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Analysis of the compliance of prescription of high alert medication for onco-hematologic patients in a teaching hospital

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Abstract

Objective: To analyze the compliance of High Alert Medication (HAM) prescriptions for onco-hematologic patients regarding the safety requirements of the Protocol for Prescription, Use and Administration of Medicines from Ministry of Health. **Method**: Cross-sectional study, with prescriptions for onco-hematologic patients in a university teaching unit in the Midwest region of Brazil. The variables were defined as recommended by the Ministry of Health protocol. Data were analyzed using STATA 14.1 software. **Results:** 57 prescriptions were analyzed and a total of 659 medications were prescribed, of which 20.2% (n=133) were HAM. The most prescribed HAM were tramadol 21.0% (n=28), morphine 19.5% (n=26) and glucose 13.6% (n=18). Regarding non-compliance, 88.0% (n=117) of HAM showed at least one disagreement regarding protocol. Medications prescribed for the central nervous system were the most associated with non-compliance. In all, 266 non-compliance were identified, among which the majority, 18.4% (n=49) were related to the use of vague expressions, 16.2% (n=43) to the absence of infusion time and 11.8% (n=31) the presence of abbreviations. **Conclusion:** Most HAM prescriptions showed non-compliance regarding Ministry of Health protocol. The main were related to the inappropriate use of vague expressions, omission of infusion time and use of abbreviations. These findings highlight the need to improve the quality of prescriptions and the development of strategies to intercept errors, such as checklists and informational materials.

Key words: high-alert medication; medication errors; pharmacoepidemiology; inpatient; patient safety.

Análise da conformidade da prescrição de medicamentos de alta vigilância de pacientes onco-hematológicos em um hospital de ensino

Resumo

Objetivo: Analisar a conformidade das prescrições de medicamentos de alta vigilância (MAV) para pacientes onco-hematológicos quanto aos requisitos de segurança do Protocolo de Prescrição, Uso e Administração de Medicamentos do Ministério da Saúde. **Método:** Trata-se de um estudo transversal, desenvolvido a partir de prescrições de MAV para pacientes onco-hematológicos em uma unidade de internação de clínica médica, de um hospital universitário na região Centro-Oeste do Brasil. As variáveis estudadas seguiram o preconizado no protocolo do Ministério da Saúde e os dados foram analisados por meio do *software STATA* 14.1. **Resultados:** Foram analisadas 57 prescrições. Um total de 659 medicamentos foram prescritos, dos quais 20,2% (n=133) eram MAV. Os MAV mais prescritos foram tramadol 21,0% (n=28), morfina 19,5% (n=26) e glicose 13,6% (n=18). Em relação às não conformidades, 88,0% (n=117) dos MAV apresentaram ao menos uma discordância em relação aos requisitos de segurança preconizados no protocolo do Ministério da Saúde. Medicamentos para atuação em nível de sistema nervoso central foram associados ao maior número de não conformidades. Ao todo, foram identificadas 266 não conformidades, dentre as quais, 18,4% (n=49) estava relacionada ao uso de expressões vagas, 16,2% (n=43) à ausência tempo de infusão e 11,8% (n=31) à presença de abreviaturas. **Conclusão:** As prescrições de MAV, em sua maioria, apresentaram não conformidades em relação ao protocolo do Ministério da Saúde, principalmente relacionadas ao uso de expressões vagas, omissão do tempo de infusão e uso de abreviaturas. Esses achados evidenciam a necessidade da melhora da qualidade das prescrições e da elaboração de estratégias para a interceptação de erros, como *checklists* e materiais informativos.

Palavras-chave: medicamentos de alta vigilância; erros de medicação; farmacoepidemiologia; paciente hospitalizado; segurança do paciente.

Introducion

The *To Err Is Human: Building a Safer Health System* report[1], published in the early 2000s, addressed a very important and hitherto little-discussed topic: patient safety in health institutions. According to the report, up to 98,000 people died annually in the United States due to preventable Adverse Events (AEs) and this number surpassed deaths due to traffic accidents, breast cancer and HIV infection. In addition to that, the deaths due to Adverse Drug Events (ADEs) even surpassed those due to work-related accidents. Publication of the report warned about the magnitude of AEs in hospital settings and drove a significant movement for patient safety in health institutions throughout the world[1].

With regard to medications, medication errors (MEs) are a major concern and are conceptualized as (any preventable event that can cause or lead to inappropriate medication use or harms to patients while the medication is under the control of a healthcare professional, patient or consumer)[3]. These MEs encompass from in-hospital assistance to home-based care[4].

The medication process is complex, involves many professionals and stages, and is susceptible to failures[5,6]. In hospital institutions, MEs can occur in any of the stages involving medication use: prescription, transcription, dispensing, preparation or administration[5,7], and can reach a mean of 50% of the hospitalized patients[8]. A Brazilian study evidenced that nearly 48,2% of the MEs are related to the prescription stage[7]. Another study carried out in Brazil found that half of the prescriptions analyzed did not contain enough information to guarantee technical quality of the prescription and, consequently, safety in drug administration[9]. Omission of information about the medication and/or the patient represents a risk factor for MEs in the prescription stage[10].

In addition to the risks inherent to the medication process itself, some medications have greater potential to cause harms in case of failure in their use, and they are known as High-Alert Medications (HAMs)[11]. Errors related to HAMs may not be the most frequent in hospital institutions; however, when they do occur, the patients can suffer severe adverse events, such as permanent lesions or death[12].

Aiming to promote safe practices in medication use, the Ministry of Health prepared the Protocol for Safety in Drug Prescription, Use and Administration. This protocol shows the items and characteristics of a prescription considered safe, including readability of the prescription, patient information and characteristics of the medications, in addition to highlighting the criteria that must be observed in the safe prescription of HAMs[13]. Based on this protocol, a study conducted in a Brazilian public hospital evaluated HAM prescriptions and identified 1,942 errors related to the way in which they were written. The most frequently found error was omission of treatment length in time (20.9%)[14].

Onco-hematological patients, who undergo complex treatment protocols with HAMs such as chemotherapy drugs also make use of opioids as adjuvant therapy and for the treatment of other concomitant diseases[15]. Non-conformities in the prescription stage corresponding to these medications can impair both the treatment and safety of these patients[16]. In a study carried out in 107 hospitals from Spain, it was identified that 74.5% of the adverse drug events (ADEs) were caused by at least one HAM, with the most frequent being opioids (16.5%) and oral anticoagulants (13.3%)[17].

Recurrent hospitalizations of onco-hematological patients can contribute to a higher frequency of HAM use, consequently increasing the risk of harms associated with the events. Considering the importance of safe medication use, in 2017, the Third Global Challenge for Patient Safety[18] encouraged health institutions to implement safe practices in the medication process, minimizing the occurrence of serious and avoidable harms to the patients through knowledge of the HAM prescription standards. In this context, the current study aims at describing the demographic and clinical profile of onco-hematological patients and the compliance of HAM prescriptions in a teaching hospital of the *Sentinela* Network in the Brazilian Midwest Region, using as a basis the regulations included in in the Ministry of Health's Protocol for Drug Prescription, Use and Administration.

Methods

This is a cross-sectional, descriptive and observational study, developed at the Medical Clinic hospitalization unit of the Clinical Hospital belonging to the Federal University of Goiás, in the Brazilian Midwest region. The Medical Clinic unit serves various medical specialties, including Hematology, and has 60 beds.

Patients admitted in between January 1st, 2017, and December 31st, 2018, were included, whereas those who did not undergo a complete hospitalization during the period determined in the survey were excluded, that is, those who were hospitalized before January 1st, 2017, or discharged after December 31st, 2018.

After obtaining the full list of hospitalizations (n=3,885), duplicates were excluded (n=1,267), resulting in 2,618 valid hospitalizations.

Sample size was calculated based on the sample size calculation for finite populations[19]. The hospitalizations, proportionally allocated to each Medical Clinic specialty, resulted in a sample size of 336, of which 41 represented the sample of hospitalizations for the Onco-Hematology Medical Clinic.

The Hematology hospitalizations during the study period were numbered in increasing order and 60 of them were drawn (a number that is higher than the minimum sample size of 41) by resorting to the www.sorteador.com.br website. All prescriptions for each hospitalization drawn were numbered in ascending order and the prescription to be evaluated was randomly selected via the www.sorteador.com.br website. If the prescription drawn did not have at least one prescribed medication of any pharmacological class, a new draw was performed until the resulting prescription had at least one drug. Of all 60 prescriptions drawn, three were excluded due to absence of necessary information in the medical chart to conduct the study, resulting in 57 valid prescriptions.

A pilot form was prepared to adjust the data collection instruments, validated by two duly trained members of the team.

Sociodemographic and health variables were considered for data analysis, such as age, gender and main diagnosis. The variables for the verification of safe prescriptions were obtained from the Ministry of Health's Protocol for Safety in Drug Prescription, Use and Administration (Figure 1). For the purposes of this study, any and all deviations from the safety protocol were considered as MEs[20].

The data obtained from the study were introduced in a structured database in the Research Electronic Data Capture (RedCap) software[21]. For data analysis, descriptive statistics was used to obtain relative and absolute frequencies, resorting to the STATA 14.1 software. The study was approved by the Research Ethics Committee of HC-UFG/EBSERH under CAEE No. 14501219.6.0000.5078.

Figure 1. Items used in the study for the verification of safe prescriptions.

Type of prescription	Classified as "handwritten" when handwritten, and as "typed" when typed using text editing software.
Medications prescribed	Performed based on identification of the active ingredient of each of the medications prescribed, and later classified according to the first ATC[1] level
HAM	Classified as "yes" when it was on the list of HAMs standardized by ISMP Brazil2, and as "no" when it was not.
Abbreviations	Classified as "present" when the following was included in the prescription: U (Units), IU (International Units), chemical formulas (MgSO4, KCl, NaCl, etc.) and short names of medications (HCTZ, RIPE, SMZ + TMP, MTX, CBZ, HNF, etc.), and as "absent" when no abbreviation was present.
Denomination of the medications	Classified as "generic name" when using the generic name, and as "commercial name" when using the brand name.
Medications with similar names	Classified as "compliant" when written according to the list standardized by ISMP Brazil3, and as "non-compliant" when not written according to the list or as "not applicable" when it was not a medication standardized by ISMP Brazil.
Expression of doses	Classified as "compliant" when the units (grams, milligrams, micrograms, international units) were present and legible in the prescription, and as "non-compliant" when the units of measurement were present but illegible, or when milliliter, tablet, ampoule, teaspoon, bottle or capsule were used as a measure for expressing the medication doses.
Doses	Classified as "compliant" when they were in agreement with the usual dosages recommended in the Micromedex®[4] and Up To Date®[5] databases, and as "non-compliant" when the dose was not in agreement with the databases.
Expression of the administration route	Classified as "present" when the administration routes for each medications were prescribed and legible; as "absent" when the administration routes were not prescribed; and as "illegible" when it was not possible to read them.
Administration route conformity	Classified as "compliant" when the administration route prescribed was the one recommended by the manufacturer, and as "non-compliant" when the administration route did not correspond to the one indicated for the prescribed medication.
Dosage	Classified as "present" when drug dosage was prescribed and legible; as "absent" when the medication dosage was not prescribed, and as "illegible" when it was not possible to read it.
Dosage conformity	Classified as "compliant" when the prescribed dosage was in accordance with the maximum doses recommended in the literature, and as "non-compliant" when the dosage was in disagreement with the maximum doses recommended in the literature. Given the use of protocols, this item was not evaluated for glucose.
Dilution	Classified as "present" when there was information on the diluent (type and volume) for intravenous, intramuscular and subcutaneous use medications; as "absent" when this information was not prescribed, as "illegible" when it was prescribed but illegible, as "incomplete" when some information about the diluent (type or volume) was missing or as "not applicable" when referring to medications not administered via these routes or that did not require dilution according to the Micromedex®[4] and Up To Date®[5] database[5].
Dilution conformity	Classified as "compliant" when the diluents prescribed for intravenous, intramuscular or subcutaneous use contained information on the diluent (type and volume) in accordance with the guidelines of the databases or the manufacturer, and as "non-compliant" when this information was in disagreement with the literature or as "not applicable" when referring to medications not administered via the aforementioned routes or that did not require dilution according to Micromedex®[4] and Up To Date®[5] or the manufacturer. Due to the use of protocols, dilution conformity was not evaluated for glucose.
Infusion time	Classified as "present" when the prescriptions contained information on the speed and time for the infusion of intravenous medications; as "absent" when this information was not included in the prescription; and/or as "not applicable" when referring to medications not administered via this route or that could be administered in bolus according to the Micromedex®[4] and Up To Date®[5] databases or the manufacturer.
Infusion time conformity	Classified as "compliant" when information on the infusion speed and time was present according to the guidelines of the databases or the manufacturer, and as "non-compliant" when this information was in disagreement with the literature or as "not applicable" when referring to medications that were not administered intravenously or that could be administered in bolus according to the database or manufacturer's instructions. Infusion time conformity was not evaluated for glucose.
Treatment length in time	Classified as "present" when duration of the antimicrobial and antineoplastic treatment was described; as "absent" when duration of the treatment for these medications was not described; as "illegible" when this information was prescribed but illegible; and as "not applicable" for other medications.
Use of vague expressions	Classified as "non-compliant" when the expressions "use as usual", "use as accustomed", "continuous use" or "do not stop" were present in the prescription, and as "compliant" when the "SOS", "if necessary" or "according to medical criterion" expressions were accompanied by safety information (dose, dosage, maximum daily dose, condition that determines treatment use or interruption).
Erasures	Classified as "present" or as "absent".

[1]WHO, 2021. [2]ISMP BRAZIL, 2019. [3]ISMP BRAZIL, 2014. [4]Micromedex®. [5]Up To Date.

Results

Prescriptions of 57 patients were analyzed in the current study. In relation to age, 49.1% (n=28) belonged to the age group from 18 to 59 years old, with a mean of 50.9 ± 18.4. There was predominance of the male gender with 61.4% (n=35). In relation to the diseases, 26.3% (n=15) of the patients were diagnosed with leukemia and 21.0% (n=12) with myeloma (Table 1).

Table 1. Distribution of the sociodemographic and health variables of the onco-hematologic patients hospitalized in the Medical Clinic of the Goiânia Clinical Hospital, between 2017 and 2018

Sociodemographic and health variables	n (%)
Onco-hematologic diseases	
Leukemias	15 (26.3%)
Myeloma	12 (21.0%)
Anemias	7 (12.3%)
Lymphomas	7 (12.3%)
Others	7 (12.3%)
Unknown	5 (8.8%)
Myelodysplastic syndrome	4 (7.0%)
Total	57 (100%)
Age	
18-59 years old	28 (49.1%)
≥ 60 years old	24 (42.1%)
15-17 years old	5 (8.8%)
Total	57 (100%)
Gender	
Male	35 (61.4%)
Female	22 (38.6%)
Total	57 (100%)

Regarding the type of prescription, it was observed that 93.0% (n=53) of them were typed and 7.0% (n=4) were handwritten. A total of 659 medications were prescribed, of which 20.2% (n=133) were HAMs; and, among these, the most prescribed were tramadol with 21.0% (n=28), morphine with 19.5% (n=26) and glucose with 13.6% (n=18) (Table 2). Regarding the ATC level 1 classification, the most prescribed medications were those that act on the Central Nervous System with 42.1% (n=56) antineoplastics and immune system modulating agents with 22.6% (n=30), those with action on the blood and hematopoietic organs with 21.1% (n=28), other groups with 13.5% (n=18) and general anti-infective agents with 0.75% (n=1).

In relation to the safety requirements included in the protocol, 88.0% (n=117) of the HAMs presented at least one non-conformity in their prescription. Considering the ATC classification, the group of medications most frequently involved in non-conformities was the one acting on the Central Nervous System, with 50.8% (n=135) (Table 3).

In all, 266 non-conformities were identified in the prescriptions, with 18.4% (n=49) related to use of vague expressions such as "if necessary", "IN", "according to medical criteria" and "AMC". The main medication in this regard was tramadol, with 34.7% (n=17) (Table 3). Absence of information about the infusion time represented 16.2% (n=43). Tramadol was the medication most frequently prescribed without the infusion time, with 65.1% (n=28) and, when present, it was prescribed in non-compliance in 100% (n=28) of the prescriptions (Table 4).

The presence of abbreviations was identified in 23.3% (n=31) of the HAMs, corresponding to 11.7% (n=31) of all non-conformities, with glucose as the most non-compliant HAM in this regard. In 54.9% (n=17) the denomination of glucose it was abbreviated as "GH 50%". In relation to denomination of the medications, 10.9% (n=29) were prescribed using their commercial name, with tramadol as the most frequent with 48.3 (n=14) (Tables 3 and 4).

Table 2. Frequency and Anatomical Therapeutic and Chemical classification of the high-alert medications prescribed to onco-hematologic patients hospitalized in the Medical Clinic of the Goiânia Clinical Hospital, between 2017 and 2018

Medication	ATC classification	n (%)
Tramadol	N02AX02	28 (21.0%)
Morphine	N02AA01	26 (19.5%)
Glucose	V04CA02	18 (13.6%)
Heparin	B01AB01	6 (4.6%)
Enoxaparin	B01AB05	6 (4.6%)
Thalidomide	L04AX02	6 (4.6%)
Potassium chloride	B05XA01	6 (4.6%)
Cyclophosphamide	L01AA01	5 (3.8%)
Hydroxyurea	L01XX05	5 (3.8%)
Magnesium sulphate	B05XA05	4 (3.0%)
Vincristine	L01CA02	3 (2.3%)
Methotrexate	L04AX03	3 (2.3%)
Warfarin	B01AA03	2 (1.5%)
Rivaroxaban	B01AF01	2 (1.5%)
Cyclosporine	L04AD01	2 (1.5%)
Sodium bicarbonate	B05XA02	2 (1.5%)
Amphotericin B	J02AA01	1 (0.7%)
Cytarabine	L01BC01	1 (0.7%)
Doxorrubicin	L01DB01	1 (0.7%)
Dasatinib	L01EA02	1 (0.7%)
Ruxolitinib	L01EJ01	1 (0.7%)
Ibrutinib	L01EL01	1 (0.7%)
Tretinoin	L01XF01	1 (0.7%)
Buprenorphine	N02AE01	1 (0.7%)
Codeine	N02AJ03	1 (0.7%)
Total	-	133 (100%)

Regarding treatment length in time, the majority (96.4% [n=27]) did not have this information available (number of days that the patient should use the medication and day of the protocol that the prescription referred to: D1, D2, etc...). The medications most involved in this non-conformity were antineoplastics and immune system modulating agents, with 96.3% (n=26), in addition to anti-infective agents with 3.7% (n=1) (Table 3). Regarding the presence of information about dilution, 18.0% (n=16) of the medications were in non-compliance, in 75.0% (n=12) of the cases the information was incomplete (the dilution type and/or volume was missing) and absent in 25,0% (n=4). With 75.0% (n=12), morphine was the medication that was most frequently involved in non-conformities in relation to dilution (Table 4).

Regarding medications with similar names, 10.5% (n=14) of the HAMs presented non-compliant writing, and the most frequently associated medication was cyclophosphamide with 35.7% (n=5), whose correct spelling is Cyclo**PHOSPHAM**ide[22]. In relation to expression of the dose, only 2.3% (n=3) of the medications presented non-conformities and 2.3% (n=2) had inadequate dose (Table 4). The groups of medications that were most involved in the non-conformities referring to dose were Blood and hematopoietic organs with 66.7% (n=2) and others with 33.3% (n=1) (Table 3). In 23.3% (n=31) of the HAMs it was not possible to evaluate the dose, as they were medications whose dose is calculated according to the patient's weight, which was missing in the prescriptions. No erasures were identified in the HAM prescriptions.

Table 3. Description of the non-conformities of the high-alert medications according to the Anatomical Therapeutic and Chemical classification prescribed to onco-hematologic patients hospitalized in the Medical Clinic of the Goiânia Clinical Hospital, between 2017 and 2018.

Type of non-conformity	ATC group n (%)					
	N[1]	V[2]	L[3]	B[4]	J[5]	Total n (%)
Vague expressions	33 (24.4%)	16 (29.6%)	-	-	-	49 (18.4%)
Expression of the infusion time	28 (20.7%)	15 (27.8%)	-	-	-	43 (16.2%)
Abbreviation	-	17 (31.5%)	-	14 (42.4%)	-	31 (11.7%)
Commercial name	16 (11.9%)	-	4 (9.1%)	9 (27.3%)	-	29 (10.9%)
Infusion time conformity	28 (20.7%)	-	-	-	-	28 (10.5%)
Treatment length in time	-	-	26 (59.1%)	-	1 (100%)	27 (10.1%)
Expression of the dilution	12 (8.9%)	4 (7.4%)	-	-	-	16 (6.0%)
Medication with a similar name	-	-	14 (31.8%)	-	-	14 (5.3%)
Dilution conformity	12 (8.9%)	-	-	-	-	12 (4.5%)
Dosage conformity	1 (0.7%)	-	-	4 (12.1%)	-	5 (1.9%)
Expression of the dose	-	1 (1.9%)	-	2 (6.1%)	-	3 (1.1%)
Dose	-	1 (1.9%)	-	2 (9.1%)	-	3 (1.1%)
Expression of the administration route	2 (1.5%)	-	-	-	-	2 (0.8%)
Administration route conformity	2 (1.5%)	-	-	-	-	2 (0.8%)
Expression of the dosage	1 (0.7%)	-	-	1 (3.0%)	-	2 (0.8%)
Total	135 (50.8%)	54 (20.3%)	44 (16.5%)	32 (12.0%)	1 (0.4%)	266 (100%)

[1]Central Nervous System. [2]Others. [3]Antineoplastics and immune system modulating agents. [4]Blood and hematopoietic organs. 5Anti-infective agents.

Discussion

Age group from 18 to 59 years old, male gender and leukemia (onco-hematological disease) were the most observed, in line with two studies: one that evaluated MEs in onco-hematological patients, with a predominance of males (52.7% [n=156]), mean age of 48 years old and higher frequency of leukemia with 42.6% (n=126) followed by myeloma with 15.9% (n=47)[23]; and another conducted in a university hospital from Ceará, which also observed leukemia as the most frequent disease (30%), followed by myeloma (15%)[24]. These findings show that the sociodemographic profile of the onco-hematological patients is similar even in different Brazilian regions, helping to develop strategies for the prevention of MEs, especially those related to HAMs.

Regarding the type of medication prescribed, we observed that opioid analgesics were the most frequent. Similar results were observed in a study conducted in a university hospital that identified a frequency of 18.2% (n=724) of HAMs and, with opioid analgesics as the most frequently prescribed class, with 31.2% (n=226)[25]. Although the populations of both studies are different, these findings can be partially explained by the fact that opioid analgesics are used for sedoanalgesia both in intensive care settings and in medical clinics[25], in addition to being a class frequently used to treat cancer pain[26]. These findings are important because they show that, regardless of the institution's patient profile, HAMs, and especially opioids, are widely used, and that the implementation of safety measures in the use process can be instituted regardless of the type of patient.

In our study, we observed that most of the HAMs were prescribed in non-compliance and that opioids were related to slightly more than half of them. These results were similar to those of a systematic review on HAM prescription errors in hospitals and identified that opioids were the medications most frequently associated with errors[27]. Likewise, a study that identified MEs in a large-size Australian hospital concluded that HAMs were associated with half the number of errors and that the most commonly involved medications were narcotics (17.9%)[28].

A study carried out in France showed that the MEs involving opioids led to severe outcomes (n=25; 69.4%), of which 50.0% (n=18) were involved in hospitalizations, 8.3% (n=3) in life-threatening situations and 2.8% (n=1) in deaths[29]. These findings reinforce the importance of developing strategies to mitigate the risk for MEs, such as better dissemination of patient health information among the multiprofessional team members[29]. The verification of risk factors related to the patient (comorbidities, age, gender and previous therapy with opioids) and to the prescription (total daily dose, number of opioids prescribed and different formulations of the same drug) by a clinical pharmacist can contribute to safe opioid use in hospitalized patients[30].

In our study, glucose was the second medication with the highest number of non-conformities with the protocol and the main non-conformity was related to the use of abbreviations. Our results were similar to those of a study conducted in a tertiary-level hospital, which evaluated HAM prescription errors according to the protocol guidelines. In that study, glucose accounted for 17.6% (n=343) of the non-conformities related to writing of the prescription and the most frequent was use of abbreviations with 82.7% (n=62)[14].

The use of abbreviations can generate doubts and misinterpretations by health professionals, compromising patient safety[31]. Such findings reinforce the importance of the elaboration of educational measures by pharmacists regarding the inappropriate use of abbreviations[32], as well as the elaboration of lists of standardized and prohibited abbreviations in the institution[31].

We observed that the main non-conformity identified was related to the incorrect use of vague expressions, most of which were associated with opioids. A study conducted at a community pharmacy in São Paulo, which also used the protocol for evaluating the prescriptions, observed that 18.8% of the manual prescriptions were non-compliant with regard to the use of vague expressions[33].

Table 4. Frequency of the non-conformities of the HAMs prescribed to onco-hematologic patients hospitalized in the Medical Clinic of the Goiânia Clinical Hospital, between 2017 and 2018.

Medications	Type of non-conformity n (%)															
	Expvg[1]	Exptinf[2]	Abrev[3]	Ncomer[4]	Cdinf[5]	Durto[6]	Expdil[7]	Lasa[8]	Cddil[9]	Cdpos[10]	Expdose[11]	Dose[12]	Expvia[13]	Cdvia[14]	Exppos[15]	Total
Tramadol	17 (34.7%)	28 (65.1%)	-	14 (48.4%)	28 (100%)	-	-	-	-	-	-	-	-	-	-	87 (32.7%)
Glucose	16 (32.7%)	15 (35.7%)	17 (54.9%)	-	-	-	4 (25%)	-	-	-	1 (33.3%)	1 (33.3%)	-	-	-	54 (20.3%)
Morphine	15 (30.6%)	-	-	1 (3.4%)	-	-	12 (75%)	-	12 (100%)	1 (20%)	-	-	2 (100%)	2 (100%)	1 (50%)	46 (17.3%)
Potassium chloride	-	-	5 (16.1%)	-	-	-	-	-	-	2 (40%)	2 (66.7%)	2 (66.7%)	-	-	-	11 (4.1%)
Cyclophospha-mide	-	-	-	-	-	4 (14.8%)	-	5 (35.7%)	-	-	-	-	-	-	-	9 (3.4%)
Enoxaparin	-	-	-	5 (17.3%)	-	-	-	-	-	1 (20%)	-	-	-	-	-	6 (2.3%)
Thalidomide	-	-	-	-	-	6 (22.3%)	-	-	-	-	-	-	-	-	-	6 (2.3%)
Vincristine	-	-	-	-	-	3 (11.1%)	-	3 (21.4%)	-	-	-	-	-	-	-	6 (2.3%)
Methotrexate	-	-	-	-	-	3 (11.1%)	-	3 (21.4%)	-	-	-	-	-	-	-	6 (2.3%)
Heparin	-	-	5 (16.1%)	-	-	-	-	-	-	-	-	-	-	-	-	5 (1.9%)
Hydroxyurea	-	-	-	2 (6.9%)	-	3 (11.1%)	-	-	-	-	-	-	-	-	-	5 (1.9%)
Magnesium sulphate	-	-	4 (12.9%)	-	-	-	-	-	-	-	-	-	-	-	-	4 (1.5%)
Cyclosporine	-	-	-	-	-	2 (7.4%)	-	1 (7.1%)	-	-	-	-	-	-	-	3 (1.1%)
Doxorrubicin	-	-	-	-	-	1 (3.7%)	-	1 (7.1%)	-	-	-	-	-	-	-	3 (1.1%)
Warfarin	-	-	-	2 (6.9%)	-	-	-	-	-	-	-	-	-	-	-	2 (0.8%)
Rivaroxaban	-	-	-	2 (6.9%)	-	-	-	-	-	-	-	-	-	-	-	2 (0.8%)
Sodium bicarbonate	-	-	-	-	-	-	-	-	-	1 (20%)	-	-	-	-	1 (50%)	2 (0.8%)
Tretinoin	-	-	-	1 (3.4%)	-	1 (3.7%)	-	-	-	-	-	-	-	-	-	2 (0.8%)
Codeine	1 (2%)	-	-	1 (3.4%)	-	-	-	-	-	-	-	-	-	-	-	2 (0.8%)
Amphotericin B	-	-	-	-	-	1 (3.7%)	-	-	-	-	-	-	-	-	-	1 (0.4%)
Cytarabine	-	-	-	-	-	1 (3.7%)	-	-	-	-	-	-	-	-	-	1 (0.4%)
Dasatinib	-	-	-	-	-	-	-	1 (7.1%)	-	-	-	-	-	-	-	1 (0.4%)
Ruxolitinib	-	-	-	-	-	1 (3.7%)	-	-	-	-	-	-	-	-	-	1 (0.4%)
Ibrutinib	-	-	-	-	-	1 (3.7%)	-	-	-	-	-	-	-	-	-	1 (0.4%)
Total	49 (18.4%)	43 (16.2%)	31 (11.8%)	29 (10.9%)	28 (10.5%)	27 (10.2%)	16 (6.0%)	14 (5.3%)	12 (4.5%)	5 (1.9%)	3 (1.1%)	3 (1.1%)	2 (0.8%)	2 (0.8%)	2 (0.8%)	266 (100%)

[1]Vague expression. [2]Expression of the infusion time. [3]Abbreviation. [4]Commercial name. [5]Infusion time conformity. [6]Treatment length in time. [7]Expression of the dilution. [8]Medication with a similar name. [9]Dilution conformity. [10]Dosage conformity. [11]Expression of the dose. [12]Dose. [13]Expression of the administration route. [14]Administration route conformity. [15]Expression of the dosage.

Both in hospital and outpatient environments, absence of complete information regarding the maximum dose and dose range can lead to toxic events and compromise patient safety[34]. The prescription of high daily doses of opioids can lead to serious harms; therefore, these findings reflect the importance of improving opioid prescription practices among health professionals[35].

Regarding treatment length in time, we noticed that more than 90% of the drug prescriptions containing antineoplastics did not include information regarding duration of the treatment. No other studies were found that evaluated compliance of this parameter in relation to the protocol. However, these results are important, as antineoplastics have complex protocols and low therapeutic index and can lead to serious ADEs in case of errors[36]. It is noteworthy that the presence or treatment length in time in the hospital prescription allows assessing treatment continuity by the pharmacist at discharge.

Regarding spelling of the medications with similar names, we observed that antineoplastic drugs were the ones that most presented this problem. This finding is important, as these errors can lead to switching medications due to their similarity, which can lead to confusion between brand/generic, generic/generic or brand/brand names, for example[37].

Although the risk for MEs with medications with similar names involving HAMs is a reality in health institutions[38], incorporating adoption of the differentiation of these drugs using the *Tall Men Lettering* method[39] in the prescription requires an electronic prescription system so that the parameterizations are made with the help, for example, of specific software program[40]. However, this is not the reality of most public health institutions in the country. Other strategies can be used, such as reducing the variability of human behavior, which involves limiting distractions and work interruptions, in addition to adopting strategic storage[41].

Even considering the limitations of this study, such as absence of important information in the medical records and the outdated protocol itself, the current study showed the most frequent non-conformities related to the HAM prescription stage and signaled the potential risk of serious harms related to them.

These findings highlight the need to improve quality of the prescriptions. For this purpose, training sessions can be carried out for prescribers, as well as identification of the reasons for the non-conformities, in addition to the profile of the prescribers responsible for them. It is also suggested to adopt checklists with the items addressed in the protocol, plus information on the standardized HAMs, in order to support an evaluation of the prescriptions by the pharmacist; in addition to encouragement and support from the institutions' management in the elaboration of strategies to intercept MEs related to HAMs, such as preparing informative materials and training sessions regarding safe prescription of these medications in order to improve the practices performed by the multiprofessional team.

Conclusion

Non-conformities in the drug prescription stage can compromise highly complex HAM treatments and the safety of onco-hematological patients. Non-conformities related to these medications can result in severe adverse events or even related deaths.

We identified that 88% of the HAM prescriptions were non-compliant with the Ministry of Health's protocol. The main non-conformities were related to use of vague expressions, omission of the infusion time and use of abbreviations. According to the ATC first level classification, the group of medications most frequently associated with non-conformities corresponded to those that act on the Central Nervous System.

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Collaborators

LTF, PRM, ACFM and LTS contributed to the conception, planning, data analysis and interpretation, and were in charge of writing and critically reviewing the content. TXAMF, JCM, and PCSG participated in the relevant critical review of the intellectual content. All those involved approved the final version to be published.

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Conflict of interest statement

Os autores declaram que não há conflito de interesse

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