



Optimizing the Treatment of Seizure and Status Epilepticus Patients in the ED

Edward P. Sloan, MD, MPH

Professor
Department of Emergency Medicine
University of Illinois at Chicago
Chicago, IL

Case Presentation

A 37 year old male is being brought to you by paramedics because of a seizure at home. The patient supposedly was observed to have a generalized, tonic/clonic seizure by family, who are familiar with this patient's prior seizures. The paramedics gave 5 mg of diazepam IV, at which time the seizure resolved. The total time for this seizure was approximately 5-10 minutes. The patient had a remote history of traumatic brain injury, and was on phenobarbital and Dilantin. He has been known to be non-compliant with his medications in the past. He has had no recent illness or recent changes in his seizure frequency or medication regimen.

In the ED, the patient is postictal, is slow to respond, but is becoming more responsive to verbal stimuli and is appropriate. He has a non-focal neurological exam. He has no evidence of acute trauma or toxicity. Within 10 minutes of ED arrival, as his mental status improves, he has recurrent generalized tonic-clonic seizure.

When considering all ED seizure patients, is this patient an outlier?

What is the optimal management for his recurrent seizure?

What is his risk of going into status epilepticus?

Key Clinical Questions and Learning Points

What are the important issues related to seizure/SE epidemiology and pathophysiology?

The greatest risk for SE is in elderly patients. As the population ages, the frequency with which emergency physicians will have to treat SE will rise, such that familiarity with an SE treatment protocol and the availability of SE therapeutics in the ED will be critical.

In general, any compensatory mechanisms in the setting of SE will begin to fail after 20-40 minutes, such that there will be relatively diminished cerebral blood flow, brain injury especially in the hippocampus, and the potential for long term sequelae. As such, ED patients should begin to demonstrate improvement in mental status within 20-40 minutes of the resolution of a generalized tonic-clonic seizure. If this does not occur, the diagnosis of “subtle” SE should be considered.

What are key concepts related to seizure/SE classification?

Seizures are classified as partial or generalized, involving either a part of one cerebral hemisphere or both cerebral hemispheres during the seizure. The most common type of seizure presentation is that of a partial onset seizure (ie an aura) that later generalizes.

Nonconvulsive SE is classification that refers to a generalized seizure that does not involve tonic-clonic seizure activity. One type of nonconvulsive SE is seen in absence or complex partial SE, in which there are minimal motor manifestations of the seizure. The other type of nonconvulsive SE is “subtle” SE, which is a late manifestation of a prolonged generalized tonic-clonic seizure. This is a grave situation, one that is manifested by unresponsiveness and minimal partial motor activity (facial or finger twitching). Although benign in appearance, this type of SE must be aggressively diagnosed via EEG and treated, preferably prior to EEG confirmation, when able.

What protocols for the ED treatment of seizure/SE patients exist?

Very few protocols for the treatment of seizures and SE have been published or studied in a clinically robust manner. The VA cooperative study (Treiman, NEJM, 1998) utilized four treatment regimens in the only randomized study of SE, demonstrating that lorazepam, phenobarbital, and diazepam and phenytoin in combination all are equally effective in treating SE patients. This study demonstrates the fact that any antiepileptic drug, when used quickly and in adequate mg/kg doses, will terminate most episodes of SE.

What do these SE protocols tell us about ED therapies and treatment timing?

Most SE protocols that have been published or are available on internet websites suggest the following:

When evaluating and treating patient with prolonged seizures and SE, it is important to quickly manage the airway and vital signs, check for hypoglycemia, and initiate therapy in a matter of minutes. With tens of minutes, patient should receive one or more antiepileptic drugs (AEDs), which should be fully dosed in a full mg/kg dose prior to initiating a subsequent therapy.

In general, most SE patients, both adult and pediatric, should be initially treated with infusions of a benzodiazepine, a phenytoin, and either phenobarbital or valproate. Within 60-90 minutes, all AED injections should be completed, and continuous infusions of anesthetic agents such as midazolam or propofol should be initiated. During the next 60-90 minutes, CT evaluation, neurology consultation, EEG monitoring, and ICU disposition should be arranged.

What clinical questions does the 2004 ACEP Seizure/SE Clinical Policy address, and what does it tell us about ED diagnosis and treatment?

The 2004 ACEP clinical policy addresses the need for laboratory testing, neuroimaging, AED administration, and hospital admission for new onset seizure patients. In general, these new onset seizure patients should receive directed laboratory testing and neuroimaging in a timely manner. AED administration and hospitalization are only indicated if the patient is at high risk for going into SE, or if other features of the patient's clinical presentation or support system require that these be done.

The policy addresses the issue of phenytoin loading, stating that any of the current loading strategies can be used, based again on the patient's clinical presentation and support system.

The treatment of patients in SE is addressed, asking what therapies should be provided in patients who continue to seize despite the administration of a benzodiazepine and a phenytoin. Given that there is no published data that conclusively suggests one therapy over another for these refractory SE patients, the policy simply states what therapies should be considered in these patients, and includes the AED therapies commonly listed in the published and internet posted SE protocols.

Lastly, the clinical policy stated that EEG monitoring is indicated when SE patients remain comatose, suggesting "subtle" SE, and when paralytic agents or continuous anesthetic infusions are used to manage the airway or to treat the SE itself.

What do the 1993 EFA SE guidelines suggest, and what impact will the update of the EFA guidelines have on clinical practice?

The EFA guidelines suggest the need to utilize a protocol and to rapidly provide AEDs serially in full mg/kg basis, regardless of what specific AED is used in what order. These 1993 guidelines provided a consensus view of how SE patients should be treated, prior to the use of evidence based clinical policies and guidelines. Unfortunately, there are few subsequent evidence based recommendation that can be made as the guidelines are being revised, given that there are limited numbers of randomized therapeutic trials in SE that have indicated what therapies are optimal when attempting to terminate the seizure in SE patients.

What is SeizureStat©, and how can it be used in clinical practice?

SeizureStat© is a PDA software that will soon be available on the FERNE website. It includes four main sections: written materials on seizures and SE, a section with a full description of how to use the 10 most common parenteral AEDs in the setting of seizures and SE, a SE protocol with timed therapies and actions, and a full description of the main recommendations from the six questions addressed in the 2004 ACEP seizure/SE clinical policy. Via handheld technology, this software will allow ED health care providers to understand current recommendations, to know how to provide AED therapies, and to use a protocol that directs these emergent treatments over time.

Who is FERNE and what is available on the FERNE website www.ferne.org ?

FERNE is a group of emergency physicians committed to the following:

- * Patients with neurological emergencies deserve quality emergency care.
- * The emergency care for neurological emergencies can be enhanced through quality scientific research.
- * Emergency medical care providers can provide optimal medical care for patients with neurological emergencies through participation in quality medical education that highlights state-of-the-art neurological care.

As such, FERNE promotes quality emergency care through innovative research and educational efforts. FERNE works with ACEP's Emergency Medicine Foundation to promote funding for neurological emergencies research, and offers small seed grants directly.

The FERNE website, www.ferne.org, includes the written materials and slide presentations from over 300 lectures by 160 speakers at more than 40 meetings. The written materials most often include a clinical case, a description of the optimal ED diagnosis and management, references, an annotated bibliography, and questions with answers. The slide presentations are available as a PPT file or a PDF file. Both are available for downloading and local use. Lastly, there are audio and video files that can be viewed from the website so that the learner can listen to these presentations at a later time, when necessary.

Also available on the FERNE website are other lectures and resources (stroke PDA software, topic reference search engine, clinical scoring tools) that should make it possible for emergency health care workers to optimize the care of patients who present to the ED with acute neurological emergencies requiring urgent care.

Patient Case Outcome

From the introductory clinical case, the following is an example of how the ED medical record can be documented as a status epilepticus patient is examined, treated, and dispositioned.

ED History & Physical Document

- 37 yo male
- EMS to ED
- Generalized seizure at home,
- CFD: IV diazepam, GTCS resolved
- Hx TBI (remote) as seizure etiology
- On phenobarbital and dilantin
- Non-compliance in past
- No recent illness
- No new trauma

- Vital signs: VS OK, pulse ox OK, POC glucose OK
- HEENT: Pupils midrange, reactive, no papilledema, airway OK
No head trauma noted
- Neck: No Bruits, no nuchal rigidity, NT
- Chest: BSBE No Rales
- Cardiac: No afib, no gallops or murmurs
- Abd: No evidence of AAA, peritonitis
- Ext: No DVT or pedal edema evident
- Skin: No cellulitis or wounds
- Neuro: No toxidrome noted. Pt postictal, slow to respond initially.

- CN: No mouth droop, no lid weakness
- Motor: No hemiparesis noted
- Sensory: No light touch abnormalities
- Reflex: No pathologic reflexes
Normal corneals, normal gag reflex
- Cerebellar: No truncal ataxia, sitting in cart OK
- Visual/Neglect: None noted
- Language: No dysarthria, expressive aphasia, no receptive aphasia
- LOC: Slightly somnolent, responds to verbal stimuli, GCS=13-14

ED Management and Patient Outcome

- Recurrent generalized TC seizure in ED
- Lorazepam 2 mg IVP x 6 over 25 min given
- Generalized seizure continues, IV access lost, re-established
- Fosphenytoin 1 gram PE over 10 min
- Fosphenytoin 500 mg PE over 5 min
- Seizure ended after 45 minutes, pt remained obtunded

- Non-contrast CT negative
- Metabolic tests normal
- Toxicology screening negative
- Sub-therapeutic phenytoin level
- Sub-therapeutic phenobarbital level
- Neurology aware, to obtain EEG upon arrival in ICU

- **Diagnosis:** Status Epilepticus due to sub-therapeutic AED levels

Hospital Course and Patient Outcome

The patient had an EEG performed in the ICU, within 120 minutes. Neurology consultation confirmed that the patient was not in subtle SE. The patient awoke completely within 12 hours, and was discharged from the ICU the next day. He had no morbidity related to this SE episode. He was discharged home two days later, and was told to take his medications as prescribed. He was scheduled to have neurology follow-up one week later, and was found to have no sequelae from this SE episode.