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The Use of Activated Charcoal in Toxicology and Implications for APRN Practice

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Abstract
This Research to Practice article is designed to help aid advanced practice registered nurses (APRNs) with up-to-date research guidelines in order to establish evidence-based changes in clinical practice within emergency medical care. The article, "Activated Charcoal and Poisoning: Is It Really Effective?" by Aksay et al. (2022), examines whether the usage of activated charcoal (AC) in current treatment protocols for ingested poisonings adds benefits, given recent controversies in its use. Study variables included clinical findings in relation to the drug being ingested, the frequency and usage of an antidote, the rate of being intubated, and the duration of being hospitalized comparing poisoned patients who received AC with those who did not. APRNs need to be aware of the current guidelines to help establish the appropriateness of use when administering AC and be able to evaluate patients during and after the administering of AC. Improved awareness and education regarding the different treatment modalities for toxicology patients such as AC can help with certain kinds of poisonings in the emergency department. **Key words:** activated charcoal, detoxification, overdose management, poisoning, toxicology

THE CASE

Logan Samuels, a 22-year-old man, transported through emergency medical services (EMS), presented after a reported consumption of an unknown quantity of extra-strength (500 mg) acetaminophen 70 min prior to arrival as a suicide attempt. According to EMS, the patient's college roommate found him "lying on the floor and barely breathing," with an almost empty bottle of newly purchased extra-strength acetaminophen (500 mg tablets) at his bedside. The roommate immediately notified emergency personnel. Upon their arrival, the patient was awake, acting "confused," and complaining of abdominal pain and nausea. EMS administered a 1,000 ml intravenous 0.9% sodium chloride bolus en route to the emergency department (ED).

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Upon arrival, the patient appeared drowsy but was responsive to questions. He stated that his only medical history was depression and anxiety for which he takes daily fluoxetine 40 mg and lorazepam 1 mg as needed. This was the patient's first self-harm attempt, but 3 months ago he was involuntarily admitted for psychiatric evaluation for suicidal ideation. He admitted that he was taking acetaminophen tablets because "he can't take the stress anymore." His review of systems was positive for nausea and abdominal cramping. He denied vomiting up any pills, melena, hematemesis, shortness of breath, or chest pain.

The patient stated that he was a full-time chemical engineering PhD student. He denied smoking, drinking alcohol, or recreational drug use. He reported compliance with his daily medications and admitted to increased use of lorazepam, twice daily, in the past week due to worsening anxiety. He stated that he sees a counselor on campus three times per week for his depression and anxiety. But, over the last month, he had only scheduled one meeting stating, "I'm too busy with class." He denied having a significant other. His family lived out of state.

His review of systems was significant for recent increased "migraines" that he treated with acetaminophen, anxiety, and abdominal pain and nausea that began this morning. All other systems were negative. In addition to the acute ingestion of the extra-strength (500 mg) acetaminophen bottle 70 min prior to arrival, he admitted to a chronic overdose of acetaminophen by stating that he had been taking between 8 and 10 extra-strength (500 mg) acetaminophen tablets daily for the past 2 weeks for headache relief.

On the physical examination, the patient was tearful, drowsy, and uncomfortable. He presented clutching his abdomen and grimacing in pain. He was currently oriented to person, place, and situation with a Glasgow Coma Scale (GCS) score of 12. His vital signs presented with a temperature of 36.3 °C; heart rate of 101 beats per minute; respiratory rate of 33 breaths per minute; blood pressure of 155/92 mmHg; SpO_2 of 96% on room air (RA); and weight of 66 kg. Breath sounds were tachypneic and clear, with no evidence of respiratory distress. Heart sounds were tachycardic without murmurs, gallops, or rubs. Peripheral pulses were 3+ with a brisk capillary refill. His skin was pale, warm, and moist. His abdomen presented as scaphoid, with active bowel sounds, soft with tenderness when palpating in the right upper quadrant without rebound, guarding, or hepatosplenomegaly. His neurological examination stayed intact and nonfocal with 2+ reflexes.

His workup included completing an electrocardiogram, which presented as sinus tachycardia with a heart rate of 101 beats per minute, normal intervals, and no acute ST-segment changes or abnormalities. A urine toxicology screen resulted as negative, and his serum toxicology screen was positive only for benzodiazepines. Serum acetaminophen levels were pending. A liver function test (LFT), complete metabolic panel (CMP), lipase, complete blood cell (CBC) count, coagulation studies, and arterial blood gases (ABGs) were obtained, resulting in acute transaminitis with elevations of aspartate aminotransferase (AST) of 5,000 IU/L, alanine aminotransferase (ALT) of 1,000 IU/L, and a total bilirubin level of 2.8 mg/dl. The CMP showed mild hypokalemia with a potassium of 3.2 mEq/L; hypoglycemia with blood glucose levels of 62 mg/dl and hypophosphatemia of 2.1 mg/dl. The ABG showed a wide metabolic acidosis gap: pH, 7.19; pCO_2, 27 mmHg; HCO_3^-, 13 mmol/L; and an anion gap of 12. His coagulation studies had a prolonged prothrombin time (PT) of 18 s and an international normalized ratio (INR) of 1.8. While awaiting a psychiatric evaluation, the patient's intravenous 0.9% sodium chloride infusion was continued at a rate of 100 ml/hr, and his nausea was treated with ondansetron 4 mg intravenously.

REVIEW OF ARTICLE

Aksay, E., Kaya, A., Gulen, M., Acehan, S., Isıkber, C., Sahin, G., & Satar, S. (2022). Activated charcoal and poisoning: Is it really

effective? *American Journal of Therapeutics, 29*(2), e182–e192. doi:10.1097/mjt.0000000000001422

STUDY PURPOSE, DESIGN, AND METHODS

The primary purpose of Aksay et al.'s (2022) retrospective cohort study was to compare drug-specific clinical outcomes (neurological and cardiovascular findings), laboratory abnormalities (e.g., liver function, ABG, electrolytes), usage of an antidote, needing intubation, and the length of being hospitalized between poisoned patients who had been administered activated charcoal (AC) within 4 hr after drug intake with poisoned patients who were not given AC due to the lack of availability. Specific drug levels of ingested toxins were not measured or included in assessing the effectiveness of AC on symptom resolution or clinical outcomes.

The study sample included ED chart data obtained from a tertiary hospital treating patients admitted for poisonings between May 1, 2011, and May 22, 2012, when AC was not available with patients admitted from August 1, 2014, to August 31, 2015, when AC was readily available for administration (Aksay et al., 2022). There were a summative total of 2,036 cases in this study. The study inclusion criteria included adults (18 years or older), patients presenting to the ED within the first 24 hr following a suicidal or accidental toxic, oral drug ingestion, and ingestion of a drug for which AC is indicated in management. Exclusion criteria for the study included patients who were deceased within 24 hr of drug ingestion, patients for whom treatment duration was not able to be determined, patients who declined treatment and had unknown outcomes, and poisonings where the use of AC was contraindicated.

DATA ANALYSIS AND RESULTS

Two thousand thirty-six patients were admitted to the ED presenting with a chief complaint of poisoning during the study periods. Of these, 877 (43.1%) were administered AC, 48.1% within the first hour, and 1,159 (56.9%) received no AC (Aksay et al., 2022). Four hundred seventy-seven patients were reportedly excluded from the final comparisons for failing to meet all study inclusion criteria (Aksay et al., 2022).

The mean patient age was 29 years, with 70.5% being female, and 94.9% took drugs for suicide. In 48.1% of cases, AC was administered within the first 60 min of admission to the ED. The median time to being admitted to the ED following drug ingestion was 2 hr (Aksay et al., 2022). Of the total sample, 99.4% were ultimately discharged and mortality data were not studied (Aksay et al., 2022).

Clinical findings related to toxic ingestion developed in 20.9% of patients. These effects were compared between the cases in which AC was administered and those that did not receive AC using logistic regression modeling. The authors found no statistically significant differences in central nervous system findings, cardiovascular findings, ABG alterations, or rates of intubation. However, hepatobiliary findings and electrolyte disturbances were significantly higher among cases that were not administered AC (Aksay et al., 2022). Interestingly, tachycardia, speech abnormalities, coma, and respiratory acidosis were significantly higher, whereas coagulation parameters presented significantly lower among cases that did receive AC (Aksay et al., 2022). Patients receiving AC were also found to have slightly lower drug-related clinical findings and shorter hospitalization durations than those not given AC. When ingestion outcomes of specific drugs were compared, variations in hospitalization duration were found among cases receiving AC and those also given antidotes (Aksay et al., 2022).

Based on these findings, the authors (Aksay et al., 2022) concluded that administration of AC in the first 90 min after drug ingestion may not add benefit in reducing clinical signs and symptoms needed for intubation, duration of hospitalization, or antidote use despite its widespread use in the treatment of poisonings. The authors further concluded that

there are many factors that affect signs and symptoms of drug toxicity clinically, and the effectiveness of AC appears to vary depending on how much drug was ingested, when it was ingested, the patient's gastrointestinal motility, and how much AC is given. These factors make studying the effects of AC challenging and support that further research on AC benefits on clinical outcomes is needed (Aksay et al., 2022).

Study limitations include the limitations of a retrospective chart review design. A significant methodological limitation is that the authors did not measure specific drug levels or use them in their analysis of clinically related outcomes. Therefore, the effectiveness of AC on actual drug level (toxic dose) and duration of toxicity, a critical variable in this type of study, was missing. Although the authors concluded that their methodology was sound because the sample size was large, and a few of their comparisons of clinical outcomes showed statistically significant differences between the patients receiving AC and those who did not, the lack of randomization and failure to assess toxic dose levels limit their conclusion that AC may not be beneficial in treating poisoned patients. In addition, the authors did not study mortality rates among those receiving AC and those who did not, another important outcome when studying whether AC should remain a component of treatment in the management of toxicology patients.

AUTHORS' COMMENTS

According to the American Academy of Clinical Toxicology and European Association of Poison Centres and Clinical Toxicologists (1999) and Chyka et al. (2005), the current usage of AC remains a component in the management of accidental or intentional oral poisonings. AC is widely used for gastric decontamination and elimination of absorbable toxins and is recommended to be administered within the first hour following ingestion.

Recently updated Australian Toxicology and Toxicology treatment guidelines, based on a review of evidence and expert consensus of emergency physicians and toxicologists, discuss that the controversy regarding the use of AC may be due to a "misperception" of the 1-hr window for AC administration (Chiew, Buckley, Graudins, & Munir, 2021). According to the updated guidelines, AC may be effective in gastric decontamination for a maximum of 2 hr following consumption of an immediate-release medication, 4 hr after modified-release medication, and even later for large ingestions because massive ingestions can slow gastrointestinal motility, delay absorption, and prolong the period of toxicity where AC may be effective in gastric decontamination (Chiew et al., 2021).

Because patients who intentionally overdose may also intentionally withhold information about the amount and timing of their overdose, the use of AC, despite the controversy, may still be beneficial in reducing systemic absorption and in reducing hepatotoxicity (Meehan, 2022). Current recommendations for the administration of AC are summarized in Table 1. Although an effective antidote of *N*-acetylcysteine (NAC) is available, the additional usage of AC can support the patient's clinical outcome if given in the

Table 1. Criteria for administration of activated charcoal for acute oral poisoning

Time since ingestion (less than 2 hr)
Massive ingestion
Anticholinergic properties
Highly toxic agents: Cyanide, colchicine, calcium channel blockers, cardioglycosides, cyclopeptide mushrooms, cocaine, salicylates, cirutoxin, tricyclic antidepressants
Substance can be absorbed by AC
Patient is alert and willing to drink the suspension
An effective antidote is not available
Patient is not at risk of aspiration

Note. AC = activated charcoal.

appropriate time frame while awaiting serum acetaminophen levels to determine NAC dosing. According to the American Academy of Clinical Toxicology and European Association of Poison Centres and Clinical Toxicologists (1999) and Chyka et al. (2005), both single- and multiple-dose AC administration protocols are recommended. However, multidose administration is only recommended for lethal ingestions of dapsone, carbamazepine, phenobarbital, quinine, or theophylline. Administration of drug-specific antidotes is recommended either in lieu of or in addition to AC.

The mainstay approach to any patient presenting with poisoning includes a detailed history to determine what toxin was ingested, the amount ingested when the ingestion occurred, and if any co-ingested substances were taken that may cause an adverse drug–drug interaction. The patient's comorbidities and psychiatric history should also be obtained either from the patient or from EMS, friends, or family members. A review of systems can assist in determining what type of toxin was ingested if the patient is not cooperative or cannot disclose due to altered mental status. Similarly, vital signs, neurological and cardiovascular status, pupillary response, and symptom-specific assessment may help in determining what type of drug was ingested when patients are unable or unwilling to disclose.

Diagnostic studies should include point-of-care glucose, CBC, CMP, liver and renal function tests, urinalysis with pregnancy, urine toxicology screen, acetaminophen levels, serum ethanol, ABGs, serum lactate, and, if appropriate, serum drug levels. The current mainstay of treatment in poisoning cases includes intravenous peripheral access, gastric decontamination (administration of AC), and administration of an appropriate antidote. According to Wightman and Nelson (2020), AC should be considered in the management of an acute acetaminophen overdose if initiated within 4 hr of ingestion. This is in contrast to Meehan's (2022) guidance that it is not necessary to administer, given the availability of the acetaminophen antidote, NAC, also known as Acetadote. However, because the use of AC is not contraindicated in a conscious and cooperative patient with a toxic acetaminophen overdose, its use can aid in reducing the peak serum concentrations of acetaminophen immediately postingestion while waiting for pending serum acetaminophen levels. Early gastric decontamination with AC may add to reducing absorption and facilitating elimination, improving a patient's clinical outcome, and reducing the risk of hepatotoxicity while awaiting serum acetaminophen levels (Chiew et al., 2017).

CASE REVISITED

The emergency nurse practitioner (ENP) contacted the local poison center to aid in decision-making while awaiting serum acetaminophen levels. Because the ingestion of acetaminophen was 70 min prior to arrival, the medical toxicologist recommended gastric decontamination with AC to help reduce the serum concentrations of acetaminophen, which may further decrease the requirement for the antidote NAC. The ENP decided to order the administration of AC because the patient had ingested a large amount of extra-strength (500 mg) acetaminophen approximately 70 min prior to arrival and admitted to excessive use of extra-strength (500 mg) acetaminophen with eight to 10 tablets daily over the past few weeks, increasing his risk of life-threatening and severe complications (Heard, 2018; Zellner et al., 2019). In addition, his acute hepatotoxicity, that is, elevated LFTs and total bilirubin, and significant metabolic disturbances, that is, hypokalemia, hypophosphatemia, hypoglycemia, prolonged coagulation, and metabolic acidosis along with a reported ingestion time of 70 min, supported AC use. The patient was given an initial dose of 50 g of AC within 15 min of ED arrival (Zellner et al., 2019).

Approximately 4 hr after ingestion, the patient's initial acetaminophen level resulted as 200 mcg/ml. Using the Rumack–Mathew nomogram, the ENP interpreted the resulting levels as probable toxicity that requires treatment with the antidote NAC (Chomchai, Mekavuthikul, Phuditshinnapatra, & Chomchai., 2022). Because of the patient's nausea and risk for aspiration, the ENP chose to administer an intravenous formulation of NAC instead of the PO route and monitored for adverse effects such as pruritus and bronchospasms. Using the Food and Drug Administration (FDA)-approved three sequential infusions protocol determined by the hospital, the ENP determined the loading dose (150 mg/kg) of the patient to be 9,900 mg mixed in 200 ml of 5% dextrose (D5W), infused over 60 min (Chyka, 2015). Because the patient was not experiencing respiratory distress that would indicate respiratory compromise, that is, SpO_2 96% RA, was speaking in complete sentences without breaking for a breath, had no retractions, or was unconscious, the ENP decided against intubation. However, the patient would be carefully monitored for acute respiratory instability.

After administering ondansetron, AC, and the loading dose of NAC, the ENP noted that the patient remained alert and oriented and his nausea had improved. Repeat laboratory studies showed an improvement in laboratory abnormalities: ABGs pH, 7.33; pCO_2, 36 mmHg; HCO_3^-, 18 mmol/L; potassium, 3.5 mEq/L; glucose Level of 82 mg/dl; and phosphate, 3.2 mg/dl. However, he continued to show signs of hepatoxicity with minimal improvement in transaminases, that is, AST 3,000 IU/L and ALT 850 IU/L, total bilirubin level 2 mg/dl, and his coagulation studies remained elevated PT 15 s, and INR of 1.6. Upon repeat physical examination, the patient continued to complain of right upper-quadrant tenderness with palpation. Given his persistent abnormal diagnostic studies and physical examination findings, he was admitted to a medical unit after starting the second infusion of 50 mg/kg NAC in 500 ml D5W over 4 hr and continued monitoring for improvement of hepatoxicity and metabolic disturbances. The third infusion was administered over 16 hr. At 42 hr postingestion, repeat acetaminophen levels and AST/ALT levels were elevated, resulting in hepatic failure with a peak ALT of 2,000 IU/L and INR of 7.5. The patient's liver function returned to baseline after 14 days in the hospital. Once medically cleared, he was admitted for inpatient psychiatric evaluation and management of depression, anxiety, and suicidality.

CONCLUSION

The usage of AC as a universal antidote in poisoned patients remains widely debated. Unfortunately, the strength of their conclusions and study design of Aksay et al.'s (2022) study on AC does not sustain or support discontinuing using AC in the current care and treatment of poisonings. As we discussed, there remains controversy in the use of AC among the leading toxicological guidelines as well as in recommendations by practicing clinicians (Meehan, 2022; Wightman & Nelson, 2020; Zellner et al., 2019). Ultimately, its usage in clinical practice and ED settings may depend on the clinician's personal preference or standards of practice within an institution. However, consulting early on when deciding the appropriate treatment modality and collaborating alongside a toxicologist or a local poison center can further support decision-making. Its usage in current treatment modalities for a cooperative patient who presents with no risk of aspiration may outweigh any perceived risk or lack of benefit. Despite that the clinical guidelines for use of AC set by the American Academy of Clinical Toxicology and the European Association of Poisons Centres and Clinical Toxicologists have not been revised since 2005, ENPs should adhere to evidence-based toxicology guidelines along with consultation from a medical toxicologist. It is hoped that new evidence will continue to inform practice and contribute to updates in the management of poisoned patients to improve outcomes and reduce risks.

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