	0.007
Serum calcium, mg/dL	8.44 (0.88)	8.30 (1.38)	0.532
Serum phosphate, mg/dL	3.02 (1.12)	3.79 (2.27)	0.037
Total cholesterol, mg/dL	168.08 (49.37)	158.87 (57.92)	0.555
Serum albumin, g/dL	3.52 (0.66)	2.73 (0.93)	<0.001
Serum ALT, U/L	533.67 (61.28)	147.63 (275.02)	0.052
Serum AST, U/L	82.78 (102.35)	171.36 (205.69)	0.031
Total bilirubin, mg/dL	1.04 (0.79)	1.84 (1.49)	0.017
Alkaline phosphatase, mg/dL	111.31 (81.39)	106.89 (88.13)	0.857

Note: Data presented as mean (standard deviation) unless indicated otherwise.
Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Table 4 Treatment and treatment outcomes of patients with SE categorized by type of hospital discharge

Factors	Good outcome N=120	Poor outcome N=91	*P*-value
SE time prior to treatment, minutes	150.83 (257.64)	159.19 (344.43)	0.848
SE treatment time to control SE, minutes	88.81 (175.08)	191.47 (621.38)	0.143
Total SE time, minutes	225.77 (268.90)	360.09 (723.49)	0.108
Recurrent SE, n (%)	13 (10.83)	39 (42.86)	<0.001
Interictal time, hours	5.54 (12.24)	1.16 (6.59)	0.001
Numbers of AED use	2.55 (1.71)	2.44 (1.35)	0.612
Types of AED use			
Primary AED			
Diazepam, n (%)	91 (75.83)	69 (75.82)	0.747
Phenytoin, n (%)	26 (21.67)	21 (23.08)	0.747
Sodium valproate, n (%)	3 (2.50)	1 (1.10)	0.747
Secondary AED			
Phenytoin, n (%)	91 (98.91)	77 (100)	0.359
Sodium valproate, n (%)	1 (1.09)	0	0.359
Others			
Midazolam, n (%)	0	3 (0.03)	0.079
Propofol, n (%)	0	2 (0.02)	0.185
Length of hospital stay, days	4.69 (6.12)	5.69 (7.50)	0.287
Duration of respirator use, days	1.83 (3.92)	4.18 (6.21)	<0.001
Aspirated pneumonia, n (%)	33 (27.50)	20 (21.98)	0.360

Note: Data presented as mean (standard deviation) unless indicated otherwise.
Abbreviations: AED, antiepileptic drug; SE, status epilepticus.

plasma glucose levels. An increase of 1 mg/dL of plasma glucose increased the risk of having poor discharge status by 1.2%.

A previous study from Singapore also showed that in SE patients with a hyperglycemia equal to or more than 7 mmol/L (126 mg/dL), these levels were associated with poor outcomes of SE.[8] In animal models, hyperglycemia causes hippocampal damage and also aggravates seizures.[9,10] Therefore, glucose control may be important in SE patients, particularly in Asian populations. These results may not apply to Western populations. Two studies from Switzerland did not have findings similar to this study.[11,12] Hyperglycemia was, however, shown to be associated with poor outcome in acute ischemic stroke.[13]

Some factors such as serum albumin or aspartate aminotransferase were significantly different between the good and poor SE outcomes by univariate logistic analysis or descriptive statistics. Both factors, however, were not statistically significant in the multivariate logistic regression analysis. These results implied that only plasma glucose was an independent factor or predictor for SE outcome.

The population of this study may be different from other previous studies in terms of causes of SE. In the current study, acute stroke, alcohol related causes, and septic encephalopathy accounted for 41.23% of the entire subjects. Unlike in Western populations, AED withdrawal was found only in 9%. The previous study from Thailand found that the mortality rate of SE was 35%,[2] while refractory SE may have a mortality rate of 50%.[14,15] The poor outcome rate of this study was 43.13%. The poor discharge statuses were one of the following: death; not improved or discharged against advice; or presence of a neurological deficit.

The strengths of this study were the quite-large sample size and different causes of SE as compared with previous studies.[11,12] There are some limitations. Retrospective data collection may not have complete data, particularly laboratory findings such as HbA_{1c} levels or history of previous medications that may affect plasma glucose levels such as steroid use. Also noted was that the population in this study was mostly not refractory SE; only three and two patients had received midazolam and propofol, respectively. Further studies are needed particularly in refractory SE. The results of this study may apply only to Asian populations or other countries in Southeast Asia.

Conclusion

Initial plasma glucose is associated with poor discharge status in patients with SE.

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Disclosure

The authors report no conflicts of interest in this work.

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