Seizures – Emergency Treatment

Simon R. Platt BVM&S MRCVS
Dipl. ACVIM (Neurology) Dipl.ECVN
College of Veterinary Medicine, University of Georgia

Emergency Seizures

SEIZURE CLASSIFICATION

- Cluster seizures - 2 or more generalized convulsive seizures in 24 hours
- Status Epilepticus - 2 or more seizures without a "break" or 1 seizure lasting more than 5 minutes

Epidemiology

- SE seen in 59% of dogs with seizures of any cause
- SE seen in 5% of dogs / 19% of cats with idiopathic epilepsy
- Australian Shepherds / Border Collies predisposed
- SE cause = 27% idiopathic epilepsy / 32-35% structural epilepsy / 25-30% unknown cause / 7-11% reactive epilepsy / AEM related in 6%

STATUS EPILEPTICUS

SYSTEMIC EFFECTS

- Compromised respiration
  (1) Mechanical impairment
  (2) Respiratory center impairment
  (3) Autonomic dysfunction

STATUS EPILEPTICUS

SYSTEMIC EFFECTS

- Cardiac compromise
  (1) Autonomic dysfunction
  (2) Hypoxia / ischemic damage
  (3) End result is arrhythmia

STATUS EPILEPTICUS

SYSTEMIC EFFECTS

- Renal compromise
  (1) Hypotension
  (2) Hyperthermic damage to muscle
  (3) Myoglobinuria & poor perfusion
STATUS EPILEPTICUS

NEURONAL EFFECTS

• Hypoxia & Hypoglycemia
  (1) Cerebellum / hippocampus / cerebrum
  (2) Irreversible damage after 90 minutes
• Acidosis / Electrolyte / Excitotoxin abnormalities

STATUS EPILEPTICUS

ADMISSION MANAGEMENT

• Concurrent history taking
• Rectal temperature – cool if >104°F/40°C
• Blood work – Electrolytes/ Ca++ / Glucose / bile acids / Toxicity screen / PCV / TP
• +/- Dextrose 10% solution; 100 mg/kg IV vs. Karosy whole PO
• Oxygen administration – ‘flow by’
• +/- IV catheter

 treats

• Only available water soluble BZD
• Delivered IV, CRI, IM, IN and buccally
• Can be mixed with saline or glucose
• Poor and erratic availability (0-50%) rectally with prolonged Tmax
• 0.066 - 0.22 mg/kg IM or IV
• IM midazolam more efficacious than IV lorazepam in people!

STATUS EPILEPTICUS

STEP ONE

BENZODIAZEPINES

• Diazepam 0.5 - 1.0 mg/kg IV
• Diazepam 0.5 - 2.0 mg/kg rectally
• Diazepam 0.5 - 2.0 mg/kg nasally
• Midazolam 0.2 mg/kg IV/IM/IN

STATUS EPILEPTICUS

STEP TWO

PHENOBARBITONE

• Phenobarbitone 2 - 4 mg/kg IV or IM
• Onset of action in 20 minutes
• Repeat at 30 minute intervals if needed
• Total cumulative dose – 20 - 24 mg/kg / 24 hours
LOADING DOSE

Total Phenobarbitone loading dose
18 to 24 mg/kg intravenously over 24 hours

STATUS EPILEPTICUS
STEP THREE (a)

CONSTANT RATE INFUSION BZD

- Diazepam 0.5 - 2.0 mg/kg/hour IV CRI in 0.9% saline
- Midazolam 0.2 mg/kg/hr IV CRI in 0.9% saline
- Adheres to PVC and light sensitive
- Respiratory depression possible
- Reduce dose q3-6 hr to effect

STATUS EPILEPTICUS
STEP THREE (b)

- Levetiracetam (Keppra) IV & IM
- 100 mg/ml
- Anticonvulsant and anti-epileptic
- 10-60 mg/kg IV over 10 minutes lasts 8 hours – repeat if necessary
- Higher dose if on PB already
- Mean time to peak concentration 40 mins

IV Levetiracetam in Dogs

- A randomized, placebo-controlled, double-masked study including 19 dogs with SE or cluster seizures
- IV LEV in addition to diazepam resulted in 56% response compared to placebo and diazepam alone (10%)
- Dogs in the placebo group required significantly more boluses of diazepam compared with the LEV group [Hardy et al., 2012]

STATUS EPILEPTICUS
STEP FOUR

PROPOFOL COMA

- Anticonvulsant Properties
- Bolus 1-4 mg/kg IV to effect
- Constant Rate Infusion (0.1-0.6 mg/kg/min)
- Consider expense

Propofol

- Propofol infusion syndrome (>48hrs)
- Impairment of mitochondria resulting in energy mismatch
- Metabolic acidosis, hyperlipidemia, elevated CK, rhabdomyolysis, hyperkalemia, renal failure and cardiovascular collapse
- Risk of oxidative damage to RBC of cats
- Heinz body formation
- Haemolytic anaemia
STEP FIVE - Ketamine
- First used in 1998 for SE in people
- Used for refractory convulsive SE & super-refractory SE
- 1-5 mg/kg IV (IM?) then 5 mg/kg/hr
- Metabolized by liver in dog
- Midazolam added to prevent emergence reactions

STEP SIX? - Lacosamide
- Available since 2009 as IV solution
- Functionalized amino acids
- Low protein binding
- No effect on plasma concentrations of other AEDs
- Eliminated renally
- Effective for SE in animal models
- Overall human SE success 56%

STEP SIX? - Fosphenytoin
- Phosphate ester pro-drug of phenytoin
- After injection, phenytoin is cleaved by phosphatase enzymes
- Toxicity is related to phenytoin
- Ataxia and vomiting.
- A dose of 15 mg/kg was tolerated
- ~80% of fosphenytoin converted to phenytoin by 30 minutes suggesting rapid metabolism in dogs

STATUS EPILEPTICUS
STEP SEVEN
Last Ditch!!
- Inhalational Anesthesia
- Dexmedetomidine 5-15 μg/kg IV/IM/SQ bolus or per hour
- Potassium bromide rectally – 100 mg/kg q4hrs 6 doses

STATUS EPILEPTICUS
STEP EIGHT
CEREBRAL EDEMA
- Steroids?
- Furosemide 1 mg/kg IM, IV
- Mannitol 20% 0.5 g/kg IV
- Flow by oxygen vs. Hyperventilation?

STATUS EPILEPTICUS
STEP NINE
POST - SEIZURE MANAGEMENT
- Thoracic and Abdominal imaging
- Urinalysis / Indwelling urinary catheter
- ECG
- CT / MRI
- CSF
- +/-Gastric lavage
**CLUSTER SEIZURES**

**OPTION 1**
- Diazepam 0.5 - 2.0 mg/kg rectally / nasally
- Adjunct to maintenance medications
- Reduce number of clusters and number of seizures per cluster
- Poor effect if already on PB – use higher dose

**CLUSTER SEIZURES**

**OPTION 2**
- Clorazepate 0.5 mg/kg q8-12 hrs PO
- Metabolized to nordiazepam
- Tolerance develops but slower than to diazepam
- Useful for ‘breakthroughs’ as only effective for 2 months

**CLUSTER SEIZURES**

**OPTION 3**
- Oral pulsed levetiracetam
- Instant release 20mg/kg q8h PO
- XR 20mg/kg q12-24h PO

**Emergency Seizures**

**SUMMARY**
- SE is a life threatening emergency
- Quick approach to prevent brain damage
- No single approach always effective
- Cluster treatment is mix of chronic and acute therapy advice