Clinical timeline & novel therapeutic options for presumptive Strychnine toxicity in a dog

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Grand Rounds: April 14 2011
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Objectives

- Case summary
- Toxicokinetic and toxic principles
- Literature review
- Novel management strategies
Apollo

- 5-year-old castrated male Labrador Retriever
- Weight = 43 kg (94lbs)

Owner’s history: Apollo was out wandering the property, came back with a paper plate hanging out of his mouth and seemed completely normal.

- 10 minutes later – ataxia → rigidity → recumbency
Emergency Clinic

- Ambulatory but having tremors
- $T = 41.5 \text{ C (106.7F)}$
- $P = 130 \text{ bpm}$
- R= panting
- MM: hyperemic

- CBC - NSF
- Serum chemistry: Na (162mmol/L; reference range 140-150mmol/L)

- 3 more seizure-like episodes
  - Cyanotic – flow by O2 support
  - Diazepam (15 mg; 4 times)
  - Butorphanol (0.3mg/kg)
  - Methocarbamol (4.6mg/kg)
  - Phenobarbital (4.6mg/kg)
  - Normasol - 2ml/kg/hour
  - External cooling
UMN ER (6.5 hours)

- T – WNL, P- WNL
- R – 60
- Severe hyperesthesia and muscle rigidity
- Intermittently laterally recumbent
- Mild stimuli → contraction of all four limbs and neck in an opisthotonic manner
- If sitting sternal, the dog would fall laterally and become more rigid whenever touched
First Night (hrs 6-14)

- Transport to ICU (8 hrs)
  - Grand mal seizure – 0.5mg/kg diazepam

- ICU stabililization
  - IVF (PLyte 148) – 2ml/kg/hr
  - Grand mal seizure (10 hrs)
    - Mannitol, Diazepam, Pheno load
  - Ucath, nasal cannulae (12 hrs)
Critical Care Day 1
(hrs 14-18.75)

- TPR WNL, 5% dehydrated
- Intermittently tremors and hyperesthesia
- Recumbent, non ambulatory, blind
- Methocarbamol
- Client communication
  - Ddx: epilepsy, brain, toxin
The page... (18.75 hours)

- **Gopher Bait 50**
  - active ingredient of Strychnine alkaloids 0.50%.
Day 2 – Polypharmacy (hours 24-48)

- His anxiety and hyperesthesia worsened overnight (hours 24-36)
  - Diazepam, hydromorphone, Diazepam CRI

- Still non ambulatory and non-visual
  - Phenobarbital, acepromazine, cotton balls, masks
  - Diazepam CRI – up, down, off...

- No changes

- Flailing around cage
Bliss (hours 48-60)
3rd Day (hours 60-72)

- Cough
- BAR, Eating and drinking, Visual
- Walking

Day 4 (hours 84-90)
- Home!
Follow Up

- SAP – WNL
- USG 1.050
Strychnine

- Crystalline alkaloid naturally found in the seeds of
  - *Strychnos nux-vomica*
  - *Strychnos ignatti*
- History: stimulant and laxative
  - Avicide and rodenticide
  - Since 1990, most baits traditionally containing strychnine (gopher and mole baits) have been replaced by zinc phosphide. (Ettinger & Feldman, 1995)
Toxicity

- Dogs are the most commonly affected animals
  - inhalation, swallowing or absorption through the eyes or mouth
- Bitter
- Malicious poison for dogs
Pharmacokinetics

- LD50 - 0.75mg/kg
- Onset - 10-120 minutes post ingestion
- MOA - inhibitor of glycine at the postsynaptic sites in the spinal cord
  - This inhibition causes unchecked stimulation of motor neurons
- 10-20% of the dose - excreted unchanged in urine 24 hours later
- 70% excreted in first 6 hours
- Generally complete within two days though the animal generally dies within 1-2 hours if left untreated.
"Ugly way to die"

- Restlessness and stiffness
- Trismic grin
- Extensor muscle rigidity
- Generalized tonic-clonic seizures often occur
- Moderate hyperthermia
- Respiratory paralysis
- Cyanosis
- Death
- Necropsy: agonal hemorrhages in the heart and lungs and cyanotic congestion and rapid rigor mortis.

Diagnosis

- history
- isolated from the stomach, vomitus, liver, kidneys or urine
- DDx:
  - Anticholinesterase insectisides
  - Organophosphates
  - Carbamates
  - Diethyltoluamide (DEET)
  - Organochlorines
  - Dichlorodiphenyltrichloroethane (DDT)
  - Bromethalin
  - Nicotine
  - Fluoroacetate
  - Zinc Phosphide
  - Avermectin/Ivermectin
  - Tremorgenic Mycotixins
  - Penitrem A
  - Roquefortine
  - Cocaine
  - Amphetamines
  - Methylxanthines
  - Mushrooms
  - TCAs
  - Metronidazole
Therapy

- no antidote
- Decontamination?
- Supportive care:
  - control of seizures and anxiety
  - prevention of ventilator arrest
  - management of sequelae
    - lactic acidosis
    - muscle breakdown
    - acute renal failure
Limitation and assumptions

- not confirmed via urine testing or gastric contents
- the found container of strychnine toxin does make the presumptive diagnosis very likely.
- Based on calculations, the patient would have needed to ingest 32.25 mg or 6.45 grams (0.2 ounces) of the 0.50% Gopher Bait 50 to reach toxic levels.
Prevalence

- Alberta Canada – 31/57 (54%)
  - Of analyzed stomach contents
- KSU – 7%
  - Of all small and large animal tox 1975-1980


161 cases 1/1992-12/2008
132 (82%) of the cases were canines
93 (57%) had signs of strychnine toxicity
- SEIZURES, tremors, rigidity, stiffness, panting, hyperthermia, vomiting, ataxia, hyperesthesia
10% euthanized or died

Safdar A. Khan, DVM, MS, PhD, DABVT, Mary Kay McLean, BS Toxicology
Brief: Epidemiology and management of strychnine poisoning.
VETERINARY MEDICINE  Jun 1, 2010
Atypical course

- Clinical 10 hrs post
- Pain, stiffness, regurgitation, hyperesthesia
- Died 15 min after onset
- No seizures

Trazodone

- Antidepressant – SARI
  - approved by the Food and Drug Administration in 1981
- Anxiolytic, hypnotic effects, off-label for insomnia
- MOA: 1* = 5HT antagonist (predominantly 5 HT 2a)
  - 2* inhibit serotonin reuptake
  - Serotonin-1 receptor agonist
  - +/- attenuated inhibitory tone of GABA
- Mean peak blood levels 1-2 hour after ingestion
- Metabolism: <1% eliminated unchanged, metabolized in liver to m-CPP
- Biphasic elimination (T1/2 1 3-6 hours and T1/2 2 5-9 hours).
- One retrospective study of trazodone used in dogs with anxiety disorders, demonstrated it was well tolerated and may provide an additional treatment modality in controlling anxiety in dogs.
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Videos!
Further Knowledge gained

- Use of diazepam?
- Limitations to methocarbamol
- Acepromazine
- Urine acidification
- Sensory deprivation
Thanks!!

- The Golden Interns!
- ECC department and everyone that listened to Apollo scream for 2 days before I discovered Trazodone
- Apollo and the Turry family for trusting someone who had been a doctor for 5 weeks
Questions?