Position paper update: gastric lavage for gastrointestinal decontamination

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Context. The first update of the 1997 gastric lavage position paper was published by the American Academy of Clinical Toxicology and the European Association of Poisons Centres and Clinical Toxicologists in 2004. This second update summarizes the 2004 content and reviews new data. Methods. A systematic review of the literature from January 2003 to March 2011 yielded few studies directly addressing the utility of gastric lavage in the treatment of poisoned patients. Results. Sixty-nine new papers were reviewed. Recent publications continue to show that gastric lavage may be associated with serious complications. A few clinical studies have recently been published showing beneficial outcomes, however, all have significant methodological flaws. Conclusions. At present there is no evidence showing that gastric lavage should be used routinely in the management of poisonings. Further, the evidence supporting gastric lavage as a beneficial treatment in special situations is weak, as is the evidence to exclude benefit in all cases. Gastric lavage should not be performed routinely, if at all, for the treatment of poisoned patients. In the rare instances in which gastric lavage is indicated, it should only be performed by individuals with proper training and expertise.

Keywords Gastrointestinal decontamination; Poisoning; Gastric lavage

Introduction
Poisoning is a common form of injury throughout the world.1 A challenge for clinicians managing poisoned patients is to promptly identify those who might benefit from gastric lavage. Gastric lavage has been used as a treatment for poisoned patients for over 200 years. During the last decades there has been concern that complications associated with gastric lavage might outweigh the possible benefits to patients. As a consequence, a panel of experts from the American Academy of Clinical Toxicology and the European Association of Poisons Centres and Clinical Toxicologists was convened to evaluate the literature regarding gastric lavage. The panel’s findings were published first in 1997 and then were updated in 2004.2,3 In both instances, the papers concluded that there was no conclusive evidence to support the continued use of gastric lavage for poisoned patients. As a consequence, poison centers seldom recommend gastric lavage today4 and its use in emergency departments has declined steadily4 (level of evidence [LOE] 4 and 2c). Another potential consequence of the Gastric Lavage Position Papers is reduced availability of equipment or expertise to perform gastric lavage (LOE 4).6 The purpose of this second update of the Gastric Lavage Position Paper is to briefly summarize the content of its forerunners and to present any relevant new data that have been published in the medical literature since then.

Method
An expert panel consisting of nine members (authors) was appointed by the American Academy of Clinical Toxicology (AACT) and the European Association of Poisons Centres and Clinical Toxicologists (EAPCCT) to update the 2004 Gastric Lavage Position Paper.

The National Library of Medicine’s PubMed database was searched using gastric lavage as textwords for 2009–11, gastric lavage/humans for 2003–08, and (gastric OR stomach) AND therapeutic irrigations[mh]. International Pharmaceutical Abstracts (via Ebsco), the Science Citation Index (via Web of Science), the Cochrane Database of Systematic Reviews, and the Cochrane Central Register of Clinical Trials were searched without limits using the term “gastric lavage”. A separate search was performed for animal studies using National Library of Medicine’s PubMed database using gastric lavage and (poisoning OR overdose) as textwords, limiting the species to animals. The search was performed over the time period from January 2003 to March 2011 and yielded 683 articles. Sixty-nine of these offered the possibil-
ity of applicable human data and were therefore incorporated into an evidence table showing the key characteristics of each article (see Supplementary Appendix 1 to be found online at http://informahealthcare.com/doi/abs/10.3109/15563650.2013.770154). Each article was assigned a level of evidence (LOE) based on the Oxford Centre for Evidence-based Medicine Levels of Evidence for Therapy/Prevention/Etiology/Harm, March 2009 (Appendix 2). The rejected articles focused on specialized lavage for removal of phytobezoars or diagnosis of gastric cancer, mentioned gastric lavage only in passing, or were review articles that did not provide any new information. Ultimately, 15 articles contributed to this revision of the Position Paper and their LOEs are noted.

After review of the evidence, an updated Position Paper draft and evidence table was prepared by two panel members and submitted to the rest of the panel for comment. Panel member comments were collated and returned to the main authors in an anonymous format. The lead authors responded to the comments and made revisions to the draft accordingly. The revised draft was distributed to the panel for approval or content objections. Any objections to the revised second draft required evidence-based support and then revision by the main authors. Each revised draft was distributed to the panel for comment and vote. When all panel members approved the manuscript draft, it was posted on the websites of AACT and EAPCCT for 6 weeks for comment by members of the organizations. All organization members were sent an email notification regarding the posting and request for review. All external comments were addressed by the main authors and a final draft was prepared, distributed to all panel members, and approved. This final draft was sent to the Boards of Directors of AACT and EAPCCT for review and endorsement. Comments from the Boards were addressed in the same manner as previous comments and drafts. The final product is endorsed by the Boards of both sponsoring clinical toxicology organizations.

Animal studies

Summary of prior position paper 2004

Animal studies suffer from several inherent flaws that may limit their generalizability to humans. Animals that are anesthetized and given analgesics can have slowed gastrointestinal motility. In most studies the animal is given a single drug in dosage forms that may not mimic human exposure.

Three animal studies examined the utility of gastric lavage in reducing the bioavailability of various markers.7–9 In one study dogs were given sodium salicylate 500 mg/kg as broken tablets by esophageal tube and then lavaged at 15 minutes or 1 hour post administration.7 The mean portion of salicylate recovered was 38% (range 2–69%) at 15 minutes, and 13% (range 0–40%) at 1 hour. In two studies barium sulfate was used as a marker. The mean portion of marker recovered was 26%8 and 29%9 when lavage was initiated within 30 minutes. Marker bioavailabilities dropped to 13%7 and 8.6%8 when lavage was performed at 60 minutes. A fourth study compared lavage plus activated charcoal to no treatment in a simulated aspirin overdose. In this study, dogs were given aspirin 500 mg/kg and then lavaged and given activated charcoal (1.5 g/kg) 30 minutes after drug administration. The peak plasma salicylate concentrations were reduced by 37% when compared to no treatment.10

New studies

Since 2004 there have been no new animal studies published addressing the utility of gastric lavage as a treatment for poisoning.

Experimental studies in volunteers

Summary of prior position paper 2004

A major limitation of human volunteer studies is that doses used in mock overdoses are substantially lower than doses actually encountered during real overdoses. Smaller mock doses used are potentially absorbed faster than the larger, real doses seen clinically. As a result, gastric lavage may make less of an impact in reducing the bioavailability of a drug during experimental studies than is seen clinically. In addition, the studies may utilize lavage times that are not feasible within most clinical settings or may utilize sub-optimal methods to calculate dose absorbed. With these limitations in mind, there were four studies that examined the utility of gastric lavage using simulated drug overdoses.11–14 The drugs studied included ampicillin (5 g),11 aspirin (1.5 g),12 and two multi-drug studies involving the same combination of temazepam (10 mg), verapamil (80 mg), and moclobemide (150 mg).13,14 The reductions in absorption were 32% for ampicillin, and 8% for aspirin when lavage was performed at 1 hour after ingestion. The aspirin study utilized urinary salicylate recovery to estimate absorbed aspirin doses. In the multi-drug study the reductions in peak plasma concentrations were not statistically significant for any of the medications when lavage was implemented within 30 minutes; however, the drug doses were small and the patients were lavaged in the sitting position. Three studies examined the effect of lavage on recovery of markers instead of drugs in healthy human volunteers. In these studies the markers used were cyanocobalamin,15 Tc99m,16 and radiolabeled water.17 The recoveries ranged from 84% (radiolabeled water lavaged 5 minutes after ingestion) to 30% (Tc99m capsules lavaged a mean of 19 minutes after ingestion).

New studies

No new marker study in volunteers has been reported since the most recent position paper on gastric lavage was published.

Experimental studies in poisoned patients

Summary of prior position paper 2004

Post-lavage endoscopy was used to evaluate the thoroughness of gastric decontamination in 17 patients ranging in age from 16 to 72 years and lavaged with 2.5–5.5 L of tap water using a Faucher tube size 33.18 After lavage was
completed, 88% of the patients had solid debris still visible in the stomach. Another approach has been to administer nontoxic markers to poisoned patients before lavage in hope of bypassing some of the dose and physiological issues associated with using volunteers to simulate poisoned patients. Even though patient generalizability may be improved, it is possible that marker recoveries falsely inflate recoveries compared to real-life poison retrievals because the markers are administered immediately before lavage, the markers do not fully homogenize with gastric contents, and there is always a delay from time of ingestion to time of lavage. There are two poisoned patient marker studies that have been published.\textsuperscript{19,20} One used radiovisible polyethylene pellets and the other used a liquid 100-mg thiamine preparation. The pellet study required each patient to ingest 20 pellets 5 minutes before lavage and observed an overall pellet retrieval rate of 48%.\textsuperscript{19} In the thiamine study, 100 mg of injectable thiamine was washed into the patients stomach through a lavage tube with 100 mL of 0.9% sodium chloride. When lavage was performed 5 minutes later, 90% of the marker was retrieved.\textsuperscript{20} It is unclear how close these values relate actual lavage retrieval rates in poisoned patients.

New studies

No new marker study in poisoned patients has been reported since the most recent position paper on gastric lavage was published.

Case reports

Summary of prior position paper 2004

Continued drug absorption is known to occur after gastric lavage has been performed. Sharman et al.\textsuperscript{21} recovered drug hours after gastric lavage in 19 patients when hourly nasogastric aspirates were obtained. Lavage can also be ineffective when drug concretions form during overdose. Schwartz described a 56-year-old patient who developed a concretion when drug concretions form during overdose. Computed tomography revealed a large number of tablets in her stomach. Gastric lavage was used to successfully remove drug and to assist with rewarming efforts. The patient recovered fully over 3 days. The authors suggested that lavage could play a more important role in overdose patients suffering from concomitant hypothermia because of hypothermia-induced gastric atony and because lavage can prevent poison absorption and assist with rewarming efforts. Kimura et al. reported two cases in which computed tomography was used to identify large numbers of tablets in the stomachs of patients presenting past a 1-hour cut-off point and where nasogastric lavage was used to retrieve tablet fragments. One case involved a 16-year-old girl who overdosed on unknown medications and presented with anticholinergic findings (mydriasis, decreased bowel sounds, tachycardia).\textsuperscript{27} After computed tomography confirmed tablets in her stomach and duodenum, a nasogastric tube was used to aspirate tablet debris over 5 minutes and then to instil activated charcoal. The patient recovered and confessed to ingesting a 100-tablet combination of sulpiride, maprotiline, biperiden, and quetiapine 10 hours before arriving at the emergency room. The other case was an 83-year-old man with a medical history of diabetes mellitus and hyperventilation who presented with tachycardia, confusion, and disruptive behavior.\textsuperscript{28} He later admitted to ingesting 100 ursodeoxycholic acid tablets 5 hours prior to admission in a suicide attempt. Computed tomography was performed to evaluate the patient for cerebrovascular disease and possible aspiration pneumonia and showed numerous tablets in the gastric fundus. The patient was lavaged with a nasogastric tube using 6 L of fluid until returns were clear. A dose of activated charcoal was then administered. The patient recovered over a day. In none of these cases were the gastric aspirates assayed so drug amounts could be quantitated. It is also unclear how important nonconventional lavage methods and ancillary treatments (activated charcoal and supportive care therapies) were in the eventual recoveries of these patients.

Clinical studies

Summary of prior position paper 2004

There are a number of studies that have examined the utility of gastric lavage in specific types of overdose using the amount of drug recovered as a surrogate marker for treatment effectiveness. For barbiturates, the recoveries have ranged from 0 to greater than 450 mg, with most studies recovering less than 200 mg.\textsuperscript{29–32} Recoveries dropped with the passage of time and as the number of tablets ingested decreased. Recoveries were virtually nonexistent after 4 hours. The mean recovery for tricyclic antidepressants was 94 mg (range 6–342 mg) at a mean of 2.5 hours after ingestion.\textsuperscript{33} Salicylate recoveries of greater than 1000 mg were obtained in 6 of 23 salicylate poisoning cases\textsuperscript{32} and for jimson weed, 8 of 14 had evidence of seeds in their lavage aspirates.\textsuperscript{34} Plasma acetaminophen concentrations dropped by a mean of 39% (± 14.67) when
patients were lavaged. \(^{35}\) Unfortunately, these studies did not address the impact of lavage over time since the initial doses were not known for any of the patients. With the exception of the jimson weed study, these studies did not examine the impact of lavage on clinical recovery.

Other investigators have examined the value of gastric lavage on cohorts of overdose patients without restricting observations to a single agent. An early study by Comstock et al. \(^{36}\) reported the lavage recovery rates for a sample of patients reporting to a large metropolitan hospital. Recovery rates were expressed as the percentage of patients in whom more than 10 therapeutic doses were recovered. Recovery varied from 6% (short-acting barbiturates) to 33% (amitriptyline) with an overall rate of 14%. Later prospective, pseudo-randomized studies compared the frequency of clinical deterioration or clinical improvement in patients treated with gastric lavage plus activated charcoal to patients treated with activated charcoal alone\(^ {37,38}\) or patients treated with lavage plus activated charcoal compared to patients treated with syrup of ipecac followed by activated charcoal. \(^{39}\) Lavage did not influence the clinical course of patients when contrasted to its comparator group, even when patients were further stratified by clinical severity plus time since ingestion in two of three studies. The only exception was in the study by Kulig et al., where a higher proportion of obtunded patients presenting within an hour and receiving gastric lavage plus activated charcoal improved (16/56) compared to the proportion of similar patients that improved after receiving activated charcoal alone (3/32). \(^{37}\) Subset comparison groups were small in the three studies, and vulnerable to subjective interpretation, potentially making negative results susceptible to Type II error.

**New studies**

Li et al. \(^{40}\) performed a qualitative systematic review of controlled studies to determine the strength of evidence that gastric lavage was useful as a treatment for organophosphorus pesticide poisoning. The investigators searched PubMed, Embase, the Cochrane database, the Chinese National Knowledge Infrastructure database, and the internet using Google. The review consisted of 56 controlled studies from China, including 16 variations on lavage procedures (e.g., multiple lavage versus single lavage). Lavage was a component of all control groups. Twenty-three studies were randomized controlled trials. All of the randomized clinical trials were small. All of the studies suffered from either poorly described methodology or unclear study results (e.g., inadequate blinding, poorly described randomization methods, unbalanced study groups, unknown inclusion and exclusion criteria, lack of quantitative confirmation of pesticide in lavage washings, imbalances in concomitant treatments, unclear outcome definitions) (LOE 4). All 56 studies reported positive results in their intervention groups. Although the studies are intriguing, the authors of the paper concluded that their systematic review was inconclusive, and that the Chinese observations need to be replicated using higher quality clinical methods before their results can be accepted.

There have been two other clinical studies published that were not part of this systematic review. Wang et al. examined the effect of gastric lavage on mortality rates associated with tetramine poisoning in China. \(^{41}\) Tetramine is found in Chinese rodenticides and causes life-threatening seizures by irreversibly binding to gamma-aminobutyric acid receptors. The investigators identified 409 tetramine exposures presenting to one Chinese hospital over a 3-year period of time (January 1999 to December 2002). Patients treated with gastric lavage had a lower fatality rate compared to patients not lavaged (5.85% vs. 38%, \(p < 0.01\)). When patients were categorized by severity of their intoxication (no effect, mild poisoning, severe poisoning), fatality rates rose from 0% to 14% as the severity of intoxication increased. Lavage appeared to provide protection even within the severely intoxicated groups (fatality rate of 9% vs. 31%, \(p < 0.01\)). Logistic regression showed that gastric lavage was the most important factor influencing fatality rate in this series. The authors concluded that gastric lavage was useful in the treatment of tetramine poisoning (LOE 4). Since this was a retrospective review it is likely that there were many uncontrolled variables (e.g., dose, supportive care therapies, time to presentation) in the lavage versus the nonlavage groups. Amigó and colleagues performed a prospective cohort trial in which they compared the outcomes of patients treated according to a gastrointestinal decontamination algorithm versus those not treated according to the algorithm (LOE 4). \(^{32}\) The algorithm allocated patients to treatment with ipecac, gastric lavage, gastric lavage plus activated charcoal, activated charcoal alone, or no decontamination based on patient clinical condition, agent ingested and time since exposure. The study outcomes were worsening of clinical condition and increasing drug concentrations. There were 94 patients enrolled in the study with 70 in the algorithm group and 24 in the nonalgorithm group. There was less clinical deterioration in the group managed with the algorithm than in the group not managed with the algorithm (14% vs. 33%, \(p = 0.041\)). There was no distinguishable difference in the drug disposition profiles between the two groups. Only eight patients were treated solely with gastric lavage and individual decontamination treatments were not compared in this study, so the contribution of gastric lavage to patient improvement is unclear.

**Contraindications**

In the extraordinary situations where gastric lavage seems to be a potential treatment option, the clinician must carefully consider whether potential harms outweigh theoretical benefits. Patients with craniofacial abnormalities, concomitant head trauma, or a number of other bodily injuries may not tolerate the lavage procedure. Gastric lavage is contraindicated if the patient has an unprotected airway, such as in a patient with a depressed level of consciousness without endotracheal intubation. Gastric lavage is also contraindicated if its use increases the risk and severity of aspiration (such as a patient who has ingested a hydrocarbon with high aspiration potential). Patients who
are at risk of hemorrhage or gastrointestinal perforation due to pathology, recent surgery or other medical condition, could be further compromised by the use of gastric lavage. If a patient refuses to cooperate and resists, it should be considered at least as a relative contraindication for performing gastric lavage because complications may be more likely.43–45

Complications

Summary of prior position paper 2004

The complications associated with gastric lavage have been well described in the medical literature and include aspiration pneumonia,32,39,46,47 laryngospasm,48,49 arrhythmia,49 esophageal or stomach perforation,32,37,50–55 fluid and electrolyte imbalance, and small conjunctival hemorrhages.56

Aspiration pneumonia has been reported as a complication even in lower risk settings such as when patients are awake, have been intubated, or have ingested a nonhydrocarbon substance.32,39,46,47

New studies

Many reports continue to be published documenting the complications associated with gastric lavage.

Eddleston et al.57 observed gastric lavage as it was being performed by practitioners in Sri Lanka. In their series, 14 patients presented to four hospitals after intentionally overdosing on a wide variety of agents. Half of the patients developed likely aspiration and three died soon after the procedure. The practitioners did not follow usual safety precautions including airway protection or exclusion of patients who refused to cooperate. No airway protection was provided and, in half the cases, patients were physically restrained during the procedure. In 3 of 14 cases, the lavage fluid was “poured” until the patient vomited around the lavage tube. The authors noted that in many cases gastric lavage was taking precedence to more important supportive care therapies. The series illustrated the many problems and potential risks associated with deploying traditional poison treatment techniques in developing countries (LOE 4).

Several studies have been published illustrating the risks associated with performing lavage in patients who have ingested hydrocarbons or pesticides. Jasyashree et al.58 identified the predictors of poor outcome in 48 children who ingested aliphatic hydrocarbon and were admitted to a pediatric intensive care unit in India (LOE 4). All of the patients in this series presented with some degree of respiratory distress. The nine patients who received gastric lavage had a higher frequency of hypoxemia (8/9 vs. 11/39, p < 0.05) and leucocytosis (5/9 vs. 13/39, p < 0.05) and a greater need for mechanical ventilation (5/9 vs. 3/39, p < 0.05) than patients who were not lavaged. The investigators examined cases retrospectively, so it is unclear whether patients who were lavaged aspirated before or after the procedure. Wang et al.59 retrospectively identified predictors of pneumonia after cholinesterase inhibitor poisoning in Taiwan (LOE 4). In this series, lavage was either performed at a peripheral hospital (122/155) where the details of the procedure were not available or they were lavaged at the study hospital (33/155) where gastric decontamination was performed using a nasogastric tube and activated charcoal was administered through the tube (1 g/kg in 300–800 mL of normal saline) while the patient was in the left decubitus position. Overall 34/155 (22%) of the patients developed pneumonia, and 32/34 (94%) of them had respiratory failure. Forty-four percent (15/34) of patients with pneumonia died. Of the patients lavaged at the study hospital 21/33 (64%) developed respiratory failure. Three of these patients (3/21, 14%) developed pneumonia. Only one patient developed both respiratory failure and pneumonia after gastric lavage. None of the patients without respiratory failure had pneumonia. Patients who were lavaged at a peripheral hospital were 6.23 times (95% CI 1.52–25.98) more likely to develop pneumonia than patients lavaged at the study hospital. Charcoal contamination of sputum was one of the main predictive factors for respiratory failure indicating that the adverse effects were related to the combination of gastric lavage and activated charcoal.

Gokel et al.60 documented electrolyte abnormalities associated with gastric lavage by prospectively monitoring serum calcium, ionized calcium, magnesium, and sodium concentrations at baseline, 15 minutes, 6 hours, and 12 hours after lavage in 30 patients who presented within 2 hours of amitriptyline intoxication (LOE 4). Gastric lavage with normal saline was performed. There were statistically significant decreases in serum calcium, ionized calcium, and serum magnesium concentrations at all three post-baseline measurement times, but no patient had clinical signs of hypocalcemia or hypomagnesemia. It is unclear how much of the electrolyte dilution was due to the lavage procedure since patients were also receiving intravenous fluids during their treatment.

Griffiths et al.61 described a case of esophageal perforation as a complication of gastric lavage during a review of all esophageal perforations occurring at a large 767-bed hospital in the United Kingdom (LOE 4). Over a 13-year period, there were 39 cases of esophageal perforation. One case (3%) involved an overdose patient treated with gastric lavage. This patient had taken 30 tablets of paracetamol-codeine combination and 20 of acetylsalicylic acid. She became anxious, agitated, and had shortness of breath 3 hours after the lavage. She developed neck swelling and surgical emphysema. A radiographic study showed a leak of contrast media at the thoracic inlet. She recovered over 20 days. There were no details on placement of lavage tube other than that it was a “difficult procedure.”

Indications – place in therapy

Summary of prior position paper 2004

The evidence showing that gastric lavage provides therapeutic benefit to poisoned patients is weak. Experimental studies in animals and in humans show that gastric lavage will reduce the bioavailability of markers in simulated overdoses; however, the results are highly variable and diminish with the elapsed time since ingestion. Clinical studies have failed to show that gastric lavage improves the severity of illness,
recovery times, or the ultimate medical outcomes of treated patients even when the treatment is started within 60 minutes. Given that gastric lavage may be associated with a number of life-threatening complications (aspiration pneumonitis, aspiration pneumonia, esophageal or gastric perforation, fluid and electrolyte imbalances, arrhythmia), it should not be performed routinely if at all. In the rare situation where gastric lavage might seem appropriate, clinicians should consider treatment with activated charcoal or observation and supportive care in place of gastric lavage. No specific examples of when “gastric lavage might seem appropriate” were included.

New studies
Since the publication of the 2004 position statement there has been continued growth of medical literature showing that gastric lavage can cause harm to patients but very little growth of the literature showing that gastric lavage could provide benefit. There are case reports showing that gastric lavage occasionally produced impressive returns (LOE 4).26–28 Nearly all of the clinical studies showing that gastric lavage might provide clinical benefit have been written in Chinese and published in the Chinese medical literature.30 These studies were designed to examine the therapeutic value of gastric lavage for the treatment of organophosphorus pesticide poisoning. These studies are not readily available to non-Chinese clinicians or investigators. A systematic review of the Chinese lavage studies suggests that they all potentially suffer from significant methodological flaws that threaten their internal validity (LOE 4).40

At the same time, there is at least one indicator that clinicians might not be adequately equipped or skilled at performing gastric lavage. A recent survey of hospital emergency departments in the United Kingdom found that 95% of respondents rarely or never performed gastric lavage.6 Fifty percent of respondents stated they did not have the equipment, and 38% stated they did not have adequately skilled personnel available to perform lavage. This survey had only a 50% response rate, was only published as an abstract, and awaits further confirmation in other parts of the world (LOE 4).

At present, the evidence supporting gastric lavage as a beneficial treatment for poisoned patients is weak. Older experimental studies show that retrieval is variable and time-dependent. Newer clinical studies suffer from methodological faults and often fail to show that gastric lavage improves outcome even when initiated within an hour of ingestion. At present, the evidence supporting situations where gastric lavage would provide benefit to patients (e.g. lethal ingestion, recent exposure, substance not bound to activated charcoal), is either based on theoretical grounds or is based on case reports (LOE 4). However, evidence to exclude that gastric lavage could be beneficial in those situations is also lacking. Until methodologically sound clinical studies are published demonstrating or excluding that lavage hastens clinical recovery rates or improves patient outcomes, the conclusion remains the same as in 2004: gastric lavage should not be performed routinely, if at all, for the treatment of poisoned patients. In the rare situation where gastric lavage might seem appropriate, clinicians should consider treatment with activated charcoal or observation and supportive care in place of gastric lavage. New evidence since 2004 suggests the need to emphasize that gastric lavage should be performed only where the expertise exists (Appendix 3).

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Declaration of interest
The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References
Supplementary material available online

Supplementary Appendix 1–3.