



EPILEPSY REVIEW

Marisha Trelinski, FNP-BC
Neuroscience Associates

HOW WILL YOU INTERACT WITH AN EPILEPSY PATIENT?

- **Well visit** at your primary care practice
- In **consultation** for other issues at your specialty practice
- **First time seizure** presenting at your pediatric practice
- Patient with seizures who establishes care at your **OB-GYN clinic**
- Patient who experiences **a fall after a seizure** and presents to your **urgent care**
- **Inpatient** on your service has a seizure
- Patient has a seizure in your **clinic's waiting room/exam room**

TYPES OF SEIZURES-QUICK REVIEW

- **Seizure types:**
 - **Simple partial-** no loss of awareness; could be a simple motor movement, sensory, visual or speech changes
 - **Complex partial-** loss of awareness, confusion; could be tonic/clonic movements, or behaviors like lip smacking
 - **Primary generalized-** occurs from both sides of the brain simultaneously; can be generalized tonic-clonic “grand mal” or absence “petit mal”
 - **Secondary generalized-** begins as a simple partial or complex partial seizure, but then spreads quickly to include both hemispheres and involves convulsions

SEIZURE CAUSES AND TRIGGERS

- The most common **causes** of seizures are: head trauma, stroke, brain tumor, brain infection, effects of drugs, alcohol intoxication, genetic causes (Tuberous sclerosis, mitochondrial diseases, etc.), and metabolic derangement (ex. hyponatremia), and idiopathic causes
- **Seizure triggers** may include: missed medication, lack of sleep, stress, alcohol, drug abuse (illegal drugs such as cocaine, amphetamines, and psychedelic drugs), interactions between prescription drugs, menstruation (for those with epilepsy), photosensitivity, stimulants (caffeine in high doses), over the counter medications such as diphenhydramine (Benadryl) (for those with epilepsy), pseudoephedrine or phenylephrine (cough and cold medicines)

DRUG MONITORING FOR SOME COMMON ANTIEPILEPTICS

- **valproic acid (Depakote)**
 - Therapeutic level 50-100 mcg/mL
 - Liver function baseline, platelets, coagulation at baseline, ammonia
 - Adverse reactions: hepatotoxicity, pancreatitis, SIADH, hyponatremia
- **lacosamide (Vimpat)**
 - Creatinine at baseline, ECG at baseline if conduction issue or severe cardiac disease
 - Adverse reactions: PR prolongation, AV block, ventricular tachyarrhythmias, afib
- **lamotrigine (Lamictal)**
 - Drug levels (baseline while not pregnant, monthly during pregnancy and postpartum), creatinine at baseline
 - Adverse reactions: severe rash, Stevens-Johnson syndrome, toxic epidermal necrolysis
- **oxcarbazepine (Oxtellar XR, Trileptal)**
 - Creatinine at baseline
 - Adverse reactions: hyponatremia, SIADH, anaphylaxis, angioedema
- **phenobarbital**
 - Therapeutic level 10-40 mcg/mL; toxic >50 mcg/mL
 - Creatinine at baseline, folate, CBC, liver function
 - Adverse reactions: respiratory depression, erythema multiforme, Stevens-Johnson syndrome
- **phenytoin (Dilantin)**
 - Therapeutic level 10-20 mcg/mL (total), 1-2 mcg/mL (free); toxic >20 mcg/mL
 - Baseline creatinine, CBC, liver function tests
 - Adverse reactions: bradycardia, hepatotoxicity, thrombocytopenia, pancytopenia

ANTIEPILEPTIC DRUG INTERACTIONS TO AVOID (SOME EXAMPLES-NOT AN ALL INCLUSIVE LIST)

Antiepileptic	Drug interaction	Effect	Practice
carbamazepine (Carbatrol, Tegretol)	Oral contraceptives	Induces estrogen metabolism; Reduces effectiveness of contraception	Avoid combination; ensure females are taking folic acid supplementation
	Antibiotics: clarithromycin, erythromycin, troleandomycine	Inhibits carbamazepine metabolism causing elevated serum levels	Avoid macrolide antibiotics that inhibit CYP3A4
lamotrigine (Lamictal)	Oral contraceptives	Induces lamotrigine metabolism; reduces serum concentration and seizure control	Avoid combination; follow lamotrigine levels, increase dose of lamotrigine
Valproic acid (Depakote, Depakene)	phenobarbital	Inhibits phenobarbital metabolism; could cause toxic phenobarbital level	Avoid combination, reduce phenobarbital; follow levels
Carbamazepine (Tegretol), phenobarbital, phenytoin (Dilantin), primidone (Mysoline)	warfarin (Coumadin)	Induces warfarin metabolism, reducing serum concentration of warfarin that would make it ineffective as an anticoagulant	Avoid combination, increase warfarin dose to maintain therapeutic INR

CBD AND EPILEPSY

- **Cannabis** is also known as marijuana. Marijuana refers to the leaves and female flowers of the cannabis plant. Medical cannabis is whole plant marijuana or chemicals in the plant used for medical purposes.
- **Cannabinoids** are substances in cannabis that act on cells in the body. Two major cannabinoids include tetrahydrocannabinol, or **THC**, which **causes psychoactive effects** like ("getting high") and cannabidiol, or **CBD**, which **does not cause psychoactive effects**.
- **United States Pharmacopeia (USP) standards** do not exist to provide the identity, purity, or quality of any cannabis product. There are **over 80 active compounds derived from the cannabis plant** with various pharmacologic actions. To develop guidelines for use of cannabis products, an evidence-based approach has to be taken regarding the development and application of the products.
- **Epidiolex is a plant-based formulation of CBD**; approved by the FDA to treat seizures for people 2 years of age and older with **Dravet syndrome** (rare, drug resistant epilepsy that causes prolonged seizure with fever) and **Lennox-Gastaut syndrome** (severe form of epilepsy; multiple types of seizures, intellectual development impaired)
- Epidiolex testing: Randomized double-blind, placebo-controlled trial completed at 30 clinical centers:
 - People with LGS (age range 2 to 55 years) who had had two or more drop (atonic) seizures each week during a 28-day baseline period were included. They were randomly selected to receive CBD oral solution at a dose of either 20 milligram per kilogram of body weight or 10 milligram per kilogram of body weight or placebo.
 - During the treatment period, drop seizures decreased from baseline by:
 - 41.9% in the 20-mg CBD group
 - 37.2% in the 10-mg CBD group
 - 17.2% in the placebo group
- The most common side effects of CBD included **sleepiness, diarrhea, fatigue, and decreased appetite**.



CBD AND EPILEPSY

- CBD is an inhibitor of CYP3A4 and CYP2D6
 - CYP3A4 metabolizes about a quarter of all drugs; **CBD may increase serum concentrations** of drugs like macrolides, calcium channel blockers, benzodiazepines, antihistamines, haloperidol, antiretroviral, and some statins
 - CYP2D6 metabolizes some antidepressants; CBD **may increase serum concentrations** of SSRIs, tricyclic antidepressants, antipsychotics, beta blockers, and opioids
 - Examples of antiepileptic interactions with CBD: clobazam (Onfi) (raises serum metabolites), valproic acid (Depakote) (increases liver enzymes)

CBD AND EPILEPSY

American Epilepsy Society Position Statement on Cannabis as a Treatment for Patients with Epileptic Seizures

- “Persons with epilepsy must use caution because there is a vast array of other cannabis products, and availability is dependent on individual state laws. Of importance, **the purified, pharmaceutical formulation of CBD described above cannot be obtained from a marijuana dispensary.** When patients purchase cannabis-based products from a dispensary, it is extremely important to understand that the product they select, **may not contain just CBD, but also other phytocannabinoids such as THC (which is psychoactive), pesticides, and other dangerous impurities, of which the concentrations are unknown.** Independent laboratory testing of samples of cannabis products have shown that the labels on products in the dispensaries claiming to have **a certain percentage of CBD or THC are often incorrect.**”
- “AES urges that cannabis’ status as a Federal DEA Schedule 1 controlled substance be reviewed. **AES’s call for rescheduling is not an endorsement of the legalization of cannabis, but is a recognition that the current restrictions on the use of cannabis products for research continue to stand in the way of scientifically rigorous research into the development of cannabis-based treatments.** We also encourage USP to continue its efforts to establish recognized guidance for cannabis as well as individual, therapeutically promising cannabinoids.”

AES Position Statement on Cannabis as a Treatment for Patients with Epileptic Seizures. (2019, February 19). Retrieved February 1, 2020, from [https://www.aesnet.org/about_aes/position_statements/AES Position on Medical Marijuana](https://www.aesnet.org/about_aes/position_statements/AES%20Position%20on%20Medical%20Marijuana)

FUTURE OF CANNABIS FOR MEDICAL USE IN SC

- SC Compassionate Care Act
- Sponsors: Senators Davis, Hutto, McLeod and Kimpson
- Introduced in the Senate on January 15, 2019
- Currently residing in the Senate Committee on Medical Affairs

CBD AND EPILEPSY

In summary:

- CBD oil available online and from local stores has variable purity and ingredients that cannot be verified
- Currently, there are no evidence based guidelines for dosing of CBD oil (available online and from local stores)
- More research on CBD is needed
- Epidiolex, for now, is mostly for LGS and Dravet Syndrome. Insurance coverage for Epidiolex outside these diagnoses is unpredictable.
- **Effectiveness of CBD oil (available online and bought from local stores) in reducing seizure frequency in my patients has been variable. Most patients have stopped taking CBD oil due to cost and no perceivable benefit.**

CONSIDERATIONS FOR FEMALES WITH EPILEPSY



- **Menstrual cycle**
 - seizures may increase around a woman's menstrual cycle
- **Contraception**
 - Oral contraception may **lower lamotrigine** (Lamictal) levels; many AEDs may **decrease the effectiveness of oral contraceptives**
 - To avoid decreasing effectiveness of an AED, females should take a birth control with at least 50 micrograms of ethinyl estradiol (estrogen); and or consider long-acting forms of contraception that are not affected by seizure medicines, such as IUDs, hormone injections (Depo-Provera), or an implant.
- **Osteoporosis**
 - 10 million Americans have osteoporosis; of those, 8 million are women
 - Patients who have taken phenytoin (Dilantin), carbamazepine (Tegretol, Carbatrol), primidone (Mysoline), and/or valproic acid (Depakote) are at increased risk for developing osteoporosis and fractures
 - **Calcium**-Women under 50 need 1000 mg calcium daily; 50 and older should get at least 1200 mg calcium daily
 - **Vitamin D**-Vitamin D is needed for best calcium absorption; Women under 50 need 400 to 800 international units (IU) daily; Women over 50 need 800 to 1000 IU daily
 - Consider **bone density testing** (DEXA scan)

CONSIDERATIONS FOR FEMALES WITH EPILEPSY CONTINUED

- **Pregnancy**

- If women do not have an adequate amount of folic acid early in their pregnancy, they are more likely to have babies with birth defects; specifically neural tube defects. All women in childbearing age should consume 400 micrograms (mcg) or 0.4 milligrams (mg) of folic acid daily. For women with epilepsy, **4 mg of folic acid daily is recommended.**
- The risk of having a baby with a birth defect in the general population is 2 to 3%; in females with epilepsy who take an antiepileptic drug, the risk is 4 to 6%
- Antiepileptic drug levels should be monitored during pregnancy

- **Antiepileptic drugs to avoid in pregnancy**

- when valproic acid (Depakote) is taken during pregnancy, there is 1% to 2% risk of neural tube defects (lack of spinal cord closure) and an overall 10% risk of causing any major congenital malformation. Women who take valproic acid during pregnancy are more likely to have children with lower IQ and an increased risk of autism.
- topiramate (Topamax) taken during early pregnancy increases the risk of having an infant with cleft lip or palate

- **After delivery**

- Change diapers on the floor, bathe the infant with other adults present; consider sponge bathing
- Get adequate sleep after the baby is born to reduce the risk for breakthrough seizures
- Have drug levels monitored after delivery of the baby as medication levels may need to be adjusted

- **Breastfeeding**

- Antiepileptic drugs are present in breast milk; however, breastfeeding should be encouraged. The baby has been exposed to the drugs throughout the pregnancy; the amount of exposure to the drug during breastfeeding is small

OTHER TREATMENTS FOR SEIZURES

- Dietary therapies
- Vagal nerve stimulation (VNS)
- Responsive neurostimulation (RNS)
- Deep brain stimulation (DBS)
- Epilepsy surgery



HOSPITAL DISCHARGE BEST PRACTICE FOR SEIZURE PATIENTS

- Was your patient started on a **NEW antiepileptic medication** during hospitalization?
 - Consider your patient's type of insurance coverage; will they be able to afford this medication?
 - Contact/visit neurology on call NP (2C area) to inquire about AED drug cards
 - Avoid discharging a patient with a new medication on Friday or the weekend as their insurance company may want a prior authorization before covering this medication
- Did you or someone else provide enough **medication refills** to bridge your patient to neurology or primary care follow up?
- Was your patient and family counseled regarding **seizure precautions**?
 - i.e. Per SC State Law, an individual must be seizure free for 6 months in order to drive, do not take tub baths or go swimming alone, avoid climbing heights or operating dangerous equipment

Visit epilepsy.com/FirstAid to learn more

SeizureFirstAid

What to do in the event of a seizure

1

STAY with the person until they are awake and alert after the seizure.

- Start timing the seizure
- Remain calm and check for medical ID.



2

Keep the person **SAFE**.
Move or guide away from **harmful objects**.



3

Turn the person onto their **SIDE** if they are not awake and aware.

- **Don't block airway**, put something small and soft under the head, loosen tight clothes around neck.

Do **NOT** *restrain*.



Do **NOT** put any objects in their mouth.

- Rescue medicines can be given if prescribed by a health care provider.



Call 911:

- ▲ Seizure lasts longer than 5 minutes
- ▲ Repeated seizures
- ▲ Person is injured, pregnant, or sick
- ▲ Difficulty breathing
- ▲ First time seizure
- ▲ Seizure occurs in water
- ▲ Person does not return to their usual state

© 2019 Epilepsy Foundation of America, Inc.



SEIZURE FIRST AID

PROVIDER, PATIENT, AND FAMILY RESOURCES

International:

The International League Against Epilepsy

<https://www.ilae.org>

National:

American Epilepsy Society

<https://www.aesnet.org>

Epilepsy Foundation

<https://www.epilepsy.com>

Local:

South Carolina Advocates for Epilepsy (SAFE)

<https://www.scepilepsy.org>

REFERENCES

AES Position Statement on Cannabis as a Treatment for Patients with Epileptic Seizures. (2019, February 19). Retrieved February 1, 2020, from [https://www.aesnet.org/about_aes/position_statements/AES Position on Medical Marijuana](https://www.aesnet.org/about_aes/position_statements/AES_Position_on_Medical_Marijuana)

Johannessen, S. I., & Landmark, C. J. (2010). Antiepileptic Drug Interactions - Principles and Clinical Implications. *Current Neuropharmacology*, 8(3), 254–267. doi: 10.2174/157015910792246254

Medical Cannabis - doh. (n.d.). Retrieved March 5, 2020, from [https://doh.dc.gov/sites/default/files/dc/sites/doh/publication/attachments/Medical Cannabis Adverse Effects and Drug Interactions_0.pdf](https://doh.dc.gov/sites/default/files/dc/sites/doh/publication/attachments/Medical_Cannabis_Adverse_Effects_and_Drug_Interactions_0.pdf)

Patel, A., & Kiriakopoulos, E. (2019, May 31). Medical Marijuana and Epilepsy. Retrieved February 1, 2020, from <https://www.epilepsy.com/learn/treating-seizures-and-epilepsy/other-treatment-approaches/medical-marijuana-and-epilepsy>

Shafer, P.O., & Sirven, J.I. (2020, Feb 28). About Epilepsy: The Basics. Retrieved February 1, 2020, from <https://www.epilepsy.com/learn/about-epilepsy-basics>

Silvestro, S., Mammanna, S., Cavalli, E., Bramanti, P., & Mazzon, E. (2019). Use of Cannabidiol in the Treatment of Epilepsy: Efficacy and Security in Clinical Trials. *Molecules*, 24(8), 1459. doi: 10.3390/molecules24081459

Wirrell, E., & Shafer, P.O. (2019, Nov. 12). First Aid for Seizures - Stay, Safe, Side. Retrieved February 10, 2020, from <https://www.epilepsy.com/learn/seizure-first-aid-and-safety/first-aid-seizures-stay-safe-side>

Zagnoni, P. G., & Albano, C. (2002). Psychostimulants and Epilepsy. *Epilepsia*, 43, 28–31. doi: 10.1046/j.1528-1157.2002.043s2028.x

Ziemba, K. (n.d.). Bone Health. Retrieved February 10, 2020, from <https://www.epilepsy.com/learn/challenges-epilepsy/bone-health>

2019-2020 Bill 366: SC Compassionate Care Act - South ... (n.d.). Retrieved March 5, 2020, from https://www.scstatehouse.gov/sess123_2019-2020/bills/366.htm