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REVIEW ARTICLE

Position paper update: ipecac syrup for gastrointestinal decontamination

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Context. An update of the first position paper on ipecac syrup from 1997 was published by the American Academy of Clinical Toxicology and the European Association of Poison Centres and Clinical Toxicologists in 2004. The aims of this paper are to briefly summarize the content of the 2004 Position Paper and to present any new data. **Methods.** A systematic review of the literature from the year 2003 forward. **Results.** The literature search yielded a limited number of meaningful articles, and there remains no convincing evidence from clinical studies that ipecac improves the outcome of poisoned patients. Furthermore, the availability of ipecac is rapidly diminishing. **Conclusions.** The routine administration of ipecac at the site of ingestion or in the emergency department should definitely be avoided. Ipecac may delay the administration or reduce the effectiveness of activated charcoal, oral antidotes, and whole bowel irrigation. There is not sufficient evidence to warrant any change in the previous ipecac position papers. There are, however, insufficient data to support or exclude ipecac administration soon after ingestion of some specific poisons in rare situations.

Keywords Gastrointestinal decontamination; Poisoning; Gastric lavage

Introduction

The hospital mortality from acute poisoning in the Western world is less than 1%,^{1–7} and the challenge for clinicians is to identify promptly those who are at risk of developing serious complications and who might potentially benefit from gastrointestinal decontamination. Ipecac syrup (ipecac) has previously been promoted widely and vigorously as an emetic for patients who have ingested poisons. However, there is evidence from case reports and clinical studies that the administration of ipecac is associated with little benefit and some complications. In 2004, these findings were summarized in the Ipecac Syrup Position Paper of the American Academy of Clinical Toxicology and the European Association of Poison Centres and Clinical Toxicologists.⁸ This paper was an update of the first Ipecac Syrup Position Paper from 1997.⁹ In keeping with these data, poison centers seldom recommend the use of ipecac today,¹⁰ and its use in emergency departments has declined steadily¹¹ (level of evidence [LOE] 4). Another important consequence of the Ipecac Syrup Position Papers is that the presence of ipecac in callers' homes as well as in pharmacies has declined considerably during recent years^{12,13} (LOE 6 and 4). The results of one study suggested that the decreased use of

ipecac in children at the site of ingestion has not led to an increase in resource utilization or impairment in patient outcome.¹⁴ The aims of this second update of the Ipecac Syrup Position Paper are 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. Regarding the pharmacologically active components of ipecac, its dosage regimen and different formulations, the reader is referred to the 2004 Ipecac Syrup Position Paper.⁸

Method

MEDLINE (via PubMed), International Pharmaceutical Abstracts (via Ebsco), and 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 single term “ipecac” from 2003 to 31 March 2011. Where possible, the term was entered as a truncation (e.g., ipecac*) to capture articles using related names for the product (e.g., ipecacuanha). The initial search yielded 157 unique articles that were reviewed by one of the authors. Forty-two of these offered the possibility of applicable human data and were therefore incorporated into an evidence table showing the key characteristics of each article (Supplementary Appendix Table, published online only). The rejected articles either mentioned ipecac only in passing or were review articles that did not provide any new information. Each article in

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the evidence table 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 (Table 1). Ultimately, 12 articles contributed to this revision of the Position Paper and their LOEs are noted.

Animal studies

Summary of prior position paper 2004

The value of ipecac in reducing marker absorption has been investigated in four studies.^{15–18} In these studies, the mean recovery of ingested material was highly variable (17.5–62.0%). In general, the amount of material removed by ipecac-induced emesis depended on the time elapsed between the toxin administration and the onset of emesis. When ipecac was administered within 30 minutes of dosing, the mean recoveries ranged from 17.5% to 52.1%.^{15–18} When ipecac was administered 60 minutes after dosing, the mean recoveries were 36.8% and 31.0%.^{15,16} Since the 2004 Ipecac Syrup Position Paper was published, no new animal study has been published.

Volunteer studies

Summary of prior position paper 2004

All of the volunteer studies have the same basic limitation—it is difficult to extrapolate data from simulated overdoses in volunteers (with nontoxic amounts) to real overdoses (with large amounts) because the amount ingested affects dissolution, absorption, and gastric emptying rates. Furthermore, the time from ingestion to ipecac administration differs and makes the comparison of studies difficult. Eleven volunteer

Table 1. Levels of evidence.*

Level of evidence	Description of study design
1a	Systematic review (with homogeneity) of randomized clinical trials
1b	Individual randomized clinical trials (with narrow confidence interval)
1c	All or none (all patients died before the drug became available, but some now survive on it; or when some patients died before the drug became available, but none now die on it.)
2a	Systematic review (with homogeneity) of cohort studies
2b	Individual cohort study (including low quality randomized clinical trial)
2c	“Outcomes” research
3a	Systemic review (with homogeneity) of case-control studies
3b	Individual case-control study
4	Case series, single case reports (and poor quality cohort and case control studies)
5	Expert opinion without explicit critical appraisal or based on physiology or bench research
6	Abstracts

*Adapted from OCEBM Levels of Evidence Working Group. Levels of Evidence. Oxford Centre for Evidence-Based Medicine, 2009. Available from: <http://www.cebm.net/index.aspx?o=1025>.

studies have investigated the value of ipecac in preventing the absorption of marker substances.^{19–29} In these studies, the recovery of material was highly variable. In general, the amount of ingested material removed by ipecac-induced emesis depended on the elapsed time between ingestion and the onset of emesis. If ipecac was administered at 5 minutes after dosing, the mean recoveries in two studies were 54.1%²⁸ and 83.0%.²⁵ In another study, the mean plasma concentrations for various drugs were reduced to values between 21.0% and 48.0% of control if ipecac was administered at 5 minutes after dosing.¹⁹ A study using acetaminophen as a marker showed a 67% reduction in bioavailability if ipecac was administered within 5 minutes.²⁹ When ipecac was administered at 10 minutes after dosing, the mean recoveries in two studies were 28.4%²² and either 46.9% or 47.2%.²⁷ Ipecac administered at 30 minutes after dosing resulted in a mean recovery of 59.0%.²⁵ In another study, the bioavailability of acetaminophen was the same as control when ipecac was administered at 30 minutes or longer after ingestion.²⁹ If ipecac was administered at 60 minutes, the mean areas under the curve were reduced to 79.0%²⁶ and 62.0%²³ of control. In another study, the mean recovery of marker from the GI tract was 44.0% when ipecac was given at 60 minutes.²⁵ No new volunteer study has been published since the most recent position paper on ipecac was published.

Marker studies in poisoned patients

Summary of prior position paper 2004

In three studies, markers were administered to emergency department patients presenting with potentially toxic ingestions. The objective in each study was to measure recovery of the marker after ipecac-induced emesis. Corby et al.³⁰ gave 14 children magnesium hydroxide 1 g prior to ipecac 20 mL. The mean elapsed time to emesis was 15 ± 2.8 minutes (range 5–41 minutes) and the mean recovery of magnesium hydroxide was 28 ± 7% (range 0–78%). The incomplete collection of vomitus in three children might have contributed to the low recovery. However, the very large range of recovery of magnesium hydroxide implies a large variability in the value of ipecac. Similarly, Auerbach et al.³¹ administered liquid thiamine 100 mg mixed with ipecac 30 mL ($n = 51$) that produced emesis in a mean time of 21 minutes. The mean amount of thiamine recovered in the emesis was 50 ± 35%. The recovery of thiamine exceeded 70% in 28% of the patients. In a randomized, controlled, single-blind study, Saetta et al.³² administered 20 barium-impregnated 3-mm polythene pellets with ipecac 30 mL and water to 20 patients. Emesis started 5–20 minutes after ipecac administration. Abdominal X-rays performed 15–80 minutes after ingestion of the pellets showed that a mean of 41.5% of the pellets had been removed from the gastrointestinal tract. A control group (no stomach emptying procedures) had X-ray imaging performed 30–70 minutes after pellet ingestion. In the ipecac group, 39.3% of the ingested pellets had moved into the small bowel compared to 16.3% of the pellets in the control group. The authors suggested

that in some situations ipecac could enhance gastric emptying with the potential to facilitate drug absorption. No new marker study has been published since the most recent position paper on ipecac was published.

Case reports

Summary of prior position paper 2004

Tenenbein³³ reported two cases and Landsman et al.³⁴ one case in which ipecac-induced emesis failed to remove iron-containing tablets from the stomach. Peterson and Fifield³⁵ reported a potentially severe case of iron poisoning in a child in whom ipecac-induced emesis led to the recovery of some but not all of the iron-containing tablets.

New studies

Lynn and Hurley³⁶ reported a case of intentional ingestion of 50 iron tablets (ferrous sulfate 324 mg) by a woman (LOE 6). An X-ray performed within 1 hour after the overdose showed her stomach to be filled with radiopaque tablets. Gastric lavage failed to recover more than a few fragments. Ipecac was on hand, and the poison center recommended its use. Thirty millilitre of ipecac was given and vomiting quickly ensued. Thirty-eight iron tablets were recovered in clumps. A new X-ray showed nine tablets in the duodenum and whole bowel irrigation was performed. The serum iron concentration peaked at 49 µg/dL (8.8 µmol/L). The patient remained asymptomatic and was discharged about 18 hours after ingestion of the iron.

Clinical studies

This section contains studies with a variety of study designs with varying strengths and weaknesses.

Summary of prior position paper 2004

In a study of children with nontoxic serum acetaminophen concentrations, the mean serum acetaminophen concentration was reduced by 52.6% when emesis was induced up to 59 minutes after ingestion.³⁷ In a study of 50 children with estimated acetaminophen overdoses of > 150 mg/kg, Amitai et al.³⁸ compared the effects of early (26 ± 8 minutes) and late (83 ± 13 minutes) administration of ipecac on the measured acetaminophen plasma concentrations and found significant differences in favor of the early group. Two clinical studies have demonstrated no benefit on clinical outcome from the administration of ipecac before activated charcoal versus activated charcoal alone.^{39,40} Most studies^{14,41–45} had limitations such as exclusion of the use of ipecac in life-threatening intoxications or no group that received ipecac as the sole intervention so it is difficult to determine any clinical benefit of ipecac administration.

New studies

Beuhler et al.⁴⁶ (LOE 4) analyzed the management of 57 531 cases from the 1995–2005 Toxic Exposure Surveillance

System (TESS) database of the American Association of Poison Control Centers. All were children less than 6-years of age who had ingested mushrooms without co-ingestants. The study population was divided into three groups: ipecac alone ($n = 27\,729$), single-dose activated charcoal (SDAC, $n = 6455$), and no GI decontamination ($n = 25\,347$). The results showed no major outcomes in the ipecac group versus six each in the two other groups. Furthermore, 0.2% of the cases in the ipecac group had major or moderate outcomes versus 1.4% in the SDAC group and 0.8% in the no GI decontamination group ($p < 0.001$ for ipecac vs. either of the other groups). Although the results of this retrospective cohort study were statistically significant, it is difficult to draw conclusions from it considering the multiple factors that might have influenced the choice of initial treatment (for instance, type of suspected mushroom and amount ingested) and the fact that 99.3% of the children did well. In a systematic review of randomized trials with human volunteers, quasi-randomized studies, and non-randomized studies of GI decontamination interventions for acetaminophen overdose available up to 2005,⁴⁷ the authors concluded that “All the observational studies and studies in volunteers found that activated charcoal, gastric lavage, or ipecacuanha, shortly after ingestion, are able to reduce the absorption of paracetamol. Whether this translates into clinical benefits is not clear” (LOE 2a). Two case series on the use of ipecac in “body stuffers” have been reported in forensic medicine journals after the 2004 Ipecac Syrup Position Paper was published. “Body stuffers” are people who suddenly swallow illicit drug packets in order to prevent their discovery. In a letter to the editor, Marc⁴⁸ (LOE 4) briefly reported 50 “body stuffers” given ipecac in a hospital emergency department within 2 hours after suspected ingestion. Of the 50 patients, 47 vomited within 30 minutes with drug packets recovered from 21. Abdominal radiography was a very poorly sensitive test (33%). No detailed discussion of medical outcomes was provided. In a short original communication, Püschel et al.⁴⁹ (LOE 4) reported on 683 drug packets recovered from 154 “body stuffers” by induced emesis. Among the 154 patients, 1–55 drug packets were recovered in about 70–80% of the cases. Ninety-six percent of the packets contained cocaine. No case of intoxication was observed, but a 20-year-old man with a previously unknown toxic cardiomyopathy died 3 days after a sudden cardiac arrest that followed the forced application of ipecac via a correctly placed nasogastric tube. There were no substance concentrations detectable in the blood after resuscitation although gastroscopy helped to remove 41 crack cocaine rocks from his stomach.

Contraindications

Because of the risk of aspiration, ipecac-induced emesis is contraindicated if the patient has compromised airway protective reflexes (including impaired consciousness and convulsions), has ingested a substance that might compromise airway protective reflexes, or if there is an anticipated

need for advanced life support within the coming hour. Ipecac should not be administered following ingestion of hydrocarbons with high aspiration potential, after the ingestion of a corrosive substance such as an acid or alkali, in debilitated, elderly patients, or those with medical conditions that could be further compromised by the induction of emesis.^{50–52}

Complications

Considering that over 3 million patients received therapeutic doses of ipecac during the 14-year period of 1983–96,¹⁰ ipecac appears to have a high margin of safety. The potential complications of the therapeutic use of ipecac are well-documented, but serious sequelae occur rarely. An important concern is that the use of ipecac can delay the administration of activated charcoal by 1–2 hours.^{39,42,53} The most common complications or adverse consequences of using ipecac are diarrhea,^{53–55} lethargy/drowsiness,^{54–56} and prolonged (> 1 hour) vomiting.^{54,57} Less frequent complications include irritability/hyperactivity,^{54,55} fever,⁵⁷ and diaphoresis.⁵⁵ Rare but more serious adverse consequences include Mallory–Weiss tears,^{58,59} pneumomediastinum,⁶⁰ and aspiration pneumonia.^{53,61} Fatalities associated with the therapeutic use of ipecac include one case each of traumatic diaphragmatic hernia,⁶² intracranial hemorrhage,⁶³ and gastric rupture.⁶⁴ Albertson et al.⁵³ conducted a controlled study of the complication rate among 200 adult patients presenting to an emergency department with potentially toxic ingestions. The patients were randomized to receive ipecac and activated charcoal or only activated charcoal. The group receiving ipecac plus activated charcoal had a statistically significantly higher complication rate (5.4% vs. 0.9%). Myopathy and cardiomyopathy following repeated abuse of ipecac by patients with eating disorders have been reported both in previous^{65–82} and in more recent publications^{83,84} (LOE 4 and 4). Four of the patients died.^{65,70,73,75} Ipecac has been implicated as an instrument of child abuse in Munchausen syndrome by proxy.^{85–93}

Indications – place in therapy

Summary of prior position paper 2004

Clinical studies have not confirmed the benefit of ipecac administration after poison ingestion. There are, however, descriptive reports that indicate that ipecac occasionally produces impressive returns. There are insufficient data to support or exclude ipecac administration soon after poison ingestion. Based on experimental and clinical studies, ipecac should be considered only in an alert patient who has ingested a potentially toxic amount of a poison and if it can be administered within 60 minutes of the ingestion. Even then, clinical benefit has not been confirmed.

Discussion – Conclusions

In a practice guideline on the use of ipecac out of hospital developed by a panel of toxicologists and based on a

systematic review of the English language literature from 1966 to 2002,⁹⁴ the following conclusion was stated: “The use of ipecac syrup might have an acceptable benefit-to-risk ratio in rare situations in which: there is no contraindication to the use of ipecac syrup; and there is substantial risk of serious toxicity to the victim; and there is no alternative therapy available or effective to decrease gastrointestinal absorption (e.g., activated charcoal); and there will be a delay of greater than 1 hour before the patient will arrive at an emergency medical facility and ipecac syrup can be administered within 30–90 minutes of the ingestion; and ipecac syrup administration will not adversely affect more definitive treatment that might be provided at a hospital.” No examples of such circumstances were provided (LOE 2a). In an editorial⁹⁵ commenting on this guideline the author concluded: “Ipecac produces emesis, but that is the extent of the evidence. There is no basis for the recommendation that ipecac may be useful in rare circumstances. The use of ipecac syrup should be abandoned and the conclusions of this guideline should be disregarded” (LOE 5). This debate reflects the controversy of ipecac use in acute poisoning today. Should ipecac be kept for use in rare specific situations or should it be abandoned completely? Since the publication of the Ipecac Syrup Position Paper in 2004, no new evidence that supports the latter opinion has been published except for some reports indicating that the availability of ipecac is decreasing^{11–13} (LOE 4, 6 and 4) and probably unavailable in vast areas worldwide. In fact, the manufacture of ipecac in the United States has stopped.⁹⁶ However, some reports supporting continued use of ipecac in special situations have been published recently although none of them provides a high level of scientific evidence. While there is some recent evidence suggesting possible benefits of ipecac in rare situations in the management of iron poisoning³⁶ (LOE 6), toxic mushroom ingestion⁴⁶ (LOE 4) and “body stuffers”^{48,49} (LOE 4 and 4) but not “body packers”, the quality of this evidence is not sufficient on which to base treatment recommendations. There is not sufficient evidence to warrant any change in the previous ipecac position statements. The routine administration of ipecac at the site of ingestion or in the emergency department should definitely be avoided.

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Declaration of interest

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

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Supplementary material available online

Supplementary Appendix. Table to be published online only at <http://informahealthcare.com/doi/abs/10.3109/15563650.2013.770153>).