ACTIVATED CHARCOAL (AC)

Activated charcoal (AC) has been used for over 100 years for the treatment of toxic ingestions, and continues to be the most common form of gastrointestinal decontamination for the poisoned patient. Activated charcoal works by adsorbing poison in the gastrointestinal tract (GIT) and decreasing the extent of systemic absorption of the poison. In order for AC to work, it must physically come into contact with the poison. To maximize AC absorption of the toxicant, the administration of AC should be implemented as soon as possible, as delayed administration reduces its effectiveness.

Medicinal charcoal must meet BP, USP or similar standards for adsorption, microbial contaminants and purity. Activated charcoal is created by controlled pyrolysis of petroleum, coconut shells, lignite (coal), peat, and wood, which then produces charcoal. Once charcoal is created, it is activated by heating it at high temperatures (600-900°C) with steam, air, or carbon dioxide. Finally, charcoal is washed with inorganic acids and dried. This activation process results in a small particle size, a large surface area (950 to 2,000 m²/g), and a highly developed internal pore structure which contributes to adsorptive properties and extent of adsorption at equilibrium. The carbon moieties (carbonyl, hydroxyl) of the adsorptive surface of AC contribute to the varying binding affinity. For example, non-polar compounds bind to AC well, while heavy metals and alcohols (i.e., ethylene glycol) are not absorbed by AC; xylitol is also poorly bound to AC. In general, in vitro adsorption to AC reaches equilibrium in less than 30 minutes. While desorption of toxicants to AC can occur, as binding to AC is a reversible process, this clinical effect is not known or well described. The addition of a cathartic may be considered to help promote GIT transit time to help decrease the time for desorption to potentially occur. Activated charcoal may also contain preservatives, various types of cathartics, or even sodium bicarbonate or povidone, which may contribute to complications later discussed in this lecture.

The American Academy of Clinical Toxicology (AACT) and European Association of Poisons Centres and Clinical Toxicologists (EAPCCT) created a position paper in 1997 (revised again in 2004) which clearly stated that “single-dose AC should not be administered routinely in the management of poisoned patients... [as]... there is no evidence that administration of AC improves clinical outcome.” Since then, the use of AC in human medicine has continued to steadily decline, according to the American Association of Poison Control Centers Toxic Exposure Surveillance System (from 7.7% to 5.9% in 2003). Despite human medicine’s move away from AC, should veterinary medicine be following this similar declining trend in detoxification of poisoned patients? (Short answer: No).

HUMAN AND ANIMAL STUDIES

Numerous human and animal studies have evaluated AC administration and effect based on timing of ingestion. The position paper on single-dose AC evaluated the results of 122 studies, and compared 46 drugs, the absolute amount of charcoal (0.5-100 g) administered, and the time of administration (up to 360 minutes after ingestion). Of these 122 cases, 84 (69%) had AC administered within ≤ 5 minutes. In the studies where AC was administered within 30 minutes, there was a mean reduction in absorption of 51.7% (n=7); at 60 minutes, the mean reduction was 38.1% (n=16); at 120 minutes, the mean reduction was 34.5% (n=8); at 180 minutes, the mean result was 21.1% (n=3); at 240 minutes, the mean reduction was 29.3% (n=3), and at 360 minutes, the reduction was 14% (n=1). The data from 48 comparisons involving 26 drugs, which all used at least 50 g of AC, showed a mean reduction at 30 minutes after dosing at 47.3% (n=3); the mean reduction at 60 minutes was 40.1% (n=12); at 120 minutes, 16.5% (n=3); at 180 minutes, 21.1% (n=3), and at 240 minutes, the mean reduction was 32.5% (n=2). Unfortunately, in these studies, certain factors could not be controlled (i.e., influence of food in the stomach, presence of a poison that may delay gastric emptying, etc.). Based on these studies, the administration of AC in human medicine beyond one hour is generally not recommended; however, the beneficial potential beyond 1 hour cannot be excluded.

When it comes to animal studies, limited veterinary literature exists. Often, these studies are performed in mice and rats, and it is important to consider the differences in comparative anatomy, metabolism, GI motility, morphology, absorption rate and site, and elimination. A recent prospective study evaluated the effect of AC alone vs. emesis and AC on carprofen absorption following experimental overdose in dogs, and found that AC alone is as effective. Due to the paucity of prospective clinical research in veterinary medicine, further studies are warranted.

In veterinary medicine, it is almost impossible to administer AC within ≤ 5 minutes. 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 (i.e., syringe feeding, orogastric tube, etc.), administration is often delayed to 30 minutes, up to an hour or more. As time since ingestion is often unknown (i.e., pet owner coming home from work to find their pet poisoned), decontamination 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 (i.e., extended or sustained release) or undergoes enterohepatic recirculation (see multi-dose AC below). More importantly, the variable modalities
of therapy [i.e., antidotes (such as digoxin-specific antibody fragments, 2-PAM, etc.), plasmapheresis, hemodialysis, mechanical ventilation, etc.], along with financial limitations of pet owners, warrant the aggressive use of AC in veterinary medicine, as this is often our last line of defense in adequate decontamination of a patient.

**DOsing**

Current recommended dosing for single dose AC is: 1-5 g of AC/kg with a cathartic (i.e., sorbitol) to promote GIT transit time.

**Multi-dose Activated Charcoal**

Certain situations or toxicities warrant multi-dose administration of AC. Drugs undergoing 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; however, multi-dosing should not contain cathartics with additional doses, due to increased risks for dehydration and secondary hypernatremia via fluid losses from the GIT. 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 multi-dosing AC, provided the patient is well hydrated and monitored appropriately.

- **Dose**: 1-2 g of AC *without a cathartic* per kg of body weight, PO q 4-6 hours for 24 hours

**Availability**

There are several types of AC commercially available (i.e., granules, capsules, tablets, aqueous suspension, powder), and the labeled directions should be followed appropriately for each specific type, as the dose is dependent on the product used and concentration. Many types already contain a cathartic within the AC (i.e., typically 70% sorbitol), and it is important to ideally have two types available (AC alone, AC with cathartic). Finally, some pet owners may have access to AC tablets and capsules; however, these are not generally recommended, as they are not as effective as AC liquid slurries or aqueous solutions. In human medicine, the aqueous suspension is significantly more effective than tablets or capsules.

**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 (i.e., a depressed state of consciousness, excessive sedation, etc.), the use of AC is contraindicated without endotracheal intubation.

**Cathartics**

Cathartics are designed to increase the speed and transit time of the GIT, promoting fecal excretion of the toxin, but more importantly, decreasing the time allowed for toxin absorption through the GIT. Typical cathartics used in veterinary medicine comprise of osmotic cathartics: saccharide (i.e., sorbitol) vs. saline cathartics (i.e., sodium sulfate, magnesium citrate, or magnesium sulfate). Sorbitol is most commonly used, as it aids in the expulsion of the poison from the GIT, while also masking the grittiness and poor palatability of AC with its sweet taste. Side effects of sorbitol administration include vomiting, dehydration, secondary hypernatremia, abdominal cramping or pain, and possible hypotension. The contraindications for cathartics are similar to those that exist for AC. Another important consideration in veterinary medicine is that mineral oil is no longer recommended as a cathartic due to the high risks of secondary aspiration. In general, if AC does not contain a pre-existing cathartic (for the first dose administered), one can potentially add in sorbitol (70% solution) for a one dose dosing at: 1-2 ml/kg, PO, given within 60 minutes of toxin ingestion.

According to the position paper on cathartics endorsed by the AACT and EAPCCT, the use of cathartics in human medicine “has no role in the management of the poisoned patient and is not recommended as a method of gut decontamination.” If considered, the use of cathartics should be limited to a single dose to prevent known complications from multi-dosing of cathartics. There are no published clinical studies investigating the use of a cathartic (with or without AC) in reducing the bioavailability of drugs, or improving the clinical outcome of poisoned patients. Finally, the position statement of cathartics warns about serious adverse effects from multi-dosing of cathartics, including dehydration and electrolyte abnormalities, including hypernatremia and hypermagnesemia (when using a sodium- or magnesium-containing cathartic). In addition, those patients with renal dysfunction or pre-existing dehydration may be at increased risk. In veterinary medicine, we still recommend a first dose dosing of AC with a cathartic; however, the use of multi-dose AC should *not* contain cathartics to prevent these clinically recognized, but rare, complications.

Unfortunately, there is limited literature evaluating the use of cathartics in veterinary medicine, and no studies prospectively evaluating its use in the clinical poisoned veterinary patient. Experimental animal studies do exist; in one study evaluating mice administered paraquat, the combined use of AC with magnesium citrate (30 minutes post) increased survival from 31% (controls) to 94%, with a significant p<0.01. In a canine study evaluating sorbitol, mannitol, and AC administration in dogs given acetaminophen, the area under the curve (AUC) was 75% greater with cathartics and AC compared to charcoal alone (p=0.07),
and the peak plasma concentration was 80.4% greater (p=0.012) after cathartics plus AC compared to AC alone.\textsuperscript{4} When AC was given with sodium sulfate to rats treated with salicylate, pentobarbital, chlorpheniramine, and chloroquine, peak plasma concentrations were significantly reduced (p<0.001) compared to the control.\textsuperscript{5} Finally, when sodium sulfate with superactivated AC was used in rats given a lethal dose of T-2 mycotoxin, survival and survival times increased (p<0.01).\textsuperscript{6}

**COMPLICATIONS**

In both human and veterinary medicine, there are relatively rare reports of AC-related adverse events, especially when considering the widespread use of AC in both human and veterinary medicine.\textsuperscript{1} Complications include respiratory complications (i.e., aspiration pneumonia, acute respiratory distress syndrome), corneal abrasions (if accidental contact to the eye occurs), intubation/endoscopy difficulty (due to the presence of AC in the oropharynx), constipation, vomiting, and fluid, electrolyte and acid-base abnormalities (including hypernatremia, hypokalemia, hypermagnesemia, and metabolic acidosis). In humans administered multi-dose AC, complications of ileus and small intestinal obstruction (from charcoal bezoars) requiring surgical intervention have been reported. When AC is used appropriately in a hydrated patient, the majority of adverse events are not directly related to AC; rather, it may be due primarily to the cathartic affect, or from complications arising when aspiration of AC occurs or when AC is directly administered (iatrogenic) into the lung. Finally, additional preservatives or contents (i.e., povidone) in AC can result in severe respiratory problems. Rarely, anecdotal reports of hypernatremia have been clinically reported with AC administration. This is likely due to the sorbitol effect, which acts as a cathartic, resulting in excessive free water loss. Initially, the use of a one-time dose of a cathartic is recommended to help promote GIT motility, to prevent desorption from occurring between the toxin and the AC within the GIT. However, continued use of cathartics (with multi-dosing) can result in profound dehydration, fluid losses, and hypernatremia.

Burkitt et. al evaluated the use of a commercial AC, Actidose-Aqua, in a prospective, clinical trial in 6 dogs to determine if AC suspension containing propylene glycol (PG) and glycerol had any effects on serum osmolality, osmolal gap, and lactate.\textsuperscript{7} Samples were also evaluated for acid-base status, and concentrations of sodium, potassium, BUN, and glucose. In this study, dogs \((n=6)\) were given 4 g/kg of AC, and samples were taken before and 1, 4, 6, 8, 12, and 24 hours post-AC.\textsuperscript{7} In this study, mean serum osmolality, osmolal gap, and lactate concentration were significantly increased after suspension administration compared to baseline, typically increasing at 1 hour after AC administration, peaking at 4 hours, and returning to baseline by 24 hours. Hypernatremia was not detected in any of the study dogs; however, mild hypokalemia was seen (P<0.05). Serum osmolality increased from 311 mOsm/kg at baseline to 353 mOsm/kg, osmolal gap increased from 5 to 52 mOsm/kg, and lactate concentration increased from 1.9 to 4.5 mmol/L after suspension administration (P < .01).\textsuperscript{7} All 6 dogs drank frequently after AC administration, but water intake or urine output was not recorded. In addition, 3/6 dogs vomited within 1-3 hours of administration of AC, while 4/6 of dogs were lethargic.\textsuperscript{7} While this study was important in evaluating complications from AC, this particular AC did not contain sorbitol or a cathartic (Actidose with Sorbitol). A prospective study evaluating the use of a cathartic with AC would be important to evaluate the prevalence of hypernatremia seen with AC and cathartic administration.

**CLINICAL APPLICATION**

Prior to administration of AC with or without a cathartic, the patient should be assessed for hydration status. Appropriate fluid supplementation (SQ, IV) should be used to prevent dehydration and hypernatremia. In addition, the concurrent use of parenteral (i.e., IV) anti-emetics should be considered, due to the high prevalence of vomiting from cathartic administration (or from the emetic previously used to decontaminate the patient): Cathartics should not be used in a dehydrated patient, due to the risks of voluminous fluid losses through the GIT and secondary hypernatremia. For patients receiving either multi-doses of AC with or without cathartics, serum sodium levels should be monitored, along with hydration status. Those patients that are dehydrated, vomiting, fasted, predisposed to hyperosmolality disorders (such as renal disease, poorly regulated diabetes mellitus, psychogenic polydyspia, diabetes insipitus, etc.) may be more at risk for developing significant, clinical hypernatremia from the cathartic agent in AC.

**CONCLUSIONS**

In veterinary medicine, the primary treatment for toxicant exposure should be decontamination and detoxification of the patient to inhibit or minimize further toxicant absorption and to promote excretion or elimination of the toxicant from the body.\textsuperscript{1} 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**