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ARTICLE

Iatrogenic intravenous medication errors reported to the PIC Erfurt

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Background. We investigated the iatrogenic intravenous medication errors (IIME) reported to the Poisons Information Center (PIC) Erfurt. **Methods:** All IIME over a ten year period were analyzed retrospectively and categorized into error types, age groups, drugs involved, and estimated risk of toxicity. **Results.** From 1997 to 2006 the PIC Erfurt registered 132 cases of IIME. They increased from 7 in 1997 to 31 in 2006. Children accounted for 31.1% of the patients affected and adults for 68.9%. The drug classes (ATC classification) involved most frequently were antipsychotics (9.8%) and antihistamines for systemic use (7.5%). The main types of IIME were overdose (53.1%) and incorrect route of administration (29.7%). The estimated risk of toxicity was: 14.4% none, 71.2% risk of toxicity, and 14.4% unpredictable risk. Medical treatment was recommended in 82%. The outcome of 104 of the 132 (78.8%) courses was unknown. In the 28 cases followed to a known outcome, 9 (32%) were asymptomatic and 19 (68%) symptomatic with minor (9 cases), moderate (1 case), and severe features (6 cases) but mostly complete recovery. Two IIME resulted in hypoxia-induced brain damage and one in death despite of resuscitation. **Conclusion.** Approximately 0.1% of all calls registered by the PIC Erfurt from 1997 to 2006 concerned IIME. Thirty-two percent of IIME followed to a known outcome resulted in severe symptoms. These data show that IIME can be harmful.

Keywords Iatrogenic intravenous medication errors; Potassium chloride; Sucralfate; Vancomycin

Introduction

Medication errors can be harmful, especially if they involve the intravenous (IV) route of administration. There have been reports of toxicity and fatalities following errors involving the wrong drug, dose, diluent, or cross contamination errors with intravenous medications (1,2). Recent investigations in British hospitals showed errors in about half of the IV administered drug doses. These errors were evaluated as harmful in about a third of cases (3). In a German non-university hospital one or more errors were observed during preparation and administration of 58 of 122 IV drug doses (4). Previous studies have identified medication errors in preparing and administering intravenous medicines of 13% to 84% in hospitals in several countries (5). By contacting the poisons center immediately on recognition of these events, health care providers may ultimately lessen eventual toxic effects through appropriate intervention (6). However, very few studies have investigated the incidence of iatrogenic intravenous medication errors (IIME) and their outcomes reported to a poisons

information center. Therefore, we analyzed retrospectively the IIME received by the Poisons Information Center (PIC) Erfurt, Germany.

Methods

The PIC Erfurt serves a population of 10.9 million inhabitants in four federal states (Mecklenburg-Western Pomerania, Saxony, Saxony-Anhalt, and Thuringia). All calls regarding iatrogenic intravenous medication errors (IIME) registered by the PIC Erfurt all of 1997 to 2006 were analyzed retrospectively. An IIME was defined as a deviation in preparation or administration of a drug from a doctor's prescription, the hospital's intravenous policy, or the manufacturer's instructions. The clinical appropriateness of the prescription was not assessed. Cases met study criteria when a "therapeutic misadventure" involved a patient within a health care facility or under the care of a licensed health care provider. All cases in which the PIC Erfurt was consulted for treatment following an IIME were included in the study. Data were categorized into error type, patient age groups, drugs involved, and estimated risk of toxicity. Error types involved preparation, dosing, route of administration, administration of the wrong medication, and extravasation of injection. Age groups were: baby (<1 year), toddler (1 to 6 years), schoolchild (6 to 13 years),

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child of unknown age (younger than 14 years), adolescent (14 to 18 years), adult of the mean age group (19 to 65 years), senior (older than 65 years), adult of unknown age (older than 18 years). The IIME outcomes were classified according to the Poisoning Severity Score (7). Estimation of toxicity risk were nontoxic, toxic (severity unknown), minor toxic, moderate toxic, severe toxic, and unpredictable. The drugs involved in IIME were classified according to the Anatomical Therapeutic Chemical (ATC) classification (8,9). The case causality was assessed according to the WHO-UMC system (10).

Results

Frequency, patients, and drugs involved

The PIC Erfurt received 132 cases of IIME from 1997 to 2006. Intravenous administration errors increased from 7 in 1997 to 31 in 2006 (Fig. 1). IIME represented 0.1% of all calls and 10% of all calls concerning medication errors received by the PIC Erfurt during the investigation period.

Approximately 31% of the patients were children (76% of them babies and toddlers) and 69% adults. Among adults, 32% were between 18 and 65 years old and 19% were seniors, but 49% were of unknown age (Fig. 2).

The most commonly involved drug classes are in Table 1 and the substances involved in severe outcomes are in Table 2. Lidocaine (2 cases) and succrulfate (3 cases) were implicated multiple times with severe outcomes.

Types of errors

The main types of errors were overdose (52.3%) and wrong route of administration (29.5%). Other errors were administration of the wrong medication (7.6%), preparation errors (6.1%), and extravasated injections (4.5%) (Fig. 3). Errors in children involved in dosing errors (43%), administration of the wrong medication (39%), incorrect route of administration (15%), and preparation errors (13%). There were extravasations in children (Fig. 3).

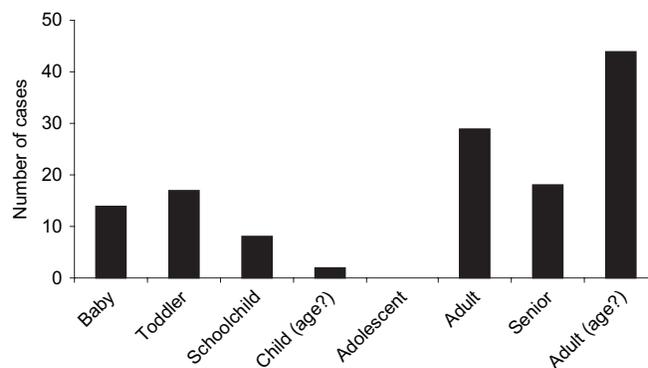


Fig. 2. Age of patients affected by intravenous medication errors registered by the Poisons Information Center Erfurt from 1997 to 2006.

Estimated risk of toxicity

The estimated risk of toxicity was: 14.4% none, 71.2% risk, and 14.4% unpredictable risk. In 16 cases (12.1%) poisoning was estimated to be severe (among them 14 cases of overdose, one case of administration of the wrong medication and one case of incorrect route of administration) (Fig. 4). In one child the risk was estimated to be severe (Table 2).

Medical treatment was recommended in 82% of cases. The outcome of 104 of the 132 (78.8%) courses was unknown. In the 28 cases followed to a known outcome, 9 (32%) were asymptomatic and 19 (68%) symptomatic with minor (9 cases), moderate (1 case with intermittent granulocytopenia), and severe features (6 cases with coma, seizures, respiratory insufficiency or sudden cardiac arrest) but mostly with complete recovery. In two cases sudden cardiac arrest was reported followed by hypoxia-induced brain damage despite of resuscitation (Table 2). In another patient, the erroneous intravenous administration resulted in sudden cardiac arrest and death despite immediate resuscitation (Table 2).

Discussion

From 1997 to 2006 we observed a fourfold increase of IIME reported to the PIC Erfurt. An analysis of the number of publications in PUBMED reporting IIME showed an increase from 16 publications in 1997 to 126 in 2006. The increase of IIME observed by the PIC Erfurt may reflect a growing awareness of the risk of IIME. However, previous studies have identified medication errors in preparing and administering intravenous medicines of 13% to 84% in hospitals in several countries (5). It is estimated that at least 1% to 2% of the patients being involved in medication errors will be adversely affected (4). Therefore, the frequency of all IIME may be higher than that reported by the PIC Erfurt; our data may not be representative but may give an idea about IIME outcomes.

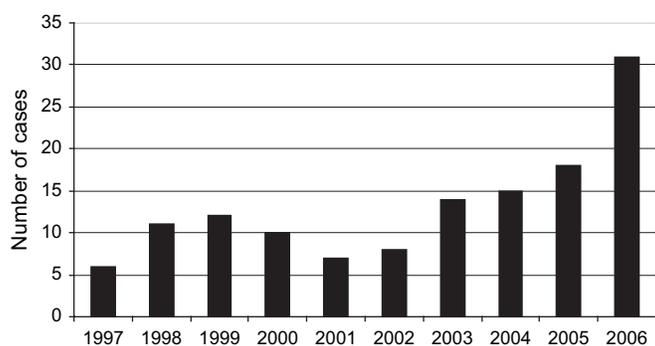


Fig. 1. Frequency of registered intravenous medication errors by the Poisons Information Center Erfurt from 1997 to 2006.

Table 1. Drugs involved most frequently in intravenous medication errors registered by the Poisons Information Center Erfurt from 1997 to 2006

ATC Code	Drug class	Number of medication errors					
		Total	Preparation error	Dosing error	Wrong route of administration	Administration of the wrong medication	Paravenous injection
N05A	antipsychotics	13		4	9		
R06A	antihistamines for systemic use	10		2	8		
L01B	antimetabolites	8		5		1	2
J05A	direct acting antivirals	7		7			
R03D	other systemic drugs for obstructive airway diseases	7	1	5	2		
N01B	local anaesthetics	7		1	4	2	
N02B	other analgetics antipyretics	6		5	1		
D08A	antiseptics and disinfectants	5	1	2	1	1	
R03C	adrenergics for systemic use	5			5		
B01A	antithrombotic agents	4	1	3			
J01F	macrolides, lincosamides and streptogramins	4	1	1	2		
N03A	antiepileptics	4	1	3			

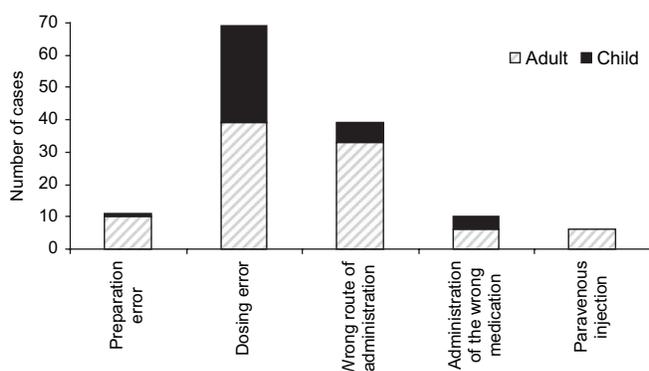


Fig. 3. Types of intravenous medication errors registered by the Poisons Information Center Erfurt from 1997 to 2006.

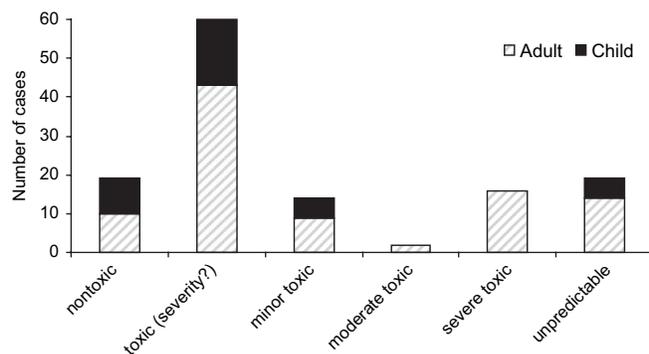


Fig. 4. Estimated risk of toxicity caused by intravenous medication errors registered by the Poisons Information Center Erfurt from 1997 to 2006.

Little information is available in the literature about medication errors reported to a PIC, and even less data can be found on IIME. Ballesteros et al. (11) observed that at least 31.5% of all iatrogenic medication errors received by the Spanish Poison Control Center in Madrid were IIME. The two main error types of IIME were route of administration (53%) and dose (37%). In contrast, the proportion of all cases concerning IIME received by the PIC Erfurt was 20.7% of all iatrogenic medication errors and 0.1% of all calls, with the most frequent errors also route of administration (29.5%) and dose (52.3%). Unfortunately, an estimation of toxicity of IIME was not published in the study by Ballesteros et al. (11). In a previous study, all medication errors reported to the PIC Erfurt from 2000 to 2004 were investigated and the estimated risk of toxicity was: 52% none, 34% risk of toxicity, 13% unpredictable risk, and 1.8% severe risk (12). In our study of IIME, only 14.4% of errors were estimated to be of no risk while 12.1% were severe risk was (Fig. 4). While the frequency of IIME is lower than of other medication errors, the consequences are probably more severe. Ballesteros et al. (11) reported that in 56.2% of intravenous dosing errors the patient was a child younger than two years in a pediatric inpatient setting. The common administered drugs were antimicrobial agents and vaccines (23.9%), neurological agents (17.1%), dermatological agents (16.2%), respiratory agents (9.9%), and antineoplastic agents (4.8%). In our study, 31% of the patients affected in our present study were children (76% of them babies and toddlers) and the drugs most frequently involved were neurological agents (18,9%), respiratory agents (16.7%), antimicrobial agents and vaccines (8.3%), antineoplastic agents (6.1%), and dermatological agents (3.8%). Of the nine patients severely affected by IIME eight were adults and one was a 5-year-old boy.

Table 2. Iatrogenic intravenous medication errors with severe outcome registered by the Poisons Information Center Erfurt from 1997 to 2006

Case number	Administered substance	Type of IIME	Patient	Symptoms	Treatment and outcome, causality assessment
1	5 mL sucralfate IV instead of PO	wrong route of administration	adult, age unknown	tachycardia, respiratory insufficiency	intubation and ventilation, administration of deferoxamine because of aluminium overdose, recovered completely, causality: probable
2	less than 5 mL sucralfate IV instead of PO	wrong route of administration	80-year-old woman	respiratory insufficiency, dermal rash	intubation and ventilation, recovered completely, causality: probable
3	1000 mg lidocaine IV instead of 100 mg IV because of VES	overdose	68-year-old woman	seizure one minute after administration	cardiac massage, intubation and ventilation, stimulation by percutaneous pace maker, causality: possible
4	15 mg midazolam IV in case of suspected amphetamine overdose	overdose	32-year-old woman	coma	monitoring of respiratory and cardiac function, administration of flumazenil, recovered totally, causality: probable
5	50 mg chlorpromazine IV because of vomiting during chemotherapy	overdose	5-year-old boy	coma, seizure	monitoring of respiratory and cardiac function, diazepam, the following day somnolent, differential diagnosis was not finished at that time, causality: possible
6	250 mg vancomycin IV	possibly overdose, possibly to fast injection	man, age unknown	asystolia, renal insufficiency	resuscitation, severe hypoxia-induced brain damage, causality: possible
7	35 mL potassium chloride 7.5% peridurally instead of IV	wrong route of administration	55-year-old woman	1.5 h after application paresthesia of the legs, after 2.5 h reduction of vigilance, paraplegia, after 3.5 h respiratory insufficiency, hypertonus, tachycardia, sweating, mydriasis	monitoring of respiratory and cardiac function, intubation and ventilation, peridural infusion of sodium chloride 0.9% 50 mL/h over 5 h. After 4 h increase of muscle tonus, after 11 h no neurological symptoms, causality: probable
8	1000 mg lidocaine IV during resuscitation	overdose	woman, age unknown	coma	monitoring of respiratory and cardiac function, comatous 18 h after administration, hypoxia-induced brain damage suspected, causality: probable
9	unknown dose of sucralfate IV instead of PO	wrong route of administration	man, age unknown	cardiac arrest	resuscitation over 45 min, death, causality: probable

Independent of the drug administered, IIME may result in thrombus formation, hypersensitivity reaction, or infection. Injection of substances with low water solubility can result in pulmonary microembolism with reactive asystole. The substances that resulted in severe outcome in our study (chlorpromazine, midazolam, potassium chloride, vancomycin, lidocaine, sucralfate) were not necessarily the most frequent drugs of IIME.

Cases of erroneous epi- or peridural administration of potassium chloride have been reported (13,14). In our case number 7, a 55-year-old woman received 35 mL potassium chloride 7.5% peridurally instead of intravenously. Ninety

minutes after administration paresthesia of the legs started. After 2.5 hours a reduction of vigilance and paraplegia were observed. After 3.5 hours, respiratory insufficiency, hypertonus, tachycardia, sweating, and mydriasis occurred. Intubation and ventilation were necessary. The patient was given a peridural infusion of sodium chloride 0.9% 50 mL/h over 5 hours. Four hours after the start of the infusion the muscle tonus increased and after 11 hours no neurological symptoms were detectable. The causality was assessed as probable.

Cardiopulmonary arrest occurred in a 57-year-old diabetic woman undergoing peritoneal dialysis following vancomycin 1 g IV bolus over 2 minutes for the treatment of enterococcal

peritonitis. The authors suggested that rapid IV infusion of vancomycin could result in neuromuscular blockade or ventricular dysrhythmias (15). In our case number 6, the IV administration of 250 mg vancomycin in a man resulted in asystole and renal insufficiency. Despite resuscitation, severe hypoxia-induced brain damage developed. The causality was assessed as possible.

Sucralfate, used for treatment and prophylaxis of gastric and duodenal ulcers, should not be administered intravenously because of its low water solubility. No cases of sucralfate IIME have been reported in the literature. The PIC Erfurt had three cases of IV administration of sucralfate in adults (case number 1,2,9). In all three cases cardiac and respiratory insufficiency required resuscitation shortly after IV administration of sucralfate. In two cases patients recovered totally after resuscitation. One patient died despite 45 minutes of resuscitation. We postulate that the IV toxicity of sucralfate might be related to the formation of insoluble microemboli with obstruction of small pulmonary vessels resulting in reactive cardiac depression or asystole. In all three cases the causality was assessed as probable.

In our present study, 32% of IIME followed to a known outcome resulted in severe symptoms. These data show that IIME can be harmful. In literature, there is little information about sequelae and treatment of IIME of individual substances. A PIC may play an important role in accumulating knowledge for treatment of IIME. Collection and publication of IIME and their treatment by a PIC could enhance the awareness of IIME and may improve their outcome. A PIC can be utilized not only after the exposure has occurred, but also for prevention through formal and informal educational programs and possible evaluation of potential environmental and therapeutics toxicities.

Limitations

Our study had several limitations. The main limitation was that only 21.2% of cases (or courses) were followed to a known outcome. One explanation for the small proportion of cases followed to a known outcome is that an IIME is a delicate issue. Many callers felt guilty, nervous, and worried about the error and feared for the safety of the patient and possible disciplinary action. Therefore, we did not insist on the caller giving us non-voluntary information. Another explanation for the small number of cases followed to a known outcome is that the present study is retrospective and the data were not intended to be included into a study at the time of receiving them. Another limitation of our study is the small proportion of IIME reported to our PIC compared to IIME in hospitals. We assume that a PIC may be more likely

contacted in severe cases of IIME to lessen eventual harmful effects so that there is a bias to more severe cases in our study.

Conclusions

Approximately 0.1% of all calls registered by the PIC Erfurt from 1997 to 2006 concerned IIME. Thirty-two percent of IIME followed to a known outcome resulted in severe symptoms. These data show that IIME can be harmful. In literature, there is little information about sequelae and treatment of IIME of individual substances. A PIC may play an important role in accumulating knowledge for treatment of IIME.

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