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ORIGINAL RESEARCH

Characteristics and Consequences of Medication Errors in Pediatric Patients Reported to Ramathibodi Poison Center: A 10-Year Retrospective Study

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Purpose: This study was performed to evaluate the clinical characteristics of, consequences of, and factors associated with medication errors (MEs) that cause harm to pediatric patients (<15 years of age) treated in the hospital setting.

Patients and Methods: We performed a 10-year retrospective study (January 2011–December 2020) by analyzing data from the Ramathibodi Poison Center. MEs were classified into categories A to I according to the severity of the outcome.

Results: In total, 121 patients were included in the study. Most (51.24%) patients were male. Their median age was 1 year (range, 1 hour–14 years). Infants, newborns, and toddlers were the three most common age groups in which MEs were reported. Most MEs occurred during the afternoon shift [n = 60 (49.59%)] and in the inpatient department (66.12%). The most common type of MEs was a dose error (64.46%). Antibiotics, sedative agents, and bronchodilators were the three most common classes of ME drugs. Four patients died. Three deaths occurred because of a dose error. One patient was a 1-year-old girl who received an iatrogenic intravenous phenytoin overdose of 10 times the normal dose, resulting in a phenytoin level of 72.4 mcg/mL. She died 22 hours after the ME occurred. The work shift was the only factor that significantly differed between patients with category C and D MEs and those with category E to I MEs.

Conclusion: Small children were at highest risk for MEs. MEs induced harm and deaths in some patients. A preventive and safety system, including appropriate shift work administration, should be emphasized and implemented to prevent and/or decrease the occurrence of MEs.

Keywords: children, deaths, outcomes, pediatrics

Introduction

A medication error (ME) is defined as any failure in the treatment process that potentially leads to harm to the patient while the treatment is in the control of the health care professional.[1,2] MEs are classified by seriousness according to the type and/or stage at which the ME occurred such as incorrect drug errors, incorrect administration technique errors, or dose errors.[3]

Although MEs are a major concern in different age groups, children have specific demands with respect to medication ordering, dispensing, administration, and monitoring. They also require weight-based dosing calculations.[4] Children are at greater risk of MEs because of their wide variation in body mass, necessitating calculation of unique drug doses based on the patient's body weight or body surface area.[5,6] The incidence of ME is reportedly higher in pediatric patients than in adult patients.[1,7]

The consequences of MEs include morbidity and mortality.[1,7] MEs also affect patients, their families, and health care providers by increasing hospital expenses, prolonging the length of hospital stay, and causing psychological impacts. Some patients develop serious clinical effects from ME. Therefore, health care organizations should consider improving their medication safety system to prevent patient harm caused by MEs.

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In a systematic review of MEs in Southeast Asian countries,[1] the most commonly reported types of administration errors were incorrect time errors, omission errors, and dose errors. Factors contributing to MEs were shortages of medical personnel, high workload of nurses, doctor/nurse distraction, and misinterpretation of prescription/medication charts.[1] All studies included in the systematic review were performed in specific wards or involved patients in the hospital/inpatient setting, usually in only one hospital. Most studies in this review are carried out in adult patients.[1] No studies involving poison centers were included. The clinical consequences of the reported MEs were not investigated in most studies involved in this review.[1] Moreover, few epidemiological data are available regarding MEs in specific groups of patients, such as pediatric inpatients, especially in Thailand.[8–10] One study demonstrated that the data of MEs reported to poisons information centers, could help characterize and detect of trends of MEs taking place in both a domestic setting and across the healthcare facilities and also promote the pharmacovigilance.[7]

The Ramathibodi Poison Center (RPC) was established in the Faculty of Medicine Ramathibodi Hospital, Mahidol University in Bangkok in 1996. Currently, the center is mainly involved in consultations by medical personnel from every region in Thailand (approximately 20,000–30,000 consultations/year). The RPC might be able to provide timely, high-quality surveillance data on the conditions and types of MEs occurring across the health care system in Thailand.

The present study was performed to clarify the clinical characteristics of, consequences of, and factors associated with MEs that cause harm to patients during the prescribing, dispensing, administering, and monitoring of drugs in hospitals in Thailand. We also aimed to characterize the trends in MEs occurring across the health care spectrum.

Materials and Methods

Study Design

We performed a 10-year retrospective analysis (January 2011–December 2020) using data from the RPC Toxic Exposure Surveillance System. The primary outcomes were the clinical characteristics of patients with MEs during their treatment in hospitals and the consequences of these MEs. The secondary outcome was the factors associated with MEs causing harm to patients.

This study was approved by the Institutional Ethics Committee Board of Ramathibodi Hospital, Faculty of Medicine, Mahidol University (COA. MURA2022/32). Because this study was a retrospective study which used a pre-existing confidential database from the RPC, patient consent was waived by our hospital's ethics committee board. This study was also conducted in accordance with the Declaration of Helsinki.

Study Setting and Population

The study was performed at the RPC, a poison center of a tertiary teaching hospital in Thailand.

The RPC has supported data and advices to the general population or medical personnel for diagnosing and management of poisoning cases. Calls are received and answered by specialists in poison information (SPIs) who are nurses or pharmacists, 24 hours a day. The SPIs have to complete the course of training, pass the certification exam and are certified to have competent skill, knowledge and experience to provide poison information to medical personnel and the public. Consultations are reviewed and verified daily by senior SPIs and medical toxicologists. For complicated or uncertain cases, consultations with medical toxicologists are required and available. Most queries are from medical personnel. Follow-up calls are performed to collect patient data and the progress of cases, recommend treatment, and determine the medical outcomes of cases. All cases are recorded in the RPC Toxic Exposure Surveillance System database. All records, including the diagnosis and severity, are reviewed and verified by a team of SPIs and medical toxicologists.

Patients were included if the reason for exposure was coded as a "therapeutic error", defined according to the RPC Toxic Exposure Surveillance System as "an exposure (or incident) resulting from incorrect use of medication, whether the agent was administered by medical personnel or by a lay person".[11]

The inclusion criteria were an age of ≤15 years and the occurrence of a therapeutic error as defined by the RPC Toxic Exposure Surveillance System together with an ME caused by health care providers and occurred in health care facilities or hospitals from January 2011 to December 2020. Patients with incomplete information preventing analysis of the primary and secondary outcomes were excluded.

Data Collection

The following data were collected by the authors (P.T., P.V., A.T., P. P.) for all patients: demographic data, underlying disease, clinical characteristics, types of MEs, types of drugs associated with MEs, treatment modalities, and outcomes. The clinical toxicologists reviewed and verified the clinical characteristics, diagnosis and outcomes of all included cases from the RPC Toxic Exposure Surveillance System database.

All patients were ≤15 years of age, and the age groups were defined as newborns, infants, toddlers, preschool-age children, school-age children, and adolescents.[12]

Definitions

MEs were defined as errors during drug prescribing, transcribing, administering, dispensing, and monitoring[4] that occurred during hospitalization in both outpatient and inpatient facilities.

An administration error was defined as any difference between what the patient received or was supposed to receive and what the prescriber intended in the original order.[4,13]

A route error occurred when a medication was given by an incorrect route of administration.[4,13]

A dose error occurred when the medication dose, strength, quantity or frequency given was different from the standard dose, strength, quantity or frequency.[4,13,14]

A patient error occurred when a patient's medication was incorrectly given to another patient.[13]

Based on the ME taxonomy developed by the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP), MEs can be classified into categories A to I according to the severity of the outcome.[15] Category C and D are the errors occurred that reached patients but did not cause harm. In category D, patients are required monitoring and/or intervention to prevent harm.[15]

Categories E–I MEs are the errors occurred, reached patients, and caused temporary to permanent harm to patients including deaths.[15]

The patients' vital signs were assessed according to the normal values for each age.[16]

Acute kidney injury was identified by the Acute Kidney Injury Network criteria.[17] We assumed that patients with no underlying disease had normal kidney function prior to the ME.

Hyponatremia and hypernatremia were defined as a serum sodium concentration of <135 and >145 mEq/L, respectively.[18] Hypokalemia and hyperkalemia were defined as a serum potassium concentration of <3.5 and >5.0 mEq/L, respectively.[18]

Statistical Analysis

We used Stata version 17 (StataCorp, College Station, TX, USA) to analyze the data. Continuous data are presented as mean and standard deviation if the data are normally distributed; otherwise, the data are presented as median with minimum and maximum. Categorical data are presented as frequency and percentage.

Comparisons between groups were analyzed by Student's *t*-test if two independent continuous datasets were normally distributed; otherwise, they were analyzed by the Mann–Whitney *U*-test. Differences in categorical variables were evaluated by chi-squared analysis and Fisher's exact test.

Results

In total, 1033 patients with recorded therapeutic errors were identified. Of these, 804 patients with MEs that occurred outside hospitals or health care facilities were excluded. Patients aged >15 years were also excluded. Finally, 121 patients who fulfilled the inclusion criteria were analyzed.

The patients' clinical characteristics and demographic data are shown in Table 1. Among the 121 patients, 62 (51.24%) were male. The patients' median age was 1 year (range, 1 hour-14 years). Infants, newborns, and toddlers were the three most common age groups with reported MEs. The central region of Thailand was the most common region in which MEs were reported in our study. Most MEs occurred during the afternoon shift [n = 60 (49.59%)] and commonly occurred in the inpatient department (66.12%).

Table 1 Demographic Data of Patients

Variables	Category	Frequency
Sex	Male	62 (51.24%)
	Female	59 (48.76%)
Age group	Newborn	25 (20.66%)
	Infant	27 (22.31%)
	Toddler	25 (20.66%)
	Preschool	15 (12.40%)
	School	22 (18.18%)
	Adolescent	7 (5.79%)
Region	Bangkok (the capital)	29 (23.97%)
	Central	32 (26.45%)
	North	10 (8.26%)
	Northeast	19 (15.70%)
	East	13 (10.74%)
	South	12 (9.92%)
	West	6 (4.96%)
Type of hospital	Government	98 (80.995%)
	Private	23 (19.01%)
Shift of work	Morning	47 (38.84%)
	Afternoon	60 (49.59%)
	Night	14 (11.57%)
Underlying diseases	Yes	99(81.82%)
	No	22 (18.18%)
Location of patients' management	Emergency room/Outpatient department	41 (33.88%)
	Inpatient department (wards and intensive care units)	80 (66.12%)

The data of the processing stage during with the ME occurred, such as the prescribing or transcribing stage was not recorded in our database and hence are not shown in our study.

The most common type of ME was a dose error [n = 78 (64.46%)] (Table 2). We also analyzed the classes of drugs based on the medications that the patients received. Antibiotics, sedative agents, and bronchodilators were the three most common classes of drugs that caused MEs in our study. The most common antibiotic drugs included benzathine penicillin G (incorrect route and dose), gentamycin (incorrect dose), vancomycin (incorrect dose), and metronidazole (incorrect route and dose). The most common sedative agents were fentanyl (incorrect dose), chloral hydrate (incorrect dose, route, and administration), and morphine (incorrect dose). The bronchodilators were fenoterol/ipratropium bromide (incorrect route), albuterol (incorrect route), and aminophylline (incorrect dose).

Category F MEs occurred most frequently (39.67%). Of the 121 patients, 2 (1.65%) had category H MEs and 4 (3.31%) had category I MEs.

Table 2 Class of Drugs, Type of Medication Errors and Type of Category Error Involved in Medication Errors

Variables	Frequency
Class of drugs	
Antibiotics	19 (15.70%)
Sedative drugs	11 (9.09%)
Bronchodilators	11 (9.09%)
Cardiology drugs	9 (7.44%)
Antihistamines	9 (7.44%)
Antiepileptic drugs	7 (5.79%)
Antipyretics	7 (5.79%)
Antivirals	4 (3.31%)
Antiemetic drugs	3 (2.48%)
Iron supplements	3 (2.48%)
Opioids	3 (2.48%)
Proton pump inhibitors	3 (2.48%)
Antineoplastic drugs	2 (1.65%)
Local anesthetics	2 (1.65%)
Antipsychotic drugs	2 (1.65%)
Steroids	2 (1.65%)
Others (each for 1 case)	24 (19.83%)
Type of medication errors	
Wrong dosing	78 (64.46%)
Wrong route	17 (14.05%)
Wrong drug	21 (17.36%)
Wrong administration	5 (4.13%)
Type of category error	
Category C	3 (2.48%)
Category D	33 (27.27%)
Category E	31 (25.62%)
Category F	48 (39.67%)
Category G	0
Category H	2 (1.65%)
Category I	4 (3.31%)

Table 3 shows the clinical characteristics at the presentation when the MEs occurred and Table 4 shows the laboratory findings when the MEs occurred. Eighty-three patients received further treatments for MEs that occurred as shown in Table 5.

Intravenous fluid and oxygen supplementation were the most frequently used treatment modalities in our patients. Eleven (13.25%) patients required endotracheal intubation, seven (8.43%) required inotropic drugs/vasopressors, and four (4.82%) required cardiopulmonary resuscitation.

Table 3 Clinical Characteristics of Patients When Medication Errors Occurred

Variables	Frequency (%)
Pulse rate	
Normal	74 (61.16%)
Tachycardia	16 (13.22%)
Bradycardia	5 (4.13%)
Not available	26 (21.49%)
Blood pressure	
Normal	50 (41.32%)
Shock	45 (37.19%)
Not available	26 (21.49%)
Respiratory rate	
Normal	50 (41.32%)
Tachypnea	45 (37.19%)
Not available	26 (21.49%)
Glasgow Coma Scale	
15	10 (8.27%)
< 15	5 (4.13%)
Not available	106 (87.60%)
Oxygen saturation from pulse oximeter	
≥ 95%	44 (36.36%)
< 95%	14 (11.57%)
Not available	63 (52.07%)
Systems involvement (some patients had > 1 system)	
Neurological system*	31
Respiratory system**	15
Gastrointestinal system***	8
Dermatological system****	5
Cardiovascular system*****	4

Notes: *Drowsiness (20 patients), unconsciousness (8 patients), seizure (5 patients), agitation (1 patient), tremor (1 patient), dystonia (1 patient), headache (1 patient). **Dyspnea (8 patients), tachypnea (7 patients), bradypnea (5 patients), apnea (1 patient), desaturation (1 patient). ***Nausea/vomiting (8 patients), abdominal pain (1 patient). ****Phlebitis (5 patients). *****Palpitation (3 patients), chest discomfort (1 patient).

Table 4 Laboratory Results of Patients When Medication Errors Occurred

Variables	Frequency
Serum sodium	
Hyponatremia	7 (5.79%)
Normal	39 (32.23%)
Hypernatremia	1 (0.83%)
Not available	74 (61.16%)
Serum potassium	
Hyponatremia	10 (8.27%)
Normal	33 (27.27%)
Hypernatremia	5 (4.13%)
Not available	73 (60.33%)
Renal function	
Abnormal*	3 (2.48%)
Normal	7 (5.79%)
Not available	111 (91.74%)
Chest X-ray	
Abnormal**	3 (2.48%)
Normal	3 (2.48%)
Not available	115 (95.04%)
Electrocardiogram (EKG)	
Abnormal***	3 (2.48%)
Normal	3 (2.48%)
Not available	115 (95.04%)

Notes: *Acute Kidney Injury. **Pneumonia. ***Sinus Tachycardia.

Table 5 Management of Medication Errors Occurred

Variables	Frequency, N=83
Nasogastric lavage	1 (1.21%)
Activated charcoal administration	3 (3.61%)
Intravenous fluid	32 (38.55%)
Oxygen administration	24 (28.92%)
Intubation	11 (13.25%)
Inotropes administration	7 (8.43%)
Hemodialysis	1 (1.21%)
Cardiopulmonary resuscitation	4 (4.82%)

Four patients with MEs died (Table 6). The other patients survived and were finally discharged home. The four patients who died are described as follows.

The first patient was a 3-year-old boy (Patient 1 in Table 6) with no medical history. He presented to the emergency department with a fever and cough. Initial examination revealed tachycardia with a high-grade fever. His diagnosis was viral croup, and he was treated by nebulized adrenaline. Unfortunately, 1 mg of adrenaline (0.07 mg/kg) was unintentionally injected via an intravenous route. After the intravenous adrenaline administration, he developed marked tachypnea, tachycardia, and agitation. He was intubated, and his chest X-ray showed bilateral infiltration. He thereafter became comatose, developed cardiac arrest, and died approximately 6 hours after the ME occurred.

Table 6 Clinical Characteristics and Laboratory Results of Dead Patients (Category I)

Characteristics	Patient 1	Patient 2	Patient 3	Patient 4
Patient characteristics				
Sex/Age (year)	M, 3	M, 1 day	F, 1	F, 1
Underlying disease	No	No	ASD*	Epilepsy
Body weight (kg)	15	1.1	7	5.5
Hospital type	Private	Government	Government	Government
Location	ER	NICU	PICU	PICU
Work shift	Afternoon	Afternoon	Morning	Morning
Diagnosis	Croup	Apnea of premature	CHF	Seizure
Class of drugs	Cardiology Drug	Antiasthmatic preparation	Anticoagulant	Anticonvulsants
Drugs name	Adrenaline	Aminophylline	Heparin	Phenytoin
Type of MEs**	Wrong route	Wrong dose	Wrong dose	Wrong dose
Symptoms at presentation when MEs occurred**				
GI symptoms (yes/no)				
Nausea/vomiting, Abdominal pain, Diarrhea	No, No, No	No, No, No	No, No, No	No, No, No
Neurologic symptoms (yes/no)				
Alteration of consciousness, Seizure	No, No	Yes, No	No, No	No, Yes
Respiratory symptoms (yes/no)				
Dyspnea, Aspiration	Yes, No	Yes, No	Yes, No	No, No
Systemic effects when MEs occurred**				
Vital signs/Glasgow Coma Scale (GCS)				
BT (°C), HR (/minute), RR (/minute)	36.5, 182, 44	36.0, 200, 68	37.0, 86, 38	36.0, 87, 35
BP (mmHg)	93/58	57/37	43/34	53/16
O2 saturation (%)	90%	88%	69%	95%
GCS	9	8	8	9
Metabolic acidosis (yes/no)	Yes	Yes	Yes	Yes
Na, K, Cl, HCO3, Anion gap (mEq/L)	137, 3, 94, 13, 30	142, 5.3, 103, 13, 26	130, 4, 95, 14, 21	140, 3.3, 110, 14.4, 15.6
Acute kidney injury (yes/no)	No	Yes	No	No
BUN, Cr (mg/dL)	10, 0.7	25, 1.1	12, 0.8	20, 0.33
Treatment (yes/no)				
Oxygen therapy	Yes	Yes	Yes	Yes
Endotracheal intubation	Yes	Yes	Yes	Yes
Intravenous fluid	Yes	Yes	Yes	Yes
Dialysis	No	No	No	No
Cardiopulmonary resuscitation	Yes	Yes	Yes	Yes
Complication during hospitalization (yes/no)	No	No	Yes	No
Hospital stay (hour) after MEs** occurred	6	72	4	22

Notes: *Atrial septal defect. **Medication errors.

The second patient who died was a 1-day-old preterm boy (Patient 2 in Table 6) who was diagnosed with apnea of prematurity. The attending physician prescribed a methylxanthine to stimulate breathing. Aminophylline was injected at 44 mg/kg instead of 8 mg/kg via an intravenous route. He subsequently developed tachycardia with hypotension. High anion gap metabolic acidosis was observed. Bolus injections of intravenous fluid were administered, and norepinephrine was infused to maintain hemodynamic instability. The patient thereafter developed multiorgan failure due to profound shock. The theophylline levels at 3, 12, and 36 hours after the ME occurred were 31.0, 21.7, and 6.13 mcg/mL, respectively. He died 5 days after the ME. The attending physician concluded that the causes of death were sepsis and theophylline overdose.

The third patient who died was a 1-year-old girl (Patient 3 in Table 6) with an atrial septal defect who was hospitalized with congestive heart failure. She was erroneously injected with 600 units of heparin. She developed hemoptysis with dyspnea, and she remained hypotensive despite vigorous resuscitation. Two hours later, her prothrombin time was 95.9 seconds and her international normalized ratio was 7.86; her partial thromboplastin time was unmeasurable. Two milligrams of protamine sulfate were given by very slow intravenous injection. Five hours later, she developed

Table 7 Factors Associated with Medication Errors Causing Harm or Deaths to Patients (Type E-I)

Variables	Category of Errors		P-value*
	C-D N=36	E-I N=85	
Gender			0.157
Male	22 (61.11%)	40 (47.06%)	
Female	14 (38.89%)	45 (52.94%)	
Age (year), median (min-max)	1.6 (4.38 hours-14)	1 (1 hour-14)	0.249
Age group			0.618
Newborn	6 (16.67%)	24 (28.24%)	
Infant	11 (30.56%)	26 (30.59%)	
Toddler	6 (16.67%)	14 (16.47%)	
Preschool	4 (11.11%)	4 (4.71%)	
School	7 (19.44%)	12 (14.12%)	
Adolescent	2 (5.56%)	5 (5.88%)	
Shift of work			0.040
Morning	20 (55.56%)	27 (31.76%)	
Afternoon	12 (33.33%)	48 (56.47%)	
Night	4 (11.11%)	10 (11.77%)	
Type of errors			0.110
Wrong Dose	29 (80.56%)	49 (57.65%)	
Wrong Route	2 (5.56%)	15 (17.65%)	
Wrong Drug	4 (11.11%)	17 (20.00%)	
Wrong Administration	1 (2.78%)	4 (4.71%)	

Notes: *Student's *t*-test/Mann–Whitney *U*-test for continuous variables. Chi-squared analysis and Fisher's exact for categorical variables.

cardiac arrest and resuscitation was initiated. She remained in cardiac arrest for more than 45 minutes. Finally, there was no return of spontaneous circulation. The causes of death were reported as pulmonary hemorrhage, bacterial pneumonia, and congestive heart failure.

The last patient who died was a 1-year-old girl (Patient 4 in Table 6) with underlying epilepsy. She presented to the emergency department with seizures. She was erroneously injected with a 10-times overdose of phenytoin (total of 1100 mg; 200 mg/kg instead of 20 mg/kg) in 1 hour. An hour later, she developed seizures with profound hypotension. Valproic acid and midazolam were given to stop her seizure. She developed cardiac arrest and was resuscitated with aggressive vasopressors including dopamine, dobutamine, and adrenaline. The phenytoin level at approximately 1 hour after the overdose was 72.4 mcg/mL. She died 22 hours after the incorrect dose administration.

To analyze factors associated with MEs that caused harm including deaths (categories E–I), we compared the clinical characteristics between patients with category C and D MEs and those with category E to I MEs, as shown in Table 7. The work shift was the only factor that was significantly different between the two groups of patients. MEs resulting in harm occurred more frequently during the afternoon and night shift than during the morning shift.

Discussion

Increasing medication use results in a higher risk of harm by MEs. MEs are considered to be a worldwide health problem and have been reported in many countries around the world.[1,19–23] However, the different backgrounds of the socio-economic or health care systems among various continents or countries might affect the occurrence or pattern of MEs that occur.

The present study revealed the occurrence of MEs that also included MEs with severe and fatal outcomes among pediatric patients in Thailand. Our findings, which are based on our poison center data, represent the overall epidemiology, clinical effects, and consequences of MEs occurred in every region; medical personnel consulted our poison center after MEs occurred in their patients. The data obtained from our poison center facilitated the characterization of MEs occurring across the health care spectrum and might contribute to pharmacovigilance, especially with respect to the common MEs that occur in Thailand.

Some studies of MEs reported to the poison center showed that most MEs occur in domestic settings or outside health care facilities[7,24] and that they occur more often in pediatric than adult patients.[7,25]

The pediatric population is more susceptible to MEs and complications resulting from MEs because of various factors such as the availability of different dosage forms of the same medication or organ system immaturity.[26,27] Together with, MEs that occur in health care facilities might contribute to harm in patients. Therefore, we focused on and collected data for MEs in pediatric patients that occurred only in hospitals and were caused by medical personnel.

The demographic data of our patients showed that MEs occurred almost equally between both sexes. The occurrence of potential MEs was significantly higher in newborns, infants, and toddlers. Our findings are consistent with those of a pediatric study showing that MEs occurred almost equally in both sexes and that about 66% occurred in newborns, infants, and toddlers.[4] These findings might be explained by the difficult drug dose calculations based on the patient's age, body weight, or body surface area and the drug dilutions or small medication volumes administered, leading to confusion among medical personnel. Thus, children's characteristics of a low body weight and vulnerability might lead them to receive very high doses and resultant toxicity compared with adult patients.[28–30]

Therefore, we emphasized that pediatric patients, especially very small children, are at particularly high risk of MEs, and their safety should be highlighted in all stages of the medication process.

We found that the work shift during which MEs occurred most frequently was the afternoon shift. This finding is consistent with a study in Iran showing that the highest average MEs occurred during the afternoon and night shifts.[31]

The most common classes of drugs reported in our studies were antibiotics, sedatives, and bronchodilators. These findings are consistent with other studies showing that antimicrobials are the most common medications associated with a risk of MEs.[1,32]

Bronchodilators were not commonly reported in other studies.[7,22,32] However, bronchodilators were the third most common drug class reported in our study. Interestingly, most MEs from bronchodilators occurred because of an incorrect route (from nebulizer to intravenous route), and one patient died of adrenaline toxicity (Patient 1, Table 6). Thus, the

drugs in this drug class, especially fenoterol/ipratropium bromide and albuterol, should be emphasized when implementing a safety protocol or system to reduce harm to patients.

We found that a dose error was quite common, this finding was consistent with the other studies' finding.[1,7,23] Almost all of our patients had category D to I MEs; therefore, almost all of them had to be monitored in hospitals longer than the time required for management of the primary disease that caused their hospitalization. These MEs also increased hospital expenses and resulted in fewer unoccupied beds for other patients.

Of the four patients who died in our study, three died because of an incorrect dose. Thus, dose calculations in pediatric patients should be strictly performed, and a system such as a computerized provider order entry (CPOE) system should be used to prevent this type of ME. Electronic entry of medication orders through a CPOE system may reduce errors from poor handwriting or incorrect transcription; such a system may also include other functionalities such as drug dosage support and clinical decision support, which may further reduce errors.[33,34]

One patient died of an intravenous phenytoin overdose and toxicity, with a very high dose of 200 mg/kg. This ME led to a high phenytoin level of 72.4 mcg/mL. One case report of a death caused by phenytoin toxicity described a 35-year-old woman who ingested 100 phenytoin tablets (300 mg each) in a suicide attempt. She presented to the emergency department with alteration of consciousness. On the seventh day, she developed encephalopathy and finally died.[35] To our knowledge, no such fatal pediatric cases have been reported in the English-language literature. Therefore, our study contains the first fatal pediatric case of intravenous phenytoin overdose and toxicity. Phenytoin toxicity by the intravenous route is postulated to cause severe clinical effects due to the diluent of propylene glycol. Propylene glycol is a cardiac depressant, and rapid infusions can lead to bradycardia, hypotension, and asystole.[36]

The factor associated with ME-induced harm in our study was the work shift. The afternoon (or evening) shift caused more ME-induced harm to patients than did other shifts. One study in Thailand showed that the evening and night shifts were associated with a higher risk of both difficulties initiating sleep and early morning awakening; thus, these shifts affect sleep health.[37]

Sleep deprivation can affect cognitive functions and impair many types of performance by reducing the ability to concentrate, slowing reaction time, and reducing the ability to remember and learn new facts and motor skills.[38–40] Therefore, shift work, especially afternoon and night shift work, should be properly managed (eg, by providing adequate medical personnel or using cognitive aids or targeted system redesign to reduce task complexity)[41] to reduce ME-induced harm.

Our findings indicate that MEs that occur in hospitals can cause severe consequences and fatal outcomes in pediatric patients. Therefore, it is necessary to emphasize and increase medical staff's awareness of the significance of MEs and implement safety protocols or systems to deliver the correct medication by the correct route, with the correct dosage form, in the correct dose, to the correct patient, and at the correct time.

Limitations

This study had several limitations. First, it is not mandatory to report MEs to the RPC. Therefore, the true incidence of MEs might have been underestimated, especially in mild cases. In addition, we could not collect data on category A and B MEs, which refer to those errors that occurred but did not affect the patient because the medications had not yet been given; these MEs were therefore not reported to the RPC. Second, because we could not retrieve data on the total prescriptions in each hospital, we could not calculate the rate of MEs per total prescriptions. Third, the retrospective study design may have resulted in missing or incomplete data. Fourth, we could not retrieve information on the MEs that occurred during each processing stage, such as prescribing, to help improve the safety system in each processing stage. Our specialist in poison information or staff might not have asked about these data because they feared that the medical personnel would feel uncomfortable answering for their mistakes. Finally, the small number of total patients and patients with severe outcomes might have limited the statistical analysis. Further larger study is warranted.

Conclusions

According to the data of RPC, we found that most MEs occurred in small children, took place during the afternoon shift and were resulted from an incorrect dose. MEs caused harm and deaths in some patients. One pediatric patient died of an intravenous phenytoin overdose and toxicity from an ME. The factors associated with MEs with harm was the work shift.

The afternoon and night shift were the high-risk shifts, during which MEs with harm occurred more commonly than in the morning shift. A preventive and safety system including appropriate shift work administration should be emphasized and implemented to prevent and/or decrease the occurrence of MEs, especially incorrect dose and route errors with drugs such as bronchodilators. ME reduction strategies should be initiated and implemented in all health care institutions to improve pediatric care management.

Disclosure

The authors report no conflicts of interest in this work.

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