International Variability in Gastrointestinal Decontamination With Acute Poisonings

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abstract

BACKGROUND AND OBJECTIVES: Identifying international differences in the management of acute pediatric poisonings may help improve the quality of care. The objective of this study was to assess the international variation and appropriateness of gastrointestinal decontamination (GID) procedures performed in children and adolescents who present with acute poisonings to emergency departments.

METHODS: This was an international, multicenter, cross-sectional prospective study including children <18 years with poisoning exposures presenting to 105 emergency departments in 20 countries from 8 global regions belonging to the Pediatric Emergency Research Networks. Data collection started between January and September 2013 and continued for 1 year. The appropriateness of GID procedures performed was analyzed using the American Academy of Clinical Toxicology and the European Association of Poisons Centres and Clinical Toxicologists' recommendations. Multivariate logistic regression was performed to identify independent risk factors for performing GID procedures.

RESULTS: We included 1688 patients, 338 of whom (20.0%, 95% confidence interval 18.1%–22.0%) underwent the following GID procedures: activated charcoal (166, 49.1%), activated charcoal and gastric lavage (122, 36.1%), gastric lavage (47, 13.9%), and ipecac (3, 0.9%). In 155 (45.8%, 40.5%–51.2%), the GID procedure was considered appropriate, with significant differences between regions. Independent risk factors for GID procedures included age, toxin category, mechanism of poisoning, absence of symptoms, and the region where the intoxication occurred ($P < .001$).

CONCLUSIONS: Globally, there are substantial differences in the use and appropriateness of GID procedures in the management of pediatric poisonings. International best practices need to be better implemented.

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Participating networks include the following: the Pediatric Emergency Care Applied Research Network, the Pediatric Emergency Medicine Collaborative Research Committee of the American Academy of Pediatrics, Pediatric Emergency Research Canada, Pediatric Emergency Research in the United Kingdom and Ireland, Pediatric Research in Emergency Departments International Collaborative, and Research in European Pediatric Emergency Medicine.

Dr Mintegi conceptualized and designed the study, supervised data collection, analyzed the data, and wrote the initial draft of the manuscript; Dr Azkunaga collaborated in the design of the data

WHAT'S KNOWN ON THIS SUBJECT: Thousands of children are managed in emergency departments annually worldwide. The American Academy of Clinical Toxicology and the European Association of Poisons Centres and Clinical Toxicologists previously have released statements on gastrointestinal decontamination (GID) procedures to guide evidence-based practice.

WHAT THIS STUDY ADDS: This study demonstrates substantial international management differences in both the prehospital and emergency department settings related to acute pediatric poisonings and specifically to GID procedures. When performed, GID procedures were not appropriate in more than 50% of the patients.

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Globally, poisoning exposures remain a major public health problem, particularly in children.[1,2] Each year, tens of thousands of children are evaluated and managed in emergency departments (EDs) around the world, frequently for unintentional ingestions of toxins that are secondary to exploratory behavior of young children and infants within their environments.[3] To our knowledge, no study has evaluated international practice variation regarding the treatment of poisoning (specifically gastrointestinal decontamination [GID]) or evaluated if its management across countries is consistent with international guidelines. It is pressing to establish whether variation exists and measure practice against standards of care to guide local and global poisoning knowledge-translation endeavors. This is a critical step in improving the quality of care that is provided to poisoned children worldwide.

Historically, preventing the absorption of an ingested toxin by the gastrointestinal tract to limit systemic toxicity was felt to be an appropriate, important management strategy for many types of poisonings.[4] The reduced absorption concept led to several GID strategies including gastric lavage, administration of an adsorbent, and induced emesis. For the last 2 decades, the American Academy of Clinical Toxicology and the European Association of Poisons Centres and Clinical Toxicologists have released international consensus statements on various GID strategies to guide evidence-based practice.[5–14] In most cases of poisoning exposure, the ingested toxicant has minimal or no clinically important toxic effects, and so GID is not recommended. These recommendations, however, are not always followed by physicians, and variation has been described both in studies of EDs[15] and in single countries.[16,17]

We hypothesized that there would be significant differences in the frequency of GID procedures that are performed in children with poisoning exposures among global regions.

The objective of this study was to assess the variation in frequency and appropriateness of GID procedures that are performed in children and adolescents who present with acute poisonings to EDs that are part of the Pediatric Emergency Research Networks (PERN), which is a global consortium of the major pediatric emergency medicine research networks around the world.[18]

METHODS

Design

This was a cross-sectional study of childhood poisoning presentations from a prospectively collected, international, multicenter registry involving 105 EDs from 20 countries in the PERN that used purposeful sampling.[19] All children (<18 years of age) presenting for an acute poisoning exposure on the fourth, 14th, and 24th days of every month had specific electronic questionnaires completed via Google Drive. EDs reported data over a 1-year period, thus collecting data for 36 days per site (10% of the calendar year) with data collection starting at the sites between January and September 2013. The purposeful sampling on 3 set calendar days per month for 1 calendar year allowed a large number of sites to participate without an overwhelming research burden and avoided bias because of seasonal variation or only sampling on a specific day of the week. The electronic poisoning-reporting system previously had been successfully used by the Spanish Society of Pediatric Emergency Medicine.[20] Questionnaires, in addition to a study manual of operations, were distributed to site investigators (ED physicians) before the initiation of the study to confirm understanding of text, suitability of data collection at all participating sites, and to ensure clarity of the final data collection. All queries regarding data collection were addressed by 1 investigator (S.M.) to maintain consistency in the data collection and quality. After patients were identified by ED physicians, the following demographic, clinical, and management data were collected via interviews of patients and caregivers: age, sex, time of presentation to the ED, the toxin involved, the mechanism of poisoning, amount of time between poisoning and ED presentation, the route of poisoning, the location of poisoning, previous similar episodes, prehospital management, clinical symptoms and signs in the ED, management in the ED, consultation with poison control centers, and patient disposition and outcome. The study questionnaires were completed by the physician responsible after ED discharge for those patients who were discharged from the hospital and after discharge for patients who were admitted to the hospital to ascertain complete patient information and ED and hospital outcomes. The completed questionnaires were then sent electronically to the principal investigator (S.M.).

Countries were categorized according to the regional classification system of the World Health Organization (Africa, the Americas, Southeast Asia, Europe, the Eastern Mediterranean, and the Western Pacific regions). Countries from the Americas were further divided into North and South America, and those from Europe were further divided per the United Nations Statistics Division's classification into Northern, Southern, Western, and Eastern Europe.

We included children <18 years of age. However, only 67 of the 105 EDs (64%) evaluated patients >14 years old, which reflects the variability in the upper age limit of patients who

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are treated in different pediatric EDs around the world.

Toxicants were categorized as follows: carbon monoxide, cosmetic, therapeutic drugs, ethanol, ethanol and illicit drugs, pesticides, plants, household products, other, and unknown. Mechanisms of poisoning were categorized as dosage errors, unintentional or accidental, recreational, suicide attempt, and other.

The appropriateness of a GID procedure was determined by 2 investigators (S.M. and J.B.) who reviewed all patients who were treated with GID procedures. Disputes were resolved with a consensus from a third investigator (S.R.D.). The appropriateness of GID procedures was determined according to the international consensus statements on various GID procedures released by the American Academy of Clinical Toxicology and the European Association of Poisons Centres and Clinical Toxicologists.[5–14] We considered a single dose of activated charcoal (AC) to be appropriate after the ingestion of a toxicant except for those known not to be bound by AC or when its use is clearly not indicated (pesticides, potassium, hydrocarbons, acids, alkali, alcohols, iron, insecticides, lithium, and solvents).[13] We considered multiple doses of AC to be potentially appropriate for the ingestion of antimalarial (quinine), dapsone, carbamazepine, phenobarbital, methylxanthines, phenytoin, digoxin, valproate, nadolol, sotolol, phenylbutazone, thyroid, and salicylates. Gastric lavage was always deemed inappropriate except in cases of potentially lethal ingestions when the toxin is known not to bind to AC. The combination of AC and gastric lavage (and administration of ipecac syrup) was considered to be inappropriate. We also determined the appropriateness of an antidote for a given toxicant. An antidote for a given toxin was considered to be appropriate if it was listed as such in the Medical Toxicology Antidote Card provided by the American College of Medical Toxicology.[21]

Ethics and Human Subjects

We obtained overall approval from the Clinical Research Ethics Committee of the Basque Country. Approval for the study was granted by the institutional review boards and ethics committees at each participating institution, which determined if informed consent was required by participants. When required, informed consent was obtained from parents or guardians, and informed assent obtained from participants when they were >12 years old was deemed appropriate.

Statistical Analysis

We described qualitative variables with frequency tables, percentages, and 95% confidence intervals (CIs). To compare categorical variables, we used the χ^2 test.

We initially performed bivariate logistic regression to evaluate associations with the use of GID. When associations with performing a GID were found, those variables were included in a multivariate logistic regression analysis that was performed to identify the independent risk factors for performing a GID procedure. We included all variables with bivariate associations of $P < .10$ in the multivariate stepwise model. In the final multivariate analysis, only variables with P values <.05 remained in the model. We reported the results of the modeling as odds ratios (ORs) and 95% CIs. We calculated the area under the receiver operating characteristic curve for the final models.

We performed all statistical analysis using SPSS Version 23.0 statistical software (IBM, Armonk, NY).

RESULTS

During the study period, there were 363 245 pediatric ED presentations to the 105 EDs on the 36 days that each site participated, of which 1727 were for poisoning exposures (0.48%). Of the 1727 episodes, 39 (2.3%) were excluded because of lack of required informed consent or because of episodes missed prospectively. The underlying mechanisms of the remaining 1688 poisonings were as follows: 1157 (68.5%) unintentional poisonings, 233 (13.8%) suicide attempts, 180 (10.7%) recreational uses of a toxicant, 64 (3.8%) dosage errors, and 54 (3.2%) other mechanisms.

In the ED, 832 (49.3%; 46.9%–51.7%) children received treatment for their poisoning. Of these, 338 (20.0%; 18.1%–22.0%) received GID procedures with the following: AC (166, 49.1%), AC and gastric lavage (122, 36.1%), gastric lavage (47, 13.9%), and ipecac (3, 0.9%). A nasogastric tube was used to administer the AC in 123 patients (42.7% of those who received AC). In 155 patients (45.8%; 40.5%–51.2%), the GID procedure was considered appropriate, with significant differences across regions. South America, Eastern Europe, Southern Europe, and the Eastern Mediterranean had low rates of appropriate use of GID when compared with North America, Western Europe, Northern Europe, and the Western Pacific regions (Fig 1, Supplemental Table 3). Independent risk factors for GID procedures being performed included the age of the patient, the toxin category, the mechanism of poisoning, the method of poisoning, the absence of symptoms, and the (global) geographical region where the intoxication occurred (area under the curve = 0.87 [95% CI, 0.85–0.89]) (Table 1). Of these independent risk factors, the global region in which the intoxication occurred had the largest effect

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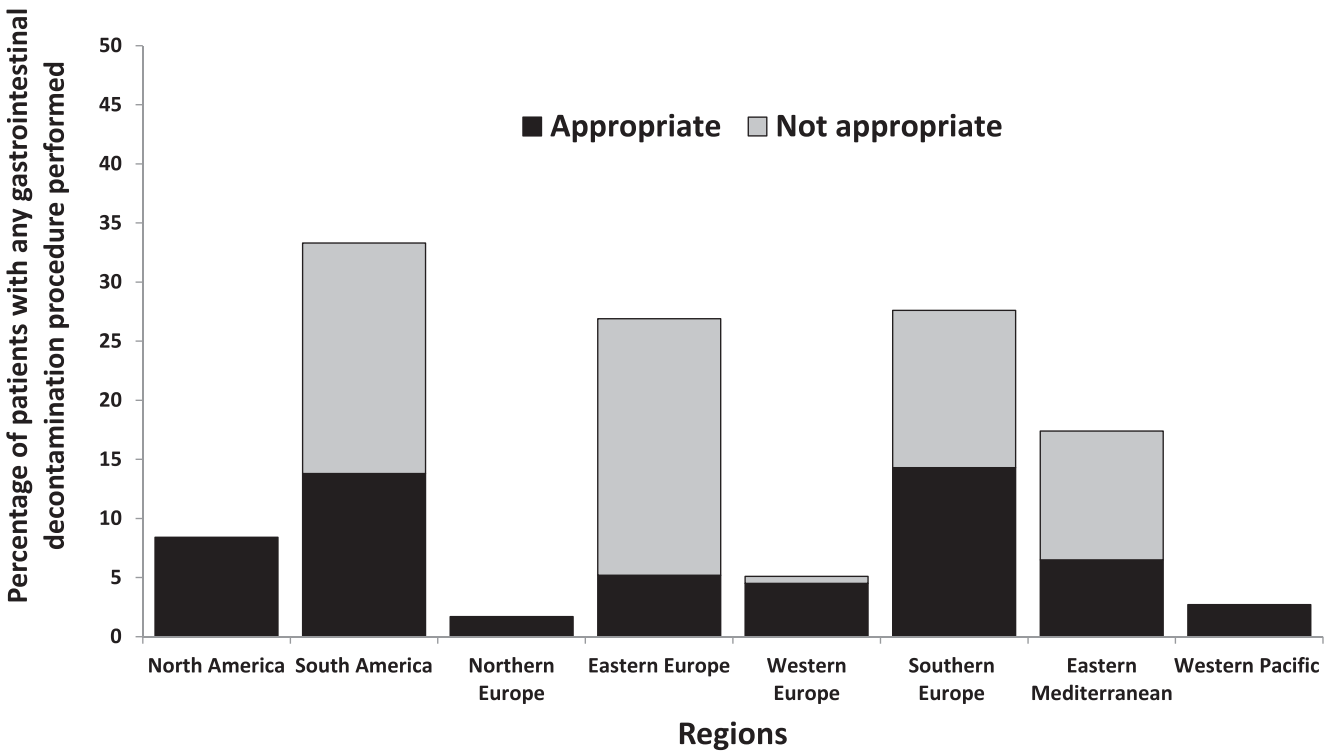

FIGURE 1
GID procedures performed in the ED.

estimate, with ORs for GID procedure use in Eastern Europe (12.8, 95% CI 6.5–25.3), South America (10.9, 95% CI 5.5–21.4), Southern Europe (8.2, 95% CI 4.4–15.1), and Eastern Mediterranean (4.7, 95% CI 1.7–13.3) being compared with North America (Table 1).

Before ED presentation, 519 patients (30.7%) contacted health professionals, and 257 (15.2%) received some treatment. Of these, a GID procedure was performed in 51 before arriving at the ED (AC [35], gastric lavage [7], AC and gastric lavage [9]). All of the gastric lavages were performed in Europe, South America, and the Eastern Mediterranean region. Of the GID procedures performed before ED presentation, 15 (29.4%) were considered to be inappropriate (Supplemental Table 4).

Variability related to other aspects of ED management (tests practices, contact with poison control centers, antidotes, admission to a ward or ICU, and suicidal patients who were reviewed by psychiatric services) is shown in Supplemental Table 5. An antidote was given to 116 children (6.9%; 95% CI 5.7%–8.1%), with significant differences across regions, and it was considered appropriate in 109 cases (94.0%) (Table 2). No patients died.

DISCUSSION

Thousands of children and teenagers with an acute poisoning are treated annually worldwide. Our study demonstrates international variability in the GID procedures performed on children with poisoning exposure. Of note, the region where the intoxication occurs was an independent risk factor for performing a GID procedure. In addition, one-half of GID procedures performed in the EDs were deemed to be inappropriate. This is particularly concerning and requires interventions to remedy.

Despite the cooperative efforts between European and North American Toxicology societies and their recommendations for developing international consensus statements on compiling the evidence to guide GID and other therapeutic strategies,[5–14] we found great variability in the use of GID procedures in our study. In addition, when performed, GID was not appropriate in >50% of the patients. Furthermore, our definition of appropriate use of AC only considered if the ingested toxicant was known to be bound to charcoal. Because of the limited data availability, we did not consider the time between ingestion and administration of charcoal in our definition of "appropriate," which potentially classified treatment as appropriate when the time between ingestion and charcoal would not have allowed for a clinically meaningful effect. Of note, in some regions (such as South America, Eastern Europe, Southern Europe,

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and the Eastern Mediterranean), it is common to combine gastric lavage and the administration of AC despite the lack of evidence that this combination is useful.[12,13] AC therapy involves the oral administration or instillation by nasogastric tube of an aqueous preparation of AC after the ingestion of a poison.[7] Sometimes, the placement of a nasogastric tube to administer AC may facilitate the performance of a gastric lavage after or before giving the AC, although there is no evidence that supports this practice. Additionally, in Eastern Europe, gastric lavage is the most commonly used GID procedure in the ED, although it is well recognized that gastric lavage should not be performed routinely.[12] On the other hand, ipecac has been nearly abandoned in EDs globally, as has been recommended.[14]

Furthermore, it should be noted that the treatment of a child with a poisoning exposure must begin as soon as possible, and GID procedures may be performed in the prehospital setting. The timing of charcoal administration is crucial to its efficacy in oral overdose, and prehospital AC does not appear to markedly delay transport or arrival of overdose patients into the ED.[22] Although it is not appropriate for many children, in our study, the rate of GID that was performed inappropriately was lower in the prehospital setting when compared with the ED, perhaps because of the difficulties performing gastric lavage in the out-of-hospital setting. In our study, one-third of the poisoned children and their families sought medical attention before going to the ED, mainly from prehospital emergency medical services. This differed significantly by geographic region. These differences may reflect the regional epidemiology of poisonings and also the differences in how health services are organized globally. In some regions, it seems that medical vehicles and/or ambulances are only used to transport patients rather than to initiate treatment.[23]

TABLE 1 Bivariate and Multivariate Analysis for the Identification of Risk Factors for Performing GID Procedures in the ED

		Bivariate	Multivariate
	P	OR (95% CI)	OR (95% CI)
Region (ref North America)	<.001		
South America	<.001	5.392 (2.917–9.967)	10.895 (5.539–21.432)
Western Europe	.215	0.578 (0.243–1.374)	1.116 (0.455–2.738)
Eastern Europe	<.001	4.009 (2.177–7.382)	12.848 (6.523–25.306)
Northern Europe	.010	0.188 (0.053–0.668)	0.220 (0.061–0.792)
Southern Europe	<.001	4.139 (2.322–7.377)	8.167 (4.424–15.077)
Eastern Mediterranean	.084	2.286 (0.894–5.843)	4.724 (1.674–13.332)
Western Pacific	.119	0.302 (0.067–1.362)	0.363 (0.079–1.672)
Age (ref <1 y), y	<.001		
1–6	.002	2.784 (1.468–5.281)	2.577 (1.240–5.358)
7–10	.397	1.485 (0.595–3.706)	1.441 (0.511–4.065)
≥11	.160	1.613 (0.827–3.142)	1.575 (0.567–4.371)
Previous contact with other medical or toxicology service (yes)	.483	1.098 (0.845–1.427)	—
Presence of symptoms (yes)	<.001	0.501 (0.387–0.649)	0.536 (0.377–0.763)
Physical examination (altered)	.001	0.595 (0.434–0.817)	
Method of poisoning (ref ingestion)	<.001		
Inhalation	<.001	0.028 (0.004–0.201)	0.104 (0.013–0.815)
Other	<.001	0.059 (0.008–0.429)	0.075 (0.010–0.587)
Mechanism of poisoning (ref unintentional)	<.001		
Recreational	<.001	0.242 (0.130–0.453)	2.032 (0.606–6.816)
Suicide attempt	.210	1.234 (0.888–1.714)	1.851 (0.784–4.368)
Dosage error	.101	0.532 (0.250–1.130)	0.345 (0.148–0.800)
Other	.407	1.303 (0.698–2.433)	1.921 (0.834–4.428)
Toxin category (ref drugs)	<.001		
Ethanol and/or illicit drugs	<.001	0.076 (0.035–0.164)	0.070 (0.023–0.211)
Pesticides	.717	0.901 (0.514–1.580)	0.523 (0.278–0.987)
Household products	<.001	0.038 (0.0.17–0.087)	0.024 (0.010–0.056)
Carbon monoxide	.997	—	—
Other	<.001	0.360 (0.146–0.526)	0.243 (0.157–0.377)
Unknown	.022	0.095 (0.013–0.709)	0.107 (0.013–0.892)
Contact with poison control center	.251	1.161 (0.900–1.498)	—

We also found significant variability related to other aspects of management in the ED. There were differences in the use of poison control centers, the types of laboratory tests performed and antidotes administered, and patient dispositions. Although poison control centers are effective gatekeepers for patients who are seeking treatment of poisonings, and others have reported them to be highly cost-effective,[24] they appear to be underutilized in certain global regions. The availability (and lack of availability) of these centers worldwide may explain some of this variability. In the United States, all are telephone based. In some countries, poison centers may offer consultation only to medical personnel. In others, the "poison center" is a treating unit within a hospital. In any case, increasing the availability of poison control centers globally and encouraging their use when a poisoning occurs may improve the quality and cost effectiveness of the care provided to these children. On the other hand, the administration of an antidote may be critical to the management of a poisoned patient. Shortcomings in the types and quantities of antidotes, antivenoms, and antitoxins have been widely reported.[25–28] In our series, an infant with methemoglobinemia did not receive the antidote (methylene blue) because of a lack of local

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TABLE 2 List of the Types, Uses, and Appropriateness of Antidotes

Antidote	Toxicant	Appropriate
Oxygen (40)	Carbon monoxide (40)	Yes
N acetyl cysteine (37)	Acetaminophen (37)	Yes
Biperiden (7)	Antipsycotics (4)	Yes
	Metoclopramide (2)	Yes
	Antiepileptic drugs (1)	Yes
Naloxone (7)	Opioids (6)	Yes
	Detergent (1)	No
Flumazenil (4)	Benzodiazepine (2)	Yes
	Atropine, propranolol, and barbiturate (1)	No
	Ketazolam, escitalopram, and otilonio bromuro (1)	No
K vitamin (4)	Pesticides (2)	Yes
	Coumarin drugs (2)	Yes
Diphenhydramine (3)	Antipsycotics (2)	Yes
	Metoclopramide (1)	Yes
Hydroxocobalamin (2)	Acrylonitrile	Yes
Physostigmine (2)	Antimuscarinic	Yes
	Mixed scopolamine, hyoscyamine, and atropine	Yes
Dimercaptosuccinic acid (1)	Lead	Yes
Pralidoxime (1)	Organophosphate	Yes
Octreotide (1)	Sulfonylurea	Yes
Glucose (1)	Insuline	Yes
Methotrexate (1)	Folic acid	Yes
Phytomenadione/phytonadione (1)	Warfarin	Yes
Paraffin oil (1)	Acetone	No
Tropatepine (1)	Risperidone	No
Pseudoephedrine (1)	Tadalafil	No
Thiamine (1)	Mixed ethanol and cannabis	No

availability. The infant received vitamin C and did well. Finally, suicide attempts are the most common mental health emergencies among adolescents.[29] A first self-poisoning episode is a strong predictor of subsequent suicide and premature death.[30] Consultation with psychiatrists and/or mental health professionals also showed great variability.

Nevertheless, all of these recommendations to improve the quality of care (such as harmonized best practices for childhood poisoning [specifically GID], better access to and utilization of poison control centers, availability of prehospital medical services and advice hotlines, more mental health evaluation referrals, and better antidote stocking) require specific resources that have to be allocated by countries, and they need political and social willpower to be realized.

This study has several limitations. The number and percentage of EDs included was not the same in all global regions, thus data from the Eastern Mediterranean and Western Pacific regions need to be interpreted with this in mind. However, the sample was sufficiently large to detect important differences in GID procedures between regions and fulfill the main objective of the study. One-third of the participating EDs only see children >14 years of age. The types of poisoning and their severity differ significantly between young children and adolescents, and this might bias the analysis of the use of GID procedures. Nevertheless, this does not alter the analysis of the appropriateness of the procedure, and the geographical region in which the poisoning exposure occurred was an independent risk factor for GID procedures in the multivariate analysis. Appropriateness of GID procedures was determined solely on the basis of the appropriateness of the GID for a given toxin without consideration of the time since ingestion. It is likely that a number of GID procedures that were undertaken may have been considered inappropriate because the time between ingestion and the GID procedure would make the decontamination futile. Thus, our overall estimate of inappropriate use of GID procedures is likely to be underestimated. In addition, the EDs involved in the study are members of PERN and are therefore self-selected and may not be truly representative of all pediatric EDs globally. Nevertheless, the EDs included both secondary and tertiary EDs; pediatric, mixed pediatric, and adult EDs; rural and urban EDs; and EDs with small and large volumes. Therefore, it seems unlikely that self-selection would have significantly biased the results. On the other hand, international differences related to poison control center availability and functionality, the availability of a telephone hotline for poisonings, and prehospital medical services may bias the number of children with poisonings who are brought to the EDs by region. However, this possibility does not limit the analysis of the management of children with poisonings presenting to EDs across broad regions of the globe.

Globally, there are substantial management differences in both the prehospital and ED settings related to acute poisonings in children and specifically to GID procedures. When performed, GID procedures were inappropriate in >50% of the patients. Predictors of receiving GID procedures included the global geographic region, the age of the patient, the toxin category, the mechanism of poisoning, and the absence of symptoms. International best practices need to be identified for the management of acute pediatric poisonings and, specifically, GID procedures. Our study also highlights the importance of international research networks

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to perform such broad and generalizable studies.

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ABBREVIATIONS

AC: activated charcoal
CI: confidence interval
ED: emergency department
GID: gastrointestinal decontamination
OR: odds ratio
PERN: Pediatric Emergency Research Networks

collection system, had oversight responsibility of data collection from all participating sites, and critically revised the manuscript; Dr Prego was the coordinator of the study in South America and critically revised the manuscript; Dr Dalziel was the coordinator for the Western Pacific region, revised various versions of the initial manuscript, and critically revised the final manuscript; Dr Arana-Arri and Ms Martinez-Indart (statistician) collaborated in the design of the study, analyzed the data, and critically revised the manuscript; Dr Acedo collaborated in obtaining the data regarding poisonings from the participating sites and critically revised the manuscript; Dr Benito revised the design of the study, drafted the initial manuscript, and critically revised the manuscript; Dr Kuppermann was the coordinator for North America, revised multiple versions of the initial manuscript, and critically revised the final manuscript; and all authors approved the final manuscript as submitted.

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