Post Stroke Seizure Management

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Disclosures

- Dr. Mathews has no financial relationships to disclose.
Objectives

- Understand what a seizure is, and how to recognize one
- Understand who is at risk for post stroke seizures and epilepsy
- Understand the relevance of post stroke epilepsy to your patients
- Understand the basic principles of treatment of post stroke epilepsy: who should be treated and how?
- Know some of the commonly used medications and the factors involved in choosing an appropriate medication
What is a seizure?

• The clinical manifestation of an abnormal, paroxysmal, excessive discharge that is synchronized throughout a localized or distributed population of neurons
• A symptom of dysfunction in gray matter
• There can be many causes
  • Metabolic derangements, infections, drug withdrawal
Seizure types

- PARTIAL (or FOCAL)
  - Arise in specific locations ("foci") governing the clinical manifestations
    - "Simple partial"
      - no alteration of consciousness
    - "Complex partial"
      - altered consciousness
      - focus usually in temporal or frontal lobe
      - seizure produces "remote" effects in both hemispheres

- GENERALIZED
  - Onset bilaterally over a wide area
  - Loss of consciousness at onset

- PARTIAL EVOLVING TO GENERALIZED
What is epilepsy?

• “A disorder of the brain characterized by an enduring predisposition to generate epileptic seizures....
• .... and by the neurobiologic, cognitive, psychological, and social consequences of this condition.”
• Minimal clinical definition: more than one unprovoked seizure
Causes of epilepsy

- Idiopathic
- Cerebrovascular
- Trauma
- Developmental
- Infection
- Tumor
- Degenerative
- Other

From W.A. Hauser
Relative risks for developing epilepsy
Incidence of Epilepsy in Rochester, MN 1935-1984

From Hauser et al.
Stroke as a cause of epilepsy

- Stroke is the presumed cause in ~ 50% of new cases of epilepsy in people over 60 years old
What is the relationship between seizures and stroke?

1. Seizures may predate stroke
   Seizures are a manifestation of acute or chronic derangement of the brain’s microcircuitry or metabolic environment

   May be the first sign of previously silent cerebrovascular disease
   - should prompt a thorough work-up

Some reports that TIA’s may manifest as seizures
What is the relationship between seizures and stroke?

2. Seizures may complicate acute stroke
   “Early” seizures (within first 2 weeks)

2-5% of acute strokes

Most (50-70%) occur in first 24 hours
   - may be the presenting sign of stroke

Predicts recurrent seizures (epilepsy) in 30%
What is the relationship between seizures and stroke?

3. Seizures can occur months to years after stroke
   “Late” seizures – occur after a latent period

3-5 % of stroke patients

Much stronger predictor of recurrence (epilepsy) than “early” seizures: ~ 90%
Who is at risk?

- ~ 10% of stroke patients will have a post stroke seizure
  - ~ 3% eventually will be diagnosed with epilepsy
- Risk factors:
  - Hemorrhagic > ischemic
  - Cortical involvement
  - Severity of initial deficit
What are the consequences?

- May worsen the stroke (particularly “early” and frequent/prolonged seizures)
- Seizures are associated with increased morbidity and mortality
  ◦ Injuries/accidents
  ◦ Loss of independence (eg. driving)
  ◦ Co-morbidities
    • Depression, anxiety
- Epilepsy is life-long, even after stroke recovery
Diagnosis of seizures

- Most important factor is recognizing seizure
- Many partial seizures are subtle:
  - Confusion, ± brief loss of consciousness
  - Patient may not be aware during event or may not recall event
  - Patient may have cognitive, communication deficits that prevent obtaining adequate history
Differential diagnosis of post stroke seizures (not everything is a seizure)

- Stroke patients typically have many comorbid conditions:
  - Cardiovascular disease, DM, autonomic dysfunction
- DDX includes:
  - Syncope
  - TIA (esp. with post-ictal weakness or aphasia)
  - Altered mental state due to other conditions (drugs, metabolic disturbances)
  - Migraine
  - Acute symptomatic seizure due to other conditions
Diagnosis of post stroke seizure

- History!
  - Education of family, caregivers on characteristics of seizures
  - Clinical cues:
    - Confusion, behavior change or unresponsiveness without loss of postural tone
    - Loss of consciousness; falls without recollection
    - Lack of presyncopal symptoms or other explanation
    - Stereotyped
Diagnosis of post stroke seizure

- Confirmatory tests
  - EEG
    - + in 25% elderly patients without epilepsy and 75% with epilepsy
    - Video-EEG monitoring is more sensitive and specific, but more costly
  - MRI
    - Confirms stroke, but not seizure
    - Useful when concern for worsening of existing stroke
To treat or not?

- Early seizure or late?
- First seizure or recurrent?
Who should be treated?

- High risk of recurrence
- Frequent or severe (complex partial, secondarily generalized) seizures
  - i.e. high risk of injury or otherwise independent
- Low risk of medication
- “Can’t afford to wait and see.”
Who might not need treatment (or not right away)?

- Low risk of recurrence
- Infrequent or mild (simple partial) seizures
Treatment of seizures
General considerations

- Antiepileptic drugs (AEDs) have a high incidence of potential adverse effects
  - Drowsiness
  - Dizziness
  - Visual symptoms (blurred vision, diplopia)
  - Gait/balance disturbance
  - Cognitive effects
Treatment of seizures

General considerations

• Post stroke seizure patients are generally elderly
  ◦ Pharmacokinetic factors
    • Many drugs are renally excreted
      ◦ Renal function decreases with age
    • Polypharmacy is the norm
      ◦ Many drug-drug interactions
  ◦ Pharmacodynamic factors
    • “Counter-regulatory” mechanisms that allow brain to adapt to change decline with age
    • Side effects are more likely & magnified
    • AEDs can contribute to and exacerbate existing cognitive deficits
Commonly used AEDs
FDA-approved first-line drugs

- Phenytoin (Dilantin)
- Carbamazepine (Tegretol, Carbatrol)
- Oxcarbazepine (Trileptal)
- Lamotrigine (Lamictal)
- Divalproex sodium (Depakote)
- Topiramate (Topamax)
Commonly used AEDs
FDA-approved “add-on” drugs

- Levetiracetam (Keppra)
- Gabapentin (Neurontin)
- Pregabalin (Lyrica)
- Zonisamide (Zonegran)
- Lacosamide (Vimpat)
What is the “best” medicine?

- It depends on the patient
- All AEDs are roughly equivalent in clinical trials
- Consider common/potential side effects and interactions in your patient’s context
- Some common choices....
Phenytoin (Dilantin)

- **Advantages**
  - Used for almost 70 years
  - Once-daily dosing
  - Injectable form (phenytoin or fosphenytoin)
    - Can be loaded rapidly
  - Relatively inexpensive

- **Disadvantages**
  - Induces P450 enzymes
    - Lowers blood level of many other drugs
  - Difficult dosing due to pharmacokinetics
    - Blood level monitoring adds to cost
Carbamazepine (Tegretol)

- **Advantages**
  - Used for almost 50 years
  - Inexpensive

- **Disadvantages**
  - No injectable form
  - Induces P450 enzymes
  - Can cause hyponatremia, particularly with concomitant thiazide diuretic
Oxcarbazepine (Trileptal)

- **Advantages**
  - Similar to carbamazepine, with fewer interactions
  - Lower toxicity compared with carbamazepine

- **Disadvantages**
  - No injectable form
  - Can cause hyponatremia, particularly with concomitant thiazide diuretic
Divalproex sodium (Depakote)

- **Advantages**
  - Available in once-daily and injectable forms
  - Few interactions
  - Relatively inexpensive

- **Disadvantages**
  - Weight gain common
  - May cause tremor, Parkinsonism
Lamotrigine (Lamictal)

- **Advantages**
  - Well tolerated (one of few AEDs studied in elderly)
  - Few drug interactions

- **Disadvantages**
  - Slow titration
Topiramate (Topamax)

- **Advantages**
  - Some evidence for ‘efficacy compared with other AEDs
  - Weight loss

- **Disadvantages**
  - Cognitive effects
Levetiracetam (Keppra)

- **Advantages**
  - Rapid titration
  - No interactions
  - Generally well tolerated
  - Injectable and once-daily forms

- **Disadvantages**
  - Irritability common
  - Not approved for monotherapy
Gabapentin (Neurontin)

- **Advantages**
  - Well tolerated in elderly
  - No interactions
  - Effective in neuropathic (diabetic) pain

- **Disadvantages**
  - Renally excreted
  - Frequent (TID) dosing
Treatment of early seizures

- Use benzodiazepine (lorazepam) acutely
  - Very effective for stopping seizures
- Then either:
  - Load with a standard AED
    - i.v.: phenytoin, divalproex, levetiracetam
  - Begin titrating an oral AED
    - Any of above, or oxcarbazepine, lamotrigine
- Discontinue after ~ 3 months
  - unless compelling evidence for high recurrence risk
Treatment of early seizures: Controversies

- AEDs may impair recovery from stroke
- Sedation, other AED side effects may reduce ability to participate in rehab
- Must weigh benefits and risks for an individual
Treatment of late seizures

- Likely to be long-term commitment, so choose AED carefully
- Start low and titrate slowly
- First line: oxcarbazepine, lamotrigine, divalproex
- Second line: levetiracetam, gabapentin
Response to treatment: VA Cooperative Study (2005)

- 50-60% new onset geriatric epilepsy patients became seizure-free on first AED
- But, only 50% remained in study at one year
Response to treatment: When treatment fails

- If first AED is not tolerated or does not control seizures, rapidly switch to 2\textsuperscript{nd} AED

- If 2\textsuperscript{nd} AED fails, consider referral to Epilepsy Specialty Clinic
  - Many reasons for treatment failure
    - Compliance, adequate doses?
  - Is diagnosis correct?
Other treatment considerations

- Driving laws vary by state:
  - MD: 3 months from last seizure
  - DC: 12 months from last seizure
- No bathing, swimming alone
- Safety alarm in home
- Medical bracelet