

POSITION PAPER

Position Paper: Ipecac Syrup[#]

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ABSTRACT

Syrup of ipecac should not be administered routinely in the management of poisoned patients. In experimental studies the amount of marker removed by ipecac was highly variable and diminished with time. There is no evidence from clinical studies that ipecac improves the outcome of poisoned patients and its routine administration in the emergency department should be abandoned. There are insufficient data to support or exclude ipecac administration soon after poison ingestion. Ipecac may delay the administration or reduce the effectiveness of activated charcoal, oral antidotes, and whole bowel irrigation. Ipecac should not be administered to a patient who has a decreased level or impending loss of consciousness or who has ingested a corrosive substance or hydrocarbon with high aspiration potential. A review of the literature since the preparation of the 1997 Ipecac Syrup Position Statement revealed no new evidence that would require a revision of the conclusions of that Statement.

SUMMARY STATEMENT

Introduction

- Overall, the mortality from acute poisoning is less than one percent and the challenge for clinicians managing poisoned patients is to identify promptly those who are most at risk of developing serious complications and who might potentially benefit, therefore, from gastrointestinal decontamination.
- Ipecac syrup is available as a nonprescription drug at pharmacies in many countries and may be administered at home shortly after an ingestion.

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Rationale

- Ipecac syrup effectively produces emesis which is intended to remove ingested poisons from the stomach. Emesis is noninvasive, utilizes a physiological mechanism, and consumes little staff time.

Animal Studies

- The value of ipecac in reducing marker absorption has been investigated in four studies (1–4). In these studies, the mean recovery of ingested material was highly variable (17.5–62.0%), though generally, the amount of ingested material removed by ipecac-induced emesis depended on the time elapsed between the dosing and the onset of emesis.
- When ipecac was administered within 30 minutes of dosing, the mean recoveries were 45.6% (1), 44.0% (2), 19.0% (3) and 42.2%, 17.5% and 52.1% (4). When ipecac was administered 60 minutes post-dosing, the mean recoveries were 36.8% (1) and 31.0% (2).

Volunteer Studies

- Eleven volunteer studies have investigated the value of ipecac in preventing the absorption of marker substances (5–15).
- In these studies, the recovery of material was highly variable, though generally the amount of ingested material removed by ipecac-induced emesis depended on the elapsed time between dosing and the onset of emesis.
- If ipecac was administered at 5 minutes after dosing, the mean recoveries in two studies were 54.1% (14) and 83.0% (11). In other studies the mean plasma concentrations for various drugs were reduced to 21.0%, 31.0%, and 48.0% of control,(5) and to 25.0% and 40.0% of control (7). A study using acetaminophen as a marker showed a 67% reduction in bioavailability if ipecac was administered within 5 minutes (15).
- When ipecac was administered at 10 minutes after dosing, the mean recoveries in two studies were 28.4% (8) and either 46.9% or 47.2% (13).
- Ipecac administered at 30 minutes after dosing resulted in a mean recovery of 59.0% (11). In another study (5), the mean plasma concentrations of three drugs were 70.0%, 98.0%, and 107.0% of control. In a third study, the bioavailability of acetaminophen was the same as control when

ipecac was administered at 30 minutes or longer after ingestion (15).

- If ipecac was administered at 60 minutes, the mean areas under the curve (AUCs) were 79.0% (12) and 62.0% (9). When total urine salicylate was measured, 70.3% (6) and 44.4% (10) were recovered. In another study (11), the mean recovery of marker was 44.0%.

Clinical Studies

- In a study in children with nontoxic acetaminophen (paracetamol) concentrations, the mean plasma acetaminophen concentrations were reduced from 33.1 mg/L to 15.7 mg/L (a 52.6% reduction) when emesis was induced up to 59 minutes after ingestion (16).
- Two clinical studies (17,18) have demonstrated no benefit on patient outcome from the administration of ipecac before activated charcoal vs. activated charcoal alone, irrespective of the time of ipecac administration.
- Most studies excluded the use of ipecac in life-threatening intoxications, so it is difficult to determine the benefit of ipecac in more severely poisoned patients.

Indications

- There are insufficient data to support or exclude ipecac administration soon after poison ingestion.
- Ipecac should be considered only in an alert conscious patient who has ingested a potentially toxic amount of a poison.
- As the effect of ipecac diminishes with time and as clinical studies have demonstrated no benefit from its use, it should be considered only if it can be administered within 60 minutes of the ingestion. Even then clinical benefit has not been confirmed.

Dosage Regimen

- The United States Pharmacopoeia (USP DI, 2003) recommends the following oral dosage regimen for Ipecac Syrup, USP.

Children up to six months of age: Ipecac syrup should only be administered under the supervision of a physician;

Children 6–12 months of age: 5–10 mL preceded or followed by 120–240 mL of water;



Children 1–12 years of age: 15 mL preceded or followed by 120–240 mL of water;

Adolescents and adults: 15–30 mL followed immediately by 240 mL of water.

The dose may be repeated in all age groups if emesis does not occur in 20–30 minutes.

- The ingestion of milk or a drug with antiemetic properties is not a contraindication to the use of ipecac. The use of ipecac that has exceeded the expiration date is not a contraindication to its use.

Contraindications

- Compromised airway protective reflexes (including coma and convulsions).
- Ingestion of a substance that might compromise airway protective reflexes or anticipate the need for advanced life support within 60 minutes.
- Ingestion of hydrocarbons with high aspiration potential.
- Ingestion of a corrosive substance, such as an alkali or strong acid.
- Debilitated, elderly patients or medical conditions that may be further compromised by the induction of emesis.

Complications

The most common complications or adverse consequences of using ipecac are diarrhea (19,20), lethargy/drowsiness (19,20) and prolonged (>1 hour) vomiting (19,21).

SUPPORTING DOCUMENTATION

Introduction

Ipecac is prepared from the dried rhizome and roots of the *Cephalis acuminata* or *C. ipecacuanha* plant. In this Position paper, the term ipecac will be used to mean Ipecac Syrup (USP), Ipecacuanha Syrup (Emetic) (APF), Paediatric Ipecacuanha Emetic Mixture (BP), and Sirop d’Ipécac (Pharmacopée Française) even though the alkaloid content may vary among formulations. In many countries, ipecac is available at pharmacies as a nonprescription drug.

Ipecac has two main pharmacologically active components: the alkaloids emetine (methylcephaeline) and cephaeline. These alkaloids represent at least 90% of the alkaloids present in ipecac; a 30-mL dose of ipecac syrup contains approximately 24 mg of emetine and 31 mg of cephaeline. Ipecac induces vomiting through both peripheral and central mechanisms. The emetic alkaloids stimulate gastric mucosal sensory receptors which activate the vomiting center in the brain. They also directly stimulate the chemoreceptor trigger zone in the area postrema in the brain.

Ipecac has been promoted widely and vigorously as an emetic for patients who have ingested poisons. However, there is evidence from experimental and clinical studies that the administration of ipecac is associated with little benefit. In keeping with these data, American poison centers recommended its use in only 0.6% of cases in 2002 (22).

Rationale

Ipecac syrup effectively produces emesis which is intended to remove ingested poisons. Ipecac may be administered at home shortly after ingestion.

Animal Studies

Experimental studies in animals are limited to four studies in dogs. The results of gastric emptying studies in experimental animals require a degree of caution when extrapolating to cases of human poisoning. Although the dogs were not anesthetized, some were premedicated to prevent spontaneous vomiting. In addition, dogs have a variable response to ipecac.

Sodium Salicylate

The value of induced emesis was investigated (1) in fasting dogs (6–10 kg) who were pretreated with chlorpromazine 25 mg or promethazine 25 mg IM or promethazine 37.5–50 mg IV to prevent spontaneous vomiting. Pretreatment occurred 30 minutes prior to the administration of sodium salicylate 500 mg/kg in broken tablet form. Ipecac 25 mL was given 11–80 minutes after the salicylate. Twenty dogs received ipecac 30 minutes (mean 18.5 minutes, range 11–30 minutes) after the salicylate; the mean recovery was 49.1% (range 9.0–75%, SD 20.8) and the mean peak serum salicylate concentration (in six dogs) was 0.247 g/L. Seventeen dogs were given ipecac >30 minutes (mean 62.6 minutes, range 40–80 minutes) after the salicylate; the mean recovery was 35.9%

(range 4.3–74%, SD 22.4) and the mean peak serum salicylate concentration (in eight dogs) was 0.40 g/L.

Barium Sulfate

Abdallah and Tye (2) studied the use of ipecac in dogs (2.2–5.4 kg) using barium sulfate 5 g suspension as a marker. Barium was administered over 30 minutes and was followed by ipecac 1.5 mL/kg at 0, 30, or 60 minutes. The mean elapsed time to emesis was 46 minutes. The mean SE recovery of barium was 3.1 ± 0.53 g (62%) in the 0-minute group, 2.2 ± 0.34 g (44%) in the 30-minute group, and 1.6 ± 0.46 g (31%) in the 60-minute group.

Emesis was also investigated in fasting puppies using two barium sulfate 1 g gelatin capsules as a marker (3). Ipecac 15–30 mL was given 20 minutes after the barium and emesis occurred, a mean of 29 ± 8.6 minutes (range 8–37 minutes) after the ipecac. Only three of the six study dogs vomited. Emesis resulted in a mean recovery of barium of $19 \pm 9\%$ (range 2–31%). If the three dogs that did not vomit are included in the analysis, the expected recovery would be $9 \pm 6\%$.

Acetaminophen (Paracetamol)

Teshima et al. (4) evaluated the efficacy of emesis in fasting dogs (10–11.5 kg) using 50 mL of a syrup that contained acetaminophen 193 mg, salicylic acid 48 mg, and kanamycin 107 mg as well as 29 mL of JP syrup simplex (a macrolide antibiotic-containing syrup) to delay gastric emptying. The intragastric pH was maintained at 1.5–2.5 by administering a HCl-glycine buffer 25 mL or pentagastrin 6 mg/kg. Ipecac Syrup (USP) 20 mL was given 10 minutes after the marker but the time to emesis was not reported. Measurements included the mean (\pm SEM) amount of drug recovered in the emesis, the peak serum concentration, and the AUC up to 8 hours. Drug recovery in emesis was $42.2 \pm 4.4\%$ for acetaminophen, $17.5 \pm 1.8\%$ for salicylic acid, and $52.1 \pm 4.8\%$ for kanamycin. For acetaminophen, the mean peak serum concentration was 2.25 ± 0.97 mg/L (vs. 4.72 ± 0.54 mg/L for control, $p < 0.05$). The peak serum concentration and AUC for salicylic acid were not significantly different from controls. Serum kanamycin concentrations were not measured.

Volunteer Studies

Limitations of Volunteer Studies

All of the volunteer studies have the same basic limitations: it is difficult to extrapolate data from sim-

ulated 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. These are considered marker studies and are categorized by agent and do not exactly simulate the overdose situation.

Acetaminophen (Paracetamol)

Ten fasting adults were given acetaminophen 3 g as 80 mg tablets in a randomized controlled crossover study (12). Sixty minutes after the acetaminophen, the treatment group received ipecac 30 mL and water 240 mL. The mean time to the first emesis was 25.5 ± 8.9 minutes. The 8-hour AUC for the ipecac group (94.32 g/mL/h) was 21% lower than the control group (109.41 g/mL/h) ($p < 0.05$). In another volunteer study (15), 10 adults, given 3.9 g of acetaminophen, received ipecac syrup at 5, 30 and 60 minutes versus control in a four-limbed cross-over fashion. Ipecac given at 5 minutes reduced bioavailability by 67%. Only the 5 minute group varied significantly from control.

Ampicillin

The administration of ipecac 30 mL with water 250 mL to 10 volunteers 60 minutes after the ingestion of ampicillin 5 g prevented 38% of the drug from being absorbed ($p < 0.01$) compared to controls (30.9 ± 73 g/mL/h vs. 50.2 ± 10.7 g/mL/h) as measured by the 12-hour AUC(9). The mean time to emesis was 16 minutes.

Aspirin (Acetylsalicylic Acid)

Ten of 12 adults completed a randomized controlled crossover study where each was given 24 aspirin tablets (81 mg/tablet) with water 240 mL following a 12-hour fast. The control group received no treatment. Sixty minutes after aspirin administration, the experimental group was given ipecac 30 mL with water 240 mL which was repeated in three subjects who did not vomit within 30 minutes of the initial dose. The mean (SD) time of emesis was 30.7 ± 7.8 minutes. Urine was collected for 48 hours and analyzed for total salicylate. The mean (SD) percentage of ingested salicylate recovered in the urine was $96.3 \pm 7.5\%$ for the control group and $70.2 \pm 12.1\%$ for the ipecac group ($p < 0.01$). The use of highly soluble pediatric aspirin tablets and the 90-minute delay in the



onset of emesis may have had a significant impact on the outcome of this study.

Danel et al. (10) also studied urinary salicylate recovery in a randomized controlled crossover study. Twelve fasting adults were given 20 aspirin tablets (75 mg/tablet) with water (200 mL). The control group received no further treatment while the emesis group received ipecac (30 mL) 60 minutes after the aspirin. The mean (SD) percentage of ingested salicylate recovered in the urine was $60.3 \pm 13.3\%$ for the control group and $55.6 \pm 10\%$ for the ipecac group ($p < 0.025$). Although the difference between the two groups was statistically significant, it was not clinically important.

Cyanocobalamin

Tandberg et al. (8) found that emesis induced with ipecac 30 mL and water 1 liter given 10 minutes after the administration of cyanocobalamin (2500 μg in 25 tablets) resulted in a mean recovery of $28.4 \pm 16.9\%$ (range 6–70%). This study may have been biased against the effectiveness of ipecac due to the large volume of water ingested with the cyanocobalamin.

In a related study (13), the efficacy of emesis in a sitting position was compared with a knee-chest position. The results were essentially identical. Ipecac 30 mL and water 640 mL were administered 10 minutes after the ingestion of cyanocobalamin 2500 μg . In the sitting position a mean of 46.9% (95% CI 40–62 μg) of the total amount of cobalt was recovered compared to a mean of 47.2% (95% CI 39.9–62.7 μg) in the knee–chest position.

Sucralfate

Vasquez et al. (11) administered $\text{Tc}^{99\text{m}}$ 1 mCi (37 MBq) human serum albumin–sucralfate (which is minimally absorbed from the GI tract and has a mean gastric clearance half-time of 90 minutes). This was followed by ipecac 30 mL and water 240 mL at 5, 30, or 60 minutes. A gamma camera scanned the GI tract immediately following administration of the marker and 60 minutes after ipecac. The mean amounts of marker removed from the GI tract were 83% (range 71–97%) for the 5-minute group, 59% (range 51–68%) for the 30-minute group, and 44% (10–65%) for the 60-minute group.

In a similar study (14), the ingestion of 30 $\text{Tc}^{99\text{m}}$ capsules followed 5 minutes later by ipecac 30 mL and water 1 liter resulted in the mean removal of $54.1 \pm 21.3\%$ (range 21–89%, 95% CI 43.9–64.4%) of the ingested material.

Multiple Drug Administration

In a controlled crossover study (5), six fasting adults ingested acetaminophen (paracetamol) 1 g, tetracycline 500 mg, and a long-acting aminophylline preparation 350 mg. Ipecac 20 mL and water 300 mL were given either 5 minutes or 30 minutes later and timed blood samples were collected for 24 hours. The mean time to onset of emesis was 14.3 ± 1.2 minutes. For acetaminophen the mean peak serum concentration was reduced significantly ($p < 0.01$) to 4.4 ± 1.5 mg/L (control 14.9 ± 2.0 mg/L) by the administration of ipecac at 5 minutes. Under these conditions the mean $\text{AUC}_{0-24 \text{ h}}$ was 35% control ($p < 0.01$). There was no statistically significant reduction in mean peak serum concentration or mean $\text{AUC}_{0-24 \text{ h}}$ when Ipecac syrup was given at 30 minutes. For tetracycline the mean peak serum concentration was reduced significantly ($p < 0.01$) in both the 5- and 30-minute treatment groups (mean peak concentrations 3.3 ± 0.4 mg/L, 0.8 ± 0.3 mg/L, and 2.1 ± 0.2 mg/L for control, 5-minute, and 30-minute ipecac groups, respectively). The mean $\text{AUC}_{0-24 \text{ h}}$ was also reduced significantly in both treatment groups ($p < 0.01$ and $p < 0.05$ for ipecac at 5 minutes and 30 minutes, respectively). For aminophylline the mean peak serum concentration was only reduced significantly ($p < 0.05$) by the administration of ipecac at 5 minutes (mean concentrations 4.0 ± 0.6 mg/L and 1.7 ± 0.7 mg/L in control and ipecac groups, respectively). The mean $\text{AUC}_{0-24 \text{ h}}$ in the 5-minute ipecac group was 49% control ($p < 0.05$) with no significant mean $\text{AUC}_{0-24 \text{ h}}$ reduction when ipecac was administered at 30 minutes. These results are difficult to interpret because of the small number of volunteers who ingested only 12 dosage forms of the study drugs. There were very large ranges for AUC values (4–110% and 26–150% for acetaminophen, 0–89% and 38–149% for tetracycline, and 0–95% and 7–155% for aminophylline) and no confidence intervals were calculated. The investigators concluded that ipecac produced emesis effectively but that it was not very effective in preventing drug absorption.

The absorption of cimetidine and pindolol was studied in a randomized controlled crossover study (7). Seven fasted adults were pretreated with metoclopramide 20 mg and 60 minutes later ingested cimetidine 400 mg and pindolol 10 mg. Five minutes after the ingestion, either water 400 mL or water 400 mL and ipecac 20 mL was given. Six of the seven subjects vomited with a mean time delay of 17 minutes. Ipecac significantly reduced the absorption of both cimetidine (25% of control) and pindolol (40% of control) as measured by mean peak serum concentrations, 48 hour



AUCs, and 48 hour urinary excretion; however, there were very large interindividual differences.

Markers in Poisoned Patients

In three studies, markers were administered to emergency department (ED) 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. (23) gave 14 children of unstated ages magnesium hydroxide 1 g at an unstated amount of time 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 $28 \pm 7\%$ (range 0–78%). The incomplete collection of vomitus in three children may have contributed to the low recovery. However, the very large (and unpredictable) range of recovery of magnesium hydroxide does not instill confidence in the value of ipecac.

Similarly, Auerbach et al. (24) administered liquid thiamine 100 mg mixed with ipecac 30 mL ($n=51$) which produced emesis in a mean time of 21 minutes. The mean amount of thiamine recovered in the emesis was $50 \pm 35\%$. The recovery of thiamine exceeded 70% in 28% of the patients.

In a randomized, controlled, single-blind study, Saetta et al. (25) administered 20 barium-impregnated 3-mm polythene pellets with ipecac 30 mL and water to 20 patients. Emesis started 5–20 minutes after ipecac. Abdominal X rays performed 15–80 minutes (mean 47.2 minutes) after ingestion of the pellets demonstrated 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 rays performed 30–70 minutes (mean 43.5 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 suggest that in some situations ipecac may enhance gastric emptying with the potential to facilitate drug absorption.

CLINICAL STUDIES

Unselected Cases of Poisoning

Kulig et al. (17), in a controlled and randomized prospective study, evaluated 592 acute oral drug overdose patients to determine if ipecac and charcoal

or lavage and charcoal were superior to the use of activated charcoal alone. They demonstrated that the induction of emesis by ipecac before administration of activated charcoal and a cathartic ($n=214$) did not significantly alter the clinical outcome of patients who were awake and alert on presentation to the ED as compared to those who received activated charcoal and a cathartic without ipecac ($n=262$). Neither the number of hospital admissions that were required after treatment nor the number of patients who were considered to have suffered clinical deterioration after presentation to the ED were shown to be statistically different ($p>0.05$) even when syrup of ipecac was administered less than 60 minutes after a toxic ingestion. The administration of activated charcoal was delayed by a mean of 2.2 hours (range 1–6.5 hours) in patients receiving ipecac. These investigators concluded that induction of emesis in acutely poisoned patients who present alert and awake in the ED was of no benefit, even when performed less than 60 minutes after a toxic ingestion.

A prospective study involving 808 consecutive overdose patients was conducted by Merigian et al. (26) to determine if patients benefited from gastric decontamination. Three hundred and fifty seven patients were symptomatic on presentation and were randomized into two treatment groups. The control group was divided, according to clinical condition, to receive either ipecac and charcoal or gastric lavage and charcoal. The other group received nasogastric aspiration and activated charcoal. There was no group that received ipecac as the sole intervention. Data were pooled to compare gastric emptying (ipecac or lavage) and charcoal with nasogastric aspiration and charcoal. The investigators found no clinical benefit from either type of gastric decontamination procedure compared to nasogastric aspiration and activated charcoal in symptomatic patients.

Kornberg and Dolgin (27) randomized 70 children less than six years of age with a history of a mild-to-moderate ingestion into either an ipecac and activated charcoal group or an activated charcoal only group. The only statistically significant differences in outcomes were the length of time to receive activated charcoal (2.6 hours in the ipecac group vs. 0.9 hours in the activated charcoal group; $p<0.0001$), emesis or activated charcoal (56% vs. 16%; $p<0.001$, respectively) and length of stay in the ED (4.1 hours vs. 3.4 hours; $p<0.05$, respectively). There were no differences in the number of admissions or the number who improved in the ED. The investigators concluded that ipecac delayed the administration of activated



charcoal, hindered the retention of charcoal and prolonged the length of stay in the ED. The conclusion of this study regarding the efficacy of ipecac is limited by the small sample size.

In a prospective randomized controlled trial, Pond et al. (18) studied 876 patients who presented to an ED after the ingestion of a toxic substance. On odd-numbered days patients received either ipecac syrup 30–50 mL followed by water 200 mL or gastric lavage, both of which were followed by activated charcoal 50 g in sorbitol. On even-numbered days no gastric emptying was performed and each patient received only activated charcoal 50 g in sorbitol. Among the alert and cooperative patients who received ipecac ($n=220$) vs. those who did not ($n=274$), there were no statistical differences in the number who improved or deteriorated regardless of whether they presented for treatment within 60 minutes or after 60 minutes from the time of the ingestion. The use of ipecac syrup and activated charcoal did not improve patient outcome when compared to activated charcoal alone.

Bond (28) analyzed the management of 55,346 children less than six years of age and found that ED referral was significantly ($p<0.0001$) less likely when the poison information specialist recommended the use of ipecac. However, because of multiple influences on the referral decision, it could not be concluded that ipecac use resulted in a clinical benefit. In a more recent study by the same author (29), data from 64 poison centers were analyzed for the years 2000 and 2001. The author concluded that the use of ipecac syrup by poison centers did not reduce utilization of medical resources, as measured by emergency department referral rates, and did not improve patient outcome.

Selected Cases of Poisoning

Acetaminophen (Paracetamol)

A study (16) evaluated the elapsed time between ingestion and emesis and compared it to mean 4-hour acetaminophen concentrations. Those who experienced emesis within 90 minutes of ingestion had a lower mean serum acetaminophen concentration (15.7–19.9 mg/L) than those in the nondecontamination group (33.1 mg/L) even though the estimated quantity ingested was greater. The authors concluded that emesis within 60 minutes of ingestion has the potential to reduce the amount of substance available for absorption by approximately 50% but that emesis delayed for more than 90 minutes conferred no benefit.

Amitai et al. (30) compared the early and late administration of ipecac on the measured acetaminophen plasma concentration following ipecac-induced emesis. The study population consisted of 50 children less than 5 years of age with an estimated acetaminophen dose of >150 mg/kg (mean=165 mg/kg) within 4 hours of ingestion. Twenty-three children received ipecac at home [mean time of administration 26 ± 8 minutes after acetaminophen ingestion] and had measured concentrations of 23 ± 0.6 mg/L. Twenty-seven children received ipecac elsewhere (mean time of administration 83 ± 13 minutes) and had measured concentrations of 44 ± 7 mg/L. The investigators concluded that the shorter the time between the time of ingestion of acetaminophen and the administration of ipecac, the more effective ipecac was in reducing plasma acetaminophen concentrations.

Underhill et al. (31) prospectively studied 60 adult patients, 21 of whom received ipecac, who presented to an ED (mean 123 minutes postingestion) following ingestion of acetaminophen 5 g or more within the previous 4 hours. Five patients at a second center constituted a control group. Plasma acetaminophen concentrations were measured prior to treatment and for 150 minutes following the first sample. The percentage change between the first and last plasma concentrations was used as a measure of the effectiveness of the procedure. The plasma concentrations of the control group rose while the ipecac group had a mean (\pm SD) percentage drop of $40.7\pm 18.3\%$. The study is seriously flawed because of the disparity in timing of initial blood sampling between the treatment and control group (approximately 130 vs. 70 minutes).

Gastroscopy Study

Endoscopy was performed in 13 overdose patients to whom ipecac had been administered a mean 3.5 hours postingestion. Tablets were observed in the stomach of three patients and in the vomitus of two other patients (32). Unfortunately, the number of tablets seen post-emesis was not quantified and the ingested number of tablets was based on the patients' histories.

Case Reports

Tenenbein (33) reported the failure of emesis and gastric lavage in two patients who ingested iron-containing tablets. A 17-month-old toddler was brought to the ED after the ingestion of ferrous sulfate. An abdominal X ray showed 10 tablets, nine in the stomach and one in the small intestine. Ipecac was administered



and three episodes of emesis ensued. A follow-up X ray showed 10 tablets still present. A 16-year-old female by history ingested 100 enteric-coated ferrous sulfate tablets and received ipecac 30 mL at least 7.5 hours after the ingestion. Four episodes of emesis expelled 15 tablets but 50 tablets were still visible on an abdominal X ray. This case demonstrates the failure of ipecac to remove ingested tablets which may not be unique to iron but its radiopacity permitted this observation.

A 15-month-old female ingested 10–15 ferrous sulfate 300 mg tablets and had a successful ipecac-induced emesis which contained several tablet fragments (34). However, an abdominal X ray revealed the presence of a large number of iron tablets in the gastric cardia. An emergency gastrotomy was performed to remove the tablets which were imbedded in the gastric mucosa. This case illustrates the ineffectiveness of ipecac in completely eliminating iron tablets and the importance of obtaining abdominal radiographs after emesis is complete.

In a similar case Landsman and colleagues (35) described a 23-month-old female who underwent an emergency gastrotomy to remove an iron tablet bezoar which developed after ingesting 60 ferrous sulfate 325 mg tablets. Syrup of ipecac induced emesis failed to remove the iron tablets from the child's stomach. These failures of ipecac may be due to peculiar properties of iron to imbed in the gastric mucosa or form bezoars.

Indications

Experimental studies indicate that the amount of marker removed by ipecac syrup is highly variable and diminishes with time. Clinical studies have not confirmed the benefit of ipecac syrup alone even when it was administered less than 60 minutes 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.

Dosage Regimen

If ipecac-induced emesis is considered appropriate, the procedure should be explained to the patient and,

in the case of children, the patient's care-provider. Patients or care-providers should be told that an oral liquid medication will be given that will make the patient vomit and may lead to a faster recovery.

The United States Pharmacopoeia (USP DI, 2003) recommends the following oral dosage regimen for Ipecac Syrup, USP.

Children up to six months of age: Ipecac should only be administered under the supervision of a physician;

Children 6–12 months of age: 5–10 mL preceded or followed by 120–240 mL of water;

Children 1–12 years of age: 15 mL preceded or followed by 120–240 mL of water;

Adolescents and adults: 15–30 mL followed immediately by 240 mL of water.

The dose in all age groups may be repeated if emesis does not occur in 20–30 minutes.

Emesis is expected to occur within 20 minutes of administration. Emesis is not delayed by the ingestion of phenothiazines, antihistamines, antiemetics, the administration of milk, or the use of outdated ipecac.

Episodes of ipecac-induced emesis are expected to occur for 20–30 minutes. It is recommended that other oral substances not be administered for 60 minutes after the onset of emesis.

Patients in whom emesis is induced should be followed for 4 hours to monitor for desired and adverse effects.

Contraindications

Ipecac-induced emesis is contraindicated if the patient has compromised airway protective reflexes (including coma and convulsions), has ingested a substance that might compromise airway protective reflexes, or if there is an anticipated need for advanced life support within 60 minutes. 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 may be further compromised by the induction of emesis. The ingestion of milk or a drug with antiemetic properties are not contraindications to the use of ipecac. The use of ipecac that has exceeded the expiration date is also not a contraindication to its use.



Complications

The potential complications of the therapeutic use of ipecac are well-documented, though in practice, serious sequelae occur rarely.

Albertson et al. (36) conducted a prospective evaluation of the outcomes of 200 adult patients presenting to the ED with potentially toxic ingestions. The patients were randomized into a group which received ipecac and activated charcoal or a group which received only activated charcoal. The patients in the ipecac group had a statistically significant greater complication rate (5.4%, $p < 0.05$). The difference in complication rates was due to four patients who had ingested a tricyclic antidepressant and aspirated following ipecac. If these patients were eliminated (because tricyclic overdose patients should not have received ipecac), there would be no difference in the complication rates. In addition, the patients in the ipecac group had a statistically greater length of stay (6.8 ± 0.3 hours), reflecting the delay in the administration of activated charcoal.

The use of ipecac may delay the administration of activated charcoal by 1–2 hours (17,27,36). The most common complications or adverse consequences of using ipecac are diarrhea (19,20,37), lethargy/drowsiness (19,20,37), and prolonged (>1 hour) vomiting (19,21). Less frequent complications include irritability/hyperactivity (19,20), fever (21), and diaphoresis (20). Rare but more serious adverse consequences include Mallory–Weiss tears (38,39), pneumomediastinum (40), and aspiration pneumonia (41). Fatalities associated with the therapeutic use of ipecac include one case each of traumatic diaphragmatic hernia (42), intracranial hemorrhage (43), and gastric rupture (44).

Considering the fact that over three million patients received therapeutic doses of syrup of ipecac during the 14-year period of 1983–96 (22), ipecac appears to have a high margin of safety, however, the risk to benefit ratio of the use of ipecac syrup has never been formally assessed.

Myopathy and cardiomyopathy following abuse of ipecac syrup in patients with anorexia nervosa and bulimia has been reported (45–62). In each report, ipecac syrup was self-administered numerous times over a period of weeks to months. Four of the patients died (45,50,53,55).

Ipecac syrup has been implicated as an instrument of child abuse in Munchausen syndrome by proxy (63–71). In two cases, patients died from the ipecac syrup administration (67,71) and in each of the other cases, the condition of the patient improved following

the limiting of visits by caretakers who had been administering ipecac syrup to the victims.

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