https://doi.org/10.22491/2357-9730.120920

Potential medication incompatibilities in pediatric oncology prescriptions

Maitê Telles dos Santos[1], Bruno Simas da Rocha[2], Gabriela Wunsch Lopes[3], Débora Kempf da Silva[3], Giovanna Webster Negretto[2], Lauro José Gregianin[1]

Clin Biomed Res. 2022;42(4):334-341

1 Programa de Pós-Graduação em Saúde da Criança e do Adolescente, Faculdade de Medicina, Universidade Federal do Rio Grande do Sul. Porto Alegre, RS, Brasil.

2 Seção de Farmácia Clínica, Hospital de Clínicas de Porto Alegre. Porto Alegre, RS, Brasil.

3 Faculdade de Medicina, Universidade Federal do Rio Grande do Sul. Porto Alegre, RS, Brasil.

Corresponding author:
Maitê Telles dos Santos
maitetelles@gmail.com
Programa de Pós-Graduação em Saúde da Criança e do Adolescente, Faculdade de Medicina, Universidade Federal do Rio Grande do Sul
Rua Ramiro Barcelos, 2350, Sala 935
90035-903, Porto Alegre, RS, Brasil.

ABSTRACT

Introduction: Pediatric oncology patients have a limited number of venous access routes and need a large number of drugs during hospitalization. This study evaluates potential medication incompatibilities (MI) in pediatric oncology prescriptions and identifies possible factors associated with the risk of their occurrence.

Methods: This cross-sectional study evaluated prescriptions from a tertiary universitary hospital from December 2014 to December 2015. The association between variables and the risk of potential incompatibilities between drugs was determined by Student's t-test and Pearson's chi-square, considering $p < 0.05$ significant. The odds ratio was calculated considering a 95% confidence interval for each drug.

Results: 385 prescriptions were evaluated. The mean age of 124 patients was 9.22 years old (SD = ± 5.10), and 50.65% were male. The most frequent diagnosis and reason for hospitalization were leukemia (27.30%) and chemotherapy (36.10%). The totally implantable catheter was the most commonly used venous access (61.30%). In 87.5% of prescriptions, there was the possibility of MI, and 2108 incompatibilities were found, considering 300 different combinations between two drugs. Age, diagnosis, reason for hospitalization, and type of venous access were risk factors for potential incompatibilities ($p < 0.05$). The following drugs present higher risk of potential incompatibilities: leucovorin, sodium bicarbonate, cefepime, diphenhydramine, dimenhydrinate, hydrocortisone, and ondansetron, with a significant odds ratio.

Conclusion: The possibility of MI in prescriptions for pediatric oncology patients is frequent. Thus, the identification of risk factors may contribute to patient safety and to the rational use of drugs.

Keywords: *Drug incompatibility; oncology service; intravenous infusions; pediatric; patient*

INTRODUCTION

Cancer in children and adolescents from 0 to 19 years old represents a group of diseases with particular characteristics that are related to histopathological profiles and clinical manifestations. It is considered a rare disease and represents 1 to 4% of malignant tumors, with short periods of latency and more aggressive manifestations. However, it has a better response to treatments and, generally, has a good prognosis[1].

Cancer treatment in children and adolescents includes different modalities, from systemic to diagnostic, according to histological type, local extension, and region. This disease can be treated with surgery, radiotherapy, and/or systemic treatment, such as chemotherapy (monotherapy or drug association), according to national and international guidelines[2].

Antineoplastic drugs are used in almost all treatments, but the undesirable effects of chemotherapy include a potential acute and late toxicity, as well as the possibility of medication interactions and drug incompatibilities. In these situations, dose reduction or even medication discontinuation should be

ISSN 2357-9730

considered, in order to limit the antineoplastic effect that impairs patient survival[2].

Medication incompatibilities (MI) are physical or chemical reactions that occur between two or more drugs in vitro (before intravenous administration) when associated in the same syringe, vial, or bag[3,4]. Physical reactions are commonly visible, with precipitate formation, color change, or gas production. However, the identification of chemical reactions requires analytical techniques that show significant loss of active components during the drug mixing process[5].

The consequences of MI can result in a reduction of the efficacy and safety of drug therapy, drug inactivation, the formation of a new innocuous or toxic active component, and in organoleptic changes in color, consistency, turbidity, as well as precipitation and crystal formation[4]. There are reports of fatal pulmonary embolism related to drug incompatibility and mechanical failure of venous catheters[5-7].

MI should be even more considered in the pediatric population, since this group has a limited number of venous access routes, such as the totally implantable catheter (Port-a-Cath), which has only one route for drug administration. Moreover, this population needs a relatively large number of drugs, in addition to water supply via the catheter[8-10].

Clinical pharmacists working on oncology wards play an important role on a multiprofessional team, with their knowledge, experience, and abilities concerning cancer patient care[11]. Among the activities that can be developed by clinical pharmacists in oncology with the focus on patient safety, we highlight the evaluation of drug incompatibilities, aiming at the rational use of drugs[12].

Based on this context, this study aims to evaluate the potential medication incompatibilities within a pediatric oncology unit and identify possible risk factors for their occurrence.

METHODS

Type of study

Cross-sectional study at the Pediatric Oncology Unit of a tertiary university hospital in Southern Brazil.

Population and sample

In order to calculate the sample size, a 50% prevalence (considering the worst-case scenario due to the lack of data about the prevalence of MI on medical prescriptions for pediatric oncology patients), 5% precision, and 95% confidence level were used. Retrospectively, 385 medical prescriptions were selected from patients aged 0 to 17 years and 11 months old admitted to the Pediatric Oncology Unit from December 2014 to December 2015.

Inclusion and exclusion criteria

The prescription chosen for analysis was related to the third day of hospitalization of patients with at least two intravenous drugs prescribed. It is important to consider that in the first and second day of hospitalization, there may be no intravenous drugs prescribed. The drug metamizole was not analyzed, since its use is not authorized in some countries, thus, it did not appear in the database used in this study to evaluate MI.

Data collection

Medical prescriptions were accessed via the hospital's electronic medical records system. A data collection form was used for the following information: patient's age and sex; reason for admission; type of venous access; number of venous access routes; oncological diagnosis described on the medical records system; number of intravenous drugs prescribed; number of intravenous drugs prescribed as "fixed" and "symptomatic"; total number of drug crossings per prescription; number of compatibilities, variable incompatibilities, untested incompatibilities, physical incompatibilities, and chemical incompatibilities; and the existence of total parenteral nutrition (TPN). MI were evaluated using the Drugdex database (Thomson Micromedex), accessed by the *Periódicos Capes* website[13]. Notably, it was not possible to observe if there was incompatibility; we can only evaluate the potentiality of its occurrence during prescription analysis.

Statistical analysis

The data were entered in Microsoft Office Excel and analyzed using the SPSS 20.0 program. The equality of proportions of categorical variables was analyzed by Pearson's chi-square test (with continuity correction for 2×2 tables) and the comparisons of averages of continuous numerical variables were performed using Student's t test. The odds ratio was calculated with a 95% confidence interval for each drug with a statistically significant difference in the chi-square test for differences between proportions. The age-adjusted odds ratio was also calculated. Statistical tests were performed considering a significance level of $\alpha = 0.05$.

Ethical aspects

The study was approved by the Research Ethics Committee of the Hospital de Clínicas de Porto Alegre (no. 15-0583).

RESULTS

A total of 385 prescriptions from 124 patients were analyzed during the study. The average age of patients was 9.22 years old (standard deviation [SD] = 5.10), and 50.65% were male. Leukemia was the most frequent disease, representing 27.30%

of cases, followed by osteosarcoma (18.20%), lymphoma (9.90%), retinoblastoma (6.75%), Ewing and synovial sarcoma (5.72%), rhabdomyosarcoma (5.45%), Wilms tumor (3.11%), medulloblastoma (2.33%), neuroblastoma (2.33%), and spindle cell tumor (2.07%), and in 9.90% of cases, no cancer diagnosis was yet defined at the time of data collection (Table 1).

Table 1: Risk factors for potential medication incompatibilities (n = 385).

Characteristic	Prescriptions with MI = 337 (87.5%) n (%)	Prescriptions without MI = 48 (12.5%) n (%)	p-value*	Total of prescriptions = 385 n (%)
Age (years)				
Mean	9.49	7.32	0.006	9.22
Standard deviation	4.97	5.60		5.10
Gender			0.923	
Female	166 (49.3)	24 (50.0)		190 (49.35)
Male	171 (50.7)	24 (50.0)		195 (50.65)
Diagnosis			< 0.001	
Leukemia	98 (29.0)	7 (14.6)		105 (27.30)
Osteosarcoma	69 (20.5)	1 (2.1)		70 (18.20)
Lymphoma	36 (10.7)	2 (4.2)		38 (9.90)
Retinoblastoma	19 (5.6)	7 (14.6)		26 (6.75)
Sarcoma (Ewing/synovial)	16 (4.7)	6 (12.5)		22 (5.72)
Rhabdomyosarcoma	19 (5.6)	2 (4.2)		21 (5.45)
Wilms tumor	10 (2.9)	2 (4.2)		12 (3.11)
Medulloblastoma	8 (2.4)	1 (2.1)		9 (2.33)
Neuroblastoma	7 (2.1)	2 (4.2)		9 (2.33)
Spindle cell tumor	3 (0.9)	5 (10.4)		8 (2.07)
Hepatocellular carcinoma	7 (2.1)	0 (0.0)		7 (1.81)
Primitive neuroectodermal tumor	4 (1.2)	2 (4.2)		6 (1.55)
Adrenoleukodystrophy	3 (0.9)	1 (2.1)		4 (1.03)
Neurofibromatosis	0 (0.0)	3 (6.2)		3 (0.77)
Sacrococcygeal tumor	3 (0.9)	0 (0.0)		3 (0.77)
Astrocytoma	2 (0.6)	0 (0.0)		2 (0.51)
Ganglioneuroma	1 (0.3)	0 (0.0)		1 (0.25)
Hemangioma	0 (0.0)	1 (2.1)		1 (0.25)
Undefined oncological diagnosis	31 (9.2)	7 (14.6)		38 (9.90)
Reason for hospitalization			< 0.001	
Chemotherapy cycle	136 (40.3)	3 (6.2)		139 (36.10)
Fever and infections	54 (16.0)	5 (10.4)		59 (15.32)
Surgery/catheter	45 (13.3)	13 (27.1)		58 (15.06)
Diagnostic research	31 (9.2)	7 (14.6)		38 (9.87)
Conducting exams	26 (7.7)	6 (12.5)		32 (8.31)
Pain management	7 (2.1)	3 (6.2)		10 (2.60)
Diarrhea/vomit management	7 (2.1)	4 (8.3)		11 (2.86)
Transplants	9 (2.7)	0 (0.0)		9 (2.34)
Cell collection for transplant	3 (0.9)	3 (6.2)		6 (1.56)
Thrombocytopenia	5 (1.5)	0 (0.0)		5 (1.30)
Other	14 (4.1)	4 (8.3)		18 (4.68)
Type of venous access			0.004	
Fully implantable catheter (Port-a-Cath)	207 (61.4)	29 (60.4)		236 (61.32)
Peripherally inserted central catheter (PICC)	60 (17.8)	2 (4.2)		62 (16.10)
Peripheral venous catheter	44 (13.0)	15 (31.2)		59 (15.32)
Double-lumen tube	17 (5.0)	2 (4.2)		19 (4.93)
Hickmann line	9 (2.7)	0 (0.0)		9 (2.33)
Number of venous access routes			0.376	
One route	311 (92.3)	46 (95.8)		357 (92.73)
Two routes	26 (7.7)	2 (4.2)		28 (7.27)
Total parenteral nutrition prescription			0.593	
Yes	2 (0.6)	0 (0.0)		2 (0.52)
No	335 (99.4)	48 (100)		383 (99.48)

* Student's t-test for numerical variables and Pearson's chi-square test for categorical variables. MI: Medication incompatibilities; SD: Standard deviation.

The most frequent reason for hospitalization was the need of chemotherapy (36.10%), followed by fever and infections (15.32%), the need to undergo surgery, including the insertion of catheters (15.06%), diagnostic research (9.87%), exams (8.31%), hematopoietic stem cell transplantation (2.34%), diarrhea and/or vomiting (2.86%), pain management (2.60%), and others.

Regarding the type of venous access, the totally implantable catheter (Port-a-Cath) was used in 61.30% of cases, followed by the peripherally inserted central catheter (PICC) (16.10%), the peripheral venous catheter (15.32%), the double-lumen tube (4.93%), and the Hickmann line (2.33%). In 92.73% of cases, the venous access used had only one lumen (one access route), while 7.27% had two routes. Only 0.52% of cases had a TPN prescription.

Table 1 shows that age, diagnosis, the reason for hospital admission, and the type of venous access were risk factors for potential MI, since they presented a statistically significant difference in the chi-square test for the proportions and Student's t-test.

In 87.5% of the prescriptions evaluated, there was the possibility of occurrence of at least one MI. A total of 2108 drug incompatibilities were evaluated, of which 300 different incompatibilities were between two drugs. Table 2 shows the prevalence of the main incompatibilities, as well as the types of MI found.

Table 2: Prevalence of the main MI between two intravenous drugs and types of incompatibilities (n = 385).

Drug A	Drug B	MI type	n prescriptions (%)	
Dimenhydrinate	Ondansetron	Untested*	251	(65.19)
Diphenhydramine	Dimenhydrinate	Untested*	184	(47.79)
Dimenhydrinate	Potassium chloride 10% + sodium chloride 20% + glucose solution	Physical	130	(33.77)
Sodium bicarbonate	Dimenhydrinate	Physical	63	(16.36)
Diphenhydramine	Hydrocortisone	Variable	63	(16.36)
Leucovorin	Sodium bicarbonate	Physical	62	(16.10)
Sodium bicarbonate	Ondansetron	Physical	61	(15.84)
Leucovorin	Dimenhydrinate	Untested*	58	(15.06)
Cefepime	Ondansetron	Physical	55	(14.29)
Sodium bicarbonate	Diphenhydramine	Physical	47	(12.21)
Cefepime	Potassium chloride 10% + sodium chloride 20% + glucose solution	Untested*	45	(11.69)
Dexamethasone	Diphenhydramine	Physical	44	(11.43)
Cefepime	Dimenhydrinate	Untested*	40	(10.39)
Dimenhydrinate	Mesna	Untested*	40	(10.39)
Dimenhydrinate	Morphine	Untested*	33	(8.57)
Cefepime	Diphenhydramine	Physical	32	(8.31)
Dimenhydrinate	Ranitidine	Untested*	26	(6.75)
Dimenhydrinate	Furosemide	Physical	25	(6.49)
Furosemide	Ondansetron	Physical	22	(5.71)
Dimenhydrinate	Etoposide	Untested*	22	(5.71)
Diphenhydramine	Furosemide	Physical	21	(5.45)
Dimenhydrinate	Doxorubicin	Untested*	21	(5.45)
Cefepime	Morphine	Variable	18	(4.68)
Dimenhydrinate	Ifosfamide	Untested*	18	(4.68)
Cytarabine	Dimenhydrinate	Untested*	16	(4.16)
Dimenhydrinate	Methotrexate	Untested*	16	(4.16)
Acyclovir	Ondansetron	Physical	14	(3.64)
Dimenhydrinate	Potassium chloride 10% + sodium chloride 20% + magnesium sulfate + glucose solution	Physical	14	(3.64)
Dexamethasone	Calcium gluconate	Variable	14	(3.64)

* Untested: the association was not tested in laboratory yet. MI: Medication incompatibilities.

Considering the variables related to incompatibilities, the mean of the total number of drugs, of both "fixed" and "symptomatic" drugs, the total number of drug crossings, and total compatibilities were higher in prescriptions with MI. The difference between the means were statistically significant (Table 3).

Table 3: Variables related to MI (n = 385).

Variables	Total = 385 Mean (SD)	With MI = 337 Mean (SD)	Without MI = 48 Mean (SD)	p-value*
Total drugs	5.28 (2.27)	5.63 (2.15)	2.81 (1.28)	< 0.001
"Fixed" drugs	3.09 (2.26)	3.32 (2.27)	1.46 (1.33)	< 0.001
"Symptomatic" drugs	2.19 (1.47)	2.31 (1.48)	1.35 (0.97)	< 0.001
Drug crossing	13.84 (12.59)	15.33 (12.66)	3.38 (4.64)	< 0.001
Compatibilities per prescription	8.32 (8.92)	9.03 (9.16)	3.35 (4.65)	< 0.001
Types of incompatibilities per prescription				
Untested	3.01 (3.00)	3.69 (3.08)	0 (0.00)	NA**
Variable	0.33 (0.47)	0.37 (0.48)	0 (0.00)	NA**
Physical	1.98 (1.99)	2.26 (1.97)	0 (0.00)	NA**
Chemical	0 (0.00)	0 (0.00)	0 (0.00)	NA**

* Student's t-test for numerical variables; ** NA: not applicable; in prescriptions without MI, no type of incompatibility is expected. MI: Medication incompatibilities; SD: Standard deviation.

For drugs with a statistically significant difference in the chi-square test for proportions, the odds ratio was calculated in order to confirm the risk of incompatibilities of these drugs individually. Leucovorin, sodium bicarbonate, cefepime, diphenhydramine, dimenhydrinate, hydrocortisone, and ondansetron were drugs with higher risk of potential MI (Table 4).

Table 4: Drugs prescribed and the risk of potential MI (n = 385).

Drugs	Total n (%)	With MI n (%)	Without MI n (%)	p-value[a]	OR	95%CI	p-value[b]
Leucovorin	64 (16.62)	64 (19.0)	0 (0.0)	0.001	22.87	1.39–375.90	0.028*
Sodium bicarbonate	67 (17.40)	67 (19.9)	0 (0.0)	0.001	23.42	1.42–384.75	0.027*
Cefepime	64 (16.62)	64 (19.0)	0 (0.0)	0.001	22.87	1.39–375.91	0.028*
Dexamethasone	75 (19.50)	71 (21.1)	4 (8.3)	0.037	2.75	1.06–9.38	0.062†
Diphenhydramine	216 (56.10)	206 (61.1)	10 (20.8)	< 0.001	5.41	2.68–11.89	< 0.001*†
Dimenhydrinate	286 (74.30)	285 (84.6)	1 (2.1)	< 0.001	244.57	51.59–4378.65	< 0.001*†
Furosemide	27 (7.01)	27 (8.0)	0 (0.0)	0.042	8.59	0.5–143.16	0.134
Hydrocortisone	66 (17.14)	66 (19.6)	0 (0.0)	0.001	23.75	1.44–390.30	0.026*
Ondansetron	323 (83.89)	288 (85.4)	35 (73.0)	0.027	2.37	1.12–4.78	0.019*†

[a] p-value in the chi-square test; [b] p-value in the odds ratio calculated by the chi-square test; * significant odds ratio; † Calculated and age-adjusted odds ratio. It was not possible to adjust for the other drugs due to the distribution of variables between groups. MI: Medication incompatibility; OR: Odds ratio; 95%CI: 95% confidence interval.

DISCUSSION

This study was developed to identify possible MI in pediatric oncology prescriptions and, thus, highlight issues related to safety in the administration of intravenous drugs. It is important to emphasize that there are few studies about MI, especially in pediatrics. To our knowledge, this is the first study to address MI in pediatric oncology. The identification of possible risk factors for the occurrence of MI may help clinical pharmacists in pediatric oncology.

The epidemiological data of the population involved in this study coincide with national statistics for this age group, with predominance of leukemia (27.30% of cases), followed by osteosarcoma (18.20%), and lymphomas (9.90%). The higher prevalence in male is also in line with Brazilian data[1].

The reasons for hospital admission are similar to another study performed in a pediatric oncology unit, in which chemotherapy was the main cause of hospitalization (36.10% vs. 67.5%), followed by complications related to the treatment, such as fever and infections (15.32% vs. 24.8%)[14]. The reasons for hospitalization were risk factors for the occurrence of MI, proving to be an important information for clinical pharmacists to analyze the MI, when prioritizing prescriptions for patients. Hospitalizations for chemotherapy and the management of complications require the use of intravenous drugs and, therefore, MI should be a concern in this group of patients.

The most frequent type of venous access in our study was the totally implantable catheter (Port-a-Cath), which was used in 61.32% of cases. This long-term central venous access is commonly used in oncology due to its comfort, as it avoids frequent venipunctures, especially in patients that need long-term treatments[15]. In 61.4% of prescriptions for patients with Port-a-Cath, the possibility of MI was

identified. A study published in 2014 showed that MI represented the major problem related to intravenous drug administration in patients in a general hospital. The authors also observed that patients with central access had more incompatibilities than patients with peripheral access[16].

TPN prescriptions occurred in only 0.52% of cases. The frequency of TPN was small due to its indication only for situations with impossibility of using oral or enteral routes in medium- and long-term periods. Moreover, the objective of using TPN is to offer favorable conditions for the therapeutic plan, maintaining the patient's vital functions[17]. Our study analyzed only the medical prescription from the third day of hospitalization, when the indication of TPN is uncommon.

We observed the possibility of the occurrence of MI in 87.5% of the prescriptions analyzed. As expected, the number of drugs in medical prescriptions with MI was significantly higher when compared with prescriptions without MI (a mean of 5.63 vs. 2.81 drugs per prescription), being a risk factor for the occurrence of MI. This data is similar to a study conducted in a Pediatric Intensive Care Unit, which showed that the number of drugs prescribed (>3 drugs) was a risk factor for MI[18].

MI are classified into four categories. They are "untested" when there is no data in the literature on the combination of two certain drugs. In these situations, it is recommended, for safety reasons, for them to not be administered concomitantly. MI are "variable" when the compatibility between two drugs depends on the type of diluent used and/or the concentration of drugs. Finally, they are "physical" and "chemical" when the incompatibility leads to a physical or chemical reaction, respectively[12]. In this study, the number of "untested" incompatibilities was higher compared with other categories, with an average of 3.69 incompatibilities per prescription. This is similar to the study performed in 2016 by Leal et al., in which they also observed a higher prevalence of "untested" incompatibilities[18].

The main possibility of incompatibility identified was between two antiemetics, dimenhydrinate and ondansetron, found in 65.19% of prescriptions. This high prevalence occurs because antiemetics are commonly prescribed for patients undergoing chemotherapy, as described in other studies[19,20], since nausea and vomiting are frequent and debilitating adverse effects directly causing a meaningful impact in patients' quality of life[20]. Antiemetics are advisable from the first treatment cycle and are also used as prophylaxis for anticipatory vomiting in other stages of treatment[21]. Another frequent incompatibility occurred between dimenhydrinate and a solution of potassium chloride 10% + sodium chloride 20% + glucose (33.77% of medical prescriptions). This solution is often prescribed for pediatric patients, for water replacement and/or maintenance and is used to maintain patients' body homeostasis while fasting, offering the necessary amount of water and electrolytes to restore the losses due to physiological processes, such as diuresis, sweating, bowel movements, and respiration[22].

The presence of leucovorin, sodium bicarbonate, cefepime, diphenhydramine, dimenhydrinate, hydrocortisone, and ondansetron in medical prescriptions allowed the occurrence of possible MI, characterizing these drugs with a higher risk for potential MI.

The presence of ondansetron, dimenhydrinate, and diphenhydramine can be explained by the fact that they were the most frequently prescribed drugs (83.89%, 74.30%, and 56.10%, respectively), despite being considered incompatible with each other. Similarly, the solution 10% potassium chloride + 20% sodium chloride + glucose was frequently prescribed (51.94% of prescriptions), despite being incompatible with dimenhydrinate, another frequently prescribed drug.

Leucovorin and sodium bicarbonate were drugs with higher risk for MI. These drugs are incompatible with each other and are part of the treatment for osteosarcoma[23], the second most frequent disease in the population of this study (18.20% of cases). Leucovorin is used as an antidote to methotrexate, which blocks the conversion of folic acid to tetrahydrofolate by binding to the enzyme dihydrofolate reductase, and is indicated after 24 hours of the infusion of methotrexate. Sodium bicarbonate is used for urine alkalinization, facilitating the excretion of methotrexate[23].

Cefepime was observed in 16.62% of medical prescriptions and presented a higher risk for MI. The use of cefepime in pediatric oncology is recommended in cases of febrile neutropenia, which is a frequent complication due to periods of spinal immunosuppression after chemotherapy[24,25].

MI requires attention from all professionals involved in patient care. Clinical pharmacists can contribute to the prevention of MI through the use of some strategies[17]. Some tools that can be adopted are standard operating procedures with specific guidelines for medication administration, analysis of prescriptions informing potential MI via a drug compatibility charts, and nursing training in the preparation and administration of drugs[18,26-30].

It is important to reinforce the interaction of clinical pharmacists with the nursing team regarding IM since knowledge about compatibility varies depending on the professional and inpatient unit[31]. Medication errors related to medication administration are frequent[32]. Mendes et al. showed that, among medication errors, in cases of concomitant administration, only 17.86% were compatible[32]. Specific nursing education interventions should be planned, including the use of applications for smartphones[33].

This study had some limiting factors, mainly due to its retrospective design. The main limitation was

the fact that the analysis was restricted to drugs in medical prescriptions. Thus, it was not observed whether these drugs were actually administered concomitantly, causing MI. The cross-sectional design and the non-inclusion of metamizole in the analyses, due to its absence in the database were other limitations of the study. Further research is needed to better understand the problems related to MI, especially laboratory studies to evaluate MI that are currently considered "untested."

This study showed that the possibility of the occurrence of MI is frequent in intravenous drug administration in pediatric oncology and should be the focus of attention of professionals in safety of drug use.

Conflicts of interest

None.

REFERENCES

1. Instituto Nacional de Câncer José Alencar Gomes da Silva (BR). *Estimativa 2020*: incidência de câncer no Brasil. Rio de Janeiro: Inca; 2019.
2. Greene RJ, Harris ND. Doenças neoplásicas. In: Greene RJ, Harris ND. *Patologia e terapêuticas para farmacêuticos*: bases para a prática da farmácia clínica. 3rd ed. Porto Alegre: Artmed; 2012. p. 638-93.
3. Taxis K, Barber N. Ethnographic study of incidence and severity of intravenous drug errors. *BMJ*. 2003;326(7391):684.
4. Trissel LA. *Handbook on injectable drugs*. 17th ed. Bethesda: American Society of Health-System Pharmacists; 2012.
5. Kanji S, Lam J, Johanson C, Singh A, Goddard R, Fairbairn J, et al. Systematic review of physical and chemical compatibility of commonly used medications administered by continuous infusion in intensive care units. *Crit Care Med*. 2010;38(9):1890-8.
6. Benlabed M, Perez M, Gaudy R, Genay S, Lannoy D, Barthélémy C, et al. Clinical implications of intravenous drug incompatibilities in critically ill patients. *Anaesth Crit Care Pain Med*. 2019;38(2):173-80.
7. Taniguchi T, Yamamoto K, Kobayashi T. Precipitate formed by thiopentone and vecuronium causes pulmonary embolism. *Can J Anaesth*. 1998;45(4):347-51.
8. Zenk KE. Intravenous drug delivery in infants with limited IV access and fluid restriction. *Am J Hosp Pharm*. 1987;44(11):2542-5.
9. Gaetani M, Frndova H, Seto W, Parshuram C. Concurrent intravenous drug administration to critically ill children: evaluation of frequency and compatibility. *J Crit Care*. 2017;41:198-203.
10. Santeiro ML, Stromquist C, Coppola L. Guidelines for continuous infusion medications in the neonatal intensive care unit. *Ann Pharmacother*. 1992;26(5):671-4.
11. Pendleton M. Recommended adult immunization schedule: 2013 updates. *Hopa News* [Internet]. 2014 [cited 2017 Nov 20];11(2):3. Available from: www.hoparx.org/uploads/files/2013/HOPA13_ScopeofPracticeBk.pdf
12. Maison O, Tardy C, Cabelguenne D, Parat S, Ducastelle S, Piriou V, et al. Drug incompatibilities in intravenous therapy: evaluation and proposition of preventive tools in intensive care and hematology units. *Eur J Clin Pharmacol*. 2019;75(2):179-87.
13. Micromedex Solutions® Healthcare Series of Database, versão 2.0 [Internet]. Greenwood Village: Thomson Micromedex; 2017 [cited 2017 Nov 20]. Available from: http://www-micromedexsolutions-com.ez45.periodicos.capes.gov.br/micromedex2/librarian
14. Sampaio GC. *Estudo de utilização de medicamentos antieméticos no serviço de oncologia pediátrica de um hospital do Sul do Brasil* [master's thesis]. Porto Alegre: Universidade Federal do Rio Grande do Sul; 2014.
15. Ortolani L, Gasparino RC, Traldi MC. Complicações associadas ao uso de cateter totalmente implantável em crianças e adolescentes. *Rev Bras Cancerol*. 2013;59(1):51-6.
16. Vijayakumar A, Sharon EV, Teena J, Nobil S, Nazeer I. A clinical study on drug-related problems associated with intravenous drug administration. *J Basic Clini Pharm*. 2014;5(2):49-53.
17. Lopes AF, Maia-Lemos PS. Terapia nutricional parenteral em crianças e adolescentes em tratamento oncológico diagnosticados com colite neutropênica. *Rev Bras Nutr Clin*. 2014;29(3):193-7.
18. Leal KDB, Leopoldino RWD, Martins RR, Veríssimo LM. Potencial de incompatibilidade de medicamentos intravenosos em uma unidade pediátrica. *Einstein (São Paulo)*. 2016;14(2):185-9.
19. Estan-Cerezo G, Jiménez-Pulido I, Rodríguez Lucena FJ, Matoses Chirivella C, Soriano-Irigaray L, Navarro-Ruiz A. Chemical stability of ondansetron hydrochloride with other drugs in admixtures via parenteral; a review. *Farm Hosp*. 2017;41(5):625-9.
20. Dewan P, Singhal S, Harit D. Management of chemotherapy-induced nausea and vomiting. *Indian Pediatr*. 2010;47(2):149-55.
21. Becker J, Nardin JM. Utilização de antieméticos no tratamento antineoplásico de pacientes oncológicos. *Rev Bras Farm Hosp Serv Saude*. 2011;2(3):18-22.
22. Somers MJ. Maintenance intravenous fluid therapy in children [Internet]. Waltham, MA: UpToDate; [cited 2017 Oct 20]. Available from: https://www.uptodate.com/contents/maintenance-fluid-therapy-in-children
23. Senerchia AA, Macedo CR, Ferman S, Scopinaro M, Cacciavillano W, Boldrini E, et al. Results of a randomized, prospective clinical trial evaluating metronomic chemotherapy in nonmetastatic patients with high-grade, operable osteosarcomas of the extremities: a report from the Latin American Group of Osteosarcoma Treatment. *Cancer*. 2017;123(6):1003-10.

24. Alvarez PA, Berezin EN, Mimica MJ. Etiologia das infecções em crianças com neutropenia febril pós-quimioterapia. *Arq Med Hosp Fac Cienc Med Santa Casa Sao Paulo*. 2014;59(1):40-2.

25. Guzmán PC, Ruiz JG. Neutropenia febril en Pediatría: ¿qué punto de corte usar? *Pediatría*. 2012;45(3):195-202.

26. Bertsche T, Mayer Y, Stahl R, Hoppe-Tichy T, Encke J, Haefeli WE. Prevention of intravenous drug incompatibilities in an intensive care unit. *Am J Health Syst Pharm*. 2008;65(19):1834-40.

27. Santos MT, Hegele V, Hoffmann TD, Chiarani F, Hennigen FW. Instrumento para avaliação da compatibilidade em Y na administração intravenosa de medicamentos em unidades de terapia intensiva. *Rev Bras Farm Hosp Serv Saude*. 2013;4(3):34-7.

28. Huddleston J, Hay L, Everett JA. Patient-specific compatibility tables for the pediatric intensive care unit. *Am J Health Syst Pharm*. 2000;57(24):2284-5.

29. Camut A, Noirez V, Gustin B, Khalife A. Improvement of antibiotics infusion practices: proposition and evaluation of a good practices' guide. *Journal de Pharmacie Clinique*. 2007;26(3):143-50.

30. Mohr A, Thiesen J, Krämer I. Development of an incompatibility-reducing infusion scheme and infusion device for pediatric oncology patients. *Krankenhauspharmazie*. 2020;41(7):251-61.

31. Neininger MP, Buchholz P, Frontini R, Kiess W, Siekmeyer W, Bertsche A, et al. Incompatible intravenous drug combinations and respective physician and nurse knowledge: a study in routine paediatric intensive care. *Eur J Hosp Pharm*. 2019;26(4):214-7.

32. Mendes JR, Lopes MCBT, Vancini-Campanharo CR, Okuno MFP, Batista REA. Types and frequency of errors in the preparation and administration of drugs. *Einstein (Sao Paulo)*. 2018;16(3):eAO4146.

33. Pourteimour S, Hemmati MalsakPak M, Jasemi M, Eghtedar S, Parizad N. The effect of smartphone-based application learning on the nursing students' performance in preventing medication errors in the pediatric units. *Pediatr Qual Saf*. 2019;4(6):e226.

Received: Dec 17, 2021
Accepted: Oct 24, 2022