International Epidemiological Differences in Acute Poisonings in Pediatric Emergency Departments

Santiago Mintegi, MD, PhD,† Beatriz Azkunaga, MD, PhD,* Javier Prego, MD,‡ Nadeem Qureshi, MD,†§ Stuart R. Dalziel, MBChB, PhD,||¶ Eunate Arana-Arri, MD,# Yordana Acedo, MD,* Lorea Martinez-Indart, MSC,# Arantza Urkaregi, MSC,** Nerea Salmon, MD,* Javier Benito, MD, PhD,*† and Nathan Kuppermann, MD, MPH,††‡‡ on behalf of the Pediatric Emergency Research Networks (PERN) Poisoning Working Group*

Background and Objective: Identifying international differences in the epidemiology of acute poisonings in children may help in improving prevention. We sought to evaluate the international epidemiological differences in acute poisonings in children presenting to emergency departments (EDs) from 8 different global regions.

Methods: This was an international multicenter cross-sectional prospective study including children younger than 18 years with acute poisonings presenting to 105 EDs in 20 countries was conducted. Data collection started at each ED between January and September 2013, and continued for 1 year.

Results: During the study period, we registered 363,245 pediatric ED presentations, of which 1727 were for poisoning (0.47%; 95% confidence interval, 0.45%–0.50%), with a significant variation in incidence between the regions. Full data were obtained for 1688 presentations. Most poisonings (1361 [80.6%]) occurred at home with either ingestion (1504 [89.0%]) or inhalation of the toxin (126 [7.6%]). Nonintentional exposures accounted for 1157 poisonings (68.5%; mainly in South America and Eastern Mediterranean region), with therapeutic drugs (494 [42.7%]), household products (310 [26.8%]), and pesticides (59 [5.1%]) being the most common toxins. Suicide attempts accounted for 233 exposures (13.8%; mainly in the Western Pacific region and North America), with therapeutic drugs (214 [91.8%], mainly psychotropics and acetaminophen) being the most common toxins. Significant differences between regions were found in both types of poisonings. Recreational poisonings were more common in Europe and Western Pacific region. No patient died.

Conclusions: There are substantial epidemiological differences in acute poisonings among children in different countries and regions of the globe. International best practices need to be identified for prevention of acute poisonings in childhood.

Key Words: Poisonings, epidemiology, global

(*Pediatr Emer Care* 2017;00: 00–00)

Globally, poisoning in childhood remains a major public health care problem.[1,2] Although fatal child poisonings have decreased substantially in recent decades in the United States,[3] millions of calls and/or referrals are made to poison control centers each year worldwide. Thousands of children are subsequently evaluated in emergency departments (EDs) mainly due to ingestions of household products, medicines, or pesticides, most of which are preventable.[1] In the United States alone, each year more than 1 million children younger than 5 years experience potentially toxic ingestions.[4,5] Other common causes of child poisonings include suicide attempts and recreational ingestions.

There are limited data regarding global morbidity and differences in poisoning epidemiology between countries. Identifying international epidemiological differences related to acute pediatric poisonings would help to identify and implement appropriate and specific preventive measures. In 2008, an electronic poisoning surveillance system established in Spanish pediatric EDs by the Spanish Society of Pediatric Emergency Medicine[6] identified regional epidemiological differences in acute poisonings in children presenting to pediatric EDs in Spain.[7,8] This national surveillance system also served as a pilot to investigate such differences between regions worldwide.

The objective of this study was to evaluate and compare the epidemiology of poisonings in children presenting to EDs that are part of the international Pediatric Emergency Research Networks (PERN), a global consortium of pediatric emergency medicine research networks.[9]

We hypothesized that there would be significant epidemiological differences in the circumstances and etiologies of poisonings among the different global regions.

METHODS

Design

This was an international multicenter cross-sectional prospective registry study of childhood poisoning presentations to 105 EDs in the PERN network. When proposed, PERN comprised representative hospitals from the 5 major pediatric emergency medicine research networks located in Europe and the Middle East (Research in European Paediatric Emergency Medicine [REPEM]), North America (the Pediatric Emergency Care Applied Research Network [PECARN], the Pediatric Emergency Care Collaborative Research Committee of the American

From the *Pediatric Emergency Department, Cruces University Hospital, University of the Basque Country, Bilbao, Basque Country, Spain; †Research in European Paediatric Emergency Medicine (REPEM), London, UK; ‡Departamento de Emergencia Pediátrica, Centro Hospitalario Pereira Rossell, Montevideo, Uruguay; §Cardinal Glennon Children's Hospital, St Louis University, St Louis, MI; ||Children's Emergency Department, Starship Children's Hospital, and Liggins Institute, University of Auckland, Auckland, New Zealand; ¶Paediatric Research in Emergency Departments International Collaborative (PREDICT), Parkville, Victoria, Australia; #Clinical Epidemiology Unit, Cruces University Hospital, BioCruces Health Research Institute, Basque Country, Spain; **University of the Basque Country, Leioa, Spain; ††Department of Emergency Medicine, University of California, Davis School of Medicine, Sacramento, CA; and ‡‡Pediatric Emergency Care Applied Research Network (PECARN), Rockville, MD.

Disclosure: The authors have no conflicts of interest to disclose.

Reprints: Santiago Mintegi, PhD, Pediatric Emergency Department, Cruces University Hospital, Plaza de Cruces s/n, E-48903 Barakaldo, Bizkaia, Spain (e-mail: santiago.mintegi@osakidetza.eus).

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.pec-online.com).

ISSN: 0749-5161

Academy of Pediatrics [PEM-CRC], and Pediatric Emergency Research Canada [PERC]), and Australasia (Paediatric Research in Emergency Departments International Collaborative [PREDICT]), in addition to several hospitals around the globe not affiliated with specific networks. Together, the 5 research networks have access to data from more than 3 million pediatric ED presentations annually, from more than 100 hospitals, in 4 of the 6 World Health Organization (WHO) regions.[9]

In the study, countries were categorized following the regional classification system of the WHO (Africa, the Americas, Southeast Asia, Europe, Eastern Mediterranean, and Western Pacific regions). Countries from the Americas region were further divided into North and South America and those from Europe were further divided per the United Nations' Statistical Department classification into Northern, Southern, Western, and Eastern Europe.

One hundred five EDs reported data over a 1-year period, with data collection starting at sites between January and September 2013. All the EDs completed a full year of data collection. Emergency departments reported the total number of visits registered for the 4th, 14th, and 24th days of each month and the number of patients presenting and/or treated for poisonings on the same days.

All patients presenting and/or treated for poisonings on the 4th, 14th, and 24th days of every month had specific electronic questionnaires completed via Google Drive by the responsible physicians. Questionnaires were initially distributed to all participating EDs to enhance the clarity of the methods and to improve the quality of collected data. The questionnaires were read to the patients by the responsible physician. The questionnaires were then completed by the responsible physician after ED discharge for those patients discharged to home, and after hospital discharge for patients admitted to the hospital to ascertain complete patient information and ED and hospital outcomes. The completed questionnaires were then sent to the principle investigator (S.M.). Patients were identified by ED physicians with the following data collected via interviews of patients and caregivers: age, sex, time of ED presentation, toxic substance involved, mechanism of poisoning (Appendix, Supplemental Digital Content 1, http://links.lww.com/PEC/A152), time between poisoning and ED presentation, route of poisoning, location where poisoning occurred, previous similar episodes, prehospital management, clinical symptoms and signs, management in the ED, consultation with poison control centers, and patient disposition and outcome. Eligible patients included those who were referred by guardians or caretakers after exposure to a toxicant (via ingestion, inhalation, dermal or mucosal exposure) regardless of the presence of any symptom. In addition a patient could be enrolled if he/she presented to the ED and was symptomatic due to an intoxication.

We included all children younger than 18 years exposed to poisons. However, only 67 (64%) of the 105 EDs included patients older than 14 years. These included all of the EDs from North America, Northern and Eastern Europe, Western Pacific, and Eastern Mediterranean regions; 85.7% from Western Europe; 50% from Southern Europe; and 42.8% from South America. This reflects the variability that exists in the upper age limit of patients treated in different pediatric EDs around the world.

Sample Size

To estimate the sample size, we used the published Spanish pilot data.[6] In that study, therapeutic drugs accounted for 56.2% of acute poisonings. The sample size was intended to identify a 10% difference in frequency between regions for the main toxic substance implicated. The final sample size thus depended both on the final point estimates of the frequencies of the types of toxic substances, and the ranges in the differences between regions. If the frequency of poisoning due to different types of toxic substances among regions varied between 45% and 60%, to find a 10% difference between regions, 90 poisoning episodes per region would be needed; if the frequency of poisonings due to different types of toxic substances among regions varied between 30% and 60%, to find a 10% difference between regions, 25 poisoning episodes per region would be needed; and if the frequency varied between 30% and 40%, to find a 10% difference between regions, 350 poisoning episodes per region would be needed (all with 80% power, α of 0.05). The inclusion of approximately 100 poisoning episodes per region was deemed sufficient to meet the primary objectives of the study.

Statistical Analysis

We calculated all incidence rates globally (with 95% confidence intervals [CIs]) from the number of new cases of poisonings evaluated at the EDs divided by the total number of ED episodes. We describe the qualitative variables in percentages with 95% CIs. We compared frequencies between regions using the χ^2 test. To identify types of poisonings, we used multiple correspondence analysis and cluster analysis.

Because the original variables obtained from the collected data were categorical, we used multiple correspondence analysis to create a reduced number of continuous variables (also known as factors) to make data interpretation easier.[10] We used the following categorical variables: location of poisoning (home, school, street, tavern/bar, other, and unknown), age (<1, 1–6, 7–10, and ≥11 years), mechanism of poisoning (dosage errors, nonintentional/accidental, recreational, suicide attempt, and other), route of poisoning (ingestion, inhalation, and other), and specific toxicant exposure (carbon monoxide, cosmetic, drugs, ethanol, ethanol + illicit drugs, pesticides, plants, household products, other, and unknown).

We then performed the cluster analysis, which organizes information from apparently heterogeneous episodes into relatively homogenous groups. We used the factors obtained in the multiple correspondence analyses as variables to perform the cluster analysis and to obtain the appropriate grouping of poisonings.[11] To create clusters, we used the squared-euclidean distance and Ward method.[12] Combining multiple correspondence analysis and cluster analysis categorize poisoning episodes into groups suggested by the data—not defined a priori—such that episodes in a given group of poisonings are similar to each other and episodes in different groups are dissimilar.

We performed all statistical analyses using SPSS vs. 22.0 statistical software (IBM, Armonk, NY) and R project.

Ethics/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/ethics committees at each participating institution who determined if informed consent was or was not required by participants. When required, informed consent was obtained from parents/guardians, with informed assent obtained from the participants when they were older than 12 years.

RESULTS

During the study period, we registered 363,245 pediatric ED presentations to the 105 EDs in the designated enrollment days, of which 1727 were for poisoning (0.47%; 95% CI, 0.45%–0.50%). There was significant variation in incidence of poisoning presentations across the global regions (Table I, Supplemental Digital Content 2, http://links.lww.com/PEC/A148). Of the 1727 episodes, 39

were excluded due to lack of required informed consent or due to episodes missed prospectively. Of the 1688 episodes analyzed, 873 (51.7%; 95% CI, 49.3%–54.1%) were in boys. Poisonings in girls were more common in North America (57.2%; 95% CI, 49.6%–64.7%) and in the Western Pacific regions (55.4%; 95% CI, 43.7%–66.4%). There was a bimodal peak age distribution (Fig. 1). Most of the poisonings (1361 [80.6%]; 95% CI, 78.7%–82.5%) occurred in the home with either ingestions (1504 [89.0%]; 95% CI, 87.5%–90.5%) or inhalations of the toxicants (126 [7.6%]; 95% CI, 6.3%–8.8%). Although unintentional poisoning was the most common mechanism of poisoning (1157 [68.5%]; 95% CI, 66.2%–70.7%), there was a significant variation in the underlying mechanisms across the different regions analyzed (Fig. 2 and Table II, Supplemental Digital Content 3, http://links.lww.com/PEC/A149). No patient died.

The multiple correspondence analyses indicated that 3 factors explained 76.3% of the global variability in the data. After applying cluster analysis to the 3 factors found in the multiple correspondence analyses, we identified 5 main groups of intoxications (Table 1). Group A was related to nonintentional inhalation of toxic substances (>50% carbon monoxide) mainly at home and, less frequently, at school; most of the children in this group were older than 10 years. Group B was related to nonintentional ingestions of household products at home by children between 1 and 7 years old. Group C was similar to group B (nonintentional, at home, and children 1–7 years old) but related to the ingestion of therapeutic drugs. Group D was associated with the intentional ingestion at home of therapeutic drugs by patients older than 10 years. These ingestions were frequently suicide attempts. Group E was related to the recreational ingestion of ethanol or, less frequently, the use of illicit drugs by children older than 10 years in the street or taverns/bars. The distribution of these groups showed significant differences between the analyzed global regions (Table 2).

Unintentional Poisonings

There were no significant differences between regions in either the season or in the day of week of presentations of unintentional poisonings. The type of exposure varied significantly, however, by international region (Fig. 3 and Table III, Supplemental Digital Content 4, http://links.lww.com/PEC/A150); therapeutic drugs were the most frequently involved substances (494 [42.7%]; 95% CI, 39.8%–45.5%), mainly psychotropics, acetaminophen, and nonsteroidal anti-inflammatory drugs, although there were significant differences between regions (Table IV, Supplemental Digital Content 5, http://links.lww.com/PEC/A151).

Of the household products, the most common exposures were to caustic agents (77 [24.8%]; 95% CI, 20.0%–29.6%) and detergents (19.6%; 95% CI, 15.1%–24.0%—most were single-unit dose liquid laundry detergent packets in North America, Northern Europe, and Eastern Europe). Nearly 90% (1029 [88.9%]; 95% CI, 87.1%–90.7%) of children with these poisonings were exposed in the child's home, with nearly one third occurring in the kitchen. In 246 (21.3%; 95% CI, 21.3%–23.6%) of the 1157 unintentional poisonings, caregivers admitted that they kept the toxic substance in a nonoriginal container (>30% in South America and Eastern Mediterranean region). Furthermore, in nearly 50% of the unintentional poisonings due to household products (138 [44.5%]; 95% CI, 38.9%–50.0%), caregivers admitted not keeping these products out of reach of children.

Suicide Attempts

Suicide attempts were more common among girls (192/233 [82.4%]; 95% CI, 77.5%–87.3%). Presentations were more common on weekdays (195/233 [83.7%]; 95% CI, 78.9%–88.4%), with therapeutic drugs being the most common toxicant (214 [91.8%]; 95% CI, 88.2%–95.3%), mainly psychotropics (72 [33.6%]; 95% CI, 27.2%–39.9%), and acetaminophen (69 [32.2%]; 95% CI, 25.9%–38.4%). Of children attempting suicide, 59 (27.5%; 95% CI, 21.5%–33.4%) took more than 1 agent, and 13 (6.0%) mixed therapeutic drugs with ethanol or illicit drugs. The therapeutic drug most commonly associated with suicide attempts varied significantly by region: acetaminophen, 21 of 28 suicide attempts involving therapeutic drugs (75%; 95% CI, 58.9%–91.0%) in Northern Europe; benzodiazepines, 10 of 14 (71%; 95% CI, 47.2%–94.7%) in South America, while 0 of 56 in North America.

Poisonings Due to Recreational Drug Use

Poisonings due to recreational/illicit drug use were more common in males (99/180 [55%]; 95% CI, 47.7%–62.2%), particularly in older adolescents (males aged <16 years, 59/115 [51%], males aged ≥16 years, 43/65 [66%]; $P < 0.01$). Poisonings from recreational/illicit drug use were more on weekends (40.0%).

Ethanol was the most common toxicant in recreational poisonings (123 [68.3%]; 15 [12.1%], mixed with illicit drugs), followed by illicit drugs (32 [17.8%], mainly cannabis). The highest rate of recreational poisonings due to illicit drug consumption was in South America.

DISCUSSION

Globally, the unintentional ingestion of therapeutic drugs and household products by young children is the most common

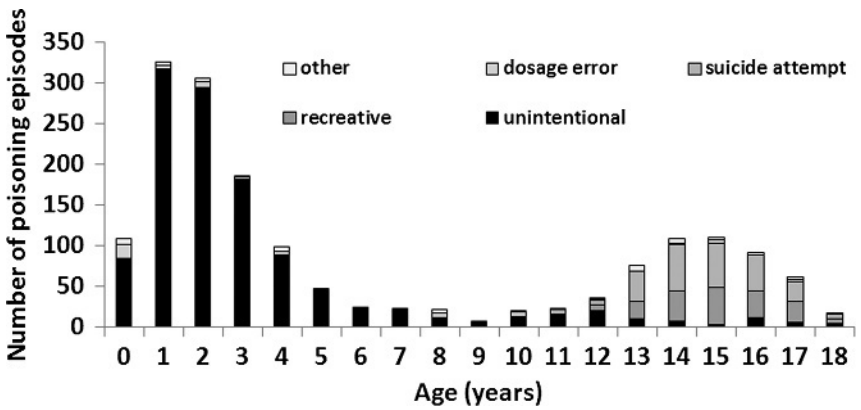

FIGURE 1. Distribution of age and underlying poisoning mechanism.

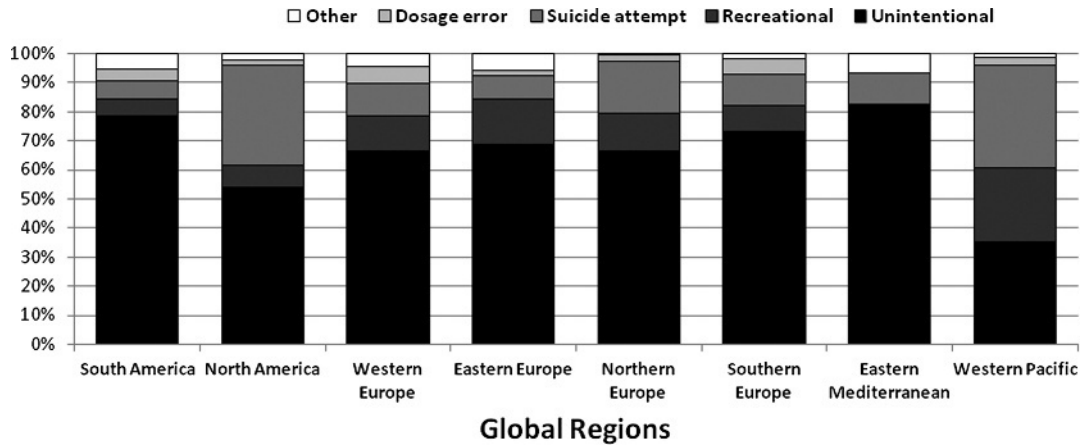

FIGURE 2. Mechanism of poisoning by international region.

TABLE 1. Description of Groups of Poisonings

Variable		Group A (n = 104)	Group B (n = 534)	Group C (n = 653)	Group D (n = 232)	Group E (n = 165)	*P*
Toxicant	Carbon monoxide	57 (54.8)	0 (0)	0 (0)	0 (0)	0 (0)	<0.001
	Household product	1 (1)	306 (57.3)	11 (1.7)	0 (0)	1 (0.6)	
	Ethanol	0 (0)	0 (0)	14 (2.1)	0 (0)	114 (69.1)	
	Ethanol + illicit drugs	5 (4.8)	0 (0)	12 (1.8)	1 (0.4)	45 (27.3)	
	Pesticides	0 (0)	58 (10.9)	3 (0.5)	0 (0)	0 (0)	
	Cosmetics	0 (0)	48 (9)	2 (0.3)	1 (0.4)	0 (0)	
	Therapeutic drugs	2 (1.9)	5 (0.9)	574 (87.9)	213 (91.8)	2 (1.2)	
	Plants	1 (1)	27 (5.1)	12 (1.8)	0 (0)	0 (0)	
	Unknown	10 (9.6)	8 (1.5)	3 (0.5)	0 (0)	1 (0.6)	
	others	28 (26.9)	82 (15.4)	22 (3.4)	17 (7.3)	2 (1.2)	
Mechanisms	Dosage errors	2 (1.9)	0 (0)	51 (7.8)	11 (4.7)	0 (0)	<0.001
	Nonintentional	90 (86.5)	527 (98.7)	537 (82.2)	0 (0)	3 (1.8)	
	Recreational	4 (3.8)	0 (0)	18 (2.8)	0 (0)	158 (95.8)	
	Suicide attempt	0 (0)	0 (0)	12 (1.8)	220 (94.8)	1 (0.6)	
	other	8 (7.7)	7 (1.3)	35 (5.4)	1 (0.4)	3 (1.8)	
Location	Home	68 (65.4)	499 (93.4)	573 (87.7)	202 (87.1)	19 (11.5)	<0.001
	Street	1 (1)	0 (0)	18 (2.8)	4 (1.7)	73 (44.2)	
	Tavern/bar	0 (0)	0 (0)	1 (2.8)	0 (0)	25 (44.2)	
	School	29 (27.9)	1 (0.2)	2 (0.3)	11 (4.7)	1 (0.6)	
	Other	3 (2.9)	32 (6)	49 (7.5)	8 (3.4)	27 (16.4)	
	Unknown	3 (2.9)	2 (0.4)	10 (1.5)	7 (3)	20 (12.1)	
Route	Ingestion	2 (1.9)	495 (92.7)	642 (98.3)	227 (97.8)	136 (82.4)	<0.001
	Inhalation	97 (93.3)	1 (0.2)	0 (0)	3 (1.3)	25 (15.2)	
	Other	5 (4.8)	38 (7.1)	11 (1.7)	2 (0.9)	4 (2.4)	
Age	<1 y	11 (10.6)	46 (8.6)	47 (7.2)	0 (0)	0 (0)	<0.001
	1–6 y	31 (29.8)	470 (88.0)	491 (75.2)	0 (0)	0 (0)	
	7–10 y	15 (14.4)	16 (3.0)	37 (5.7)	1 (0.4)	1 (0.6)	
	>10 y	47 (45.2)	2 (0.4)	78 (11.9)	231 (99.6)	164 (99.4)	

Cells show numbers and percentages of each category of different variables in each group.

Group A: nonintentional inhalation of toxic substances. Group B: nonintentional ingestions of household products. Group C: nonintentional ingestions of therapeutic drugs. Group D: intentional ingestion of therapeutic drugs, frequently suicide attempts. Group E: recreational ingestion of ethanol or, less frequently, use of illicit drugs.

The *P* values demonstrate the differences between groups among the analyzed variables. The *P* values reflect the independence between the analyzed variables, using the χ^2 test. A *P* value < 0.05 means that significant differences were found between the analyzed variables the different groups of poisonings.

TABLE 2. Distribution of Groups of Poisonings by Region

Regions	Group					*P*
	A (n = 104)	B (n = 534)	C (n = 653)	D (n = 232)	E (n = 165)	
South America (n = 223)	11 (4.9)	85 (38.1)	103 (46.2)	13 (5.8)	11 (4.9)	<0.001
North America (n = 166)	1 (0.6)	25 (15.1)	75 (45.2)	57 (34.3)	8 (4.8)	
Western Europe (n = 178)	19 (10.7)	66 (37.1)	51 (28.7)	19 (10.7)	23 (12.9)	
Eastern Europe (n = 267)	41 (15.4)	81 (30.3)	87 (32.6)	24 (7.9)	37 (13.9)	
Northern Europe (n = 176)	6 (3.4)	51 (29)	65 (36.9)	32 (18.2)	22 (12.5)	
Southern Europe (n = 558)	25 (4.5)	190 (34.1)	235 (42.1)	60 (10.8)	48 (8.6)	
Eastern Mediterranean (n = 46)	1 (2.2)	28 (60.9)	13 (28.3)	4 (8.7)	0 (0)	
Western Pacific (n = 74)	0 (0)	8 (10.8)	24 (32.4)	26 (35.1)	16 (21.6)	

Cells show numbers and percentages of each group by region.

Group A: related to nonintentional inhalation of toxic substances (>50% carbon monoxide) mainly at home and, less frequently, at school. Group B: related to nonintentional ingestions of household products at home by children between 1 and 7 years old. Group C: similar to group B (nonintentional, at home and children 1–7 years old) but related to the ingestion of therapeutic drugs. Group D: associated with the intentional ingestion at home of therapeutic drugs by patients older than 10 years, frequently due to suicide attempts. Group E: related to the recreational ingestion of ethanol or, less frequently, the use of illicit drugs by children older than 10 years in the street or taverns/bars.

The *P* values demonstrate the differences between groups in the analyzed regions. The *P* values reflect the independence between the analyzed variables, using the χ^2 test. A *P* value < 0.05 means that significant differences were found related to the rate of the groups of poisonings in the different regions.

mechanism of acute pediatric poisonings reported to poison control centers or of patients receiving care in pediatric EDs. However, we identified significant differences between international regions related to the circumstances of the poisonings and involved toxicants. It is somewhat surprising that no patient died. However, this is consistent with previous reports that fatal child poisonings have decreased substantially in recent decades.[3]

Although great efforts have been made in the last few decades in prevention, childhood acute poisoning remains a major problem.[3,5] Overall, in our study, poisoning accounted for approximately 1 in 200 visits to the EDs. Various epidemiological studies on poisoning emphasizing the importance of acute pediatric poisonings have been conducted in EDs,[6,13] National Poison Control Centers,[5,14] and prehospital settings.[15] To our knowledge, this is the first international, epidemiological study comparing presentations of childhood acute poisonings in EDs across the globe, involving 4 WHO regions. Given that most of these "accidental" poisonings can be prevented,[1] different interventions and strategies targeted to the circumstances surrounding the poisonings should be developed and implemented.[3]

As with reports from single countries,[6,13] unintentional poisonings were the most common presentations, although the frequency of unintentional poisoning and the toxicants involved varied greatly across the 8 international regions. The study was not designed to address the reason for these differences, and it is highly likely that differences are multifactorial (eg, differences in drug prescribing practices, exposure to pesticides, access to recreational drugs, parental supervision, educational structures). However, current prevention strategies within regions (eg, limiting quantity of medications prescribed, warning labels, and

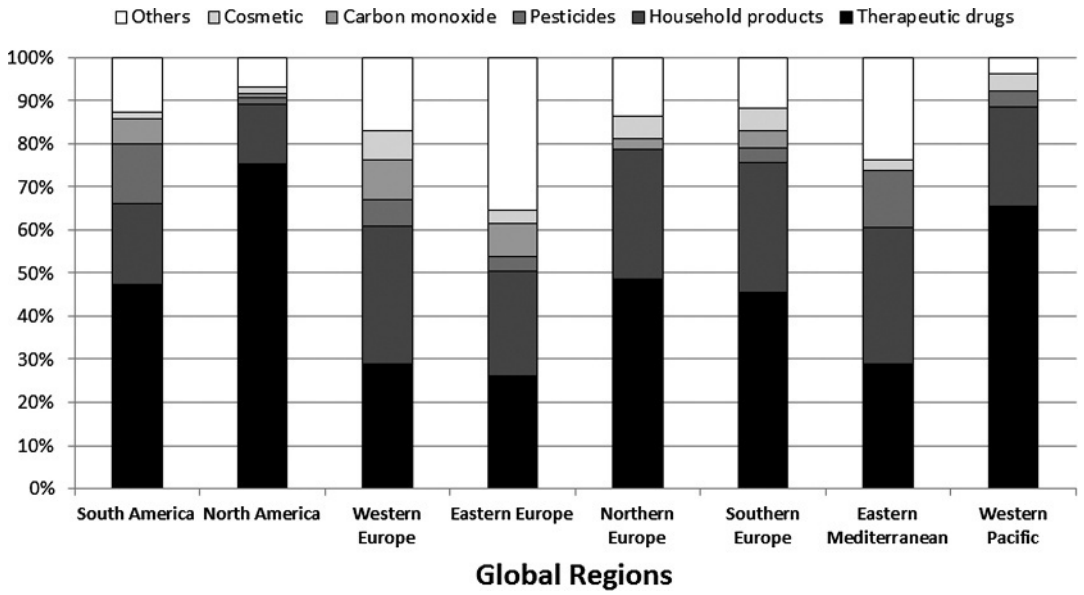

FIGURE 3. Toxicants involved in unintentional poisonings by international region.

community outreach and messaging) also play an important role in overall poisoning rates. With the identification of differences across regions, further studies can explore the effectiveness of specific public health prevention measures within countries. Among children with nonintentional poisonings, the most common culprits were therapeutic drugs, although in some regions, poisonings due to household products were more common. In addition, we also observed significant regional differences between therapeutic drugs involved. These differences should be addressed when designing prevention programs.

This study also confirms the substantial international incidence of laundry detergent pod ingestions in children[16,17] and the need for increased efforts to prevent exposure of young children to these products,[17] mainly in Europe, where the rate of poisonings due to household products was particularly high. Pesticides are a leading cause of poisoning in South America and the Eastern Mediterranean, where most reported cases related to direct exposure to rodenticides used in and around the home.

There remains a pressing need for universal prevention messages for childhood poisonings of all types. In this study, 20% of caregivers did not store potential toxicants in the original packaging, and 30% of caregivers did not store these out of reach of children. Regardless of the role of legal regulations about the packaging of therapeutic drugs or household products in poisoning prevention efforts, effective education of families about the methods and strategies to store these products at home[3,18,19] remains critical, particularly in South America and the Eastern Mediterranean region.

There was also a striking rate of suicide attempts among children seen in the EDs of North America and Western Pacific region, particularly among older adolescents. Suicidal ideation and suicide attempts are the most common mental health emergencies among adolescents,[20] and suicide is the third leading cause of death among individuals aged 10 to 24 years in the United States.[21] We were somewhat limited in comparisons of suicide attempts by region; however, because some of the participating EDs attended children only to 14 years of age. Regardless, screening for mental health issues and suicidality is a strategy that must be considered in pediatric EDs worldwide, particularly in those regions most notably affected.

Approximately 10% of pediatric poisonings were due to recreational/illicit drugs. These events typically involved ethanol, despite most countries having legislation that limits the sale of alcohol to minors. As previously reported,[7] alcohol intoxication was more common in certain regions. The WHO European Region has reported the heaviest alcohol consumption in the world,[22] and alcohol-related harm is disproportionately high among young people.[23] As a consequence, ED visits related to alcohol and illicit drug consumption are increasing.[7] The ED may provide a critical and unique opportunity to screen for alcohol use and initiate care and prevention strategies of these adolescents.[24–26]

Our study emphasizes the importance of these surveillance systems. Although some countries, such as the United States, have excellent poison control center surveillance systems, the information directly recorded in the ED may help to identify most common exposures in those settings (some of which never are reported to poison control centers).[27] In addition, the availability of poison control centers varies across the world. Although most of the developed countries have well-established facilities for poison control services, this is rarely the case in developing countries.[28]

This study has several limitations worth noting. The number/percentage of EDs included was not the same in all the regions; thus, data from Eastern Mediterranean and Western Pacific regions need to be interpreted with this in mind. However, the sample was sufficiently large to detect important epidemiological differences between regions and to fulfill the main objective of the study. Of note, some of the participating EDs attend to children up to 14 years of age and others up to 18 years, thus limiting the ability to make comparisons between regions in the older adolescent group. The results regarding suicide attempts also do not include suicide attempts by inflicted self-harm (and not by poisoning) and therefore should not be used as a comparison of total suicide rates across regions. In addition, the EDs involved in the study are members of the PERN research network, and are therefore self-selected and may not be truly representative of all pediatric EDs globally. However, the EDs included both secondary and tertiary EDs, pediatric and mixed pediatric and adults EDs, rural and urban EDs, and EDs with small and large volumes, and it therefore seems unlikely that self-selection would have significantly biased the results. On the other hand, international differences related to poison center presence and functionality, the availability of a telephone hotline for poisonings, and prehospital medical services, in addition to other factors, may bias the number of children that are brought to the EDs by region. However, this possibility does not limit the analysis of the study population of children with poisonings presenting to EDs across broad regions of the globe. Finally, our study reflects that pediatric poisonings are more common in EDs from certain regions, which should be taken into account in the organization and provision of services by region.

In conclusion, there are substantial epidemiological differences in acute poisonings in children evaluated in EDs across different countries and regions of the globe. These differences should be taken into account when designing effective local prevention interventions. The role of pesticides in South America and Eastern Mediterranean regions and household products in some European regions, the striking rate of suicide attempts in North America and the Western Pacific regions, and, finally, the low use of the poison control centers are concerning issues to be considered when designing preventive measures. Furthermore, comparisons of outcomes from different treatment practices can inform current practices internationally.

ACKNOWLEDGMENTS

When the study was approved, Executive Committee members of the PERN included the following*: Nathan Kuppermann, MD, MPH (PECARN, USA); Javier Benito, MDPhD (REPEM, Spain); Yehezkel Waisman, MD (REPEM, Israel); Martin Osmond, MD, CM (PERC, Canada); David Johnson, MD (PERC, Canada); James Chamberlain, MD (PECARN, USA); Charles G. Macias MD, MPH (PEMCRC, USA); Anupam Kharbanda, MD (PEMCRC, USA); Franz E. Babl, MD (PREDICT, Australia); Stuart Dalziel, MBChB, PhD (PREDICT, New Zealand).*

Pediatric Emergency Research Networks (PERN) Intoxications working group: Site investigators:

Pediatric Emergency Care Applied Research Network (PECARN), USA: *University of California, Davis School of Medicine: Nathan Kuppermann, Mark Sutter; Nationwide Children's Hospital & The Ohio State University: Daniel Cohen, Julia Lloyd; Children's Hospital of Michigan, Detroit, MI: Elizabeth Duffy, Prashant Mahajan; Children's Hospital Colorado, Aurora, CO: George Sam Wang; Ann Arbor, MI: C.S. Mott Children's Hospital: Stuart A Bradin.*

Pediatric Emergency Medicine Collaborative Research Committee (PEM-CRC) of the American Academy of Pediatrics, USA: *Arnold Palmer Hospital for Children Emergency Department, FL: Jose Ramirez, Samuel Stephenson.*

Paediatric Research in Emergency Departments International Collaborative (PREDICT): AUSTRALIA: *The Royal Children's Hospital and Murdoch Children's Research Institute, Melbourne: Anna Carison, Franz E. Babl; Monash Medical*

Centre, Melbourne: Simon Craig; Dandenong Hospital, Melbourne: Andis Graudins; Casey Hospital, Melbourne: John Cheek. ***NEW ZEALAND:*** *Starship Children's Hospital, Auckland, New Zealand: Stuart R. Dalziel, Megan Bonish.*

Research in European Paediatric Emergency Medicine (REPEM): BELGIUM: *University Hospital Ghent: Patrick Van de Voorde, Said Hachimi Idrissi.* ***CZECH REPUBLIC:*** *University Hospital Motol, Prague: Alexandra Petrovska.* ***FRANCE:*** *Hôpital Robert Debré, Paris: Jean Christophe Mercier, Laurence Morin; Necker Enfants Malades Hospital, Paris: Gerard Cheron.* ***HUNGARY:*** *"Csolnoky Ferenc" Teaching Hospital Veszprem Hungary: Eva Szabo, Richard Nagy; Heim Pal Children's Hospital, Budapest: Zsolt Bognar; "Szent Gyorgy" Teaching Hospital Szekesfehervar: Gabor Simon; University of Debrecen Hungary: György Balla, Éva Juhász.* ***IRELAND:*** *National Children's Hospital, Tallaght, Dublin 24: Ciara Martin, Rincy Koshy; Temple Street Children's University Hospital, Temple Street, Dublin 1: Roisin Mc Namara.* ***ISRAEL:*** *Schneider Children's Medical Center of Israel: Yehezkel (Hezi) Waisman, Lisa Amir.* ***ITALY:*** *Ca'Foncello Hospital.Treviso: Liviana Da Dalt; Departamento della Salute della Donna e del Bambino, Azienda Ospedaliera-Universitá di Padova: Carlo Moretti; IRCCS Burlo Garofolo, Trieste: Stefania Norbedo; IRCCS G. Gaslini Genova: Renna Salvatore, Carla Debbia; Ospedale dei Bambini Brescia: Alberto Arrighini; DEA Meyer Firenze: Patrizia Botarelli; IRCCS Ospedale pediatrico Bambino Gesù Roma: Mara Pisani; Spedale Santobono, Napoli: Eduardo Ponticiello, Enzo Tipo.* ***THE NETHERLANDS:*** *Sophisá Children Hospital: Henriette Moll.* ***PORTUGAL:*** *Centro Hospitalar Leiria Pombal: Xavier Bilhota; Centro Hospitalar Vila Nova de Gaia, Vila Nova de Gaia: Ana Garrido; Hospital Pediátrico–Centro Hospitalar e Universitário de Coimbra: Lia Gata, Patrícia Mação; Hospital Beatriz Angelo (Lisboa): Sofía Costa Lima; Hospital de Santa María (Lisboa): Gabriela Araújo e Sá, Sofia Almeida.* ***ROMANIA:*** *Emergency Children Hospital Louis Turcanu, Timisoara: Mihai Gafencu, Alina Babeu; Hospital Tirgu Mures, Romania: Diana Moldovan; Hospital for Children Cluj, Napoca: Daniela María Mitrofan.* ***SPAIN:*** *Basurto University Hospital, Bilbao: Francisco Javier Humayor Yanez; Complejo Asistencial Universitario de León: Ana Gloria Andrés Andrés; Complejo Hospitalario de Jaén: Tomás del Campo Muñoz; Corporació Sanitària Parc Taulí de Sabadell: Rocío Mendivil, Irene Baena Olomi; Fundació Sant Hospital de La Seu d'Urgell: Jordi Fábrega i Sabaté; Hospital Alto Deba: Itziar Iturralde Orive; Hospital de Terrassa: Andreu Roca; H. de Cabueñes: Ramón Fernández; H. de Laredo: Ana Jorda Lope, Víctor Canduela; H. Doce de Octubre: Sofía Mesa; H. del Tajo: Carlos García-Vao Bel; H. Fundación Alcorcón: Alberto Barasoain Millán; H. Mendaro: Laura Herrero; H. Miguel Servet: Carmen Campos Calleja; H. Niño Jesús: Juan Carlos Molina; H. Príncipe de Asturias; Alcalá de Henares, Madrid: Mª Ángeles García Herrero; H. Quirón Bizkaia: Carlos Canduela; H. Rey Juan Carlos, Móstoles: Pablo Bello Gutiérrez; H. Río Hortega: Roberto Velasco; H. San Joan de Déu: Lidia Martínez Sánchez; H. San Pedro (Logroño): Laura Martínez Mengual; H. U. Central de Asturias: Julián Rodríguez Suárez; H. U. Cruces: Santiago Mintegi, Nerea Salmon; H. U. Donostia: Jose Ángel Muñoz Bernal; H. U. de Salamanca: Javier López Ávila; H. U. Gregorio Marañón: Paula Vázquez López; H. U. Mutua Terrassa: Elena May; H. U. S Agustín. Linares: Juan Cozar Olmo; H. U. Son Espases, Palma de Mallorca: Victoria López Corominas; H. U. Xeral de Vigo: María Tallón García; H. Virgen de la Salud: Esther Crespo Rupérez; H. Zumarraga: Amalia Pérez Sáez; Vall d' Hebron University Hospital, Barcelona: Monica Sancosmed Ron, Pablo Velasco Puyó; Canarias University Hospital, Tenerife: Judith Mesa; Hospital Arnau de Vilanova; Lleida: Neus Pociello; Hospital de Úbeda: María Galán Mercado.* ***SWITZERLAND:*** *Children's Hospital, Zurich: Michelle Seiler; Hôpital de l'Enfance, Lausanne: Céline Rey-Bellet Gasser, Anne Pittet; University Hospitals of Geneva: Alain Gervaix, Sergio Manzano.* ***TURKEY:*** *Ege University School of Medicine. Izmir: Eylem Ulas Saz, Ali Yurtseven; Izmir Tepecik Teaching and Research Hospital, Izmir: Murat Anil; Ankara University Faculty of Medicine, Ankara: Sinan Oguz, Deniz Tekin, Funda Kurt.* ***UNITED KINGDOM:*** *Alder Hey Children's NHS Foundation Trust, Liverpool: Mary Ryan, Abi Hoyle; Bristol Royal Hospital for Children, Bristol: Mark D. Lyttle, Sarah Potter; St Mary's Hospital, Newport: Rodrick Babakhanlou.*

Other participating sites and investigators include the following:

Red de Investigación y Desarrollo de la Emergencia Pediátrica de Latinoamérica (RIDEPLA): ARGENTINA: *Hospital de Niños "Víctor J. Vilela" de Rosario: Sandra Cagnasia; Hospital de Niños "Ricardo Gutiérrez" Buenos Aires: Héctor Berzel, Elda Cargnel; Hospital del Niños de la Santísima Trinidad, Córdoba: Eugenia Gordillo, Nilda Gait; Hospital Nacional Profesor Alejandro Posadas: Marta María Méndez, Adriana I. Haas; Hospital Italiano de Buenos Aires: Maria Graciela Quevedo, Maria Macarena Parot Varela; Hospital de la ciudad de Trelew: Marcela Regnando; Hospital de Pediatría "Prof. Dr. Juan P. Garrahan": Pedro Bonifacio Rino; Hospital Universitario Austral, Buenos Aires: Verónica Torres Cerino; Hospital Pediátrico Dr, Av. Castelan de Resistencia Chaco, Chaco: Héctor Tobares.* ***BRAZIL:*** *Hospital Sao Lucas de PUCRS (Pontificie Universidade Católica do Rio Grande do Sul): Francisco Bruno.* ***PARAGUAY****: Hospital General Pediátrico Niños de Acosta Ñu. San Lorenzo: Laura Godoy, Viviana Pavlicich.* ***URUGUAY:*** *Centro Comero, Cooperativa médica de Rocha: Wilfredo Casella; Asociación Española Primera en Salud: Gustavo Alberto Giachetto Larraz; Casa Galicia: María Inés Ferreira; CASMU (Centro de Asistencia del Sindicato Médico del Uruguay): Adriana Pedemoti, Estela Antúnez; Hospital Británico; Servicio de Emergencia Pediatrica: Patricia Dall'Orso; Hospital Militar: Mariana Más, Patricia Torello; Hospital Policial: Verónica Parodi, Soledad Pandolfo; H. Pereira-Rosell, Montevideo: Javier Prego; CAMOC—Centro Asistencial Medico del Oeste de Colonia: Loreley García Gariglio; SMQS, Sociedad Médico Quirúrgica de Salto: Edit Arreseigor, Humberto Gugliemone, Lourdes Yemini.*

PAKISTAN: *Agha Khan University Hospital. Karachi: Nadeem Qureshi, Jabeen Fayyaz.*

REFERENCES

1. Holder Y, Matzopoulos R, Smith N. Poisons. In: Peden M, ed. *World report on child injury prevention*. Geneva: World Health Organization and UNICEF; 2008. Available at: http://whqlibdoc.who.int/publications/2008/9789241563574_eng.pdf. Accessed August 2015.
2. Mbeledogu CN, Cecil EV, Millett C, et al. Hospital admissions for unintentional poisoning in preschool children in England; 2000–2011. *Arch Dis Child*. 2015;100:180–182.
3. Franklin RL, Rodgers GB. Unintentional child poisonings treated in United States hospital emergency departments: national estimates of incident cases, population-based poisoning rates, and product involvement. *Pediatrics*. 2008;122:1244–1251.
4. Watson WA, Litovitz TL, Rodgers GC, et al. 2004 Annual Report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. *Am J Emerg Med*. 2005;23:589–666.
5. Mowry JB, Spyker DA, Cantilena LR Jr, et al. 2012 Annual Report of the American Association of Poison Control Centers' National Poison Data

System (NPDS): 30th annual report. *Clin Toxicol (Phila)*. 2013;51: 949–1229.

6. Azkunaga B, Mintegi S, Bizkarra I, et al. Toxicology surveillance system of the Spanish Society of Paediatric Emergencies: first-year analysis. *Eur J Emerg Med*. 2011;18:285–287.
7. Azkunaga B, Mintegi S, del Arco L, et al. y el Grupo de Trabajo de Intoxicaciones de la Sociedad Española de Urgencias de Pediatría. Changes in the epidemiology of poisonings attended in Spanish pediatric emergency departments between 2001 and 2010: increase in ethanol intoxication. *Emergencias*. 2012;24:376–379.
8. Salazar J, Zubiaur O, Azkunaga B, et al. Regional differences in acute poisoning in under 14 year-old children in Spain. *An Pediatr (Barc)*. 2015; 82:e39–e43.
9. Klassen TP, Acworth J, Bialy L, et al. Pediatric emergency research networks: a global initiative in pediatric emergency medicine. *Pediatr Emerg Care*. 2010;26:541–543.
10. Greenacre MJ (Ed). *Theory and Applications of Correspondence Analysis*. London: Academic Press; 1984.
11. Lebart L, Morineau A, Piron M (Eds). *Statistique Exploratoire Multidimensionnelle*. Paris: Dunod; 1995.
12. Ward JH. Hierarchical grouping to optimize an objective function. *J Am Stat Assoc*. 1963;58:236–244.
13. Ozdemir R, Bayrakci B, Tekşam O, et al. Thirty-three-year experience on childhood poisoning. *Turk J Pediatr*. 2012;54:251–259.
14. Jackson BF, McCain JE, Nichols MH, et al. Emergency department poisoning visits in children younger than 6 years: comparing referrals by a regional poison control center to referrals by other sources. *Pediatr Emerg Care*. 2012;28:1343–1347.
15. Vilke GM, Douglas DJ, Shipp H, et al. Pediatric poisonings in children younger than five years responded to by paramedics. *J Emerg Med*. 2011; 41:265–269.
16. Williams H, Bateman DN, Thomas SH, et al. Exposure to liquid detergent capsules: a study undertaken by the UK National Poisons Information Service. *Clin Toxicol (Phila)*. 2012;50:776–780.
17. Valdez AL, Casavant MJ, Spiller HA, et al. Pediatric exposure to laundry detergent pods. *Pediatrics*. 2014;134:1127–1135.
18. American Academy of Pediatrics, Committee on Injury and Poison Prevention. Office-based counseling for injury prevention. *Pediatrics*. 1994;94:566–567.
19. Gardner HG. Office-based counseling for unintentional injury prevention. *Pediatrics*. 2007;119:202–206.
20. King CA, Kerr DCR, Passarelli MN, et al. One-year follow-up of suicidal adolescents: parental history of mental health problems and time to post-hospitalization attempt. *J Youth Adolesc*. 2010;39:219–232.
21. Kann L, Kinchen S, Shanklin SL, et al. Youth risk behavior surveillance—United States, 2013. *MMWR Suppl*. 2014;63:1–168.
22. World Health Organization. European Status Report on Alcohol and Health 2010. Available at: http://www.euro.who.int/__data/assets/pdf_file/0004/128065/e94533.pdf. Accessed August 2015.
23. Eurocare. European Alcohol policy Alliance. Available at: http://www.eurocare.org/resources/policy_issues/youth. Accessed August 2015.
24. Newton AS, Dong K, Mabood N, et al. Brief emergency department interventions for youth who use alcohol and other drugs: a systematic review. *Pediatr Emerg Care*. 2013;29:673–684.
25. Committee on Substance Abuse, Levy SJ, Kokotailo PK. Substance use screening, brief intervention, and referral to treatment for pediatricians. *Pediatrics*. 2011;128:e1330–e1340.
26. Linakis JG, Bromberg J, Baird J, et al. Feasibility and acceptability of a pediatric emergency department alcohol prevention intervention for young adolescents. *Pediatr Emerg Care*. 2013;29:1180–1188.
27. Mowry JB, Spyker DA, Brooks DE, et al. 2014 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 32nd annual report. *Clin Toxicol (Phila)*. 2015;53: 962–1147.
28. Good AM, Kelly CA, Bateman DN. Differences in treatment advice for common poisons by poisons centres—an international comparison. *Clin Toxicol (Phila)*. 2007;45:234–239.