Refractory Seizures

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CONFIRMED SEIZURES

Idiopathic epilepsy possible*

- Assess seizure frequency

  - <2 seizures q6mo
  - ≥2 seizures q6mo

  - No therapy recommended

  - Begin single AED, with goal of monotherapy
    - Phenobarbital\(^2\) 2.5-3.5 mg/kg PO q12h
    - Potassium bromide 20-30 mg/kg q24h

  - Adequate control
    - Continue current therapy

  - Inadequate control
    - \(\approx 30\%\) of dogs are not controlled with AEDs\(^3\)

    - Consider adding AEDs
      - Topiramate 2-10 mg/kg PO q12h
      - Gabapentin 10-20 mg/kg PO q6-8h
      - Pregabalin 3-4 mg/kg PO q8h

    - Change AED
      - Phenobarbital
      - Potassium bromide
      - Levetiracetam 20 mg/kg PO q8h (extended release, 30 mg/kg PO q12h); dose may need to be increased when used with phenobarbital\(^2\)
      - Zonisamide 5-10 mg/kg PO q12h (for dogs already receiving phenobarbital, 10 mg/kg PO q12h)

  - Change seizure control goals
    - Increase interictal periods
    - Decrease seizure duration

  - Therapeutic levels reached (phenobarbital 15-35 µg/mL or potassium bromide 1-3 mg/mL)?

  - YES
    - Refractory epilepsy
  - NO
    - Maximize current AED; ensure owner compliance

ABNORMAL

Perform interictal neurologic examination

- Perform CBC, serum chemistry profile, bile acid assay, thyroid panel, and serum ammonia level tests to rule out reactive seizures

- Structural epilepsy suspected

- Consider MRI and CSF analysis

- Treat underlying disease

- Inadequate control
  - \(\approx 30\%\) of dogs are not controlled with AEDs
  - Ensure sufficient length of time for therapeutic trial (ie, that steady-state drug level has been reached)
  - Re-evaluate diagnosis; repeat neurologic examination

- No therapy recommended

- Monitor blood (ie, serum AED) levels

- Perform appropriate blood work (ie, CBC, serum chemistry profile) if applicable

- Consider adding AEDs

- Change seizure control goals

- Adequate control
  - Continue current therapy

- Inadequate control
  - \(\approx 30\%\) of dogs are not controlled with AEDs

- Change to newer AED (eg, levetiracetam to zonisamide)

- Consider tolerance to AED

- Therapeutic levels reached (phenobarbital 15-35 µg/mL or potassium bromide 1-3 mg/mL)?

  - YES
    - Refractory epilepsy
  - NO
    - Maximize current AED; ensure owner compliance
A definition of refractory epilepsy is not established for dogs, but it is generally agreed that an animal with frequent or severe seizures or intolerable side effects despite appropriate antiepileptic drug (AED) therapy is considered refractory to treatment.3

Levetiracetam and zonisamide are increasingly the drugs of choice for monotherapy by some neurologists. A recent study found no reduction in monthly seizure frequency when levetiracetam was used as a sole agent.4 However, little additional information is available in the veterinary literature on the efficacy of these medications as sole agents.

Some AEDs (eg, levetiracetam, zonisamide) have a reported “honeymoon effect,” with dogs developing tolerance over time.

Gabapentin and pregabalin are not known efficacious AEDs but anecdotally may help with seizure control in patients tolerant to other medications.

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NOTES


Suggested Reading


* Idiopathic epilepsy can be subclassified into genetic epilepsy (identified genetic background), suspected genetic epilepsy (breed prevalence >2%), or epilepsy of unknown cause (nature unknown with no structural disease). Diagnosis of idiopathic epilepsy can be suggested if there is a history of ≥2 unprovoked epileptic seizures occurring ≥24 apart, the patient’s age at epileptic seizure onset is between 6 months and 6 years, interictal physical and neurologic examinations are unremarkable (except for antiepileptic-drug–induced neurologic abnormalities and postictal neurologic deficits), and no clinically significant abnormalities are found on minimum database blood tests and urinalysis. However, diagnosis is ideally made on exclusion (ie, normal brain MRI and CSF analysis) or further supported by electroencephalography.