Brain Games

Reaching Consensus in Seizure Terminology, Diagnosis and Management

Terri Cole DVM, DACVIM
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Consensus Task Forces

- **International Veterinary Epilepsy Task Force (IVETF)**
  - 26 members -- experts in human & veterinary neurology, neuropathology
  - Published 7 consensus statements including
    - Epilepsy definition, classification and terminology
    - Diagnostic approach to epilepsy in dogs
    - Medical treatment of epilepsy in dogs in Europe

- **ACVIM**
  - Board of Regents (identifies topic, selects panel)
  - Panel (recognized experts in the field)
    - Statements derived from evidenced based data when possible
    - Provide interpretive comments when insufficient/controversial data
  - Membership input
  - 2015 Consensus Statement on Seizure Management in Dogs
  - [www.acvim.org](http://www.acvim.org)
Overview of Topics Tonight

• Seizure **Terminology** (IVETF)
  – Create terminology and classification that reflects current knowledge
  – Create terminology and classification that is concise, thus reducing errors and simplifying conversation between owners, primary care and referral clinicians

• Seizure **Diagnostics** (IVETF)
  – Standardize diagnostic approach to improve consistency in the diagnosis of canine epilepsy

• Seizure **Management** (IVETF and ACVIM)
  – Establish guidelines for predetermined, concise and logical sequential approach to seizure management
Terminology

- Seizure **Terminology** (IVETF)
  - Create terminology and classification that reflects current knowledge in veterinary medicine
    - not just use terminology and classifications borrowed from human medicine (International League against Epilepsy)
  - Create terminology and classification that is concise
    - Reduce errors and simplify conversation between owners, primary care and referral clinicians
Proposed Terminology -- Etiology

• **Idiopathic Epilepsy** (defined as a disease)
  – Idiopathic (Proven genetic)
  – Idiopathic (Suspected genetic - high breed prevalence)
  – Idiopathic (unknown cause, no evidence of structural epilepsy)

• **Structural Epilepsy**:
  – *Previously: secondary, acquired, symptomatic*
  – epileptic seizures provoked by intracranial/cerebral pathology
    (vascular, inflammatory/infectious, traumatic, anomalous/developmental, neoplastic, degenerative)
  – Causes confirmed by diagnostics including imaging, CSF

• **Unknown Cause**
  – *Previously: cryptogenic, probable/possible symptomatic*
  – Indicates ignorance – needs more work up to define cause
Proposed Terminology -- Semiology (type)

• **Focal epileptic seizures** *(previously petite mal, partial)*
  – Characterized by lateralized/regional signs
  – May present as:
    • Motor – facial twitches, repeated head jerks, rhythmic blinking, repeated rhythmic jerks of one extremity
    • Autonomic – dilated pupils, hypersalivation, vomiting
    • Behavioral – short or lasting changes in behavior such as anxiousness, restlessness, unexplainable fear etc

• **Generalized epileptic seizures** *(previously grand mal)*

• **Focal evolving to generalized** *(previously partial or focal with secondary generalization)*
Name the type of event
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International veterinary epilepsy task force consensus proposal: diagnostic approach to epilepsy in dogs

• Goal in creating consensus was to improve consistency in the diagnosis of epilepsy
• Goals for patient presenting with history of suspected epileptic seizures are two fold
  – Defined if events are truly seizures
  – Define cause of seizures
Diagnostic Approach

- **WHO**: is it?? is it a Seizure??
- **WHAT**: is it the Cause???
- **WHERE**: is the evidence I can call it Idiopathic? Tiers I-III confidence levels for diagnosis of idiopathic epilepsy
- **WHEN**: should I do advanced diagnostics (CT, MRI/CSF)??
- **WHY**: should I care about this??
WHO: Is it? Is it a seizure????

- Episodic Events
  - Syncope
  - Neuromuscular weakness
  - Paroxysmal behavioral changes (compulsive disorder)
  - Paroxysmal dyskinesia
  - Narcolepsy/cataplexy
  - Idiopathic head tremors
  - Seizures
WHO: Is it? Is it a seizure????

Criteria for diagnosis of epileptic seizure

- If possible observe the events – This may be one of few times it is helpful for clients have phones with them in the exam room – VIDEOS!!
  - Still not “perfect”. 2015 Packer et al Study -- Only fair agreement between observers if an event was an epileptic seizure
- Good physical and neurological examination
- Consider the age and breed of the patient
WHO: Is it? Is it a seizure????
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Is this a seizure??
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WHAT: is the cause??

– Reactive seizures *(disease outside the brain)*
  - Response from **normal** brain tissue to transient disturbance (metabolic or toxic).
  - Reversible when the cause/disturbance is resolved.

– Epilepsy *(disease of the brain)*
  - Structural
  - Idiopathic
  - Unknown Cause
WHAT: is the cause??

**Reactive Seizures**

- **Systemic metabolic disorders**
  - Hypoglycemia
  - Electrolyte disorders (hypocalcemia)
  - Portosystemic Shunts

- **Intoxications**
  - Ethylene glycol
  - Metaldehyde
  - Organophosphates
  - Lead poisoning

- **History is important!!**
  - Acute onset more common. One study 41% of dogs with reactive seizure presented in status epilepticus
  - Neurologic signs may be preceded by other signs (i.e. GI)
WHAT: is the cause?

**Structural Epilepsy**

- Structural forebrain disorders
  - Degenerative
  - Anomalous
  - Neoplastic
  - Inflammatory/Infectious
  - Traumatic
  - Vascular
WHAT: is the cause?

**Structural Epilepsy**

- Neurologic exam is *often* but *not always* abnormal
  - Asymmetric neurologic deficits may be seen in patients with lateralized brain lesions
  - Patients with inter-ictal neurologic abnormalities are more likely to have structural lesions
- Normal inter-ictal exam however does *not* rule out structural epilepsy
  - Focal lesions in “clinically silent” parts of the forebrain may cause seizures without other neurologic signs
    - One study 23% of dogs with structural epilepsy had normal neuro exam in inter-ictal period
Structural Epilepsy

- Epileptic seizure type (focal vs generalized) should *not* be used as isolated variable to predict presence of structural disease
  - One study of dogs with structural epilepsy 93% had generalized and 7% had focal seizures
WHERE: is the evidence I can call it idiopathic?? IVETF Diagnostic Criteria

- Tier 1 confidence level for diagnosis of idiopathic epilepsy
  - History of 2 or more unprovoked seizures >24 hours apart
  - Age of onset 6 months- 6 years
  - Unremarkable inter-ictal physical and neuro examination
  - NSF on labwork and UA

- Tier 2 confidence level for diagnosis of idiopathic epilepsy
  - Tier 1 PLUS
  - Normal fasting and post prandial bile acids
  - Normal MRI
  - Normal CSF

- Tier 3 Evidence
  - Tier 1 and 2 PLUS
  - EEG consistent with seizure disorder
WHEN: should I do advanced diagnostics.

IVETF Diagnostic Criteria

- Recommend performing MRI of the brain and routine CSF analysis in dogs with
  - age of epileptic seizures onset <6 months and >6 years
  - Inter-ictal neurologic abnormalities
  - Status epilepticus or cluster seizures at onset
  - Previously presumptive diagnosis of idiopathic epilepsy and drug resistance with a single agent titrated to highest tolerable dose
WHY: should I care about this??

• Using standardized terminology and classifications leads to:
  – Concise communication between owner, primary care physician and referral sources
  – Ability to generate comparable data

• Using standardized diagnostic plan leads to:
  – A concise, clear plan to present to clients
  – A higher level of confidence in classification
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  – Establish guidelines for predetermined, concise and logical sequential approach to seizure management
ACVIM 2015 Consensus on Seizure Management in Dogs

• Goal was to establish guidelines for concise and logical sequential approach to chronic seizure management in dogs

• ACVIM consensus panel based its recommendations for clinical practice based on the current published evidence (peer reviewed literature and conference proceedings) with 4 levels of recommendation based on scientific merit and expert panel consensus
ACVIM Consensus Topics

- When should treatment be started?
- Which drug should be used first?
- How should monitoring be performed?
- What are the risks of treatment?
- When should a second AED be started and which should I use?
- What alternative nonpharmacologic treatments are available?
- What are the guidelines for Success and Quality of Life?
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What are your goals for AED therapy?

• Goals in seizure management are:
  – Decrease or eliminate epileptic events
  – Decrease seizure severity
  – Avoid adverse effects
  – Decrease seizure-related mortality and morbidity
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When Should Treatment Be Started?

- Panel recommendations to initiate AED treatment:
  - Identifiable structural lesion is present or prior history of brain disease or injury
  - Acute repetitive seizures or status epilepticus (ictal event ≥5 minutes or ≥3 more generalized seizures within 24 hour period)
  - 2 or more seizures within a 6 month period
  - Prolonged, severe or unusual postictal periods
  - Epileptic seizure frequency and/or duration is increasing and/or seizure severity is deteriorating over 3 interictal periods (IVETF)
Which Drug Should Be Used First?

- Anti-epileptic drug selection factors:
  - Efficacy (choose the most appropriate AED and dosage)
  - Know if and when to monitor serum AED concentrations and adjust treatment accordingly
  - Know when to add or change to a different AED
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### Which Drug Should Be Used First?

<table>
<thead>
<tr>
<th>Drug</th>
<th>Level</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenobarbital</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Bromide</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Primidone</td>
<td>II</td>
<td>D</td>
</tr>
<tr>
<td>Imepitoin</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Levetiracetam</td>
<td>IV</td>
<td>C</td>
</tr>
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</table>

**Level of Study Design**
- Level I: well designed controlled studies
- Level II: case controlled, cohort studies
- Level III: case reports or series
- Level IV: expert opinion only

**ACVIM Panel Recommendation Grades**
- A: high recommendation, likely effective
- B: moderate recommendation, most likely effective
- C: low recommendation, may not be effective
- D: not recommended, may be ineffective/dangerous

Adapted from Podell M et al, J Vet Intern Med (2016)
Which Drug Should Be Used First?

Phenobarbital

- Longest history of AED use in veterinary medicine
- High bioavailability
  - Rapidly absorbed within 2 hours
  - Peak plasma concentration in 4-8 hours after oral administration
  - Individual variability in absorption, excretion and elimination half life
- 8 studies evaluated as monotherapy, total of 289 dogs
  - >50% reduction in seizures in 82% of dogs
  - Cumulative seizure free rate of 31%
  - Failure rate (no improvement) 15%
  - Boothe DM et al JAVMA (2012) compared phenobarbital vs bromide as first line AED.
    - Randomized clinical trial
    - 85% PB dogs became seizure free vs 52% Br dogs
Phenobarbital

- Primarily metabolized by liver
- P450 inducer
  - Increases reactive oxygen species → increases risk of hepatic injury
  - Contraindicated in patient with pre-existing liver disease
  - Also increases PB clearing overtime (metabolic tolerance)
    - This stabilizes ~30-45 days after starting
  - Can alter kinetics of other drugs including other AEDs, corticosteroids, cyclosporine, metronidazole, digoxin
  - Drugs that inhibit P450 (cimetidine, ketoconazole etc) may inhibit PB metabolism and increase serum concentrations
Which Drug Should Be Used First?

Phenobarbital

- Dosing
  - Starting dose 2.5mg/kg q12 hours
  - Cluster seizures/status: Loading dose 15-20mg/kg IV, IM or PO divided in multiple doses of 3-5 mg/kg over 24-48 hours to obtain rapid therapeutic concentrations (i.e. 3-5mg/kg dose every 4-6 hours until reach 15-20mg/kg dose)
  - PB concentrations can be measured 1-3 days after loading
Potassium Bromide

- First documented AED in humans (1857), used in veterinary medicine since 1980s
- Usually given as liquid although tablet form available
- Slowly metabolized with median elimination half life of 15.2 days
- Steady state concentrations fluctuate in dogs due to individual differences in clearance and bioavailability
  - High chloride diets result excessive renal excretion (decreased blood levels)
  - Excreted in urine, no known hepatic metabolism
Which Drug Should Be Used First?

Potassium Bromide

- **Single study as first line therapy**
  - Boothe DM et al. JAVMA (2012)
  - 23 dogs treated with KBr
  - 73.9% (17/23) had >50% reduction in seizures
  - 52% (12/23) were seizure free first 6 months

- **Dosing**
  - Starting dose is 40mg/kg/day
  - Loading dose may be indicated to achieve steady state more rapidly (125mg/kg daily x 5 days. Divide each daily dose into 3-4 administrations)
    - Stop loading if serious side effects occur (vomiting, weakness)
Which Drug Should Be Used First?

Primingdone

- Only AED specifically approved for dog in the US
- Rapidly metabolized to phenobarbital
- Less well tolerated than phenobarbital
- Less effective than phenobarbital in a number of studies
Imepitoin

- Approved in Europe in 2013
- Novel and selective mechanism of action -- potentiates GAGAergic inhibition acts as low affinity partial agonist at benzodiazepine site of GABAA.
- Compared to phenobarbital in randomized study 226 dogs both drugs were equally effective but fewer side effects with imepitoin
- Extensively metabolized in the liver however impaired liver function is not reported to greatly impact pharmacokinetics
- Dosed 10-30mg/kg q12 hours
  - Start lower end, up-titrate if needed
Which Drug Should Be Used First?

Levetiracetam

- Approved for humans in 1999 for refractory focal seizures in adults
- Favorable pharmacokinetic properties in dogs
  - Rapid, complete absorption after oral administration
  - Minimal protein binding
  - Lack of hepatic metabolism
  - Primary urinary excretion
  - Wide margin of safety
- Rapidly metabolized, elimination half life 4-8 hours
- No published reports as first line AED in dogs
- Dose (recommended as add-on AED) 20mg/kg q8 hours
Which Drug Should Be Used First?

Zonisamide

- Sulphonamide based anticonvulsant
- Exact mechanism unknown
- Well absorbed after oral administration
  - Mean peak concentrations 3 hours after administration
  - Relatively long elimination half life (15 hours)
- Hepatic metabolism via cytochrome P450
- Limited studies (1 monotherapy, 2 as add on AED)
  - Monotherapy study (10 dogs) 60% had ≥ 50% seizure reduction
- Dose (recommended as add-on AED)
  - 5mg/kg q12 hours
  - 7-10mg/kg q12 hours with phenobarbital
Which Drug Should Be Used First?

Figure 1 Pyramid of hierarchy describing the recommendation of AEDs based on the assessment of their efficacy and quality of evidence.

Why Should Monitoring be Performed?

• Objectives of monitoring:
  – Determine effective drug concentrations after initiation of therapy
  – Determine if drug failure is because pharmacokinetic factors (drug dose too low, dose interval too long) or pharmacodynamic factors (functional tolerance)
  – Determine if treatment failure is caused by inadequate or changed drug concentration
  – Prevent toxic side effects
  – Aid with individualization of treatment
How Should Monitoring be Performed?

• When to monitor:
  – Ideally at the same time after dosing (if prior testing)
  – Trough concentration is helpful if:
    • Seizures occurring prior to next schedule drug dose
    • For drugs with short elimination half lives
How Should Monitoring be Performed?

Phenobarbital

- Timing of recheck blood level
  - 2 weeks = First steady state
  - 6 weeks = Steady state clearance time (enhanced clearance from P450 induction)
  - Every 6 months (ideally along with CBC, chemistry +/- bile acids)
  - 2 weeks after any dose change
  - Additional monitoring if the patient has >2 seizures

- Ideal time of day would be fasted, trough in morning
  - When this is not feasible then a consistent time post dosing/feeding

- Therapeutic range 15-35ug/ml
  - Efficacy can be seen with lower concentrations

- Metabolic tolerance can occur
  - Progressive dose increase without concurrent increase in serum concentration. May be due to other p450 inducers
How Should Monitoring be Performed?

Potassium Bromide

• Timing of recheck
  – 1 month (especially if loading) and 3 months = First steady state
  – Once yearly
  – 1-3 months after dose change (and maybe diet change)
  – If > 3 seizure occur before next scheduled evaluation
  – If signs of toxicity are suspected.

• Ideal time of day: Any (ideally >2 hours post dosing)

• Therapeutic range
  – Monotherapy 1000-3000mcg/ml
  – Add-on therapy 800-2500mcg/ml
  – Efficacy can be seen with lower concentrations

• Dose increases can be calculated:
  – \((\text{Target Steady state concentration} - \text{Actual serum steady state concentration}) \times 0.02 = \text{mg/kg/day ADDED to existing dose}\)
How Should Monitoring be Performed?

Levetiracetam

- Timing of recheck
  - Serum levels not routinely checked
    - Wide therapeutic window
    - Lack of strong correlation between levetiracetam concentration and response or side effect
  - Consider checking when used in combination with phenobarbital
    - Phenobarbital increase clearance of levetiracetam
    - Serum levels may help determine if dose increase is indicated
    - Therapeutic range extrapolated from humans (12-46mcg/ml)

Imepitoin

- Therapeutic drug monitoring is not indicated or commercially available
How Should Monitoring be Performed?

Zonisamide

- Timing of recheck
  - 1-2 weeks after treatment initiation or dosage
  - Additional monitoring if the patient has >2 seizures
- Ideal time of day would be trough (1 hour prior to dose)
  - Trough and peak may be indicated if poor seizure control
- Therapeutic range 10-40ug/ml (extrapolated from humans)
- Baseline CBC and chemistry is recommended prior to starting and every 6 months
What are the risks of treatment?

<table>
<thead>
<tr>
<th>Drug</th>
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<th>Type 2</th>
<th>Type 3</th>
<th>Type 4</th>
</tr>
</thead>
<tbody>
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<td>Y</td>
<td>N</td>
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Type 1: predictable, dose related  
Type 2: idiosyncratic, potentially life threatening  
Type 3: cumulative with long term treatment and potentially life threatening  
Type 4: delayed (carcinogenic, teratogenic) and life threatening

Adapted from Podell M et al, J Vet Intern Med (2016)
What are the risks of treatment?

Phenobarbital

- **Type I:** restlessness/sedation typically resolve 1-2 weeks
- **Type II:**
  - Rare immune mediated neutropenia, anemia, thrombocytopenia
- **Type III:**
  - Chronic PU/PD, polyphagia
  - Hepatotoxicity 😞
    - More commonly when serum PB concentrations >35mcg/ml
    - MONITOR CHEMISTRY (bile acids if indicated/ideal) q6 months
      - ALP can be elevated (induced) but ALT elevation is a red flag!

Primidone

- Similar to PB however higher frequency of hepatotoxicity (hepatic necrosis, fibrosis, cirrhosis). Monitor chemistry every 3-6 months if used
What are the risks of treatment?

Bromide

- Type I: PU/PD, polyphagia. Ataxia at higher concentrations
- Type II: pancreatitis, GI intolerance
- Type III: high serum levels signs of intoxication can include pelvic limb ataxia, weakness, altered behavior

Levetiracetam

- Type I: Randomized study only ataxia was different from baseline however sedation, restlessness, vomiting, decreased appetite have been reported
- Type II-IV not reported in dogs
What are the risks of treatment?

Zonisamide

- Type I:
  - sedation, ataxia, vomiting, inappetance
  - Some dogs may require dose reduction due to side effects. Gradual up-titration may permit tolerance
- Type II:
  - idiosyncratic reactions are rare but possible particularly in patient with history of prior reactions to sulfonamide medications (KCS, polyarthropathy). Very rare acute hepatopathy, renal tubular acidosis
  - Ideally baseline labwork and periodic rechecks
- Type III: may decrease T4 (fT4 and TSH remain normal)

Imepitoin

- Type I: transient mild PU/PD, hyperactivity, polyphagia
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When Should a Second AED Be Started?

• Strict criteria for Add-on AED are lacking in veterinary medicine however consider when:
  • first line AED is optimally/maximized dosed and seizure frequency/severity or quality of life are unacceptable
  • need to decrease/discontinue a first line AED due to side effects

• Factors to consider:
  – Select an add-on AED with a different mechanism of action
  – Determine risk/benefit of polypharmacy
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Adapted from Podell M et al, J Vet Intern Med (2016)
What Second AED Be Started?

- **Levetiracetam**
  - Decrease in seizure frequency >50% in most studies
  - “honeymoon” effect may occur
  - Packer R et al. Assessment into the usage of levetiracetam in a canine epilepsy clinic. BMC Veterinary Res 2015; 11:25
    - 52 dogs, retrospective study comparing a pulse therapy protocol vs maintenance protocol of levetiracetam for dogs with cluster seizures
    - Pulse protocol: 60mg/kg after a seizure OR pre-ictal signs were recognized, followed by 20mg/kg q8 hours until seizure free x 48 hours
    - 69% dogs >50% seizure frequency reduction, 15% seizure free
    - No significant difference between maintenance and pulse therapy

- **Bromide**
  - As add-on decreases seizure number and severity by 21-72% of dogs. Studies were noted to have high degree of bias. Charalambous M et al: BMC Vet Res 2014
What Second AED Be Started?

- **Zonisamide**
  - As add-on reported to have 58-80% efficacy to decrease seizure frequency by ≥ 50%
  - In one study 3/8 dogs had subsequent increase in seizure frequency when followed longer term (7-17 months)
  - Dogs in all studies were able to have first line drug (phenobarbital, bromide or both) doses reduce.

- **Imepitoin**
  - Not yet available in the USA
  - Received grade “C” due to only very limited published information on add-on therapy (added to phenobarbital or primidone treated dogs in one study, 17 dogs)

- **Phenobarbital**
  - Used primarily as first line drug, no clear studies on its use as a add-on AED
## Summary of AED therapy

**Table 2.** Qualified criteria recommendations for AED drug use.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Seizure type</th>
<th>Seizure etiology</th>
<th>Other</th>
<th>Drug monitoring</th>
<th>Cautions and risks</th>
<th>Initial dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenobarbital</td>
<td>All</td>
<td>All</td>
<td></td>
<td>2 and 6 weeks, q6m, or 2 weeks after dose change; Range: 15–35 µg/mL Increases clearance of levetiracetam and zonisamide</td>
<td>Hepatotoxicity Idiosyncratic blood dyscrasia Necrolytic dermatitis</td>
<td>2.5 mg/kg q12h</td>
</tr>
<tr>
<td>Add-on</td>
<td>All</td>
<td>All</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potassium Bromide</td>
<td>All</td>
<td>Idiopathic</td>
<td>Low initial frequency Liver disease</td>
<td>1 and 3 months, q12m or 1 month after dose change Range: 1000–3000 mcg/mL (mono) or 800–2500 mcg/mL with phenobarbital</td>
<td>Pancreatitis Sedation Ataxia</td>
<td>40 mg/kg/day</td>
</tr>
<tr>
<td>Add-on</td>
<td>All</td>
<td>All</td>
<td></td>
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</tr>
<tr>
<td>Imepitoin</td>
<td>All</td>
<td>Idiopathic</td>
<td></td>
<td>NR</td>
<td></td>
<td>15 mg/kg q12h</td>
</tr>
<tr>
<td>Monotherapy</td>
<td>All</td>
<td>NR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Add-on</td>
<td>All</td>
<td>All</td>
<td>Liver disease</td>
<td></td>
<td>Renal disease</td>
<td>20 mg/kg q8h</td>
</tr>
<tr>
<td>Levetiracetam</td>
<td>All</td>
<td>All</td>
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</tr>
<tr>
<td>Zonisamide</td>
<td>All</td>
<td>All</td>
<td></td>
<td>2 and 3 months, q6m and 2 weeks after dose change Range: 10–40 mcg/mL</td>
<td>Idiosyncratic renal and hepatic disease with phenobarbital</td>
<td>5 mg/kg q12h</td>
</tr>
<tr>
<td>Monotherapy</td>
<td>All</td>
<td>All</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Add-on</td>
<td>All</td>
<td>All</td>
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</tr>
</tbody>
</table>

NR = not recommended.

Alternative nonpharmacologic treatments

• **Vagal nerve stimulation**
  – Approved for use in humans (50% will experience >50% seizure reduction)
  – Randomized, placebo-controlled crossover study in 10 dogs with medically refractory idiopathic epilepsy (Munana et al 2002)
    • no significant difference in seizure frequency, severity or duration
    • Some dogs did have decrease in seizure frequency in last 4 weeks of the study.
    • Humans may have delayed improvement in control for up to 24 months
    • Current clinical at UGA, noninvasive method of vagal nerve stimulation

• **Dietary alterations**
  – No benefit of ketogenic diet (high fat, low carb) in randomized double blinded controlled trial in dogs. 1/3 of dogs developed pancreatitis
  – A MCT diet trial did report decreased seizure frequency (modest)
Guidelines for Success & QOL

Owner perspectives/tolerance
- Acceptable frequency of drug administration
- Tolerance of having an epileptic dog in the household
- Economic considerations

Patient quality of life
- Adequate control of seizures
- Acceptable side effects
References

References

- Runfeldt et al. Efficacy, safety, and tolerability of Imepitoin in dogs with newly diagnosed epilepsy in a randomized controlled clinical study with long-term follow up. BMC Veterinary Res 2015; 11:228
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- Hulsmeyer et al. International veterinary epilepsy task force’s current understanding of idiopathic epilepsy of genetic or suspected genetic origin in purebred dogs. BMC Veterinary Research 2015 11:175
QUESTIONS???