Seizure Disorders Care Guide

May 2023

CALIFORNIA CORRECTIONAL HEALTH CARE SERVICES

Information contained in the Care Guide is not a substitute for a health care professional's clinical judgment. Evaluation and treatment should be tailored to the individual patient and the clinical circumstances. Furthermore, using this information will not guarantee a specific outcome for each patient. Refer to "Disclaimer Regarding Care Guides" for further clarification.

https://cchcs.ca.gov/clinical-resources/

Summary

GOALS

- Identify and classify type of seizure
- Avoid drug-drug interactions
- Minimize seizures through appropriate therapy
- Minimize adverse events, including potentially avoidable hospitalizations

ALERTS

- Signs and symptoms of drug toxicity
- Seizures lasting more than 5 minutes
- Patients with traumatic brain injury (TBI), structural brain abnormalities on neuroimaging are not good candidates for AED withdrawal
- Contraception, pregnancy, and menopause
- Monitor "Vitamin D, 25-hydroxy" in patients taking AEDs, Carbamazepine, Phenytoin, Primidone, and Valproic acid for ≥ 2 years

TREATMENT OPTIONS

Initiating Medication

- Medication is not indicated after a first seizure in most patients. Evaluate need for therapy on an individual basis.
- Offer AEDs after first tonic-clonic seizure if:
  1. Prior history of absence, myoclonic or focal seizures
  2. Congenital neurologic defect
  3. Electroencephalography (EEG) with epileptic discharge
  4. Recurrence risk unacceptable to patient
- Medication selection is dependent in part on seizure class and epilepsy syndrome.
- Optimize monotherapy before considering second agent.
- Encourage adherence, monitor side-effects, ensure good control is maintained and educate patient.
- AEDs usually not indicated for provoked seizures. Treat underlying cause if possible. Discontinue prophylactic AEDs unless seizures reoccur.
- Monitor dental side effects of the medication, i.e., gingival hyperplasia, periodontal disease, increase caries risk.

Drug-Resistant Seizures

- If seizures are uncontrolled, or patient is not seizure free at maximally tolerated doses of initial AED, consider changing to a different first line AED. Titrate new medication to therapeutic level prior to tapering initial AED.
- Consider psychogenic nonepileptic seizure diagnosis. Pseudoseizures may have physiologic or psychogenic etiology.
- E-consult neurology if seizures are not well controlled on two medications.

CDCR Housing/Activity Restrictions

- Complete a CDCR 7410, Comprehensive Accommodation Chrono for bottom bunk.
- Consider lower tier also in selected cases.
- Issue restrictions on driving, operating heavy equipment, working with heat, and working at heights.

Status Epilepticus

- The principal goal of treatment is to emergently stop seizure activity. The initial treatment strategy includes simultaneous assessment and management of airway, breathing, and circulation (obtain intravenous access, administer O2, and secure the airway as needed), check vital signs, finger stick glucose, seizure abortive drug treatment (i.e., lorazepam) and emergent transport to a higher level of care

MONITORING

- Measure baseline CBC, BUN/creatinine, LFTs, electrolytes, and albumin prior to starting AED therapy.
- Monitor CBC

- Monitor for adverse effects and assess medication adherence
- Obtain AED level to establish baseline when stable dose is achieved for agents where drug levels are useful to monitor adherence or when seizure control changes. (AEDs are sometimes drugs of abuse in CDCR/CCHCS.)
- Primary Care Provider (PCP) follow-up frequency will vary on case-by-case basis. Well-controlled patients may be seen at 180-day intervals.
- Regular dental evaluations to monitor oral side effects of medication.
- AED dosing is based primarily on side effects and seizure control, rather than AED levels.

EVALUATION

Diagnosis

Epilepsy is a neurologic disorder characterized by recurring seizures (altered cerebral function due to excessive and abnormal electrical discharges of brain cells).

Differential Diagnosis

Acute symptomatic or "provoked" seizures: seizures which occur in the setting of stroke, traumatic brain injury, metabolic derangement (e.g., hypoglycemia, hyponatremia, drug/alcohol withdrawal, drug intoxication, medications, and encephalitis). Unless seizures recur, they are not considered epilepsy.

Nonepileptic paroxysmal disorders: syncope, psychological disorders, sleep disorders, paroxysmal movement disorders, migraine, miscellaneous neurologic events. In the elderly: transient ischemic attack, transient global amnesia, drop attacks.

Classification

- Identify seizure type and/or epilepsy syndrome.
- Distinguish between focal or generalized seizures.

Clinical Factors and Diagnosis

- Identify what happened before, during, and after the attack as well as any potential triggers.
- EEG if epilepsy is suspected.
- For new onset seizure, perform magnetic resonance imaging (MRI) of the head without and with contrast if epilepsy is suspected.
- Computed tomography (CT) head without contrast is preferred in new-onset posttraumatic seizure, for urgent assessment, or when MRI is contraindicated.

History

- Obtain past medical history of seizures. Attempt to obtain pre-incarceration history and medical records.
- Identify seizure type or description, number, and frequency of seizures.
- Assess for changes in seizure control.

Medication Review

- Assess drug adherence: Failure to respond to usual AEDs should prompt a review of epilepsy diagnosis and adherence to medication(s).
- Consider drug interactions when new medications are added, AEDs are added or changed, or seizure control changes.
- Monitor for adverse effects/toxicity, drug interactions, efficacy, and AED levels when indicated.

Diagnostic Evaluation

- EEG has limited use in management of chronic seizures/epilepsy.
- Consider EEG with changes in patient's seizure pattern or class or worsening mental status.
- Neuroimaging: Perform emergently when a new focal deficit, persistent altered mental status, fever, acute head trauma, intractable headache, history of cancer, or suspected immune deficiency is present.

AED Discontinuation and Withdrawal

- Discontinuation of AEDs in patients with clearly established seizure disorders is not generally recommended due to the high risk of seizure recurrence, even after long seizure free intervals on therapy.
- When discontinuation of AED is considered (e.g., for patient in whom epilepsy diagnosis is unclear or those who have been seizure free for two years), most schedules aim for a six to nine month taper, with dose reductions at three-month intervals. More rapid tapers have been studied but are associated with higher rates of seizure recurrence.

SEIZURE TYPES

PSEUDOSEIZURES OR PSYCHOGENIC NONEPILEPTIC SEIZURES

DEFINITION: Psychogenic nonepileptic seizures (PNES) are episodes of movement, sensation, or behaviors resembling epilepsy unaccompanied by physiologic central nervous system dysfunction.

DIAGNOSIS:

- Often misdiagnosed with epilepsy (epilepsy may also be present in 5-10% or more of PNES patients). More than 2/3rds of PNES patients are female.
- Diagnosis is based on a constellation of findings, the probability of PNES increases with the number of features unusual in epilepsy. Detailed history, physical examination, observation during seizures, and psychological evaluation are required for diagnosis.
- Video-electroencephalography (vEEG) is useful for diagnosis of PNES. Observation of typical seizures without accompanying EEG abnormalities is diagnostic.

FINDINGS SUGGESTIVE OF PNES

Clinical Features

- Gradual onset of seizures
- Long seizure duration (2-3 minutes or more)
- Waxing and waning symptoms during seizure, non-physiologic progression
- Disorganized, asymmetrical motor activity, side to side head movements, pelvic movements (especially thrusting), opisthotonos
- Eyes often closed, resistance to eye opening during seizure (highly suggestive of PNES)
- Ictal crying, weeping
- Seizures triggered by suggestion
- Rapid recovery after seizure, awake and oriented
- Rare incontinence, tongue biting on tip (not side of tongue)

Historical Features

- High seizure frequency
- No response to AEDs or possibly increases in seizures with AED therapy
- Associated psychiatric disorders
- History of sexual or physical abuse
- No history of injury from seizures
- Recurrent status epilepticus with frequent emergency room visits or hospitalizations
- Failure to respond to therapy for status epilepticus
- Seizures occur only when alone or only when others are present

Treatment of PNES

- Thoughtful approach to informing patient of diagnosis
- Withdrawal of prescribed AEDs
- Treatment of underlying psychological disorders

NEW ONSET SEIZURE

Diagnostic evaluation of patients with first time seizures:

- Establish whether or not the event was a seizure. Obtain a complete description of the seizure including behaviors, movements, duration, level of consciousness, etc. (both ictal & postictal), from the patient and observers.
- Consider possible correctable systemic problems such as an acute medical condition (e.g., hypoglycemia, hyponatremia), syncope, arrhythmia, neurologic illness, or injury (e.g., TIA, stroke, TBI, movement disorder, meningitis, anoxic encephalopathy).
- Perform and document a complete physical and neurological examination.
- Labs: Obtain blood tests to identify abnormalities in electrolytes, glucose, calcium, magnesium, hepatic and renal function, and a toxicology screen when clinically indicated.
  1. Depending on the clinical situation, a lumbar puncture may also be indicated to rule out infection, hemorrhage, etc.
  2. Serum prolactin measurement- Prolactin elevation (greater than 2 times baseline), measured 10 to 20 minutes after a suspected event, is a useful adjunct for the differentiation of generalized tonic–clonic or complex partial seizure from a psychogenic non-epileptic seizure but it is not sensitive enough to rule out epilepsy (i.e., does not distinguish an epileptic seizure from syncope).
  3. EEG: Perform an EEG if epilepsy is suspected. A Negative EEG does not rule out epilepsy.
     a) When indicated, the EEG should be completed soon after the seizure (within 2 weeks).
     b) Photic stimulation (to detect any light/visually triggered epileptic response) and hyperventilation should generally be part of the standard EEG assessment.
     c) Imaging: MRI should be performed if epilepsy is suspected. MRI with and without contrast is the modality of choice for brain imaging in most patients with epilepsy. CT has a role in the urgent assessment of seizures, or when MRI is contraindicated.
  4. Indications for referral/hospitalization at provider discretion:
     a) Patients presenting with a first unprovoked seizure
     b) Seizure characterized by a prolonged postictal state or incomplete recovery (status epilepticus)
     c) Seizure associated with a systemic illness that may require evaluation and treatment
     d) History of head trauma (loss of consciousness, retrograde/anterograde amnesia, mental status changes, vomiting)
- Seizure type: Seizure class and epilepsy syndrome are classified on clinical grounds, assisted by neurophysiologic and imaging studies. Seizure class has important implications in the choice of antiepileptic drugs.
- Medications: Carbamazepine, Phenytoin, and Valproic Acid are all formulary medications and can all be regarded as first-line for all seizure types

POST-TRAUMATIC SEIZURES

- Seizures following TBI:
  1. Older age (greater than 65 years) is a risk factor for post-traumatic epilepsy.
  2. The risk of post-traumatic epilepsy is slightly higher in women.
  3. Neuroimaging (MRI or CT) is indicated in all patients with a new seizure after trauma.
- Early seizures (occurring within first week after TBI) commonly due to intracranial hematoma, depressed skull fracture, and/or severe injury:
  1. 25% of early post-traumatic seizures occur within the first hour.
  2. 50% of early post-traumatic seizures occur within the first 24 hours.
  3. Although early seizures after TBI may not recur, patients are often treated with AEDs due to the risk of status epilepticus or aggravation of other injuries.
- Late seizures (occurring more than 1 week after TBI) are likely to represent epilepsy.
- Long term AED treatment is recommended after a first late post-traumatic seizure due to high rate of recurrence.
- Prophylactic AEDs are NOT recommended to prevent late seizures or post-traumatic epilepsy in patients who have NOT had a late post-traumatic seizure.
- The more severe the head injury, the longer the patient is at risk for late seizures.
- Approximately 80% of post-traumatic epilepsy develops within two years of a head injury.

- Patients with traumatic brain injury (TBI), structural brain abnormalities on neuroimaging are not good candidates for AED withdrawal.

STATUS EPILEPTICUS

- Status Epilepticus refers to the occurrence of a continuous unremitting clinical and/or electrographic seizure activity with a duration longer than five minutes, or recurrent seizure activity without recovery between seizures.
- Status epilepticus requires emergent, targeted treatment to reduce patient morbidity and mortality. Status epilepticus can lead to brain injury and must be treated without delay.
- Causes:
  1. Non-adherence with AED treatment
  2. Drug (alcohol, barbiturates, baclofen, and/or benzodiazepines) withdrawal syndromes
  3. Brain injury from trauma, subarachnoid hemorrhage, tumors or cerebral metastases, stroke, infection, cerebral anoxia, or hypoxia
- Metabolic disturbances (e.g., hypoglycemia, hepatic encephalopathy, uremia, pyridoxine deficiency, hyponatremia, hyperglycemia, hypocalcemia, hypomagnesemia)
- Prognosis: Depends most strongly on the underlying etiology and duration of the status.

SUDDEN UNEXPECTED DEATH IN EPILEPSY (SUDEP)

- Defined specifically as the sudden, unexpected, witnessed, or unwitnessed, non-traumatic, or non-drowning death in patients with epilepsy with or without evidence for a seizure, and excluding documented status epilepticus, in which autopsy does not reveal a structural or toxicological cause of death.
- SUDEP causes 2-18% of all deaths in patients with epilepsy and as high as 0.5-1% a year in those with refractory epilepsy. Noted risk factors:
  1. Frequent convulsive seizures (more than 1 per month)
  2. Medication non-adherence
  3. Subtherapeutic AED level
  4. Age 20 to 45 years
  5. Generalized tonic-clonic seizures
  6. Polytherapy
  7. Duration of epilepsy (more than 10 years)
  8. Alcoholism
  9. Male gender
- Possible etiologies suggested include:
  1. Cardiogenic. Ictal bradycardia and even asystole
  2. Pulmonary. Ventilator failure with ictal hypoxemia and hypercapnia
  3. Primary neurologic. Sudden, persistent cerebral electrical silence after a seizure
- Aggressive treatment of refractory epilepsy, including referral to a comprehensive epilepsy center and consideration of epilepsy surgery is appropriate in high-risk patients.

The American Epilepsy Society and the Epilepsy Foundation have determined that information regarding the risk of SUDEP should be disclosed to all patients with a diagnosis of epilepsy as part of a comprehensive educational program.

EPILEPSY: CONTRACEPTION, PREGNANCY, AND HORMONE REPLACEMENT THERAPY

- Preconception counseling is recommended to minimize risk of complications.
  1. Be aware of established drug-drug interactions between AEDs and oral contraceptive therapy.
     a) Contraceptive therapy failure may occur with AEDs, which are inducers of the cytochrome P-450 system.
- Folic acid supplementation (0.4 to 0.8 mg daily) is recommended for all women of child-bearing age to minimize the risk of neural tube defects.
  1. Women taking AEDs (especially Carbamazepine or Valproic Acid) are recommended to take 10 times the recommended dose of folate supplementation (4 mg daily) by the American College of Obstetrics and Gynecology.
  2. AEDs are associated with major fetal malformations (e.g., neural tube defects) and impaired cognitive outcomes in newborns.
- Prenatal screening for patients being treated with AEDs is recommended.

1. Determine need for AEDs and minimize AED dosing during pregnancy, while still controlling seizures.
   a) If possible, avoid Valproate and multi-AED therapy during the first trimester of pregnancy to reduce the risk of major congenital malformations.
   b) If possible, avoid Phenytoin and Phenobarbital during pregnancy to prevent cognitive impairment in the newborn.

- Monitor both total and free plasma AED levels during pregnancy; (Lamotrigine may need more frequent monitoring):
  1. At 5 to 6 weeks, 10 weeks, and then at least once each trimester.
  2. Also measure in the first or second week postpartum.
- Advise oral vitamin K supplementation (10 to 20 mg/day) in the last month of pregnancy for women taking enzyme-inducing AEDs (e.g., Phenytoin, Phenobarbital, Topiramate, Carbamazepine, Oxcarbazepine).
- Breast-feeding is not contraindicated with AED therapy, though use of Lamotrigine or sedating drugs may be exceptions.
- Among post-menopausal women, AED use is associated with greater bone density loss.

ANTIEPILEPTIC DRUGS

Many have important drug-drug interactions and potential adverse effects. While AED selection is typically done by a neurologist, PCPs should be aware of the important characteristics, interactions, and potential adverse effects of these common medications.

Generic Substitution:
The CCHCS pharmacy will switch from brand to generic medication unless “Do Not Substitute” and “Non-formulary” processes are followed.

Note: The American Academy of Neurologists does not recommend automatic generic substitution of AEDs without physician’s approval due to the variation allowed by the FDA between brand and generic medications. These small variations may have adverse effects for patients. However, generic substitution of AEDs may be appropriate with patient and physician approval.

AED Adverse Effects and Drug-drug Interactions:

1. AEDs have many side effects and drug interactions. Refer to product information for full details for specific drugs.
2. AEDs significantly interact with each other. Whenever an AED is added or removed from a treatment regimen, close monitoring for changes in efficacy or adverse effects of other AED agents is required.
3. AEDs significantly interact with many other medications. Review of product information is important when adding or changing medication regimens.
4. Anticonvulsants variably interact with many contraceptive medications. Refer to product information for full discussion. Alternate contraceptive methods are usually required.

- Therapy with anticonvulsants should not be abruptly discontinued to avoid rebound effects.
- Monitor for emergence/worsening of depression, suicidal thoughts/behavior, and/or unusual changes in mood or behavior.
- Monitoring of AED blood levels is often done inappropriately. In many cases, levels were obtained before steady state or without recording collection time. Furthermore, many levels were obtained without a clear medical indication. Levels are generally useful to monitor drug adherence or to identify an effective therapeutic level for a particular patient.

MEDICATION SELECTION

- The choice of AED is complex and though the American Academy of Neurology (AAN) and American Epilepsy Society (AES) released an evidence-based practice guideline for managing adult patients after a first unprovoked seizure in 2015, there are few head-to-head comparison trials to guide the choice of pharmacologic treatment. It is important to understand that both medication-and patient-related factors influence appropriate drug selection. The goal is to provide the best chance for seizure freedom with the lowest risk for potential side effects (i.e., tolerability).

- Patient Characteristics: Patient demographics including age, sex, and race should be considered. For example, prior to initiation with Carbamazepine, patients of Asian descent should be tested for the HLA B*1502 allele, which is associated with increased risk of Stevens-Johnson syndrome and toxic epidermal necrolysis. Treatment of women with epilepsy is a unique challenge as hormonal variations may affect seizure frequency, and there is always the concern of potential pregnancy in those of childbearing age and teratogenic risk based on available data must be considered and discussed. In addition, the interaction of AEDs and oral contraceptives is a frequent concern to discuss with the patient during AED selection.
- Seizure Characteristics: The treatment initiation decision is dictated by the circumstances of a patient's seizure event(s) (e.g., provoked versus unprovoked, single versus repeated episodes). AEDs are often divided into narrow spectrum medications that are useful in treating focal onset seizures or broad spectrum that are useful in treating both focal onset and generalized onset seizures.
- Medication Factors: The mechanism of action (MOA), half-life, drug-drug interactions, metabolism, and/or excretion and side effects of each AED should be considered. These factors can lead to poor tolerability, decreased adherence, increased morbidity, and worsened seizure control, which may increase a patient's risk of death.
- Side Effects: Drowsiness and cognitive impairment are common side effects of most AEDs although the degree of side effects varies among medication classes. Topiramate is more often associated with cognitive side effects, than in pairwise comparison are significantly worse than side effects of Carbamazepine, Lamotrigine, Levetiracetam, Oxcarbazepine, Phenytoin, and Valproic Acid. Side effects can be additive and can impact daily functioning among patients with baseline cognitive impairment.
- Ease of administration can greatly affect patient adherence to treatment. The use of an extended-release formulation should be considered when possible. Certain AEDs are available in liquid solution or intravenous formulation for patients with dysphagia.
- Cost Consideration: Many AEDs are available in generic formulations that can be considered first, if medically appropriate, and this should be addressed. Few AEDs with a narrow therapeutic index (NTI) for which small fluctuations in drug levels found in generic formulations may lead to lost efficacy at low doses or to side effects at high doses. Only Phenytoin and Carbamazepine are classified as NTI AEDs by the FDA.
- Combining Drugs and Rational Polypharmacy: Combination therapy should be considered if monotherapy fails. Before prescribing combination therapy, it is important to understand different AED mechanisms of action. The goal of combination therapy is to maximize efficacy and minimize adverse effects, termed rational polypharmacy to decrease the risk for toxicity and side effects. A good rule of thumb is to use an AED that could treat a comorbidity (e.g., headaches or a mood disorder) whenever possible, to limit polypharmacy. Using AEDs with different mechanisms of action provides superior efficacy of combination therapy versus lower efficacy when drugs with similar mechanisms of actions are combined (e.g., Phenytoin and Carbamazepine).
- AEDs and Special Populations: Patient groups (age older than 60 years, psychiatric conditions, liver and kidney disease, HIV infection, and patients with malignancies), may require avoidance of certain medication classes and dose adjustments. All comorbid conditions should be considered when choosing AED medications.

END OF SEIZURE DISORDERS CARE GUIDE SUMMARY