Fits, Faints and Fosphenytoin: Pediatric Seizures

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Objectives

- Review common seizure types and epilepsy syndromes seen in children
- Review current medical therapies for epilepsy in children
- Review additional epilepsy therapies including diet, surgery, and alternative medications
Overview

• Seizure and Epilepsy definitions
• Specific Pediatric Syndromes
• Differential Diagnosis of Seizures
• Treatment options
  • “Old” Medications
  • “Newer” medications
  • Cannabinoids (CBD)
  • Ketogenic diet
• Surgery
  • Vagal Nerve Stimulator (VNS)
  • Resection
Brain Complexity

Billions of neurons in our brains that make trillions of connections with each other

Problems happen......
Seizure

An electrical discharge of neurons in the brain that causes an observable change in behavior
Epilepsy

2 or more unprovoked seizures

Classification:
- Generalized
- Partial
  - Simple
  - Complex
EEG (electroencephalogram)

Records electrical activity of the brain

Can be used to determine if normal patterns are present
Example, age related patterns

Can be used for epilepsy-related patterns
Example: spikes, sharp waves
Useful for diagnosis of type of epilepsy and specific syndromes
Generalized Seizures
Childhood Absence Epilepsy

Clinical presentation of staring spells

“petit mal”

Age 4-10

Characteristic EEG changes

Most patients outgrow syndrome by age 11-15
Generalized Tonic Clonic (GTC)

“The Big One”
Stiffness (tonic phase) followed by rhythmic shaking (clonic phase)
Longer than 5 minutes a medical emergency (status epilepticus)
- treatment lorazepam (Ativan), valium (Diastat), fosphenytoin

Can be as a GTC or start focally and spread to become GTC
Infantile Spasms

Typically start around age 6 months
“Startle”-like movements
One common cause is tuberous sclerosis
EEG- hypsarrhythmia

Treatments
- ACTH
- vigabatrin
- topiramate (Topamax)
Hypsarrythmia

Figure 1. Hypsarrythmia in a 4-month-old female infant with cryptogenic infantile spasms.
Lennox-Gastaut Syndrome

Multiple Seizure types
- “Atypical” Absence Seizures
- Tonic Seizures (during sleep)
- Atonic Seizures

Abnormal development, mental retardation
Specific EEG Changes
Generally occurs before age 10
Juvenile Myoclonic Epilepsy (JME)

Generalized Epilepsy
- Absence Seizures
- GTC Seizures
- Myoclonic jerks (AM often)

Tends not to remit

Usually easily treated with valproic acid (Depakote) or levetiracetam (Keppra)
Juvenile Myoclonic Epilepsy
Focal (Partial) Seizures

- Simple
- Dyscognitive (Complex)
  - altered mental status
Benign Rolandic Epilepsy (BRE)

- Benign epilepsy with centro-temporal spikes (BECTS)
- Diagnosis based on clinical presentation and EEG
- Relatively common
- Often nocturnal seizures
- Starts age 2-12 years, most 5-10 years
- Most patients grow out of it by age 16
Excess Mortality Rate of Epilepsy Patients who have Seizures ≈ 1%

- Olafsson et al. Epilepsia 1998

Diagram: Proportion surviving over years from diagnosis.
Sudden Unexpected Death in Epilepsy (SUDEP)

- the patient has epilepsy
- died unexpectedly while in reasonable health
- fatal attack occurred suddenly
- death occurred during normal activities
- obvious medical cause cannot be found
- excluded in status epilepticus or acute trauma
Mimickers of Epilepsy

- Breath-holding spells
- Syncope
- Hemiplegia
- Migraine
- Movement Disorders
- Febrile Seizures
- “Pseudoseizures”
non-epileptic seizures/spells
Syncopal Events

- Shared Pathophysiology of Syncope, Breath Holding Spells, others
  - Events that occur at the hairdresser, church, dentist, blood draw, etc.

- Vagal-mediated bradycardia with brain hypoperfusion
  - altered mental status
  - potential anoxic seizure
Overall Treatment Strategies - Medical

- Why treat?
  - seizure control
  - quality of life, education, development
  - minimize SUDEP

- Many drugs now
- Better side effect profile
- Medications should be selected based on syndrome, patient specific issues, tolerability, side effects
- **Levetiracetam (Keppra)**
  - focal and generalized seizures
  - well tolerated generally
  - may cause irritability behavioral issues (role for vitamin B6)
  - mechanism: binds presynaptic protein SV2A, may inhibit Ca channels

- **Oxcarbazepine (Trileptal)**
  - partial seizures
  - hyponatremia
  - can make generalized seizures worse
  - mechanism: sodium channel inhibitor

- **Carbamazepine (Tegretol, Carbatrol)**
  - partial seizures
  - can make generalized seizures worse
Treatments - Medical

zonisamide (Zonegran)
  - good for generalized and partial seizures
  - long half life

topiramate (Topamax)
  - good for generalized and partial seizures
  - can cause language delay, cognition
  - weight loss

ethosuximide (Zarontin)
  - generalized (absence) only
- lamotrigine (Lamictal)
  - very good drug for multiple types of seizures
  - risk of bad rashes even Stevens-Johnson Syn.
  - “start low, go slow”

- valproic acid (Depakote)
  - very effective
  - well known side effects
  - may be best drug still for many generalized seizures
Newer Medications

- Rufinamide (Banzel)
  - Mechanism: ? Sodium channel inactivator
  - Side effects: ?

- Lacosamide (Vimpat)
  - Mechanism: ? Sodium channel inactivator
  - Side effects: ?
Newer Medications

- **perampanel (Fycompa)**
  - Mechanism: AMPA (glutamate) receptor antagonist
  - Side effects: concern for aggression, even homicidal tendencies!

- **clobazam (Onfi)**
  - Mechanism: GABA receptor agonist
  - Side effects: sedation
Less commonly used older medications

- phenobarbital
- phenytoin (Dilantin)
- carbamazepine (Tegretol)
- felbatol (Felbamate)
- tiagabine (Gabatril)
Ketogenic diet

- Ancient treatment
- Modern revival 1980’s
  *(Atkins and South Beach)*
- Appeals to some as “natural”
- Still need to recognize side effects and problems like any intervention
- Many patients respond, food refusal can be an issue
- Mechanism of action unclear
Ketogenic Diet (4:1 fat: (protein/carbs))

**Breakfast:** 28 g egg, 11 g bacon, 37 g of 36% heavy whipping cream, 23 g butter and 9 g apple.

**Snack:** 6 g peanut butter and 9 g butter.

**Lunch:** 28 g tuna fish, 30 g mayonnaise, 10 g celery, 36 g of 36% heavy whipping cream and 15 g lettuce.

**Snack:** 18 g of 36% heavy whipping cream, 17 g sour cream, 4 g strawberries and artificial sweetener.

**Dinner:** 22 g minced (ground) beef, 10 g American cheese, 26 g butter, 38 g cream, 10 g lettuce and 11 g green beans.
Cannabinoid Oil (CBD)

- Legal in TN, illegal Federal Law
- TN Law
  - Have epilepsy
  - Be resident of TN
  - Use CBD with <0.9% THC
- Side Effects
  - Minimal
- Drug interactions
  - Clobazam levels increased, maybe others
Treatments-Surgical

- Some patients have seizures from one defined area
- Medications ineffective
- Many tests done to determine area of seizure origin and whether other important regions are nearby
  - (is surgery going to be effective and safe?)
Left Hemisphere

Primary Motor Cortex
Vagal Nerve Stimulation

- FDA approved
- “open loop” intermittent stimulation, does not detect seizures
- Similar efficacy as adding a new drug
- No drowsy side effects

Advantages:
- Not a medicine, no major side effects

- Disadvantages
- Surgery, expensive, may not work
Vanderbilt New Onset Seizure Clinic
Problem

- Children with neurological problems need to be seen quickly!
  - Scared families
  - Medical necessity
  - Worried PCP
- Outpatient clinics have a long wait time
- ED and inpatient admission usually not best forum
Who?

- First time seizure
- Complicated febrile seizure
  - Focal and/or prolonged
- Breath holding spells/syncope (few please)

Exclusion Criteria

- Already on anti-seizure medications (unless just started)
- Has a neurologist
Clinic Structure

- Several slots for new patients held each week
- EEG also available same day

Staffing
- Melanie Franklin, NP
- Epilepsy specialists as back-up

Contacting Us
- 615-936-5536
Questions?