

The Changing Indications of Gastrointestinal Decontamination in Poisonings

Kennon Heard, MD^{a,b,c,*}

^a*Division of Emergency Medicine, University of Colorado School of Medicine,
Denver, CO, USA*

^b*Medical Toxicology, University of Colorado School of Medicine, Denver, CO, USA*

^c*Rocky Mountain Poison and Drug Center, Denver, CO, USA*

Gastrointestinal (GI) decontamination is the therapy that is most commonly administered to patients who have had acute oral exposure to poisons. These techniques were used in almost 200,000 poisoning cases reported to North American Poison Centers in 2001 [1]. The theory behind GI decontamination is simple: poisons that are not absorbed into the blood cannot cause systemic toxicity. This principle has been recognized since the fifth century BC [2]; hence decontamination has become accepted without rigorous scientific data. Over the past several years, as practitioners demand quality data to guide treatment decisions, we have observed a deconstruction of “standard” poisoning management. The purpose of this article is to describe the commonly used techniques of decontamination, review the literature that describes their efficacy, and, finally, provide summary recommendations for the use of GI decontamination in the treatment of poisoned patients.

Emesis

Syrup of ipecac is currently available in many countries as a non-prescription product. It is prepared from the *Cephaelis* plant, which contains the alkaloids emetine and cephaeline. These alkaloids are potent emetics,

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* Division of Emergency Medicine, University of Colorado School of Medicine, 4200 East 9th Avenue, B215, Denver, CO 80262.

E-mail address: kennon.heard@uchsc.edu

inducing vomiting by both direct local GI effects and central nervous system actions. Syrup of ipecac is administered at a dose of 30 mL followed by 240 mL of water. Emesis following syrup of ipecac ingestion typically occurs within 20 minutes and persists for 30 to 120 minutes [3].

The use of syrup of ipecac in the management of poisoned patients has declined [1]. A recent position paper lists several studies that describe the efficacy of ipecac-induced vomiting in reducing systemic absorption of many drugs [3]. This effect is highly time dependent and is unlikely to be clinically relevant beyond 30 minutes post-ingestion. One study of adult patients that compared ipecac-induced vomiting to ipecac plus activated charcoal (AC) reported a longer emergency department (ED) stay and more complications in the ipecac-treated group. Outcomes (admission rate and ICU admission) were not different between the groups [4]. In this study, aspiration pneumonitis occurred in 3 of 93 patients who received ipecac and none of 107 patients treated with AC alone.

Two additional studies have compared ipecac plus AC to ipecac alone as one arm of a study to evaluate gastric emptying [5,6]. Both studies assigned asymptomatic patients to either an AC group or an ipecac-induced vomiting group followed by AC group using an alternate-day protocol. Neither study reported any advantage of ipecac therapy over AC alone. One study patient became obtunded after receiving ipecac. This patient vomited and went on to develop an aspiration pneumonitis.

In summary, no studies demonstrate that the use of ipecac in the treatment of acute poisoning changes clinical outcome. Several studies have shown that ipecac use may result in complications and prolonged ED course. The US Food and Drug Administration has considered removing ipecac from over-the-counter status, and the American Academy of Pediatrics no longer recommends home stocking of ipecac [7]. These positions reflect an established movement to eliminate ipecac as an acceptable therapy, and this author believes that ipecac has no role in the routine management of acutely poisoned patients.

Gastric lavage

Reports of the use of gastric lavage (GL) in the poisoned patient date as far back as the early nineteenth century. GL is not the same as nasogastric aspiration. GL is performed by placing a large-bore (36–40 French) orogastric tube and instilling, then removing several liters of water to wash out stomach contents [8]. In contrast, for gastric aspiration, a smaller nasogastric tube is placed and gastric contents are aspirated without instilling any water. Nasogastric aspiration may be effective in cases of liquid poison ingestion [9], but it is not adequate for ingestion of pills.

In order for GL to be performed, patients must be able to maintain their airways or be intubated. Additionally, lavage should not be performed on patients who have ingested medications that may cause seizures or abrupt

central nervous system deterioration unless the patient has been intubated. Patients should be on a cardiac monitor and pulse oximetry. Emergent airway equipment and suction should be immediately available. Before one inserts the tube, it should be used to estimate the distance from the lips to the epigastrium. The patient is placed in the left-lateral decubitus position, the tube is placed in the mouth, and the patient is asked to swallow. The tube is then gently advanced until the estimated length from lips to epigastrium has been inserted. The patient should then be asked to phonate to assure that the tube has not been placed in the trachea. At this point, 200 to 300 mL aliquots of warm saline or tap water are instilled in the tube and allowed to drain by gravity. The endpoint of GL is poorly defined. Most recommend that the procedure be continued as long as pill fragments are observed in the drainage. However, there is no clear definition of when to end the procedure if pill fragments are not observed [8].

A recent position statement concisely summarizes several volunteer studies demonstrating that significant amounts of poison may be removed from the stomach [8]. As with vomiting, the effect is clearly time dependent, and little effect is expected when treatment is delayed beyond 60 minutes. One study using radiographic markers suggested that GL may actually propel gastric contents past the pylorus, moving the poison into the small intestine, where most of the drug will be absorbed [10].

Although the preclinical studies show that GL may decrease drug absorption, three clinical trials have failed to demonstrate improved outcomes when GL is added to AC for the management of undifferentiated symptomatic poisoning patients. Two of these studies used a similar design [5,6]. Symptomatic patients who presented with a history of self-poisoning were assigned on an alternating-day basis to either AC by nasogastric tube or GL followed by AC. The main outcome was the proportion of patients in each group who deteriorated following the treatment.

The similar design and outcome of these study arms permit some general criticisms. First, the use of undifferentiated poisoned patients results in a low power to detect a difference between groups. It is possible that some subgroups would benefit from gastric emptying, even though the overall results of the study were negative. Second, the use of alternate-day assignment results in nonblinded treatment allocation. This process could lead to selection bias, and therefore the two treatment groups would have dissimilar baseline characteristics. Third, the outcome in these studies was highly subjective, and no measure of reliability is provided for any measure. This limitation is further exacerbated by the unblinded assessment of outcome. However, the main limitation to this analysis is the interpretation of the outcomes. Although the proportions of clinical manifestations that resulted in patients being classified as “symptomatic” are not reported, it is likely that most of the patients in this group were classified as “symptomatic” because they had decreased levels of consciousness. The act of GL would certainly be expected to result in an increase in “alertness” more than would the

administration of AC. Although this “improvement” is attributable to the treatment, it is unlikely to have been of any clinical significance.

The specific results for these two studies were similar. Kulig and colleagues [5] reported that 22% of patients assigned to GL deteriorated, compared with 27% treated with AC alone. Pond and colleagues [6] reported that 7% of patients assigned to lavage deteriorated, compared with 13% in the AC-alone group. Kulig also performed a post-hoc subanalysis on patients who presented within 60 minutes of ingestion. This analysis found that more patients treated with GL within 60 minutes of ingestion improved when compared with those treated with AC alone. However, the authors relied on a χ^2 analysis rather than a Fischer’s exact test (the appropriate test given the results). Applying the more appropriate statistical test results in a non-significant outcome. Because Kulig had identified this potentially important subgroup, Pond and colleagues included a planned subanalysis of patients presenting within 1 hour in their study design. Pond’s study also reported a statistically significant difference between the treatment groups (this time using the appropriate statistical analysis). The authors attributed this effect to a baseline difference between the treatment groups in severity of symptoms. They then performed a stratified analysis and suggested that, after adjustment for severity, the beneficial effect of GL is not significant. However, the authors of neither paper discuss a more striking limitation. Patients assessed on days when the protocol resulted in an emptying procedure were statistically less likely to be classified as alert than patients assessed on days when the protocol called for AC alone (*RR* 0.87 for Kulig and 0.79 for Pond; *P* < .01 for both studies). Given that the assessors were not blinded to treatment assignment, this finding demonstrates selection bias. Such bias would result in patients with milder symptoms being assigned to receive GL and could dilute any treatment effect.

Merigian and colleagues [11] performed the third major study of gastric emptying. This study used a similar treatment protocol to those of Pond and Kulig. However, the authors’ outcomes in this study were proportions of patients (1) admitted to the hospital, (2) requiring intubation, and (3) admitted to the ICU. They also compared the rates of aspiration pneumonia. This study found that patients who received gastric emptying (the authors did not analyze ipecac and GL separately) had a similar rate of hospital admission to those who received AC alone (58% in both groups). However, patients who received gastric emptying were more likely to be admitted to the ICU (74/163 versus 40/194) and more likely to be intubated (55% versus 14%) than patients assigned to the AC-alone group. Because the baseline vital signs and mental status scores for these groups were similar, the increased rate of intubation (and subsequent ICU admission) probably reflects aggressive airway management before GL that was not thought to be required when AC was administered without lavage.

Although the three studies just described evaluated GL for the treatment of undifferentiated poisoning, one smaller study has evaluated the role of lavage

for treatment of a tricyclic antidepressant (TCA) poisoning. This method overcomes some limitations of the larger studies, because it evaluates a more homogeneous group and because TCA poisoning often produces life-threatening effects. This study compared (1) AC alone with (2) AC plus GL and (3) AC followed by GL, followed by AC. Its basis was the theory that GL could push pills past the pylorus and that prelavage administration of AC could adsorb this poison before systemic absorption. This study found no difference between the three groups in length of hospitalization, ICU stay, intubation, or duration of tachycardia. The small study size resulted in little statistical power. However, the data do not even suggest a trend toward decreased incidence of cardiac or neurologic effects in either GL group.

Complications associated with GL include GI tract perforation, hypoxia, and aspiration. GI tract perforation is a catastrophic but uncommon complication of GL. Although the exact incidence is unknown, one case of esophageal perforation was reported in the 363 patients who received GL in the three major trials discussed here [5,6,11]. Arterial oxygen tension dropped 17% during GL in one prospective study [12]. Although the clinical implications of this phenomenon are unclear, two patients in this series developed transient ST segment elevation during the GL procedure.

Aspiration is a common complication for all poisoning patients. Identifying the marginal risk associated with GL is difficult. In the largest study of gastric emptying, 5% of patients were thought to have aspirated *before* the gastric emptying procedure [6]. However, it is logical to believe that placement of a large-bore tube might impair airway protection and increase the risk for aspiration. Merigian and colleagues [11] reported that patients assigned to gastric emptying were more likely to develop aspiration pneumonia than patients treated without gastric emptying. Interestingly, all the patients who developed aspiration were intubated, and half of them “had an uncomplicated orotracheal intubation” before GL, suggesting that the aspiration occurred despite adequate airway management.

In summary, these studies report no benefit when GL is added to AC in the management of undifferentiated acute poisoning patients. Less conclusive data show no clear effect in TCA poisoning. Despite their many limitations, the studies suggest that this procedure may increase the risk of ICU admission, and the incidence of complications was higher for GL patients than for patients managed without GL in all studies.

Activated charcoal

The theory behind the use of AC is that poisons dissolved in the intestine will be adsorbed to the charcoal particles; hence the poison will remain in the gut rather than moving into the bloodstream. Several common poisons are not well adsorbed by charcoal. Most notable among these are the toxic alcohols, iron, lithium, and most other metals. However, the vast majority of medications are well bound by charcoal.

Charcoal binding is a saturable process. Ideally, the dose of charcoal should provide a large excess of binding to capture as much of the poison as possible. In reality, the dose of charcoal administered tends to be determined by the size of the bottle stocked by the pharmacy. Few studies have been performed to attempt to determine the dose of charcoal. One human study found the optimum ratio of charcoal to drug to be 10:1 (weight:weight) for para-aminosalicylate [13]. Obviously, this study is limited, because it was a volunteer study using only one drug. Current consensus recommendations are that adult overdose patients receive 25 to 100 g [14].

The efficacy of charcoal is time dependent [14,15]. Therefore, charcoal should be administered as soon as possible after the ingestion. A recent consensus statement suggests that charcoal should be administered within 60 minutes of ingestion [16]. One study demonstrated that charcoal decreased acetaminophen absorption by 22% when given 2 hours after the ingestion [17]. The effect may be even greater for sustained-release products [16] or in the setting of anticholinergic effects [18]. Although these are only volunteer studies, they suggest that charcoal may be effective for selected poisoning patients beyond the 60-minute window.

Superactivated charcoal

The property of AC to adsorb a poison is related to the surface area of the charcoal particles. Superactivated charcoal products with increased surface area have been available for more than 20 years. These products decreased systemic medication absorption when compared with standard AC in two volunteer studies [19,20]. They are also considered to be more palatable than standard charcoal products. However, no study has demonstrated a clinical benefit for these products.

Clinical efficacy of activated charcoal

Three of the four major studies described earlier compared gastric emptying plus AC to AC alone in all patients [4–6]. However, the fourth study evaluated AC versus supportive care alone in asymptomatic patients [11]. In this study, 231 patients were assigned to observation and 220 were assigned to AC. The patients were observed in the ED for a minimum of 4 hours and then for an additional 4 hours during the psychiatric evaluation. No patient in either group deteriorated, suggesting that AC provided no benefit in the management of asymptomatic poisoning patients.

Recently, a large study was published comparing AC with supportive care for symptomatic and asymptomatic overdose patients [21]. This study is described as a randomized controlled trial (RCT) where 1479 patients were assigned on an alternating-day basis to either AC or supportive care. The patients were observed for a minimum of 4 hours in the ED, and the major outcomes were the proportion of patients who deteriorated, the number of patients admitted to the hospital or ICU, and the length of stay. The study

used predetermined criteria for deterioration. No difference was found in the proportion of patients deteriorating or requiring admission to either the hospital or ICU. The mean ED stay was approximately 1 hour shorter for patients treated without AC, and there was no difference in the length of stay for admitted patients. Although the results of this study are intriguing, some limitations must be recognized. The “randomization” resulted in 399 patients receiving charcoal, whereas 1080 patients were treated with supportive care. The authors do not directly discuss the reason for this imbalance, but their description suggests that, rather than an intent-to-treat analysis, the authors performed a treatment-received analysis. This type of experiment design is subject to bias, because “less sick” patients could be allowed to forgo charcoal, whereas “more sick” patients would receive charcoal. Still, this study reported that no patients deteriorated in a large cohort (1080) of poisoning patients treated with only supportive care.

One additional RCT that has only been reported in abstract form also found that AC offers no benefit over supportive care. This study has limited numbers and is ongoing. Preliminary results suggest that the patients who were given AC had a trend toward longer ED stay and no change in mortality [22].

Several studies have also evaluated charcoal for specific poisonings. Crome and colleagues [23] reported a study of 48 patients with TCA ingestion who were treated with either AC or supportive care. This study found no difference in the duration of coma or drug levels between the two groups. However, its power was severely limited by the sample size. A carefully designed retrospective study of patients evaluated for acetaminophen ingestion reported that administration of AC to patients who ingested more than 10 g and presented within 24 hours was associated with a 64% decrease in the risk for having a toxic acetaminophen level [24]. This effect was largest in patients receiving charcoal within 2 hours of ingestion and diminished markedly after 2 hours. This finding is consistent with the expected course of acetaminophen absorption, suggesting a true effect. Although these data are based only on observation rather than on experimental results, they strongly suggest that AC may decrease the need for antidotal therapy in the setting of acetaminophen overdose.

The major complications of AC are vomiting, intestinal obstruction, and aspiration. Prospective studies have reported the prevalence of vomiting for untreated overdose patients at approximately 10% [21], whereas the prevalence in patients treated with AC is approximately 25% [6,11]. Another study has reported that the incidence of vomiting is similar between AC-treated patients and patients treated only with supportive care [22]. Given the high prevalence of vomiting, some have advocated pretreatment with antiemetics when AC is administered. Intestinal obstruction is a theoretic concern, but it has been reported when multiple-dose AC is used to enhance elimination of drugs, rather than when single doses are used for decontamination [25].

The most serious complication is aspiration. One animal model of AC aspiration demonstrated increased microvascular permeability, a fall in systemic oxygenation, and development of a metabolic acidosis [26]. This study did not show a dramatic increase in lung inflammation, and the charcoal was primarily deposited in the small airways. The authors suggest that the injury due to charcoal may have been caused by subsequent barotrauma from overdistention of the airways due to charcoal plugging. However, in practice, AC aspiration is only rarely unaccompanied by aspiration of gastric contents, so the clinical meaning of this model is limited.

Numerous reports exist of acute lung injury following aspiration of AC. In a recent review, Seger [25] discussed seven cases where charcoal aspiration was implicated as at least a contributing factor in a patient's death. This report included four additional cases where charcoal was implicated as a contributing factor in a life-threatening pulmonary complication and three cases where charcoal was instilled directly into the lung following unrecognized placement of an nasogastric (NG) tube into the trachea. A retrospective study of 50 intubated overdose patients who received charcoal reported a 2% incidence of radiographically proven aspiration pneumonia. Three additional patients in this study were treated for aspiration pneumonia despite normal chest radiographs. The only death reported in the study was unrelated to aspiration [27]. Another retrospective study of 257 patients reported a 28% incidence of aspiration. This study reported that early intubation was protective, and administration of GL and AC to nonintubated patients was associated with an increased risk for aspiration [28].

No treatment for charcoal aspiration has been used routinely. Patients are usually treated with antibiotics for aspiration pneumonia. Patients with charcoal in their sputum are treated with additional pulmonary toilet; bronchial lavage has been used to clear the airways of charcoal deposits [29].

In summary, AC limits the systemic absorption of many drugs in a time-dependent manner and may decrease the need for antidotal therapy for patients who present within 2 hours of acetaminophen ingestion. However, AC has not been shown to improve the outcomes of nonselected poisoning patients. Although serious side effects are uncommon, charcoal does appear to increase the number of patients who vomit, and rare cases of life-threatening aspiration have been reported.

Other binding agents

Two recent studies evaluated the use of magnesium hydroxide to limit the bioavailability of iron [30,31]. Both studies used subtoxic doses of iron and a 5:1 ratio of magnesium hydroxide to elemental iron. The first study administered the antidote 60 minutes after a 5 mg/kg iron dose and used a cross-over design. This study reported that magnesium hydroxide decreased the 12-hour area under the curve for serum iron concentrations by approximately 45% [30]. The second was a randomized, two-arm study.

The magnesium hydroxide was given 30 minutes after a 10 mg/kg iron dose. This study did not report a significant reduction in iron levels, although the mean peak iron level was approximately 10% lower in the treatment group [31]. The authors note that, to achieve a 5:1 ratio of magnesium hydroxide in a 60-kg adult taking 60 mg/kg of elemental iron, a dose of 225 mL of milk of magnesia would be required. This amount is similar to the volume of fluid given when a patient takes 50 g of AC.

Sodium polystyrene sulfate (SPS) is a resin that is most commonly used to treat hyperkalemia. However, SPS also effectively binds lithium. Two volunteer studies have shown that SPS administration decreases the bioavailability of lithium in subtoxic doses [32,33]. Although this technique may be of some use in selected cases, most isolated acute lithium ingestions do well with hydration alone. The increased use of sustained-release lithium products also limits the generalizability of these results in clinical practice. Cholestyramine, a steroid-binding resin, has been used to adsorb digoxin [34], and Fuller's earth has been used to bind paraquat [35]. However, the limited availability of these therapies would likely result in a delay in treatment and negate any clinical benefit over the readily available charcoal.

Whole bowel irrigation

Whole bowel irrigation (WBI) is an extension of the use of cathartics to decrease systemic availability of toxins. The use of cathartics decreases time in the GI tract, theoretically decreasing the time for the poison to be systemically absorbed [36]. The development of isotonic polyethylene glycol (PEG) solutions allows the use of cathartics without the concern of causing fluid or electrolyte alterations [37].

Effective WBI requires the administration of large volumes of PEG. The dosage used in bowel preparation is 2 to 4 L over 12 to 24 hours. The recommended dosage for WBI is 1.5 to 2 L/h. This dose is best administered through a 12-Fr feeding tube. To prevent aspiration, the patient should have the head of the bed elevated to at least 45°. If emesis occurs, the infusion should be discontinued for 30 minutes and restarted at half the previous rate. The rate is then increased as tolerated. Metoclopramide has been advocated as an antiemetic, because it increases GI motility. Patients who are awake should be provided with a bedside commode once the solution begins to pass [38].

Current recommendations are that the PEG be administered until the rectal effluent is clear. However, this endpoint probably does not completely clear the bowel of pill fragments. One study that evaluated the effect of WBI on the evacuation of coffee beans from the bowel found that, at the time of clear rectal effluent, an average of only 2.3 of 10 markers were recovered in the stool [39]. Another study found that WBI (until clear effluent) resulted in more radio-opaque markers moving into the colon at 24 hours than did standard treatment [40]. Although the clinical implications of these studies

are unclear, they demonstrate that WBI until clear rectal effluent is not likely to remove all pills from the GI tract.

Volunteer studies have shown that WBI may lower the bioavailability of lithium and ampicillin [41,42]. Although these studies suggest that this treatment may be valuable, volunteer studies use much lower doses of medications, and initiation of WBI is not always clinically feasible in the timeframe they use. No controlled evaluations of WBI for poisoning patients exist. Case reports suggest that it may be useful in the treatment of iron ingestion and sustained-release verapamil ingestion and in the treatment of body packers [43–45].

The common complications of WBI are bloating, cramping, and vomiting. As with charcoal, the main concern is aspiration. No reports exist of aspiration complicating WBI; pulmonary edema and respiratory failure have been reported as complications during bowel preparation [46].

WBI is difficult to perform effectively under most circumstances, and its clinical efficacy is unproved. A recent position paper states that WBI may be considered for ingestion of sustained-release drugs and for iron and lithium poisoning [38]. This option appears best suited for cases where there is evidence of prolonged absorption of the drug (ie, the serum levels continue to rise several hours into the ingestion or there is radiographic evidence of unabsorbed drug in the GI tract).

Summary

Overall, no conclusive data support the use of gastric decontamination in the routine management of the poisoned patient. Studies of asymptomatic patients suggest that no treatment is required, and, given the complications that have been reported, this may be a reasonable approach to most patients. Even in symptomatic patients, the only demonstrable benefit was found in a post-hoc subgroup analysis and involved an outcome of questionable clinical importance.

Given these data, it would be easy to conclude that GI decontamination has no role in the management of the poisoned patient. This conclusion is valid when considering poisoned patients as a group, but all poisoned patients are not the same. Patients with trivial ingestion do well without treatment, and their greatest risk is an iatrogenic complication. Even patients with more serious ingestions usually have good outcomes with supportive care alone. It is no longer sufficient to justify GL or forced administration of AC with the supposition that “the patient could have taken something bad.” However, there are some overdoses where limiting the systemic absorption of the poison may limit the toxic effects and prevent serious toxicity. After careful consideration of the risks, GI decontamination should be targeted at patients who, in the opinion of the treating physician, have a potentially life-threatening exposure.

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