Emergency Neurological Life Support: Status Epilepticus

Karen Berger, PharmD[1], Dionne E. Swor, DO[2], and Craig Press, MD, PhD[3]

[1]Department of Pharmacy, New York-Presbyterian Hospital/Weill Cornell Medical Center
[2]Department of Neurology, Wake Forest Baptist Health, Winston Salem, NC
[3]Department of Pediatrics-Neurology, University of Colorado, Aurora, CO

Abstract

Patients with prolonged or rapidly recurring convulsions lasting five minutes or more are considered to be in status epilepticus (SE) and should receive immediate resuscitation. Although there are few randomized clinical trials treating SE, available evidence and clinical experience suggest that early and timely treatment of SE improves patient outcomes. The current approach to the emergency treatment of SE emphasizes rapid initiation of adequately dosed first line therapy, accelerated second line antiseizure drugs and induced coma with continuous infusion of anesthetics when these fail, coupled with admission to a unit capable of neurological critical care and electroencephalography (EEG) monitoring. This protocol will focus on the initial treatment of SE and will also review subsequent steps in the protocol once the patient is hospitalized.

Key Words:

status epilepticus • seizures • antiseizure drug (ASD) • pharmacologic coma • electroencephalography (EEG) monitoring • automated external defibrillator (AED)

*Corresponding author: Karen Berger, PharmD.
†E-mail: karenberger7@gmail.com

1. Introduction

Each year in the United States (US), emergency departments (EDs) experience an average of one million seizure-related visits based on International Classification of Diseases-9 coding. These visits represent approximately 20% of ED visits for neurological problems and 1% of all ED visits.[1-3] Approximately 200,000 US patients per year have prolonged or rapidly recurring convulsions lasting more than five minutes - the defining features of status epilepticus.

The 30-day mortality of patients with generalized convulsive SE ranges from 10-27%.[4-9] Prolonged seizures are associated with higher mortality and worse clinical outcomes.[8-12] Adverse effects of SE include both indirect systemic problems arising from the convulsive state (e.g., impaired ventilation, aspiration, metabolic aberrations) and direct neuronal cellular injury from excitotoxicity, causing both immediate neuronal loss and delayed cell death.

This module is meant to give a broad framework for the principles of diagnosis and emergent management of SE, which can be adapted to reflect global and regional variations based on the local availability of diagnostic tools and treatments. Rapid control of seizures is fundamental to the emergency treatment of SE (Figure 1). Earlier termination of SE reduces neuronal injury in animal models of SE and is associated with improved clinical outcomes in human observational studies. In experimental SE, benzodiazepines are more likely to terminate seizures when given closer to seizure onset and decrease in effectiveness as seizure duration increases.

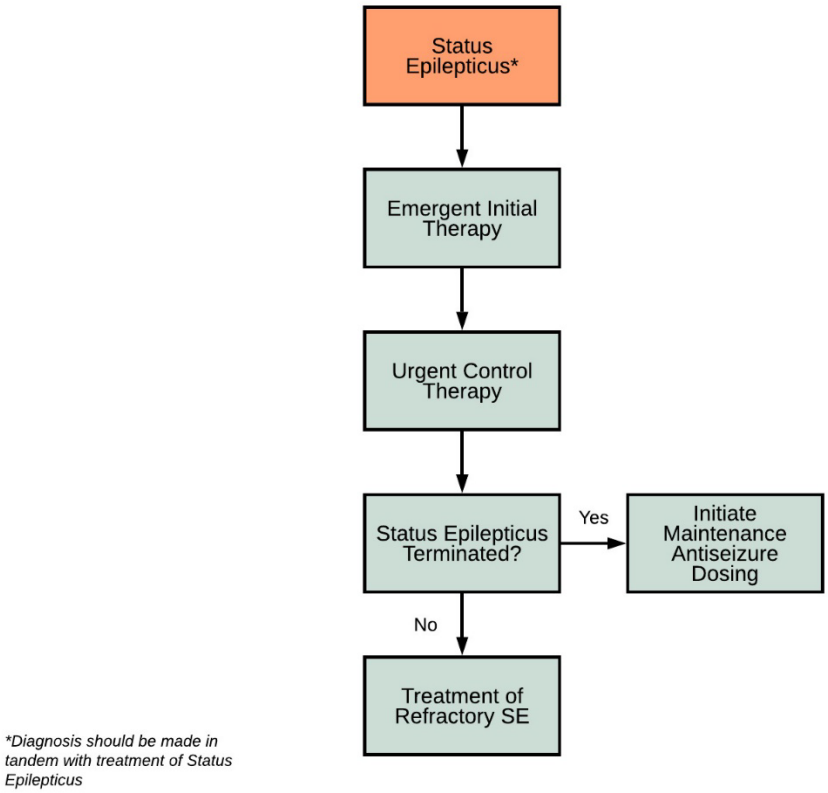

Figure 1

Caption: ENLS Status Epilepticus management protocol

The ENLS suggested algorithm for the initial management of SE is shown in Figure 1. For patients with suspected SE, it is suggested that initial diagnostic steps be performed in parallel to, but not delay treatment.

Fingerstick glucose should be checked as soon as possible as hypoglycemia is a rare, but rapidly treatable cause of SE; however, benzodiazepine administration should not await a potential diagnosis of hypoglycemia as this may lead to delays in therapy.[13,14] Unless intravenous (IV) access is already established, intramuscular (IM) midazolam should be immediately considered (buccal or nasal midazolam, or rectal diazepam may be used as alternatives if needed).[15] If IV or IO access is already established, the IV or IO route should be preferentially used in adult patients.

Table 1. Status epilepticus checklist for the first hour
Checklist
☐ Fingerstick glucose
☐ Obtain IV access
☐ Pulse oximetry, BP monitor, supplemental O_2 and fluid as needed, cardiac monitor
☐ Labs: Complete blood count, Basic metabolic panel, Calcium, Magnesium, HCG in females of childbearing age
☐ Head CT
☐ Continuous EEG (if available); notify EEG tech if available (as soon as available unless patient returns to pre-status epilepticus baseline)
☐ Consider rapid-response EEG with limited montage if continuous EEG is not available

The importance of rapid treatment of prolonged convulsions is reflected in the current definitions of SE, requiring only five minutes of unrelenting seizure activity.[16,17]

The diagnostic workup of patients with SE is pursued concurrently with treatment and stabilization, while ensuring that testing does not interfere with or delay control of seizures; treatment comes first. The diagnostic evaluation begins in parallel with Emergent Initial Therapy by ensuring airway, breathing, and hemodynamics are addressed. Evaluate for hypoglycemia, hypoxia, and hemodynamic instability. Pregnancy status should be assessed in childbearing age women to determine if preeclampsia is a potential cause of SE. Oxygen saturation and cardiac monitoring should be initiated during this phase. A rapid focused neurological evaluation should be performed including a description of ongoing convulsions, automatisms, focal deficits, pupillary changes, and level of consciousness.

Once IV access is obtained, blood and serum laboratory evaluation typically include a complete blood count, basic metabolic panel, pregnancy testing as applicable, and calcium and magnesium determinations. Selected laboratory studies that may be useful in some patients include liver enzymes, troponin, toxicology screen, lactate and blood gas determinations. Approximately two-thirds of patients evaluated in the ED for SE have a history of a prior seizure, and many have either discontinued or missed their medication or have subtherapeutic or supratherapeutic levels of antiseizure drugs. Antiseizure drug levels for specific medications, such as fosphenytoin/phenytoin, valproate, phenobarbital, and carbamazepine can be helpful to direct management. ASD levels, if available, may be useful if medication nonadherence is suspected.

If a cardiac arrhythmia or myocardial injury is suspected, ECG should be performed when possible. For patients with respiratory distress or hypoxia, supplemental oxygen should be administered, and a chest X-ray performed. Consider potential toxidromes or medications that are associated with seizures (Table 2).

Table 2: Toxidromes associated with seizures

Toxidrome	Management
Isoniazid	Treat with benzodiazepine followed by pyridoxine, max dose 5 gm.
Tricyclic Antidepressants	Evaluate for QRS widening on the ECG, treat with sodium bicarbonate.
Theophylline	Treat with benzodiazepines or barbiturates, consider gastric lavage if patient has recently (<1 hr.) ingested a significant amount or a sustained release product, administer activated charcoal, consider whole-bowel irrigation.[18]
Cocaine/Sympathomimetics	Treat with benzodiazepine.
Alcohol Withdraw	Treat with accelerating doses of a benzodiazepine and/or barbiturate
Organophosphates	Treat with atropine, midazolam, and pralidoxime.

The need for neuroimaging should be individualized but is generally warranted in patients who do not return to a normal level of consciousness, have new focal neurological findings, or have new onset seizure without an otherwise obvious identifiable etiology. Non-contrast computed tomography (CT) of the brain will identify most immediate threats and is the most typical initial imaging study obtained in the ED. A lumbar puncture should be performed in febrile patients and, when there is suspicion of central nervous system infection or subarachnoid hemorrhage, if there are not any contraindications on the CT of the brain including space occupying lesion with mass effect.

As noted in sections on hospital treatment below, EEG is necessary to identify non-convulsive SE[19] in patients who do not return to a normal level of

consciousness. EEG may also guide therapy in these patients and provide other diagnostic information. Ideally, EEG should be initiated within one hour of suspected non-convulsive SE, however many hospitals do not have access to 24/7 EEG capabilities.[20] Rapid response EEG with reduced montage may aid in quickly identifying patients with non-convulsive SE in critical care settings where continuous EEG monitoring is not available.[21]

Non-epileptic spells simulating SE (i.e., psychogenic nonepileptic seizures) may be difficult to differentiate from SE. Indicators suggestive of non-epileptic spells include preserved consciousness or purposeful movements, poorly coordinated thrashing, back arching, eyes held shut, head rolling, and pelvic thrusting.

2. Emergent Initial Therapy: Prehospital Treatment

The initial minutes after seizure onset offer the best opportunity for termination of SE. Prehospital management begins with immediate recognition of SE and emergent treatment with benzodiazepines while assessing ABCs. Airway adjuncts and/or supplemental oxygen may be needed. If present, hypoglycemia should be corrected with intravenous dextrose. In parallel, benzodiazepines should be given emergently. Since emergency medical services (EMS) response times are often 5 minutes or longer, patients found seizing upon EMS arrival may be considered in status epilepticus. EMS delivery of benzodiazepines results in a higher rate of cessation of seizures prior to arrival in the ED compared to placebo with a trend toward better outcomes.[7] In addition, IM administration of midazolam by EMS is superior to IV administration of lorazepam in terminating SE.[13] This has advantages as midazolam does not need refrigeration[22,23] and the administration of an IM drug is significantly easier and quicker than obtaining IV access.

Unless IV access is immediately available, initiate IM, PR, buccal or intranasal medications. In adults or children over 40 kg, IM midazolam 10 mg or PR diazepam 20 mg may be administered; in children 13-40 kg, the IM midazolam dose is 5 mg and in children <13 kg, the IM midazolam dose is 0.2 mg/kg (although children <13 kg were excluded from the RAMPART trial).[13] IV access can then be attempted while evaluating the effectiveness of initial therapy. If not available, consider a second dose of IM medication 5-10 minutes after the first dose if seizures persist.

When IV access is immediately available, consider lorazepam IV (adults, start 4 mg IV and repeat up to the max weight-based total dose of 0.1 mg/kg; for children, 0.1 mg/kg IV up to a maximum of 4 mg/dose). If lorazepam is not available in the area of practice, consider clonazepam 0.015 mg/kg IV (typically 1 mg IV) in adults or diazepam 0.15 mg/kg IV (up to 10 mg/dose). In one study, patients did not benefit from prehospital add-on therapy with levetiracetam IV.[24]

Respiratory depression can occur both following SE and in untreated SE; therefore, prehospital providers should be prepared to treat this irrespective of benzodiazepine use or dosing. Benzodiazepine doses recommended for SE are higher than those used for many other indications; however, the concern for respiratory depression should not prevent appropriate therapy. In fact, rates of respiratory and circulatory complications were lower with both lorazepam and diazepam as compared to placebo in the treatment of out-of-hospital status

epilepticus[7], as cardiorespiratory compromise is frequently a consequence of seizure duration and loss of metabolic reserve. While lorazepam is highly effective, it needs to be refrigerated or restocked frequently, raising logistical challenges for EMS systems. Some may find that diazepam and midazolam are preferable alternatives to stock.

3. Emergent Initial Therapy: Emergency Department

Early treatment of SE in the ED continues the care initiated by EMS. If IV access has not already been obtained, it should be achieved upon arrival in the ED, and diagnostic studies should be initiated in parallel with treatment as above.

In patients who continue to seize after initial benzodiazepine treatment, additional benzodiazepines should be administered after 5-10 minutes. Therefore, initial ED therapy will typically include IV benzodiazepines if initial EMS therapy has not succeeded. If the patient did not receive benzodiazepines prior to ED arrival and is still seizing, initial dosing should include IV benzodiazepines when IV access is immediately available. IM, PR, buccal, or intranasal benzodiazepines should be administered in parallel with IV placement when IV access is not available.

Benzodiazepines are frequently under-dosed because the labeled 4 mg initial (adult) dosing of lorazepam for SE is greater than the initial dose used for most other indications.[25] The same is true in pediatric dosing. Initial treatment failure is therefore often a result of (1) using inadequate initial doses of IV benzodiazepines due to fear of respiratory compromise, or (2) waiting too long to repeat benzodiazepine doses and advance to second line agents.[21,26,27]

As fingerstick glucose testing is widely and rapidly available in emergency departments, empiric administration of glucose is typically not warranted. However, for suspected or proven hypoglycemia, intravenous dextrose should be emergently provided.

4. Urgent Control Therapy

If SE continues after 10-20 minutes of two adequate doses of benzodiazepines, and no correctable underlying etiology is found during this time, the next step will typically be a second line agent. The best choice of second line antiseizure drugs for established SE is heavily debated, with the most used agents being phenytoin/fosphenytoin, valproate sodium, and levetiracetam. Consideration of other medical problems including renal failure, liver disease and hemodynamic status when choosing a second line agent. A recent prospective randomized double blind clinical trial evaluating the efficacy of fosphenytoin, levetiracetam, and valproate found no significant difference in the rate of seizure cessation among these drugs.[28]

Phenytoin is administered as 20 mg/kg IV (maximum rate of 50 mg/min) or 20 mg PE/kg of fosphenytoin (maximum rate of 150 mg PE/min).[29-31] Fosphenytoin is a water-soluble prodrug that is converted to phenytoin by plasma esterases. Thus, while IV fosphenytoin can be administered faster than IV phenytoin, it has the same time to effect on seizures, as it must be converted to phenytoin, which takes about 15 min. Fosphenytoin can also be administered IM if IV access is lost

or has yet to be established. In addition, fosphenytoin is compatible with many intravenous fluids making administration easier. Phenytoin and fosphenytoin are FDA-labeled for the treatment of SE in adults. They act at the sodium channel rather than the gamma-aminobutyric acid (GABA) receptor, and therefore represent a rational choice for treating patients whose seizures do not terminate with the benzodiazepine GABA agonists. Bradycardia and hypotension may occur at high infusion rates, especially in the elderly or those with significant cardiac disease. Hypotension is more profound with IV phenytoin due to its co-formulation with propylene glycol.

Valproate 40 mg/kg is given intravenously over 10 minutes, with an additional 20 mg/kg given 10 minutes after the loading dose if the patient is still seizing. Although adverse events were not statistically significantly different in the randomized study, sodium valproate probably has fewer cardiopulmonary side effects than phenytoin and may be preferred in patients with hypotension or respiratory distress. Phenytoin, fosphenytoin, and valproic acid are listed as hazardous medications according to the National Institute for Occupational Safety and Health (NIOSH) list and may require special handling per institutional guidelines.[32]

Levetiracetam is often used as a second line agent to treat SE and can be given as a 60 mg/kg dose up to a maximum dose of 4500 mg infused over 10-15 minutes.[28,33] Alternatively, a bolus of 1-3 g can be administered as an undiluted intravenous push over 2-5 minutes and may be faster than waiting for preparation of in IV piggyback dose.[34-38]

IV phenobarbital is also FDA labeled for the treatment of SE in adults and children and remains a reasonable option, but it is now less commonly chosen in adults unless other agents are contraindicated or unavailable. Phenobarbital 20 mg/kg IV is administered at a rate of 50–100 mg/min. An additional 5–10 mg/kg may be given after 10 minutes, if the patient is still seizing.

If seizures have stopped and the patient has awakened, loading doses of antiseizure medications with longer half-lives should be initiated and can be given either intravenously or orally.

Second line antiseizure drugs may be less effective, and may sometimes be contraindicated, for urgent treatment in patients with SE that is secondary to intoxications or poisonings. SE known to result from isoniazid or organophosphates should preferentially be treated with specific antidotes. Cardiac effects of tricyclic antidepressant poisoning may be exacerbated by attempting to prevent seizures with some second line antiseizure drugs.

5. Treatment of Refractory SE

Management of SE requires the use of the first and second line antiseizure drugs described above.[39] If the seizures have not stopped despite emergent and urgent drug therapy, SE is considered refractory. Intubation and drug-induced coma are recommended in these circumstances.

It is not necessary, and is usually not advisable, to delay advanced therapy with repeated trials of alternative second tier antiseizure drugs.[39] 30 minutes is usually adequate to determine if the above-described conventional approach is successful. Early administration of continuous infusion anesthetics (within 48 hours) has been associated with a shorter duration of refractory SE and better outcomes at last

follow-up. However, early administration was not associated with improved mortality or refractory status epilepticus termination.[40]

Endotracheal intubation is necessary to allow induction of coma and should be quickly performed in refractory SE (RSE). Because pharmacologic paralysis performed for purposes of intubation and mechanical ventilation will mask ongoing convulsions, it is necessary to use a short-acting neuromuscular blocker and pursue continuous EEG monitoring. If continuous EEG monitoring is not available, the patient should be emergently transferred to another facility where advanced monitoring is available.

The agents most commonly used to induce a general anesthetic state of coma are continuous infusions of midazolam or propofol.[41-44] IV midazolam infusions should be preceded by a loading dose of 0.2 mg/kg at 2 mg/min, with repeated boluses of 0.2–0.4 mg/kg every five minutes until the seizures stop, up to a maximum loading dose of 2 mg/kg. A continuous infusion should then be started at 0.05–2 mg/kg/hour. It is important to clarify the units in the electronic medical record order entry and infusion pumps since dosing for status should be in "mg/kg/hour" as compared to sedation dosing of "mg/hour" to avoid any potential dosing errors. IV propofol infusions usually include a loading dose of 1–2 mg/kg IV over 3–5 minutes, with repeated boluses of the same amount every 3–5 minutes until the seizures stop. The propofol infusion should then be maintained at a rate of 30–200 mcg/kg/min. An alternative agent may be selected when propofol doses are greater than 80 mcg/kg/min to reduce the risk of propofol infusion syndrome (PRIS) and hypotension.

Sedatives and anesthetics used for treatment of SE have a number of side effects and will frequently be associated with dose dependent hypotension requiring IV vasopressor support.[41] Hypotension may be seen with higher doses of both midazolam and propofol, however, midazolam is preferable in hemodynamically unstable patients.[41] Prolonged use of propofol at higher doses is associated with the rare-but-often-fatal propofol infusion syndrome (PRIS). PRIS is characterized by rhabdomyolysis, metabolic acidosis, and cardiac and renal failure.[45] Pentobarbital at a loading dose of 5 mg/kg followed by a maintenance infusion of 1-3 mg/kg may be used more frequently in children with refractory SE because of this adverse effect with propofol.

The use of ketamine infusion as a third line agent may be an effective adjuvant therapy for the treatment of refractory and super-refractory SE.[18,46,47] Ketamine acts as an NMDA receptor antagonist and offers a different mechanism of action than propofol and midazolam. Ketamine infusions should be preceded by a loading dose of 1-2 mg/kg IV followed by a continuous infusion of 0.5-10 mg/kg/hour.

Another IV anti-seizure medication may be added before a continuous infusion anesthetic for patients with refractory SE who cannot or should not be intubated (i.e., patient with advanced directives against intubation).[18,45,48,49] Alternate IV anti-seizure medication, such as lacosamide and brivaracetam may be useful therapeutic options in refractory SE.[18,50,51]

In the ED, sedative IV agents will usually be titrated to the cessation of clinical manifestations of convulsive or subtle SE. When continuous EEG monitoring is available, the administration rate can be titrated to the desired electroencephalographic findings, ranging from suppression of seizures to burst suppression or a completely suppressed background. Few data are available to identify the optimal treatment level of suppression.[18]

It is appropriate to continue second line antiseizure medications to attain therapeutic serum levels during the treatment of refractory SE, as these are needed to prevent seizure recurrence. Expeditious admission to an intensive care unit with a dedicated neurointensivist, with continuous EEG monitoring, is strongly recommended for RSE.

Table 3. Emergent Initial Therapy	
If no IV available:	
Adults and children >40 kg	Midazolam IM 10 mg
	If not available, Diazepam PR 20 mg
Children	Midazolam buccal 0.2-0.5 mg/kg, maximum dose 10 mg (or age based: 6m-11m 2.5mg, 1y-4y 5mg, 5y-9y 5mg, ≥10 y 10mg)
	Midazolam intranasal 0.2 mg/kg, maximum dose 10 mg
	Midazolam IM 0.2 mg/kg; 10 mg if >40 kg; 5 mg if 13-40 kg
	If not available, diazepam PR 0.5 mg/kg if 1-5yo, 0.3 mg/kg if 6-11yo, 0.2 mg/kg if >11yo
If no IV available and seizures continue, repeat x1 after 3-5 minutes	
If IV available:	
All patients	Lorazepam IV 0.1 mg/kg (up to 4 mg per dose)
	If initial dose (whether prehospital or ED) is not effective, repeat x1 after 3-5 minutes

Table 4. Urgent Control Therapy	
Adults and Children	Fosphenytoin IV 20 mg PE/kg
	Valproate IV 40 mg/kg
	Levetiracetam IV 60 mg/kg (max dose 4500 mg)
	Phenobarbital IV 20 mg/kg
Neonates	Phenobarbital IV 20 mg/kg
	Fosphenytoin IV 20 mg PE/kg
	Levetiracetam IV 40-60 mg/kg (max dose 4500 mg)

Table 5. Refractory SE	
Adult	Midazolam, 0.2 mg/kg
	If seizures continue for another 5 min, repeat dose at 0.2 mg/kg and start infusion of 0.1 mg/kg/h
	If seizures continue for another 5 min, repeat dose at 0.2 mg/kg and increase infusion to 0.2 mg/kg/h
	Propofol, 1-2 mg/kg and start infusion at 20 mcg/kg/min (range 30-200 mcg/kg/min)
	Phenobarbital 20 mg/kg, infuse no faster than 60 mg/min (adults) or 30 mg/min (children) or 1 mg/kg/min
	Ketamine, 1-2 mg/kg and start infusion at 0.5 mg/kg/hr (range 0.5-10 mg/kg/h)
Children	Midazolam, 0.1-0.2 mg/kg, start infusion 0.1-0.4 mg/kg/hr and titrate to lowest effective dose up to 1 mg/kg/hr
	Phenobarbital 20 mg/kg, infuse no faster than 1 mg/kg/min
	Ketamine, 1-2 mg/kg and start infusion at 0.5 mg/kg/hr (range 0.5-10 mg/kg/h)

6. Pediatric Considerations

Etiologies of SE in infants, children and adolescents include those encountered in adults: meningoencephalitis, trauma, stroke, hypoxemia, toxidrome, hypoglycemia and other electrolyte or metabolic disturbance, and new onset epilepsy.[52] Particular to pediatrics are febrile seizures (30-50% pediatric SE) and underlying genetic or metabolic disorders, especially in the infant and younger child.[53] Hyponatremic seizures related to improper mixing of formula or the administration of free water to neonates are not uncommon. In the first weeks of life, infants with hypoparathyroidism and hypocalcemia can present with tetany or seizures. Abusive head trauma in infants and young children frequently presents with seizures, and a history of trauma is rarely disclosed. Patients with underlying structural brain abnormalities, particularly if they are associated with abnormal neurodevelopment, are at higher risk to develop epilepsy, and may present with SE. This includes acutely antecedent or remote brain injury. Brain tumors are the most common solid tumor of childhood and can cause seizures, especially if there is associated spontaneous hemorrhage. Neonatal SE is most often focal or multifocal and rarely generalized. Seizures in neonates are often subclinical and may instead present as altered mental status with tremor, extensor or flexor posturing, apnea, eye deviation and stereotypic automatisms such as tongue thrusting and lip smacking.[54] These movements do not respond to stimulation.

In pediatrics, antiseizure drugs are similar to those in adults, and early dosing of benzodiazepines is essential.[55] Importantly, the IV midazolam formulation can be given via IM, intranasal, or buccal routes, which is preferable to delaying treatment while obtaining IV access. Intranasal midazolam and IM midazolam are likely the most effective non-intravenous medications for SE.[56] The recent ESETT trial included children ≥2 years of age and found no difference between the efficacy of IV levetiracetam 60 mg/kg, IV fosphenytoin 20 mg PE/kg or IV valproate 40 mg/kg all administered over 10 minutes as second line agents after

adequate dosing with benzodiazepines.[28] Additional recent studies have demonstrated similar effects of phenytoin 20mg/kg and levetiracetam 40mg/kg in treating pediatric SE.[57]

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Throughout resuscitation, vigilance to ABCs and cardiopulmonary support is paramount, but preparations should be made for intubation if second-line drugs fail. Practice varies between institutions, and some will trial a second second-line drug if the first fails, but third-line continuous intravenous infusions in children with refractory SE should not be delayed, as doing so may unnecessarily prolong SE and contribute to refractory SE. The risks of poor outcome and mortality increase with SE duration. High-dose midazolam infusion or pentobarbital are generally preferred over propofol in children because of concerns regarding PRIS, though propofol use during inter-hospital transport may be requested depending on patient's age and diagnosis.[40,59] Similar to adults, ketamine is also being used more frequently in children to treat refractory status epilepticus and may be considered.[60,61]

Prior knowledge of facility capabilities and identification of a center with expertise caring for neurocritically-ill children is important, as children are at risk for etiologies that may require pediatric multi-subspecialty care. Children with prolonged coma or postictal state, and those requiring intubation for SE, require EEG evaluation to rule out transition to non-convulsive SE, ongoing SE under paralysis, or titrate a third-line agent to suppress cortical electrical activity. Consultation with a pediatric intensivist or neurologist can be helpful in identifying additional measures that may be taken beyond the generally efficacious resuscitation outlined previously, in choosing a second- or third-line agent or titrating high-dose benzodiazepines or barbiturates and managing the invasive mechanical ventilation and blood pressure support typically required. If the child has a history of refractory epilepsy and is cared for by an epileptologist at a tertiary or quaternary pediatric center, they may have specific insight into what has worked for this child's seizures previously.

7. Nursing Considerations

Initial nursing care begins immediately at seizure onset. Safety is a primary focus of nursing care in the patient with seizures. Safety measures include placing the patient in lateral recumbent position, keeping the head of the bed elevated, padding the side rails of the bed and having suction supplies available at bedside. It is important not to restrain patients or insert anything into the patient's mouth as this can cause further injury.[62] Supplemental oxygen should be applied if the

patient becomes hypoxic. Vigilant monitoring of vital signs should be maintained so that instability can be treated to prevent secondary injury.

Concurrent with initial resuscitation, the nursing staff should obtain an initial neurologic examination that includes a baseline level of consciousness, pupillary evaluation, and assessment for any focal deficits. It is important to monitor and document the type of seizure activity including precipitating factors, the description of the seizure including sensory, motor and behavioral activities and the length of the seizure activity.[62] The nursing staff should be prepared to obtain IV access and administer antiseizure medications and continuous infusion anesthetics promptly at the direction of the provider team.

Nursing knowledge of medications and anticipation of potential diagnostics and procedures can save precious time in the care of the seizing patient. Nursing should ensure adequate IV access for administration of medications, monitor for response and the patient's ability to protect the airway and prompt completion of ordered diagnostics to determine etiology of seizures. The role of the nurse includes ensuring diagnostics proceed in parallel with treatment, including laboratory testing, facilitating EEG testing and neuroimaging as needed.

Nursing report between the ED and inpatient teams is imperative and communication should include a description of the type and duration of seizures, medications given, pending medications that need to be given, positive or negative response to medications already given, respiratory and hemodynamic status and what tests still need to be obtained.

8. Patient Transport

Medications, especially continuous infusions, should be continued during transport. Prescribers should ensure that patients do not miss doses of scheduled antiseizure drugs if they are scheduled for a prolonged procedure or even during transport to and during neuroimaging. Communication to the transport provider should clarify that doses should not be decreased or stopped. If possible, transport should be avoided until the patient is clinically stable as this may require disconnecting the patient from EEG and potentially missing nonconvulsive seizures. Vasopressors may be needed during transport if the patient's blood pressure is fluctuating or if continuous infusion anesthetics were recently bolused or initiated.

9. Pregnancy

Status epilepticus during pregnancy is a rare occurrence that carries a significant risk to both the mother and the fetus necessitating prompt diagnosis and treatment. The etiology of SE during pregnancy is varied, with eclampsia as the most common cause followed by underlying epilepsy, posterior reversible encephalopathy syndrome (PRES), reversible vasoconstriction syndrome (RCVS), venous sinus thrombosis, subarachnoid hemorrhage, stroke, encephalitis, tumor, and metabolic derangement.[63]

There are no guidelines for the treatment of SE during pregnancy. The general consensus is to follow the standard SE treatment algorithm with special considerations regarding the underlying etiology of SE and the teratogenicity of particular anti-seizure drugs. Benzodiazepines remain the first line agent for SE during pregnancy except for eclampsia, for which the first-line treatment is intravenous magnesium sulfate. Many second-line anti-seizure drugs are associated with increased risk of teratogenicity and should be used with caution particularly during the first trimester of pregnancy. Valproate exposure carries the highest risk of major congenital malformations followed by phenobarbital and phenytoin.[64] Newer anti-seizure drugs such as lamotrigine and levetiracetam have the lowest risk of congenital malformations.[65]

Pharmacokinetics of anti-seizure drugs are altered in pregnancy, including increased volume of distribution, changes in absorption, elevated renal excretion, and induction of hepatic metabolism.[61] These changes can result in reduced serum concentrations of anti-seizure drugs and necessitate frequent drug level checks in order to assure appropriate therapeutic dosing.

10. Communication

When communicating to an accepting or referring physician about an SE patient, consider including the key elements listed in Table 5 and relaying them to all relevant healthcare providers who are caring for the patient (i.e., accepting physician, resident/advanced practice provider, nurse, pharmacist). The nursing report should also include these key elements.

Table 6 Status Epilepticus communication regarding assessment and referral
☐ Clinical presentation
☐ Duration of status epilepticus
☐ Relevant past medical history/past surgical history
☐ Relevant labs, including anticonvulsant levels if drawn
☐ Prior medications, medications given so far (and outcomes ie; seizures resolved after drug X, no effect from drug Y)
☐ Neurological examination
☐ Brain imaging/lumbar puncture/other results (if available)

Clinical Pearls

Clinical Pearls: Management
• Early, aggressive management of patients with SE is imperative. Delay of therapy reduces the likelihood of seizure termination.
• Benzodiazepines are frequently underdosed for initial therapy, and should be dosed aggressively in SE.
• Continuous EEG is recommended for the management of ongoing SE and should be assessed frequently to monitor treatment effects; the optimal goal (seizure termination vs. burst suppression vs. complete suppression) is unknown at this time.
• Diagnostic workup should proceed in parallel with initial and urgent treatment and should continue until a source of seizures is identified.

Clinical Pearls: Medication
• Benzodiazepines such as lorazepam IV or midazolam IM (if no IV access) are first-line treatment agents for SE.
• Fosphenytoin is the prodrug of phenytoin; it can be administered more rapidly than phenytoin, is compatible in more solutions, is not formulated with propylene glycol, and can be administered IM.
• Fosphenytoin, levetiracetam, and valproic acid have comparable rates of seizure cessation in patients with SE who have failed a benzodiazepine (<50%).
• Antiseizure medication levels should be monitored frequently (typically daily during active SE) and titrated to the higher end of normal; free levels should be assessed if available (i.e., phenytoin and valproic acid); antiseizure levels for medications the patient was known to be taking (or prescribed) should be checked at presentation to assess for nonadherence or subtherapeutic levels.
• Drug/tube feed interactions, renal and hepatic dysfunction, and medication-adverse event profile should be considered when initiating and up-titrating antiseizure drugs.

Starred References

**4 (Treiman, et al): *This is one of the few randomized controlled trials conducted in SE. It established benzodiazepines as first line therapy. It also demonstrated that seizure termination efficacy diminishes with each additional agent*.

**7 (Alldredge, et al): *This study demonstrated the efficacy of benzodiazepines in the treatment of SE. In addition, the study provided useful information about the side effects of benzodiazepines in SE, particularly that there were actually more respiratory and circulatory complications in the placebo group over both lorazepam and diazepam*.

**15 (Silbergleit, et al): *This study compared midazolam IM to lorazepam IV. The results established IM midazolam as a non-inferior first line treatment option for SE*.

*20 (Brophy, et al): *These are the NCS guidelines for the management of status epileptics. They provide an in-depth overview of the diagnosis and treatment of SE*.

*41 (Claassen, et al): *This was a systematic analysis comparing the most commonly used continuous infusion anesthetics, midazolam, propofol, and pentobarbital. This review provides a comparison of agent safety and efficacy in RSE and super refractory SE*.

**28 (Kapur J, et al): *This was a randomized clinical trial that compared IV fosphenytoin, IV valproic acid, and IV levetiracetam for status epilepticus in adults and pediatrics. There was no difference in efficacy between the three treatment arms.*

**58 (Sharpe C, et al). This was a randomized, multicenter trial comparing levetiracetam (40-60 mg/kg) and phenobarbital (20-40 mg/kg) as first line treatment for neonatal seizures of any cause. The 24-hour seizure cessation rate was higher with phenobarbital than with levetiracetam.*

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