

OPTIMIZE YOUR DIAGNOSIS: PRACTICE TIPS FOR THE POISONED PATIENT SCIENTIFIC: TOXICOLOGY

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INTRODUCTION

Pet Poison Helpline, an international, 24/7 animal poison control based out of Minneapolis, MN, receives phone calls from both pet owners and veterinarians regarding toxicity cases from accidental or intentional misuse of OTC or prescription medications, common garden or outdoor toxins, and common household products. In veterinary medicine, with any poisoned patient, the primary treatment for toxicant exposure should be decontamination and detoxification, along with symptomatic and supportive care of the patient. Initial steps when presented a poisoned patient should include: immediate stabilization and triage, obtaining an appropriate history, performing a thorough physical examination, and initiating treatment (including decontamination and stabilization).

OBTAINING AN APPROPRIATE HISTORY

One of the common mistakes made in the field of veterinary toxicology is not taking the time to obtain an appropriate toxicology history. Some key questions to ask include:

- What was the product ingested? Do you know the active ingredient?
- Can you bring me the original box/container/pill vial?
- How many total tablets could have been ingested? What was the minimum and maximum amount that your pet could have been exposed to?
- Was this an extended or sustained release product? Was there an extra “letter” behind the brand name (e.g., Claritin vs. Claritin-D)?
- When did your pet get into this?
- Has your pet shown any clinical signs yet?
- Did you give your pet anything at home (e.g., hydrogen peroxide, milk, etc.) when you found out he was poisoned?

Pet owners should be instructed to do the following:

- To safely remove their pet from the area of poisoning so additional ingestion does not occur
- To not give any home remedies found circulating on the Internet (e.g., milk, peanut butter, oil, grease, salt, etc.)
- To not induce emesis without consulting a veterinarian or an animal poison control first
- To bring the pill vial in to the veterinarian so they can assess the bottle for verification of the product name
- To call the original pharmacy to find out how many total pills were prescribed, and attempt to back-count how many were taken/ingested
- To seek immediate veterinary attention

Veterinarians should do the following once presented the patient:

- To verify the spelling of the product, and confirm the active ingredient (AI)
- To evaluate if the product is a sustained-release (SR), extended release (XR), or long-acting (LA) product. These initials will follow the name of the drug on the vial.
- To evaluate if the patient should have emesis induced (see “When to decontaminate”)
- To stabilize the patient based on triage and physical examination findings (e.g., temperature, heart rate, pulse rate)
- To call for medical assistance and toxicology advice if needed

WHEN TO DECONTAMINATE

The goal of decontamination is to inhibit or minimize further toxicant absorption and to promote excretion or elimination of the toxicant from the body. Decontamination can only be performed within a narrow window of time for most substances; therefore, it is important to obtain a thorough history and time since exposure to identify whether decontamination is safe for the patient or if it will actually be beneficial for the patient. Decontamination categories may include ocular, dermal, inhalation, injection, gastrointestinal (GI), forced diuresis, and surgical removal to prevent absorption or enhance elimination of the toxicant.

One of the primary ways of decontaminating veterinary patients is via emesis induction. While gastric lavage is often more effective at removing gastric contents, it is less often performed in veterinary medicine as it requires IV catheter placement, sedation, intubation with an appropriately inflated endotracheal tube, and appropriate gavage technique. Therefore, veterinarians should be aware of which circumstances are appropriate or contraindicated if emesis induction is to be performed.

Emesis should only be induced in certain situations:

- With recent ingestion (< 1 hour) in an asymptomatic patient
- With unknown time of ingestion in an asymptomatic patient
- When ingestion of a product known to stay in the stomach for a long time is ingested in an asymptomatic patient (e.g., grapes, raisins, chocolate, xylitol gum)

Emesis should NEVER be performed in the following situations:

- With corrosive toxicant ingestion (e.g., lye, ultra-bleach, batteries, oven cleaning chemicals, etc.)
- With hydrocarbon toxicant ingestion (e.g., tiki-torch oil, gasoline, kerosene, etc.)
- In symptomatic patients (e.g., trembling, agitated, seizing, hyperthermic, weak, collapsed, etc.)
- In patients with underlying disease predisposing them towards aspiration pneumonia or complications associated with emesis-induction (e.g., megaesophagus, history of aspiration pneumonia, laryngeal paralysis, etc.)

ACTIVATED CHARCOAL (AC)

After an appropriate history, triage, physical exam, and initial decontamination procedures have been performed in the poisoned pet, the next step is the administration of activated charcoal (AC), if appropriate. AC should not be given to the poisoned patient when the toxicant does not reliably bind to AC (e.g., heavy metals, xylitol, ethylene glycol). Also, symptomatic patients who are at risk for aspiration pneumonia should not be administered AC orally. Finally, the administration of AC with a cathartic should be cautiously used in dehydrated patients, due to the potential risks for hypernatremia.

When administering AC, it should ideally be given within ≤ 5 minutes of ingestion to be most effective. In veterinary medicine, this is almost impossible due to driving time (to the clinic), lapsed time since ingestion, time to triage, and the amount of time it takes to physically deliver AC (e.g., syringe feeding, orogastric tube, etc.). As a result, administration of AC is often delayed up to an hour or more. As time since ingestion is often unknown (e.g., pet owner coming home from work to find their pet poisoned), decontamination (including emesis and administration of AC) is often a relatively benign course of action, provided the patient is not already symptomatic. As always, when administering *any* drug, it is important that benefits outweigh the risks, and that complications be prevented, when possible. In veterinary medicine, administration of AC with a cathartic as long as 6 hours out may still be beneficial with certain types of toxicosis, particularly if the product has delayed release (e.g., extended or sustained release) or undergoes enterohepatic recirculation (see multi-dose AC below). While human medicine has moved away from administration of AC with poisoned patients, the aggressive use of AC in veterinary medicine is still warranted, as this is often our last line of defense when it comes to adequately decontaminating our patients. Certain modalities of therapy [e.g., antidotes (such as fomepizole, 2-PAM, digoxin-specific antibody fragments, etc.), plasmapheresis, hemodialysis, mechanical ventilation, etc.], along with financial limitations of pet owners, limit our ability to treat poisoned pets aggressively; as a result, the continued use of AC in veterinary medicine is still warranted as a first line of defense therapy. Current recommended dosing for single dose AC is: 1-5 g of AC/kg with a cathartic (e.g., sorbitol) to promote gastrointestinal tract (GIT) transit time.

Multi-dose Activated Charcoal

Human studies have found that multi-dose AC significantly decreases the serum half-life of certain drugs, including antidepressants, theophylline, digitoxin, and phenobarbital. While veterinary studies are lacking, there is likely an added benefit from using multi-dose AC, provided the patient is well hydrated and monitored appropriately. Certain situations or toxicities, including drugs that undergo enterohepatic recirculation; drugs that diffuse from the systemic circulation back into the intestinal tract down the concentration gradient; or ingestion of sustained (SR), extended (XR), or long-acting release products will require multi-dose administration of AC. Keep in mind that multi-dose AC should *not* contain cathartics with additional doses, due to increased risks for dehydration and secondary

hypernatremia via fluid losses from the GIT. Current recommended dosing for multiple doses of AC is: 1-2 g of AC *without a cathartic* /kg of body weight, PO q 4-6 hours for 24 hours.

Contraindications of activated charcoal

Contraindications for AC include endoscopy (which would obscure visualization), abdominal surgery of the GIT, gastric or intestinal obstruction, gastrointestinal hemorrhage or perforation (due to pathology, caustic injury, etc.), recent surgery, late-stage presentation with clinical signs already present, dehydration, lack of borborygmi, ileus, hypernatremia, hypovolemic shock, compromised airway (risk for aspiration pneumonia), and ingestion of a caustic substance or hydrocarbon (due to increased risk for aspiration pneumonia). In patients that have an unprotected airway that are at risk for aspiration pneumonia (e.g., a depressed state of consciousness, excessive sedation, etc.), the use of AC is contraindicated without endotracheal intubation.

TREATMENT

When it comes to veterinary toxicology, there are only a few toxins that require or have a specific antidote (e.g., fomepizole, 2-PAM, Vitamin K₁, etc.). As a result, symptomatic supportive care is imperative and considered the mainstay therapy once decontamination (including emesis induction, gastric lavage, administration of activated charcoal, etc.) has been performed. Five broad categories of treatment are discussed below:

- 1) Fluid therapy
- 2) Gastrointestinal support
- 3) Neurologic support
- 4) Sedatives/reversal agents
- 5) Hepatoprotectants
- 6) Miscellaneous

Fluid therapy

In the poisoned pet, fluid therapy is indicated for several reasons: to aid in excretion of the drug (if it is renally-excreted); to aid in perfusion; to prevent dehydration; to diuresis nephrotoxins; and to vasodilate the renal vessels (particularly with NSAID toxicosis). In general, a balanced, maintenance, isotonic crystalloid (e.g., LRS, Norm-R) can be used at 1.5-3X maintenance. That said, the patient should be assessed carefully to ensure that volume overload does not occur (particularly if the patient has underlying cardiopulmonary disease).

Gastrointestinal support

The use of anti-emetics, antacids, anti-ulcer drugs, and gastric pH altering medications is of benefit in the poisoned patient. Those patients who have had emesis induction performed often require an anti-emetic to prevent vomiting of activated charcoal later on. Also, certain toxicants result in gastric irritation, gastric distension, etc., which may result in vomiting. In those toxicants predisposing the patient towards gastric ulceration (e.g., veterinary NSAIDs, human NSAIDs, corrosive toxicants, etc.), the use of antacids, anti-ulcer medication and gastric pH altering medications should be considered.

Anti-emetics:

- Maropitant: 1 mg/kg SQ q. 24 hours
- Ondansetron: 0.1-0.2 mg/kg IV q. 8-12 hours
- Dolasetron: 0.5-1 mg/kg SQ, IV q. 24 hours
- Metoclopramide: 0.1-0.5 mg/kg SC, IV q. 8 hours or 1-2 mg/kg/day as CRI IV

Gastric pH altering medication:

H₂ blockers:

- Famotidine: 0.5-1 mg/kg IV, SQ q. 12-24 (least p-450)
- Ranitidine: 0.5-2 mg/kg, IV, PO, SQ q. 8-12 (moderate p-450)
- Cimetidine: 5-10 mg/kg IV, PO, SQ q. 6-8 (most p-450)

Proton-pump inhibitors:

- Omeprazole: 0.5-1 mg/kg PO q. 24 hours
- Pantoprazole: 1 mg/kg IV q. 24 hours

Anti-ulcer:

- Sucralfate 100-1 g PO q. 8 hours

Neurologic support

In the poisoned patient, either stimulatory (e.g., agitation, tremors, seizures, etc.) or sedatory (e.g., severe sedation, coma, drowsiness) clinical signs are often seen with certain toxicants. ADD/ADHD drugs (which contain amphetamines) and selective serotonin reuptake inhibitor (SSRI) antidepressants may result in stimulatory signs, while certain muscle relaxants (e.g., baclofen) or sedatives (e.g., opioids, etc.) may cause severe sedation.

Appropriate anti-convulsant therapy should be used for grand-mal or petit mal seizures, while muscle relaxants (e.g., methocarbamol) should be used for tremors (e.g., pyrethrin). For comatose dogs, the use of the opioid reversal naloxone can often be used for both opioid toxicosis and baclofen toxicosis.

Anti-convulsants:

- Phenobarbital 4-16 mg/kg IV to effect
- Diazepam 0.25-0.5 mg/kg IV to effect

Muscle relaxants:

- Methocarbamol: 44-220 mg/kg IV or PO, slow to effect, not to exceed 330 mg/kg/day

Miscellaneous:

- Naloxone: 11-22 mcg/kg IV, SQ, or IM to effect

Sedatives (for anxiety):

- Acepromazine: 0.05-0.1 mg/kg (up to 0.5 mg/kg in stable patients) SQ, IV, IM to effect PRN
- Torbugesic: 0.2-0.8 mg/kg SQ, IV, IM to effect PRN
- Chlorpromazine: Dog: 1-10 mg/kg IV, IM, SQ to effect; Cat: 0.5-1.1 mg/kg IM, IV, SQ to effect

Hepatoprotectants

The use of hepatoprotectants such as S-adenosyl-methionine (SAME) are benign nutraceuticals that are beneficial for hepatotoxicants such as xylitol, blue-green algae, NSAIDs, *Amanita* mushrooms, etc. SAME acts as a methyl donor and generates sulfur containing compounds that are important for conjugation reactions used in detoxification and as a precursor to glutathione.

Miscellaneous

Other miscellaneous therapies are often used for the treatment of the poisoned patient, and include the use of beta-blockers (for severe tachycardia associated with SSRI, amphetamine, chocolate toxicosis, etc.); intravenous lipid therapy (which acts as a "lipid sink" for fat-soluble toxins such as calcium channel blockers, macrocyclic lactones like ivermectin, baclofen, etc.); vitamin K₁ therapy (for long-acting anticoagulant toxicosis), etc. Readers are referred to a toxicology resource for additional information on these topics.

CONCLUSION

Pet owners should be appropriately educated on how to pet-proof the house, and be trained on what common household products and kitchen items are poisonous. Pet owners should also be appropriately educated on crate training to help minimize toxin exposure. Once a pet is exposed to a toxicant, it is imperative to determine if emesis is appropriate, and to understand when it may be contraindicated (e.g., symptomatic patient, delayed time since exposure, hydrocarbons, etc.). Knowledge of the underlying mechanism of action, the pharmacokinetics (including absorption, distribution, metabolism, and excretion), and the toxic dose of the toxicant are imperative in determining appropriate decontamination and therapy for the patient.

REFERENCES

Peterson ME, Talcott PA. Small Animal Toxicology. Elsevier, St. Louis, Missouri, 2006.