Seizures in the Elderly Patient

Kristin Anderson, MD
Geriatrics Grand Rounds
February 4th, 2016
Definitions

• Seizure
  – A transient occurrence of signs and/or sx due to abnormal excessive or synchronous neuronal activity in the brain

• Acute symptomatic seizure
  – Provoked events not expected to recur in the absence of a particular trigger (hypoglycemia, ETOH withdrawal)

Definitions

• Epilepsy is a disease of the brain defined by any of the following:
  – 1. At least two unprovoked seizures occurring >24h apart
  
  – 2. One unprovoked seizure and a probability of further seizures similar to the general recurrence risk (60%) after two unprovoked seizures, occurring over the next 10 years

  – 3. Diagnosis of an epilepsy syndrome
ILAE Seizure Classification

- Generalized
  - Originating at some point within, and rapidly engaging, bilaterally distributed networks
  
  - Descriptors
    - Tonic-clonic
    - Absence
    - Myoclonic
    - Clonic
    - Tonic
    - Atonic

- Focal
  - Originating within networks limited to one hemisphere

  - Descriptors:
    - With(out) impairment of consciousness or awareness
    - Involving subjective sensory or psychic phenomena
    - Evolving to a bilateral convulsive seizure

- Most common seizure type in the elderly
Age-related Incidence of Epilepsy


Epilepsy Etiology

- Stroke - 50%
- Neurodegenerative - 9%
- Others (tumor, trauma) - 11%
- Unknown - 30%
Clinical Presentation

• Most seizures are focal onset

• Classic description of seizure aura uncommon

• Observers often note confusion, sleepiness, or clumsiness rather than tonic/clonic movements or automatisms

• Postictal state frequently more prolonged
  – Often ≥ 24 hrs.

The Case of Mr. A

• Mr. A is a 70 yom who presents to your clinic with a chief complaint of tingling and twitching of his left arm. Occurred two days ago while watching TV, lasted 2 minutes, spontaneously resolved. No associated weakness. Felt dizzy during episode. Felt “drowsy” for a few hours following episode. Has not had similar episode in the past. Is feeling well today.

• ROS otherwise negative
The Case of Mr. A

- **PMHx:**
  - HTN
  - HLP
  - Type II DM
  - Paroxysmal atrial fibrillation
  - CVA six years ago, no residual deficits

- **Meds:**
  - Coumadin 3 mg
  - Atorvastatin 40 mg
  - HCTZ 25 mg
  - Lisinopril 40 mg
  - Metformin 1000 mg BID

The Case of Mr. A

- **Social Hx:**
  - Married, lives with wife
  - Quit smoking 6 years ago, prior 1 ppd x 40 yrs
  - No ETOH
  - Retired RTD bus driver
The Case of Mr. A

• Physical Exam
  – VS: T 98.2, P 72, BP 144/78, R 18, 96% on RA
  – Gen: alert, pleasant male in NAD
  – CV: RRR, no murmur, no carotid bruits
  – Extremities: trace ankle edema bilaterally
  – Neuro: A&O x3, CN 2-12 grossly intact, light touch/pinprick sensation equal throughout, 5/5 muscle strength throughout, reflexes 1+ and equal throughout, finger-to-nose testing intact, normal gait
  – MMSE: 30/30

The Case of Mr. A

• You suspect that Mr. A may have had a seizure

• In general, what should you consider in your differential diagnosis?

• What work-up should be performed when you suspect a seizure?
Differential Diagnosis

- Syncope
- TIA
- Transient global amnesia
- Drop Attack
- Psychogenic nonepileptic attacks (panic attack)
- Delirium
- Rapid eye movement sleep disorder

Diagnostic Evaluation

- Reliable description of event from eyewitness is key
  - Often not available!!
- Labs
  - CMP, Ca, Mg, CBC
  - EKG
  - LP if concern for CNS infection
- Neuroimaging
  - MRI preferred given greater sensitivity for detecting abnormalities
  - CT in emergency setting to rule out bleed
Diagnostic Evaluation - EEG

- Interictal EEG is of limited diagnostic value in older patients
  - Low sensitivity and specificity
- 12% - 38% of healthy elderly individuals develop EEG abnormalities
- 33% of patients with epilepsy have a normal EEG
- Video EEG increases yield, infrequently used

Mr. A’s Results

- Blood work
  - CBC wnl
  - LFTs wnl
  - Cr 1.1, glucose 185, Ca/Mg wnl
  - INR 2.3
- EKG
  - NSR with first degree AV block
- MRI
  - No acute abnormalities, evidence of prior small infarct left parietal lobe
Mr. A’s Results

• EEG
  – Impression: Probably normal awake and drowsy EEG recording. Presence of a single sharp discharge could be a normal finding. However, in the appropriate clinical setting, it may be also consistent with a seizure disorder with focal onset.

"I stopped taking the medicine because I prefer the original disease to the side effects."
The Case of Mr. A

• You think that Mr. A likely had a seizure

• How many of you would start Mr. A on anti-epileptic therapy at this time?

Should you treat a first unprovoked seizure?

• Chance for recurrent seizure greatest within first 2 years (21%-45%)

• Clinical factors associated with ↑ risk of seizure recurrence
  – Previous brain insult (stroke, trauma)
  – EEG with epileptiform abnormalities
  – Nocturnal seizure

• Immediate AED therapy ↓ risk of seizure recurrence but may not improve quality of life

• Decision individualized based on risk factors, patient preference
What about in a patient with a TBI?

- Large variability among clinicians in practice of post-traumatic seizure prophylaxis

- Early seizures (within 7 days)
  - Prophylaxis effective to decrease risk
  - Treat x 7 days
  - Phenytoin, Keppra

- Late seizures (beyond 7 days)
  - Prophylaxis probably not effective in decreasing risk
  - Not routinely recommended

The Case of Mr. A

- You tell Mr. A that you think he likely had a seizure

- You discuss his risk of a recurrent seizure and medication treatment options

- Mr. A doesn’t like taking medications and is worried about potential side effects, does not start treatment
The Case of Mr. A

• Mr. A returns to your office six months later and this time he is accompanied by his wife. His wife tells you that since his previous visit he has had two episodes of left arm tingling and twitching accompanied by dizziness and confusion. She witnessed both episodes, twitching lasted about two minutes and she did not notice any other abnormal movements. He was confused and sleepy for about one day following each episode.

• You diagnose Mr. A with epilepsy.

Should you treat a recurrent seizure?

• Risk of additional seizures at 1 year is 57% and at 4 years 73%

• AED should be initiated given above risks

• Mr. A is agreeable to starting AED therapy. Which AED should you choose?
General Principles of Treatment

- Studies in the elderly limited by smaller number of patients and short follow-up times
- “Start low and go slow”
- Monotherapy preferred
- Efficacy often below standard therapeutic range
- Toxicity common at traditionally therapeutic levels

VA Cooperative Study 428 Group

- Randomized, double-blind study
- Determine tolerability and efficacy of lamotrigine and gabapentin as compared to carbamazepine in older patients with epilepsy
- 593 elderly patients with newly diagnosed seizures
- Randomly assigned to 1 of 3 treatment groups
  - Gabapentin 1500 mg/day
  - Lamotrigine 150 mg/day
  - Carbamazepine 600 mg/day
  *goal doses titrated over 6 weeks
VA Cooperative Study 428 Group

- Primary outcome = retention in trial for 12 months
- Secondary outcomes = seizure freedom at 12 months, time to first seizure, drug toxicity

Patient characteristics
- Mean age 72
- Cerebral infarction most common seizure etiology
- Most common seizure type was focal
- Multiple medical conditions

% of Patients Remaining in Trial over 12 Months

![Graph showing % of patients remaining in trial over 12 months for different treatments.](attachment:graph.png)

Primary Outcome

• Carbamazepine had more early terminators than either Gabapentin (p=0.008) or Lamotrigine (p<0.0001)

• Most early terminations were due to adverse drug reactions

• Very few early terminations were due to uncontrolled seizures

Secondary Outcomes

• No significant difference in seizure free rates at 12 months
  – 53.3%
  – 63.4% when 6 wk titration period excluded

• No significant difference in time to first seizure

• Adverse reactions
  – Significant: weight gain with Gabapentin, hypersensitivity rash and hyponatremia with Carbamazepine
  – No difference in neurotoxicity
Conclusion

• Lamotrigine and Gabapentin should be considered as initial therapy for older patients with newly diagnosed seizures.

• Carbamazepine standard tx choice for elderly patients

• Compare Lamotrigine to controlled-release Carbamazepine

• Observational data suggesting Levetiracetam perhaps effective in the elderly
• 359 patients randomized to 1 of 3 treatment groups
  • Carbamazepine 400 mg/day
  • Lamotrigine 100 mg/day
  • Levetiracetam 1,000 mg/day
*goal doses titrated over 6 weeks

• Primary outcome = retention to treatment at week 58

• Secondary outcome = seizure freedom at one year

• Patient characteristics
  • Mean age 71
  • Most common seizure etiology = vascular
  • 5-6 concomitant diseases
  • Focal seizures

• Primary outcome
  — Retention rate for Levetiracetam (61.5%) was significantly higher compared to Carbamazepine (45.8%)
  — Retention rates for Carbamazepine and Lamotrigine (55.6%) were not significantly different
  — Retention rates for Lamotrigine and Levetiracetam were not significantly different

• Most early discontinuations were due to adverse effects

• Secondary outcome
  — No significant difference in seizure freedom at one year
Conclusion

• This trial provides evidence supporting the use of Levetiracetam as first-line treatment for elderly patients with new-onset focal epilepsy, and points to the value of Lamotrigine as alternative.

The Case of Mr. A

• You discuss treatment options with Mr. A and decide to start Lamotrigine.

• He asks what potential side effects he should be aware of. You tell him:
  – A. Hyponatremia and cardiac conduction abnormalities
  – B. Gingival hyperplasia and effect on INR
  – C. Tremor and weight gain
  – D. Dose-associated rash and insomnia
  – E. Kidney stones and weight loss
Side Effects of AEDs

A. Hyponatremia and cardiac conduction abnormalities
   **Carbamazepine**

B. Gingival hyperplasia and effect on INR
   **Phenytoin**

C. Tremor and weight gain
   **Sodium valproate**

E. Kidney stones and weight loss
   **Topiramate**

Which AED is appropriate for my patient?

- Consider comorbidities, current medications, cost, side effect profile

- In general consider Lamotrigine, Levetiracetam as first-line treatment
The Case of Mr. A

- He also asks you what impact this will have on his driving and if you are going to report him to the DMV. You tell him:
  - A. You are required by law to report him to the DMV
  - B. Not to worry and to continue driving as usual
  - C. You are not required by law to report him, it is his responsibility to disclose his condition

Driving Restrictions in Colorado

- Physicians NOT required to report epilepsy to DMV

- Physicians may report if concerned condition affects ability to drive safely
  - No civil/criminal action may be brought against physician if they acted in good faith

- Driver license applicant must disclose a physical disability that would cause lapse of consciousness

- No seizure-free period set by the state
What if Mr. A was still working?

- Commercial Driving
  
  - Individual must receive a medical waiver before he/she may be licensed to drive commercial vehicles
  
  - Person with epilepsy may be considered for a license to drive commercially if provide a physician’s certification regarding treatment and recommendation that condition is controlled well enough to drive safely

The Case of Mr. A – Prognosis

- His wife asks you what his prognosis is and how long he will have to be treated for. You tell her:
  
  - A. 5% of patients achieve seizure remission with first AED tried
  
  - B. 100% of patients achieve seizure remission with first AED tried
  
  - C. 60% of patients achieve seizure remission with first AED tried
Prognosis

• 60% achieve seizure remission with first AED tried
• >80% achieve seizure remission with treatment adjustments
• Treatment is generally lifelong
  – Must weight risk of seizure recurrence against benefits of drug withdrawal

The Case of Mr. A

• It has now been five years since Mr. A was diagnosed with epilepsy
• He remains on Lamotrigine, tolerating well
• He has remained seizure free throughout this time
• You recommend:
  – A. MRI of the brain
  – B. DXA scan
  – C. Nothing
AEDs and Bone Health

• People with epilepsy have 2-6X greater risk of fractures than the general population

• Likely many factors contribute
  – Epileptic seizures (tonic-clonic)
  – Side effects from AEDs leading to falls (dizziness, gait instability)
  – Bone-depleting effect of AEDs

AEDs and Bone Health

• Both enzyme-inducing (phenytoin, carbamazepine) and non-enzyme inducing (sodium valproate, lamotrigine, gabapentin) AEDs associated with decreased bone mineral density

• Dose-effect relationship

• Mechanisms
  – Upregulation of enzymes that metabolize Vitamin D → inactive metabolites → 2° hyperparathyroidism → bone resorption
  – ?direct inhibitory effect on osteoblasts
  – ?direct stimulatory effect on osteoclasts
  – ?effect on intestinal calcium absorption
AEDs and Bone Health Recommendations

• Annual evaluation of 25-hydroxy vitamin D

• D3 supplementation
  – Nonenzyme-inducing: 1,000 – 1,200 IU/day
  – Enzyme-inducing: 2,000 – 4,000 IU/day

• Adequate calcium intake (1000 – 1500mg/day)

• Weight bearing exercise as tolerated

• Patients on long-term AEDs (>5 yrs) screen with DXA or FRAX

Quality-of-Life Issues

• Stigma of seizures

• Loss of independence/family overprotection

• Burden of medication

• Decline in wellbeing/decreased self-esteem

• Social isolation
Take Home Points

• Highest incidence of epilepsy is in elderly patients

• Seizures are often atypical in their presentation in the elderly

• Recognize the low sensitivity and specificity of EEG in diagnosing epilepsy

• Lamotrigine, Keppra considered first-line therapy

Thanks!
Resources


• 7. Boggs, JG. Treatment of seizures and epilepsy in the elderly patient. In: UpToDate, Pedley TA (Ed), UpToDate, Waltham, MA. [Accessed on January 28, 2016.]

• 8. Krumholz, A, Hopp, J. Driving restrictions for patients with seizures and epilepsy. In: UpToDate, Pedley TA (Ed), UpToDate, Waltham, MA. [Accessed on January 28, 2016.]


