Epilepsy in Elderly

Geriatric Residents Round

Presented by
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A 95 Year male patient, known case of late onset Epilepsy post CVA for the last 5 years on Dilantin, presented with increase falls with dizziness, his level of Dilantin is fluctuating in high range despite several correction of the dose.
What is the Best Antiepileptic Medication in Elderly?
Objectives

- Epidemiology
- Etiology
- Clinical Presentation
- Differential Diagnosis
- Diagnostic Evaluation
- Treatment
- Prognosis
25 % of new seizures > Age of 65 years.
25 % of all persons with epilepsy are elderly.
Epilepsy is the 3rd Most common Neurological condition in Elderly after CVA & Dementia.
Diagnostic Difficulties.
Complicated treatment
Significant implications:
  • Loss of independence.
  • Driving restrictions.
  • Impaired self confidence.
  • Risk of falls.
Age-related incidence of epilepsy

Incidence / 100,000

Age in years

0 50 100
Etiologies

• **1) Acute symptomatic seizures:**
  Are provoked events that are not expected to recur in the absence of a particular trigger (eg, hypoglycemia, alcohol withdrawal).

• **2) Epilepsy:**
  Is a condition in which recurrent unprovoked seizures are expected in the absence of treatment.
1) Acute Symptomatic Seizures

- Acute stroke (most common 50%):
  - 2-4 weeks after the event.
  - Risk factor: hemorrhage, large size, and cortical involvement.
- Metabolic encephalopathy (6 to 30%):
  - Hypoglycemia.
  - Nonketotic hyperglycemia.
  - Hyponatremia.
  - Hypocalcemia.
  - Uremic and hepatic encephalopathy.
1) Acute Symptomatic Seizures

- Drugs & Drug withdrawal (10 %)
  - Alcohol, benzodiazepine, or barbiturate withdrawal, others.
- Head trauma (4 to 17 %)
- Intracranial infections (<3%)
### Drugs reported to potentially cause seizures or lower seizure threshold

<table>
<thead>
<tr>
<th>Psychotropic drugs</th>
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<tbody>
<tr>
<td>Tricyclic, tetracyclic antidepressants</td>
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<tr>
<td>Serotonin reuptake inhibitors</td>
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<tr>
<td>Neuroleptic agents (phenothiazines, haloperidol, clozapine)</td>
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<tr>
<td>Lithium</td>
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<tr>
<td>Bupropion</td>
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<tr>
<td>Methylxanthines (theophylline)</td>
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<tr>
<td>Narcotic analgesics (meperidine, propoxyphene)</td>
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<tr>
<td>Antimicrobials</td>
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<tr>
<td>Penicillins, cephalosporins in high dose</td>
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<tr>
<td>Imipenem</td>
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<tr>
<td>Isoniazid</td>
</tr>
<tr>
<td>Antimalarials</td>
</tr>
<tr>
<td>Cyclosporine</td>
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<tr>
<td>Nalidixic acid</td>
</tr>
<tr>
<td>Chemotherapeutic agents (methotrexate, chlorambucil)</td>
</tr>
<tr>
<td>General anesthetics (ketamine, enflurane)</td>
</tr>
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<td>Local anesthetics (lidocaine - in toxic doses, disopyramide, bupivacaine)</td>
</tr>
<tr>
<td>Stimulants (amphetamines, cocaine)</td>
</tr>
<tr>
<td>Antiarrhythmics (verapamil intoxication, mexiletine, procainamide, propranolol overdose)</td>
</tr>
<tr>
<td>Antihistamines (diphenhydramine)</td>
</tr>
<tr>
<td>Baclofen</td>
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<tr>
<td>Antiemetics (chlorpromazine)</td>
</tr>
</tbody>
</table>
2) Epilepsy

- Stroke (Most common 30 to 50%).
  - Risk factors: same
  - Risk is highest in the 1\textsuperscript{st} year after a stroke, (remains ↑ elevated 7 years).
- Cryptogenic seizures (30 to 50%)
  - Cerebrovascular disease is also believed to underlie epilepsy.
2) Epilepsy

- Dementia (9 to 17%).
  - Alzheimer disease (AD) is a risk factor for epilepsy (usually in the later stages).
- Others (5 to 15%):
  - Head Trauma
  - Intracranial tumors.
  - AVM
Clinical Presentation

- Most seizures in elderly patients are partial onset, with or without secondary generalization.
- When generalized (partial onset unrecognized).
- Late-onset primary generalized epilepsy is very rare. (possible lifelong but undiagnosed)
Clinical Presentation

- Complex partial seizure was the most common seizure type.
- Often extratemporal, usually frontal, in origin. (atypical" clinical presentation)
- Classic descriptions of seizure aura are uncommon.
- Pre-ictal: Antecedent symptoms (nonspecific)
  - Vaguely localized paresthesias.
  - Dizziness.
  - Muscle cramps.
- Ictal: Observers often note episodic confusion, sleepiness, or clumsiness rather than motor manifestations such as tonic or clonic movements, or automatisms.
- Postictal states: frequently more prolonged.
Status Epileptics

- Convulsive or Nonconvulsive.
- First seizure in 30% of elderly individuals.
- The incidence of SE in the elderly population (90 per 100,000) is almost twice that of the general population.
- Associated mortality is also higher in older patients
  - 38% > 60 years,
  - 50% > 80 years
- Nonconvulsive status epilepticus (NCSE):
  - Common.
  - Challenging diagnosis.
    - It manifests as an altered mental status with confusion, psychosis, lethargy, or coma.
    - Delay to diagnosis (up to 5 days).
Differential Diagnosis

- Syncope
- Transient ischemic attacks (TIAs)
- Transient global amnesia
- Drop attacks
- Psychogenic factors
- Delirium
- Sleep disorders
Diagnostic Evaluation

- A reliable history and description of the event from an eyewitness are invaluable and superior to diagnostic testing. (Pre-Ictal, Ictal & Post-Ictal).
- Diagnostic Procedure should be limited (very unpleasant and intolerable).
- EEG
- Neuroimaging
- Laboratory evaluation
• In a patient with altered mental status, EEG is a useful (esp. in NCSE)
• Interictal EEG has limited utility, with low sensitivity and specificity.
• High False Positive,
  • Nonspecific EEG abnormalities such as intermittent focal slowing are seen in 12 to 38% of older individuals without seizures
• High False Negative,
  • A normal EEG does not rule out the possibility of epilepsy and is seen in about one-third of patients with epilepsy
Neuroimaging

• A brain imaging study should be obtained in all older individuals with possible epilepsy.
  • Normal CT scans 18%
  • Stroke was seen 42.6%
  • Encephalomalacia 9.1%
  • Tumors in 1.5%.
  • Other nonspecific findings (atrophy, small vessel disease, hydrocephalus) were identified in the remaining.
Laboratory Evaluation

- Electrolytes, BUN, creatinine, glucose, calcium, magnesium, and liver function tests.
- Complete blood count, differential, and platelets.
- Evaluation for stroke risk factors (e.g., fasting lipid panel).
- Lumbar Puncture (when suspicion of meningitis or encephalitis)
Treatment

- Acute symptomatic seizures
  - metabolic derangements, medication, or medication withdrawal will not require seizure treatment.
- Acute intracranial event (stroke, head trauma) are often treated for a limited time (a few weeks to a few months)
- Unprovoked seizures has high rate of recurrence (80 to 90 %) are generally treated with long-term AEDs.
Antiepileptic Drugs

- The mainstay of antiepileptic treatment. But complicated by several factors:

1) Pharmacokinetics: need small & less frequent doses.
   - ↓ Bioavailability
   - ↑ Free Fraction of Protein-Bound AEDs
   - ↑ Plasma Level Enzyme Inducing AEDS
   - ↓ Renal Elimination AEDs
Antiepileptic Drugs

2) Polypharmacy:
   • Drug interactions or lower seizure threshold.

3) Adverse effects.
   • include confusion, impaired gait, sedation, tremor, dizziness, visual disturbance & cognitive side effect.

4) Osteoporosis.
   • Especially women.
   • More with Enzyme-inducing AEDs.
   • Bone Screen, Vit. D & Ca$^{+2}$ are recommend.
Selection of AED

- Generally the newer AEDs should be considered early in the treatment of epilepsy in an elderly patient due to the lower potential for interactions, linear pharmacokinetics, and lower incidence of side effects compared with older agents.

- BUT Newer AEDs, however, have a less established track record and a less completely defined side-effect profile.
### AEDs licensed for monotherapy in focal seizures with and without secondarily GTCSs: comparison of priorities that are important in the treatment of elderly with epilepsy*

<table>
<thead>
<tr>
<th></th>
<th>Tolerability</th>
<th>Pharmacokinetics (% of perfect score)†</th>
<th>Significant drug–drug interactions</th>
<th>Titration</th>
<th>Need for laboratory tests ‡</th>
<th>Parenteral formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamazepine</td>
<td>Medium</td>
<td>Inferior (50)</td>
<td>Yes</td>
<td>Slow</td>
<td>Maximal (1 and 2)</td>
<td>No</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>Excellent</td>
<td>Moderate (73)</td>
<td>Yes</td>
<td>Very slow</td>
<td>Maximal (1 and 2)</td>
<td>No</td>
</tr>
<tr>
<td>Levetiracetam</td>
<td>Excellent</td>
<td>Superior (96)</td>
<td>Not clinically significant</td>
<td>Fast</td>
<td>Minimal</td>
<td>Yes</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>Excellent</td>
<td>Superior (89)</td>
<td>Not clinically significant</td>
<td>Fast</td>
<td>Minimal</td>
<td>No</td>
</tr>
<tr>
<td>Oxcarbazepine</td>
<td>Medium</td>
<td>Moderate (77)</td>
<td>Yes</td>
<td>Slow</td>
<td>Maximal (1 and 2)</td>
<td>No</td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>Poor</td>
<td>Inferior (57)</td>
<td>Yes</td>
<td>Slow</td>
<td>Maximal (1 and 2)</td>
<td>Yes</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Poor</td>
<td>Inferior (50)</td>
<td>Yes</td>
<td>Slow</td>
<td>Maximal (1 and 2)</td>
<td>Yes</td>
</tr>
<tr>
<td>Topiramate</td>
<td>Poor</td>
<td>Moderate (79)</td>
<td>Yes</td>
<td>Very slow</td>
<td>Maximal (1 and 2)</td>
<td>No</td>
</tr>
<tr>
<td>Valproate</td>
<td>Poor</td>
<td>Inferior (52)</td>
<td>Yes</td>
<td>Slow</td>
<td>Maximal (1)</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Table 7.19 Desirable properties are in red. *All AEDs in this table are licensed for elderly patients in monotherapy of focal seizures. In RCTs, none of the newer AEDs showed better efficacy than carbamazepine but they were better tolerated; gabapentin has shown worse efficacy in clinical practice. For more information, see summary of product characteristics and Table 7.2. For other details and citations see Table 15.3. †The % of perfect score is based on a customised rating system of 16 parameters to evaluate the pharmacokinetic profile of AEDs developed by Patsalos.††‡ (1) Monitoring for adverse drug reactions; (2) therapeutic drug monitoring.
Double-blind randomized trials

- Lamotrigine was compared with carbamazepine in a 24-week study in 150 older patients.

- Patients on lamotrigine had a higher completion rate (71 versus 42 percent), seizure-free rate during the last 16 weeks (39 versus 21 percent), and fewer number of side effects (N = 102 versus 48).

Double-blind randomized trials

- Another study comparing lamotrigine and carbamazepine in 185 patients over 65 years found no differences between groups in study completion, time to drug withdrawal, seizure remission, or treatment-emergent adverse events after 40 weeks. Neither drug appeared to be associated with significant changes in health-related quality of life compared to baseline.


Three treatment groups, lamotrigine, gabapentin, and carbamazepine were compared in 593 elderly patients with epilepsy. Early terminations (44.2, 51, and 64.5 percent, respectively) and terminations due to adverse drug reactions (12.1, 21.6, and 31 percent) were less common in those taking lamotrigine or gabapentin compared with carbamazepine. There was no significant difference in the seizure-free rates at 12 months.

Double-blind randomized trials

- Ninety-three patients with Alzheimer disease (AD) and seizures were randomized to levetiracetam, phenobarbital, or lamotrigine and compared to a control group of 68 AD patients without seizures who were not treated with AEDs. Efficacy was similar among the three AEDs; levetiracetam caused the fewest adverse effects and was associated with more favorable cognitive outcomes at 12 months.

Nonrandomized Retrospective Study

- 415 older patients (>55 years) with epilepsy found that 12-month retention rates were higher for patients prescribed lamotrigine and levetiracetam (79 and 73 percent respectively) than for carbamazepine, gabapentin, phenytoin, and topiramate (48 to 59 percent). Retention rates were lowest for oxcarbazepine (24 percent). Twelve-month seizure freedom rates were also higher for lamotrigine and levetiracetam (54 and 43 percent) compared with other AEDs.

Conclusion

- It is difficult to draw firm conclusions from trials with such short follow-up times.
- The International League Against Epilepsy treatment guidelines concluded that lamotrigine, gabapentin, and carbamazepine have demonstrated efficacy for seizure control in studies of elderly patients.
- The choice of specific AEDs in an elderly patient should be individualized.
Other Considerations

- The availability of different drug formulations (liquids, crushable).
- Dose Frequency per day.
- Medication expense.
- Generic formulations of AEDs are generally not preferred.
- Initiation at a low dose with titration up to a higher dose.
- Monotherapy is greatly preferred.
- Therapeutic drug monitoring
Prognosis

• Overall High success rate (70 %) is often quoted for treatment efficacy in older patients.
• Patients' underlying disease and comorbidity may be more important to their future morbidity and mortality.
Take Home Messages

- A first seizure is not uncommon in elderly persons.
- Cerebrovascular disease is the most common cause.
- Complex partial seizures is the most common presentation with or without secondary generalization.
- High level of suspicion for possible seizures in older patients presenting with intermittent or fluctuating confusional states.
- The usual clues to the possibility of underlying seizures are often absent.
- The choice of specific AEDs in an elderly patient should be individualized.
A reliable history and description of the event from an eyewitness are invaluable and superior to diagnostic testing.
Reference

• Seizures and epilepsy in the elderly patient: Diagnosis and treatment, Jane G Boggs, MD, last updated on Feb 2, 2011
• Seizures and epilepsy in the elderly patient: Etiology, clinical presentation, and differential diagnosis, Jane G Boggs, MD, last updated on Feb 2, 2011
Thank You...

2011

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