Status Epilepticus : Update

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Topics

- Overview
- Management
- Experienced in Khon Kaen

Physiologic definition

- Epileptic activity without complete normalization of neuro-chemical and physiological homeostasis

Clinical definition

- Recurrent seizures without full and complete recovery of consciousness
- Single prolonged convulsion lasting *over 30 minutes*

Facts

- Pre-hospital study, SE was essentially declared if a patient was still experiencing a seizure when emergency medical personnel arrived.
- More than half of seizures lasting longer than *10 min may SE.*

NEJM 2001;345:631-7, Epilepsia 1999;40:164-9

New propose definition

- SE is a continuous, generalized, convulsive seizure *lasting greater than 5 min*, or two or more seizures during which the patient does not return to baseline consciousness

Epilepsia 1999;40:120-2

Practical definition

- Continuous, generalized, convulsive seizure lasting more than 5 min.
- Unreasonable to wait 30 min before initiating AED
- Refractory SE is seizures lasting more than 1 hr.

Etiology of SE in an urban hospital and community

Etiology	Percent of cases
Withdrawal of anticonvulsants	25
Cerebrovascular disease	23
Remote symptomatic	19
Alcohol withdrawal	15
Metabolic disorders	13
Hypoxia	12
Infectious disorders	8
Tumors	5
Anoxia	4
Trauma	3
Hemorrhage	2
Drug overdose	2
Idiopathic	4

Data adapted from Churchill Livingstone 2000;697-710

Nonconvulsive Status Epilepticus in a Neurological Intensive Care Unit: Profile in a Developing Country

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Summary: *Purpose:* Nonconvulsive status epilepticus (NCSE) is an under-recognized cause of altered mental status. There are hardly any reported data on NCSE in developing countries.

Material and Methods: Prospectively 210 consecutive patients with altered mental status admitted to neurological intensive care unit (NICU) of a tertiary care center in south India were studied for the frequency of NCSE. All patients were evaluated initially with 60-min emergent EEG (EmEEG) and subsequently by continuous EEG (cEEG) monitoring.

Results: Of the 210 with altered mental status admitted to NICU, the diagnosis of NCSE was established in 22 (10.5%) patients, in 12 (55%) patients with 60-min EmEEG and in 10 (45%) after cEEG monitoring for 12 to 48 hours.

Of the 22 patients with NCSE, 32% had subtle motor phenomena, these were not an initial presenting features, but were apparent during cEEG recording. Acute medical or neurologic etiology was the risk factor in 68% of patients. Central nervous system (CNS) infections and cortical sino-venous thrombosis (CSVT), respectively, accounted for 23% and 14% of the etiologies. Intravenous midazolam terminated NCSE in 19 patients and valproate in 2. Of the 15 patients with acute symptomatic NCSE, 4 (18%) had poor prognosis (3 deaths and one persistent vegetative state). The etiological risk factors in the 9 (41%) patients with excellent outcome included epilepsy (3), remote symptomatic (2), cryptogenic (1), and metabolic and drugs (3).

Conclusions: The frequency of NCSE in the current study was comparable with those in prior reports from developed countries. CNS infections accounted for about a fifth of the etiology. Outcome was excellent in patients with nonacute symptomatic NCSE. Initial 60-min EmEEG may be performed in establishing the diagnosis of NCSE, but almost half of patients with NCSE will be missed with this approach. **Key Words:** Nonconvulsive status epilepticus—Emergent EEG—Continuous EEG monitoring—Central nervous system infections—Midazolam.

Risk factor of NCSE in ICU

- 77/3151 (2.4%) in ICU
- CNS infection 32%
- Metabolic disorder 32%
- Stroke 21%
- Other 15%
- 4.5% developed SE
- Stroke is major risk factor

Murthy JMK. Neuro India 2007:55:136-40.

Epidemiology

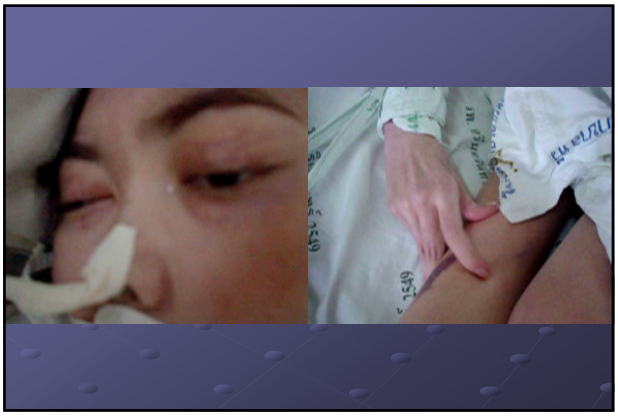
- Annual incidence GTCs SE is 18-28:100000
- Most SE developed *without a prior history of epilepsy*
  - Stroke, trauma, brain tumor, toxic, metabolic
- Pre-existing epilepsy
  - *Drug withdrawal*, severe illness, metabolic

Classification

- Convulsive status epilepticus: CSE
- Non-convulsive status epilepticus
- Generalized status epilepticus
- Partial status epilepticus

Nonconvulsive-status epilepticus

- NCSE is relatively common
- At least one third of SE
- More common in elderly
- Types
  1. Complex partial status epileptiues : CPSE
  2. NCSE in coma
  3. Typical absence status epilepticus : TAS
- Diagnosis dependent on EEG



Complex partial status epilepticus

- Behavioral change
- Commonly repeated episodes
- Mortality and morbidity usually related to underlying disease and medical complication
- Early recognition is a goal
- Sodium valproate iv, oral benzodiazepine
- Benign condition

Non convulsive status epilepticus in coma

- Common in critically ill, comatose patients
- NCSE following CSE in coma should be treated aggressive
- Poor prognosis in hypoxic encephalopathy

Treatment : Aim

- Stop epileptic activity as rapidly as possible
- Protect neurons from seizure-induced damage
- Preventing recurrences managing precipitating factors and treating complication

Pathophysiology : SE

- 2 phases
- Phase I : Compensatory mechanism of prevent cerebral damage, 30-60 min
- Phase II : Reduced compensatory mechanism, increased risk of permanent neuronal damage, last more than 60 min

General treatment of GTC SE

1. Cardio-respiratory function
2. Emergency investigations
3. Initial emergency treatment
4. Intensive care and seizure/EEG monitoring
5. Prevent and treatment complication
6. *Establish etiology*

Anticonvulsant pharmacostrategies

- BZP are drugs of choice
- Rapid onset, strong anticonvulsant action
- Peak brain concentration of DZP were achieve 1 min
- DZP : half life 28-54 hours
- LZP : half life 8-25 hours
- DZP : distribution half 0.3 hours, recurrent seizure ↑
- LZP : distribution half 2-3 hours

Early VS delay treatment

- SE treated 30 min after onset was terminated in 80%
- SE treated 120 min after onset was terminated in 40%
- Treatment SE should be initiated ASAP
- Out-of-hospital treatment

Thai CPG

Premonitoring stage

Diazepam 10 mg iv (given over 2-5 min) or rectally,
repeated once 15 minutes later
if status continues to threaten

Or

Lorazepam 4 mg iv bolus
If seizures continue or status develops

Stage of established status

Phenobarbital iv infusion of 10 mg/kg at a rate of 100 mg/min
(i.e. about 700 mg in an average adult over 20 min)

Or

Phenytoin iv infusion of 15 mg/kg at a rate of 50 mg/min
(i.e. about 100 mg in an average adult over 10 min)

If status continues after 30-60 min

Sodium valproate IV form
Small evidence base
Alternative drug in Thai Epilepsy CPG

Stage of refractory status

General anaesthesia with either:

Propofol 2mg/kg iv bolus, repeated if necessary, and then followed by continuous infusion of 5-10 mg/kg/h initially

Or

Thiopental: 100-250mg iv bolus given over 20s, with further 50mg boluses every 2-3 min until seizures are controlled

Thiopental should be slowly withdrawn 12 h after the last seizure

High mortality and morbidity

General management of RSE : GCSE

- Admit ICU
- Immediately infusion of anesthetic dose of MDZ, propofol, barbiturate
- Poor evidence of first line agent
- Burst suppression EEG pattern
- Maintained at least 24 hours
- Simultaneously AED for chronic therapy

Caution

- Routine injection of glucose is not advise
- Respiratory and/or metabolic acidosis is common but should not be treated unless pH dropped below 7.0
- Bicarbonate may lead to alkalosis which would reduce threshold for seizures

Caution

- During initial half to first hour, most patients are hypertensive
- Low blood pressure is common after the firs hour
- After the patient is stabilized and seizures are controlled the second phase of investigation should begin

Caution

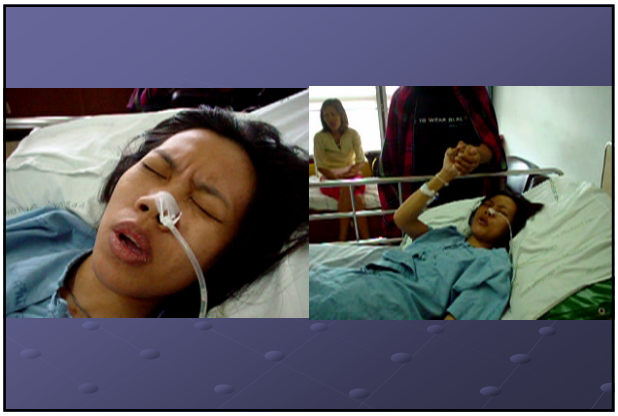
- If CNS infection is suspected and ***lumbar puncture cannot be performed immediately***
- Antibiotics should be initiated at once, after blood culture have been obtained
- Low-grade fever is a frequent result of SE itself
- Post-ictal pleocytosis

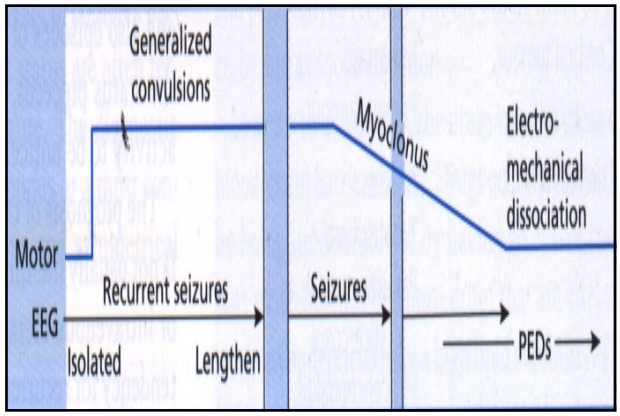
Failure to emergency treatment

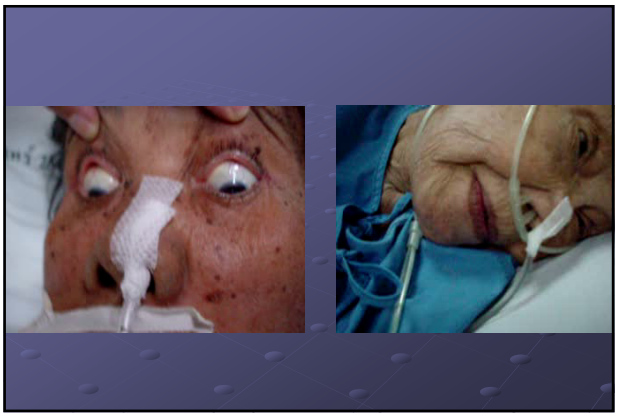
1. Inadequate drug treatment
   - too low dosage
   - too slow rate IV infusion
   - no maintenance AEDs
2. Additional medical factors
   - complication
   - causes
3. Misdiagnosis

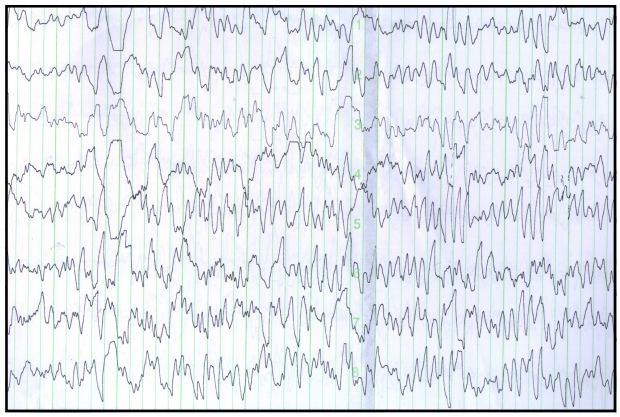
Psychogenic non-epileptic SE : PNESE

- Younger age
- Repeated PNESE
- Persistence of seizures without respiratory failure despite high-dose BZP
- Normal CK
- Usually attack in day-time









Newer therapy

- IV VPA is another choice for treatment in elderly
- Loading dose 15 mg/kg – 70 mg/kg
- Safety and tolerability of rapid infusion rate
- Low risk of hypotension,

  respiratory depression sedative

Valproate is an effective, well-tolerated drug for treatment of status epilepticus/serial attacks in adults

Olsen KB, Taubøll E, Gjerstad L. Valproate is an effective, well-tolerated drug for treatment of status epilepticus/serial attacks in adults. Acta Neurol Scand 2007: 115 (Suppl. 187): 51–54.

Objective – Status epilepticus (SE) and serial attacks (SA) represent neurological emergencies, and mortality rate for SE/SA is high, ranging from 3% to 25%, depending on cause and co-morbidity. As SE/SA become more refractory to treatment over time, rapid, appropriate treatment is extremely important. Here, we report a prospective registration of the effect of intravenous (IV) valproate (VPA) on SE/SA in a group of Norwegian patients. *Patients and methods* – Forty-one adult patients (18 males, 23 females) were included in the study. All had previously been unsuccessfully treated with diazepam. For 19, the main SE/SA seizure type was generalized tonic-clonic, while 16 had complex-partial seizures. Six had seizures that were difficult to classify. The treatment protocol recommended 25 mg/kg of VPA loading dose over 30 min, followed by continuous infusion of 100 mg/h for at least 24 h, then per oral administration. If seizures persisted after the loading dose, general anaesthesia (barbiturates/propofol/midazolam) was administered. *Results* – No serious side effects were reported. In 76% of the cases (31 of 41), SE/SA stopped and anaesthesia was not required. Of the patients treated within 3 h, only 5% needed anaesthesia, whereas of those treated after 3–24 h, 38% needed anaesthesia. Of those who waited for more than 24 h before treatment, 60% required anaesthesia. Furthermore, 60% of the patients who needed anaesthesia were given loading doses below 2100 mg. *Conclusions* – VPA seems to be a safe, effective treatment of SE/SA, but efficacy is dependent on time lapse between symptoms and VPA treatment, and administration of a sufficiently high loading dose.

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Key words: humans; serial attacks; status epilepticus; valproate

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Sodium Valproate for SE in Srinagarind hospital

- 44 events for adult GCSE, 28 male(65%)
- Mean age 50.14 yr(19-83)
- Etiologies/underlying diseases

1.Epilepsy	11	6.Renal failure	4
2.Brain tumor	7	7.CNS infection	3
3.Hypoxia	6	8.SAH	3
4.Head injury	6	9.Alcoholism	2
5.Stroke	5		

Somsak Tiamkao,et al 2007

Outcome of seizure control

- **Complete seizure controlled 56.8%**
- **Stop, then recurrent seizure 15.9%**
- **Partially seizure controlled 11.4%**
- **No seizure controlled 13.6%**

Somsak Tiamkao,et al 2007

Newer therapy

- **IV levetiracetam, July 2006 available**
- **1000 – 6000 mg**
- **23% respond (3/13)**
- **38% undetermine**
- **31% no respond**

Newer therapy in RSE

- **Topiramate nasogastric**
- **Ettectvie dose 300 – 1600 mg/day**
- **Most of cases : CPSE**

นิพนธ์ต้นฉบับ • Original Article

ภาวะลมชักวิกฤตในโรงพยาบาลศรีนครินทร์

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Status Epilepticus in Srinagarind Hospital

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Srinagarind Med J 1997;12:64-8

สาเหตุของการรักษาที่ไม่เหมาะสม generalized tonic-clonic status

สาเหตุของการรักษาที่ไม่เหมาะสม	25 ราย
1. ให้ยา phenytoin ในการ loading ทางปาก	7
2. ขนาดยา phenytoin ในการ loading ต่ำ	6
3. วินิจฉัยภาวะ SE ผิดพลาด	3
4. วินิจฉัยภาวะ SE ล่าช้า	3
5. ขนาดยา benzodiazepine ชนิดให้ทางเส้นเลือดดำต่ำ	3
6. ขนาดยา phenobarbital ในการ loading ต่ำ	2

57.5% **72 %**

การรักษา

- ถูกต้องตามแนวทางปฏิบัติ 7 ราย (28%)
- ไม่ถูกต้องตามแนวทางปฏิบัติ 18 ราย (72%)
- สาเหตุการรักษาไม่ถูกต้อง
  - แพทย์ไม่คิดถึง SE
  - จำขนาดยาไม่ได้

การเสียชีวิต

- 14/25 ราย (56%)
- รักษาเหมาะสม 2/7 (28.57%)
- รักษาไม่เหมาะสม 12/18 (66.67%)

Very High PB for RSE

- 10 RSE patients
- 18-86 years, mean 43 years
- PB 1 gm infusion every each attack
- PB dosage ranged between 40-140 mg/kg/day,(M 70)
- PB level 35.24-218.34 micro gm/ml (88.1)
- VHDPB achieved control 70%

Somsak Tiamkao,et al 2007

Conclusion

- Medical and neurological emergency
- Requiring prompt and aggressive treatment
- Duration of SE increased, clinical may become more subtle, high mortality
- Prognosis: etiology, age, type, duration, proper management