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Multiple-Dose Activated Charcoal in Treatment of Acute Poisoning

By Amberly R. Johnson, PharmD, DABAT and Austin Ulrich, PharmD Candidate 2018

Introduction

Activated charcoal (AC) is a black, odorless powder made from vegetable matter (e.g. coal, coconut shell, peat, wood, or petroleum) and is administered in poison exposures to adsorb potentially toxic substances.[1-4] In the past, activated charcoal was widely used, with US poison centers documenting charcoal administration in 145,853 poison exposures in 1999.[5] Since then its use has declined, with only 40,633 administrations in 2016, reflecting general waning of enthusiasm for gastrointestinal decontamination.[6] Activated charcoal may be administered as a single dose (single-dose activated charcoal–SDAC) or in multiple doses (multiple-dose activated charcoal–MDAC).[4] Decisions to administer either SDAC or MDAC should be based on the potential toxicity of the substance ingested and the risks and benefits of charcoal administration.[5]

Credit: Paddock Laboratories, Inc.

Activated Charcoal Mechanism of Action

Charcoal is activated by exposure to gas at high temperatures or by treatment with phosphoric acid, zinc chloride, or both.[2,4] The activation process creates an internal pore structure within the charcoal that increases its surface area from 2-4 m^2/g to 1500 m^2/g.[2] With this large surface area, AC can adsorb many potentially toxic substances through hydrogen bonding and van der Waals forces.[7] AC is most effective for substances that are dissolved and nonionized.[1] Highly ionic salts such as iron, lithium, potassium, and cyanide, and polar molecules, such as alcohol, are poorly adsorbed to charcoal.[8]

SDAC vs MDAC

SDAC is administered with the goal of decreasing absorption of a potentially toxic substance, and the single dose is most effective when administered within 1 hour of ingestion.[3-5,8] In contrast, MDAC is defined as at least 2 sequentially administered doses of activated charcoal[2,4,8] and functions to prevent ongoing absorption of substances that are slowly or erratically absorbed from the GI tract, and in some cases, enhance elimination of substances that undergo enterohepatic and enterogastric recirculation through a process termed gastrointestinal dialysis.[1,2] Certain drugs can reenter the gut via passive diffusion, and as long as a concentration gradient is maintained, with drug concentration lower in the gut lumen, these drugs can pass from the blood into the gut lumen and become adsorbed to charcoal.[1,2] Stagnant or rising drug concentrations after a poison exposure may indicate ongoing absorption or enterohepatic/enterogastric recirculation.

MDAC Efficacy

MDAC may decrease rising drug concentrations in a poisoned patient, and MDAC has been administered for a variety of substances. The American Academy of Clinical Toxicology (AACT) and European Association of Poisons Centres and Clinical Toxicologists (EAPCCT) recommends MDAC for life-threatening ingestions of only a limited number of substances, such as carbamazepine, dapsone, phenobarbital, quinine, and theophylline, based on evidence from animal, volunteer, and clinical studies.[2] The American College *(cont. on pg. 3)*

IN THIS ISSUE

POISON PEARLS

Camphor Toxicity

By Dave Jenson,PharmD and Amberly R. Johnson, PharmD, DABAT

Camphor, a common ingredient in many over-the-counter products, is frequently used as a home remedy for common cold symptoms, muscle aches, and cold sores (Table 1).[1, 4, 5] In 1983, the Food and Drug Administration restricted camphor in over-the-counter products to concentrations less than 11% after significant toxicity and death were reported from exposures to camphor-containing products. Camphor products with concentrations greater than 11% are still available in some stores, such as specialty markets, within the US and also in other countries.[1, 3,5]

In 2016, 12,833 camphor exposures were reported to US poison control centers.[2] The majority of exposures were unintentional (n=12,285) and occurred in children ≤ 5 years (n=10,573). Moderate effects occurred in 84 exposures, and major effects occurred in 10 exposures. No deaths were reported.[2]

Camphor toxicity occurs largely from ingestion, although toxicity has been reported from dermal and inhalational exposures.[4] Toxicity can occur as early as 5-15 minutes post-ingestion and generally presents as mucous membrane irritation, nausea, vomiting, and abdominal pain.[1,8] Signs of systemic toxicity include agitation, confusion, and generalized tonic-clonic seizures. Seizures are usually brief and self-limiting and occur within 1-2 hours of ingestion.[1,8] Clinical effects resolve generally within 24 hours of ingestion.[1,8] Deaths have occurred secondary to status epilepticus and respiratory failure.[1,4,5]

The American Association of Poison Control Centers referral guidelines recommend emergency department observation for patients with camphor ingestions at or above 30 mg/kg.[5] Asymptomatic patients should be observed for a minimum of 4 hours post-ingestion.[1,8]

Management of camphor toxicity consists of symptomatic and supportive care. Activated charcoal is not recommended because camphor is rapidly absorbed.[1,5] Benzodiazepines are recommended for camphor-induced seizures. If seizures are refractory to benzodiazepines, phenobarbital or propofol is recommended.[8]

If you suspect a patient has camphor toxicity, call the Utah Poison Control Center with questions.

TABLE 1: Camphor content in common over-the-counter products[5]

Product	Concentration (%)
BENGAY® Pain Relieving Cream, Ultra Strength	4
Vicks® VapoRub™ Topical Cough Suppressant	4.8
Vicks® VapoSteam™ Cough Suppressant	6.2
Mentholatum® Original Ointment	9
Campho-Phenique® Cold Sore Treatment	10.8
Tiger Balm® Ultra Strength Pain Relieving Ointment	11

References

1. Kim HK. Camphor and Moth Repellents. In: Hoffman RS, Howland M, Lewin NA, Nelson LS, Gold-frank LR. eds. *Goldfrank's Toxicologic Emergencies*, 10e. New York, NY: McGraw-Hill; 2015. http://accesspharmacy.mhmedical.com/content.aspx?bookid=1163&Sectionid=65100353. Ac-cessed January 22, 2017.
2. Gummin DD, Mowry JB, Spyker DA, Brooks DE, Fraser MO, Banner W. Mowry JB, Spyker DA, Brooks DE, Zimmerman A, Schauben JL. 2016 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 34th Annual Report. *Clin Toxicol (Phila)*. 2017;55(10):1072-1254.
3. Kusin S, Lank PM. Pediatric Overdoses. Available at: http://www.slremeducation.org/wp-content/uploads/2015/06/Chapter-158.-Pediatric-Overdoses.pdf Accessed January 16, 2017.
4. Love JN, Sammon M, Smereck J. Are one or two dangerous? Camphor exposure in toddlers. *J Emerg Med*. 2004;27(1):49-54.
5. Manoguerra AS, Erdman AR, Wax PM, et al. Camphor Poisoning: an evidence-based practice guideline for out-of-hospital management. *Clin Toxicol (Phila)*. 2006;44(4):357-70.

OUTREACH EDUCATION

National Poison Prevention Week: March 18-24, 2018

By Sherrie Pace, MS, MCHES®

The third week of March is National Poison Prevention Week (NPPW). In 1962, President John F. Kennedy signed legislation establishing NPPW, and the first observance took place that year. Since then, poison centers across the nation, along with other organizations such as medical practices, health care facilities, schools, and local health departments, have brought awareness to the poison problem during this week by advocating poison prevention in their communities.

Poisonings are preventable, yet poisoning is still the number one cause of unintentional injury death in the US. Please join the effort to reduce this alarming statistic and prevent unintentional poison exposures by promoting this important week. Visit www.utahpoisoncontrol.org to order free prevention materials to distribute, sign up to receive newsletters, download lesson plans, and learn more. Follow Utah Poison Control Center on Facebook, Twitter, and Pinterest for regular poison prevention tips and important alerts!

(cont. from pg. 1)

MDAC

of Medical Toxicology (ACMT) guidance document for management priorities in salicylate toxicity recommends considering MDAC in patients with early presentation, rising salicylate levels, or other signs of incomplete absorption.[9] However no evidence exists to show that MDAC improves clinical outcomes. Pond and colleagues performed a prospective randomized controlled trial of patients administered SDAC or MDAC for phenobarbital overdose.[10] A total of 14 patients were randomized and 10 completed the trial (MDAC n=5, SDAC n=5). The half-life of phenobarbital was reduced in patients treated with MDAC (36 ± 13 hours) compared to SDAC (93 ± 52 hours), but this did not correlate with improved clinical outcomes. No difference was found in the time patients were mechanically ventilated (SDAC 39 ± 24 hours vs MDAC 48 ± 8 hours) or hospitalized (SDAC 6 ± 2 days vs MDAC 6 ± 1 days). Four patients withdrawn from the study developed complications. SDAC patients (n=2) had worsening clinical statuses and poor perfusion. MDAC patients (n=2) developed abdominal complications; both patients had abdominal distention and 1 patient developed ischemic bowel.

Dosing and Administration

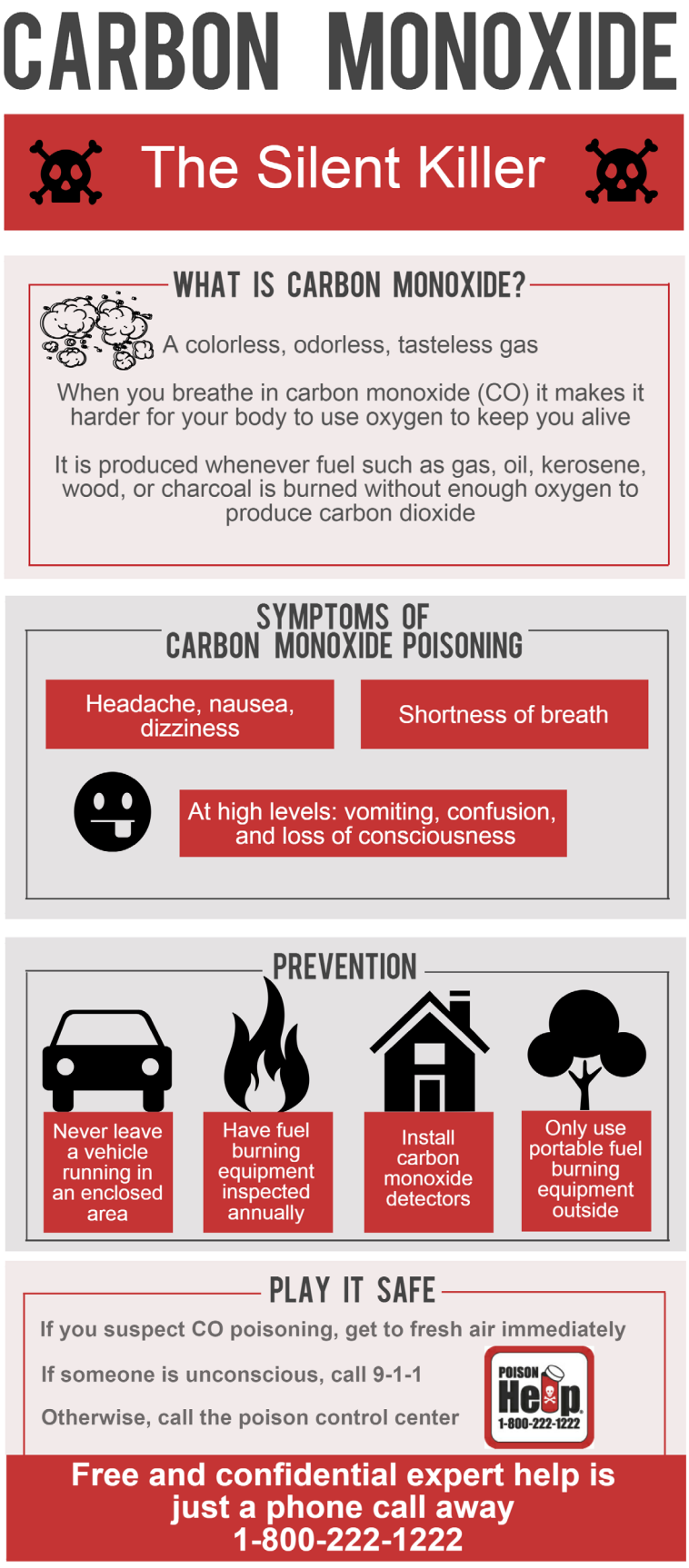
The joint AACT and EAPCCT Position Statement recommends an initial AC dose of 50-100 g in adults, followed by a 12.5 g/hr equivalent dose every 1, 2, or 4 hours.[2] Lower AC doses (10-25 g) are recommended in children due to their smaller gut capacity and usually smaller ingestions.[2] Though no recommended duration of MDAC therapy is given, administering MDAC until drug concentrations have peaked and show a significant downtrend is reasonable.[3]

Generally coadministration of a cathartic with MDAC is not recommended, especially in children.[2] Hypernatremia, hypokalemia, hypermagnesemia, and metabolic acidosis are reported with cathartic use and occur most frequently in children.[2] If cathartics are coadministered with MDAC in adults, administration should be limited to the initial 1 or 2 doses in 24 hours.[11]

Patient compliance is a challenge with MDAC administration. In 2008, a prospective randomized controlled study evaluated patient compliance rates for SDAC and MDAC.[12] Of the patients who received charcoal orally (SDAC, n=477; MDAC, n=408), more patients refused the first dose of charcoal in the MDAC group compared to the SDAC group (3.2% vs 0.6%, p=0.0045). The number of patients who refused activated charcoal appeared to increase linearly after each subsequent dose; however, percentages were only reported for the 1st and 6th doses (3.2% vs. 12.3%). Also, patients required more persuasion after each subsequent dose.

Adverse Effects

Commonly reported side effects of MDAC are nausea, vomiting,[3] black stool, and constipation.[2,8] More severe side effects include respiratory complications secondary to aspiration, bowel obstruction, and fluid/electrolyte abnormalities.[2,10] Dorrington and colleagues *(cont. on pg. 4)*



(cont. from pg. 3)

MDAC

conducted a retrospective chart review of 8 tertiary care hospitals in 4 North American cities between 1993 and 1998 to determine the frequency of complications associated with MDAC administration.[13] Patients were included if they received more than 2 doses of AC in a 12-hour period and had a primary or secondary diagnosis of poisoning (n=878). Electrolyte abnormalities were documented most frequently. Hypernatremia was documented in 53 patients (6%), and 27 patients (3.1%) had documented hypermagnesemia.[13]

No gastrointestinal obstructions were identified in the Dorrington study[11]; however, cases of obstruction secondary to MDAC administration are reported in the literature, most often in patients who have underlying gastrointestinal abnormalities.[2,8] Patients who have had a recent bowel surgery or decreased or absent bowel sounds are not candidates for MDAC due to risk of vomiting or gastrointestinal complications.[3,8] Clinically significant aspiration occurred in 5 patients (0.6%), with the majority (80%) occurring after the first AC dose.[13]

Aspiration has also occurred from error in MDAC administration. In 1993, a case report was published describing a 30-year-old man who was inadvertently administered activated charcoal and sorbitol into his right lung.[14] The patient received MDAC for a tricyclic antidepressant (TCA) overdose, and in between doses, he pulled his nasogastric (NG) tube out of position. The NG tube was inadvertently reinserted into the right bronchus, and the second AC dose was administered into the right lung. The patient developed acute respiratory distress syndrome (ARDS) and required bronchoscopic removal of charcoal. He improved with supportive care and was discharged on hospital day 14.[14]

Summary

Activated charcoal works by adsorbing poisons to prevent systemic absorption. MDAC has been shown to increase elimination and limit absorption for a very limited number of substances, and no prospective study has proven that AC improves clinical outcomes.

Dosing of MDAC is often institution and case specific, but is usually 2 or more doses of AC. Cathartics are not recommended due to adverse effects, and patient compliance is an important consideration for administration. Potential adverse effects associated with MDAC include respiratory and gastrointestinal complications and fluid, electrolyte, and acid-base disturbances.

Though not every ingestion may benefit from MDAC, in some specific poisoning situations, MDAC can be used as an adjunct therapy to minimize effects from a poison exposure. Contact the Utah Poison Control Center at 1-800-222-1222 with questions regarding the use of multiple-dose activated charcoal 24 hours a day, 7 days a week.

References

1. Smith S, Howland M. Antidotes in Depth. In: Hoffman R, Howland M, Lewin N, Nelson L, Goldfrank L. *Goldfrank's Toxicologic Emergencies*. 10e ed. New York, NY: McGraw-Hill; 2015.
2. Position statement and practice guidelines on the use of multi-dose activated charcoal in the treatment of acute poisoning. American Academy of Clinical Toxicology; European Association of Poisons Centres and Clinical Toxicologists. *J Toxicol Clin Toxicol*. 1999;37(6):731-751.
3. Hoegberg L, Gude A. Techniques Used to Prevent Gastrointestinal Absorption. In: Hoffman R, Howland M, Lewin N, Nelson L, LR G. *Goldfrank's Toxicologic Emergencies*. 10e ed. New York, NY: McGraw-Hill; 2015.
4. Juurlink DN. Activated charcoal for acute overdose: a reappraisal. *Br J Clin Pharmacol*. 2016;81(3):482-487.
5. Olson KR. Activated Charcoal for Acute Poisoning: One Toxicologist's Journey. *J Med Toxicol*. 2010;6:190-198.
6. Litovitz TL, Klein-Schwartz W, White S, et al. 1999 annual report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. *Am J Emerg Med*. 2000;18(5):517-574.
7. Gummin DD, Mowry JB, Spyker DA, et al. 2016 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 34th Annual Report. *J Toxicol Clin Toxicol*. 2017;55(10): 1072-1254.
8. Kearney T. Charcoal, Activated. In: Olson K. *Poisoning & Drug Overdose*. 6e ed. New York, NY: McGraw-Hill; 2012.
9. Guidance document: management priorities in salicylate toxicity. *J Med Toxicol*. 2015;11(1):149-152.
10. Pond SM, Olson KR, Osterloh JD, Tong TG. Randomized study of the treatment of phenobarbital overdose with repeated doses of activated charcoal. *JAMA*. 1984; 251(23):3104-3108.
11. Caldwell JW, Nava AJ, de Haas DD. Hypernatremia associated with cathartics in overdose management. *West J Med*. 1987;147(5):593-596.
12. Mohamed F, Sooriyarachchi M, Senarathna L, et al. Compliance for single and multiple dose regimens of superactivated charcoal: a prospective study of patients in a clinical trial. 2007;45(2):132-135.
13. Dorrington CL, Johnson DW, Brant R. The frequency of complications associated with the use of multiple-dose activated charcoal. *Ann Emerg Med*. 2003;41(3):370-377.
14. Harris CR, Filandrinos D. Accidental administration of activated charcoal into the lung: aspiration by proxy. *Ann Emerg Med*. 1993;22(9):1470-1473.

TOXINS IN THE NEWS

Counterfeit Medications

By B. Zane Horowitz, MD, FACMT

While cheap illegal versions of medications have been around for a long time, this newest version of the problem is substituted opiate medications. Last year, pills created to look like oxycodone 30 mg tablets were found in Tennessee to actually contain fentanyl. That spring, oblong tablets that carried an identical imprint code and shape as Norco were found in San Francisco and contained a combination of fentanyl, promethazine, and acetaminophen. A long list of fentanyl derivatives have begun to be clandestinely imported into the US and then formed in pill presses to look exactly like prescription opiates often sought after for misuse. The opiate epidemic continues to shift from prescription pharmaceuticals to heroin and now to counterfeit medications made to look like legitimate pharmaceutical products. Recently, a novel fentanyl derivative showed up in Georgia that was the previously unknown compound cyclopropyl fentanyl. Fentanyl and its analogues are opioids that are far more potent than heroin. Carfentanil, a fentanyl analogue approximately 10,000 times more potent than morphine (or 100 times more potent than fentanyl), has been identified throughout the country. Other fentanyl analogues include furanyl fentanyl, acetyl fentanyl, butyl fentanyl, "Pink" (a.k.a. U-47700), and W-18.

Multiple overdose events occurring over a short period of time *(cont. on pg. 5)*

Credit: DEA

(cont. from pg. 4)

Counterfeit Medications

in any city should trigger suspicion of a potent fentanyl analog. Clues to recognition of potential adulteration are that these counterfeit tablets fall apart easily when handled or appear slightly off-color when compared to legitimate pharmaceuticals. Suspicion of counterfeit medications appearing in your community should lead to notifications to the public health department, the poison center, and law enforcement. Consideration may need to be given to short term resource mobilization to accommodate larger numbers of victims presenting to emergency departments and increased need for pre-hospital the naloxone. Some cities in the East have had weekends with hundreds of overdose victims as these pills were sold over a short period of time.

The media has suggested that merely touching these agents could lead to dire symptoms. While the possibility of absorption through the skin has been described on the news, pharmacologically brief exposure and then washing these agents off with water is unlikely to result in any toxic effects. Due to concerns, we recommend appropriate precautions should be taken by all medical and law enforcement personnel who may come in contact with these drugs. Standard universal precautions include the use of gloves and avoidance of contact with any white powder or pill suspected of being an illicit drug.

MEET THE UPCC STAFF

Rachael Morley, BS, is from the San Francisco Bay Area of California. She completed her undergraduate food science degree at Texas Tech University in 2013 and has been working at the Utah Poison Control Center since the summer of 2015. Rachael is in her third year of pharmacy school and has been having a great time working at the poison center, with a specific area of interest in the line between medicines and toxins as is commonly seen in naturally derived products, such as colchicine and digoxin. In her spare time, Rachael enjoys reading, playing video games, and spending time with her 2 fluffy cats, Winston and Victoria.

Abimbola Bamigbola, BS, is a second year PharmD student at the University of Utah. She was born and raised in Lagos, Nigeria. She has particular interests in Clinical Pharmacy and Health Care Management. She holds a bachelor's degree in biology from Florida Memorial University, and has been part of Utah Poison Control Center since November 2015. Prior to enrolling at the University of Utah she worked for Alios BioPharma Inc. (part of the Janssen Pharmaceutical Companies) in San Francisco, California, and has led several activities relating to quality and performance improvement. She's excited for her career in Pharmacy and can't wait to share the joys of working at the poison center. In her spare time, she enjoys hiking, reading, baking, running, and traveling.

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The Utah Poison Control Center expresses its sincere thanks to the health care professionals, public health officials, and toxicology colleagues that work together to treat and prevent poisonings.

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