Drugs used in bone marrow transplantation: a study about combinations of potentially interactive antimicrobials*

MEDICAMENTOS UTILIZADOS EM TRANSPLANTE DE MEDULA ÓSSEA: UM ESTUDO SOBRE COMBINAÇÕES DOS ANTIMICROBIANOS POTENCIALMENTE INTERATIVOS

MEDICAMENTOS UTILIZADOS EN CASOS DE TRASPLANTE DE MÉDULA ÓSEA:UN ESTUDIO SOBRE COMBINACIONES ANTIMICROBIANAS POTENCIALMENTE INTERACTIVAS

Rosimeire Barbosa Fonseca[1], Silvia Regina Secoli[2]

ABSTRACT

The study aimed at characterizing the profile of the drugs and identify combinations between potentially interactive anti-microbial drugs used in patients who underwent bone marrow transplantation (BMT). The analysis covered 70 prescription medications for BMT patients hospitalized at Instituto do Coração, São Paulo, Brazil. Medications were classified according to the Alpha system, listing their interactive potential and pharmacological characteristics according to literature. Data were analyzed through descriptive statistics. Results showed that 72.7% of drugs presented an interactive potential, with precipitators (79.2%) and fluconazole (85.7%), highlighted as the most involved anti-microbial in the combinations, associated to omeprazole in 40% of the samples. BMT patients were frequently administered combinations of potentially interactive drugs. This condition, when associated with simultaneous schedules, could predispose patients to undesirable events, thus affecting the security of the therapy.

KEY WORDS

Bone marrow transplantation.
Drug interactions.
Oncologic nursing.

RESUMO

O objetivo do estudo foi caracterizar o perfil dos medicamentos e identificar combinações decorrentes da co-administração de antimicrobianos potencialmente interativos e outros agentes. 70 prescrições médicas de pacientes submetidos a transplante de medula óssea (TMO), todos internados no Instituto do Coração, São Paulo, Brasil, foram analisadas. Os medicamentos foram classificados de acordo com o sistema Alfa, e o potencial de interação e as características farmacológicas foram listados a partir da literatura. Na analise dos dados utilizou-se estatística descritiva. Verificou-se que 72,7% dos medicamentos apresentaram potencial interativo, destacando-se os precipitadores (79,2%) e o fluconazol (85,7%) como o antimicrobiano mais envolvido nas combinações, associado ao omeprazol em 40% da amostra. Nos pacientes de TMO, a co-administração de medicamentos potencialmente interativos foi freqüente, condição que, associada à polifarmácia e ao aprazamento simultâneo de horários na administração desses agentes, poderia predispor o paciente a eventos indesejados, afetando, deste modo, a segurança da terapia.

DESCRITORES

Transplante de medula óssea.
Interações de medicamentos.
Enfermagem oncológica.

RESUMEN

El objetivo del estudio fue determinar el perfil de medicamentos e identificar combinaciones por administración conjunta de antimicrobianos potencialmente interactivos y otros agentes. Fueron analizadas 70 prescripciones médicas de pacientes sometidos a trasplante de médula ósea (TMO), todos internados en el Instituto del Corazón, São Paulo, Brasil. Los medicamentos fueron clasificados según el sistema Alfa. El potencial de interacción y las características farmacológicas fueron establecidas según la bibliografía. El análisis de datos a través de estadística descriptiva. El 72,7% de los medicamentos mostró potencial interactivo, destacándose los precipitadores (79,2%) y como antimicrobiano más utilizado en las combinaciones el fluconazol (85,7%), siendo asociado al omeprazol en 40% de la muestra. La combinación de medicamentos potencialmente interactivos fue frecuente en estos pacientes, condición que asociada a la polifarmacia y a la distribución simultánea de horarios en su administración podría predisponer al paciente a efectos adversos, afectando la seguridad en el tratamiento.

DESCRIPTORES

Trasplante de medula ósea.
Interacciones de drogas.
Enfermería oncológica.

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[1] Nurse, Specialist in Oncology Nursing. Master's student in the Graduate Program in Adult Health at School of Nursing, University of São Paulo. São Paulo, SP, Brazil. meire.2310@ig.com.br [2] Nurse, PhD. Professor of the Medical-Surgical Nursing Department at School of Nursing, University of São Paulo. São Paulo, SP, Brazil. secolisi@usp.br

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INTRODUCTION

Bone marrow transplantation (BMT) represents one of the main therapeutic modalities for patients with oncologic, hematologic and congenital diseases, offering the possibility to lengthen their lifetime. In this type of therapy, initially, marrow aplasia is performed in the receptor and, later, a venous infusion of cells is done in the hematopoietic tissue, previously treated or from a compatible donor, aiming at reestablishing hematopoiesis[1-2].

Nowadays, the BMT procedure has grown noticeably, especially in developed countries. It is estimated that between 30 and 50 thousand transplants are performed every year all over the world, and this number increases from 10 to 15% per year. The European BMT registries show that 5000 autologous BMT were performed from 2000 to 2001, increasing to 7000 in 2002[3].

The BMT procedure is divided in pre-transplantation and transplantation stages (conditioning and infusion)[1]. In the pre-transplantation stage, the patient is evaluated and the type of transplantation and the donor are defined, orienting both about the procedure.

The transplantation stage is subdivided in two phases: conditioning and infusion of the bone marrow. Conditioning consists in the administration of high antineoplastic chemotherapy drugs and/or total body irradiation, aiming to induce marrow aplasia. In this phase, pharmacological therapy is also started, with antiemetic, analgesic, immunosuppressive and antimicrobial drugs, among others. The purpose of these agents is to avoid, reduce or soften undesirable effects, or even prevent complications due to antineoplastic chemotherapy[2,4-6]. Bone marrow infusion is performed with a central venous catheter and, in this phase, medication, such as corticosteroid, anti-histaminic and anxiolytic drugs, is administered intravenously, aiming to prevent transfusional intercurrences.

Hence, transplanted patients are exposed to prolonged treatment protocols, with several types of medication, especially antimicrobials - and several of these have potential for interaction[4]. It is verified that, regarding these agents, the issue of interactions is insufficiently discussed by professional teams, although all patients use this therapeutic class.

In BMT, antimicrobial therapy is used to avoid and treat infectious situations, a frequent complication responsible for serious morbidity and high death rates in this specialty[2,5-6]. Antimicrobials are prescribed in combination, i.e., they are associated agents with different modes of action. In addition, they are often administered simultaneously with drugs that act on different organic systems. This strategy, which several services invariably adopt, increases the therapeutic actions. However, the concomitant administration of agents with potentials for interaction can trigger problems related to interactions, especially in patients exposed to polypharmacy.

Drug interaction (DI) occurs when one drug (precipitator) interferes in the action of another (object)[7-9]. The occurrence of DI depends on several factors, but mainly on the characteristics of the drugs that have a potential for interaction, which are named precipitators and objects, depending on their pharmacokinetic properties[8-10].

Agents named precipitators are those with high bonding properties with plasmatic proteins (PP), which displace the object drugs from the PP linking sites. The displacement of an agent from its PP-linking site by another increases its serum level. Precipitators modify (induce or inhibit) the metabolism of others. The metabolism induction of an object agent by a precipitator can decrease the serum level of the former, while the inhibition of an object agent by a precipitator can increase the serum level of the former; they alter kidney function and the depuration of object drugs[9].

Transplanted patients are exposed to prolonged treatment protocols, with several types of medication, especially antimicrobials - and several of these have potential for interaction.

Drugs named object are those presenting a dose-response curve with an abrupt inclination, whose change in dose, no matter how small, causes an expressive change in the pharmacological effect[9].

The present study was conceived by considering that, for patients submitted to BMT, pharmacological therapy, in particular antimicrobial type, represents one of the main points for a successful procedure; that scheduling the intake of several drugs at a single time is a common practice of nurses; and that, despite medication combination being used as an important therapeutic strategy, it can result in DI, impacting the therapy and exposing the individual to risk.

OBJECTIVES

Characterize the profile of the drugs regarding the administration schedule and the potential for interaction, and identify the existing combinations between potentially interactive antimicrobials and other drugs, consequences of co-administering them to patients submitted to BMT.

METHOD

This was a descriptive exploratory research, performed at the bone marrow transplantation sector of Instituto do Coração, at Hospital das Clínicas, Faculty of Medicine of University of São Paulo.

The cases comprised 70 drug prescriptions of patients admitted from January to June, 2005, on the day before the

marrow infusion (-1), regardless of ethnicity, diagnosis, age or gender, hospitalized from January to July, 2005. The choice of day -1 happened because the introduction of prophylactic antimicrobials is initiated on this specific day. Patients transferred to the intensive care unit (ICU) were excluded, as well as those who died on the day of the study. It should be noted that each patient had only one daily medical prescription.

Regarding the clinical-demographic characteristics of the cases, male patients were predominant (52.9%), with a lymphoma diagnosis (38.6%) and submitted to autologous BMT (65.7%). Average age was 37.31 (SD 15.95) and the average number of administered drugs in the 24h was 7.97 (SD 2.34). The number of agents used per patient varied from 4 to 16, with 35.7% (n=25) of the patients receiving between 6 and 7 drugs.

The study was approved by the Review Board of the target hospital. A sheet containing variables related to patient identification (gender, age, diagnosis and BMT type), as well as data on medication (generic name, administration route and time) prescribed on day -1 was used for data collection. This instrument was previously tested and adjusted according to the study goals.

GUIAMED's Alpha classification[11] was used to define the therapeutic profile of the drugs, observing their alphabetic, therapeutic and mnemonic aspects. The drugs were classified in categories. The potential of interaction was analyzed according to authors[9] who classified the medication in precipitators and objects. The pharmacological characteristics were listed from pharmacokinetic data existing in articles present in the *Micromedex*[12] database, which was consulted through the CAPES portal for journals, with restricted online access. In this base, made up of several specific volumes on pharmacology, the *Martindale – The complete drug reference* and the *USP DI® Drug information for the health care professional* were used.

The obtained data were stored in an electronic spreadsheet – Microsoft Excel XP, and SPSS software v. 13.0 was used for descriptive analysis.

RESULTS

As for the drug scheduling profile, it was observed that the whole sample (N=70) was medicated at 10 AM and 10 PM. In the afternoon, 95.7% (N=67) had their drugs scheduled for intake at 6 PM (Figure 1).

In spite of medication schedules for all the times in the 24-hour period, Figures 1 and 2 and Chart 1 illustrate only those in which an average amount of 0.10 scheduled drugs occurred.

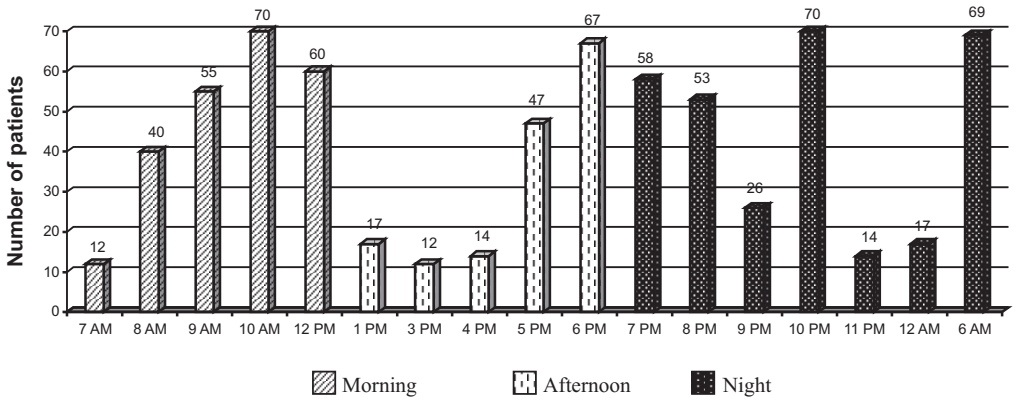

Figure 1 – Distribution of patients according to medication schedules – São Paulo, 2005.

The average of scheduled drugs at 10 AM (3.14) and 10 PM (2.90) was higher than at other times, with the highest number of simultaneously scheduled drugs found at these times (n=12) (Table 1 and Figure 2).

Table 1 – Descriptive analysis of the drugs used by patients submitted to bone marrow transplantation, according to their respective schedules – São Paulo, 2005.

TIME	DRUGS				
	Average	Median	Standard Deviation	Minimum	Maximum
07	0.23	0	0.54	0	2
08	0.94	1.00	0.93	0	3
09	1.41	2.00	1.00	0	5
10	3.14	3.00	1.26	1	9
12	1.26	1.00	0.79	0	4
13	0.24	0	0.43	0	1
15	0.17	0	0.38	0	1
16	0.24	0	0.52	0	2
17	1.19	1.00	1.32	0	6
18	2.63	3.00	1.29	0	6
19	1.53	2.00	0.92	0	3
20	1.36	1.00	0.99	0	3
21	0.63	0	0.95	0	3
22	2.90	2.00	1.70	1	12
23	0.33	0	0.75	0	3
24	1.51	2.00	0.79	0	3
06	2.51	2.00	0.92	0	6

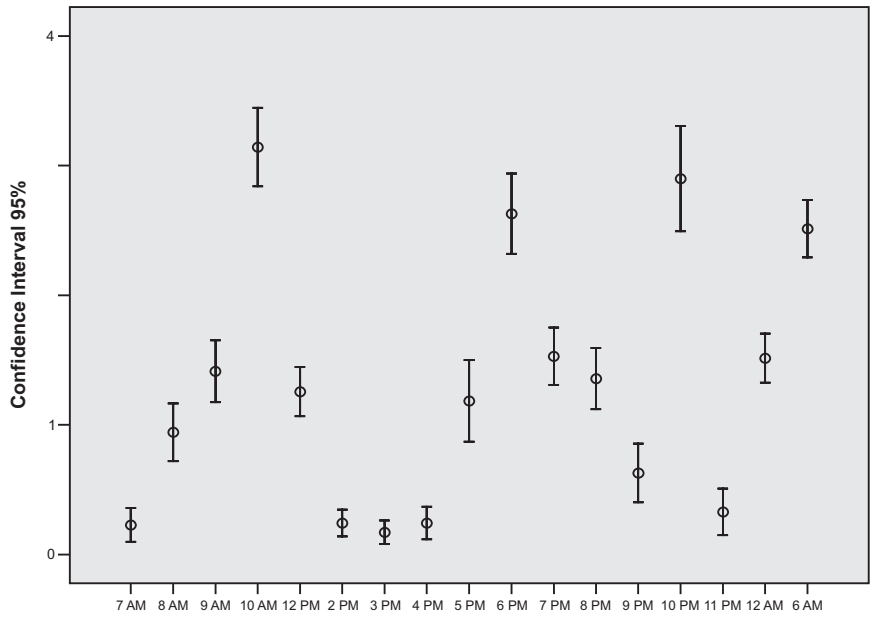

Figure 2 – Average number of scheduled drugs at the administration times – São Paulo, 2005.

In the profile of the pharmacological therapy the patients used in the BMT conditioning stage, 33 distinct drugs were identified, belonging to 8 therapeutic classes. Chemotherapy (34.0%), analgesic (21.0%) and digestive agents (15.0%) were the most frequent classes (Figure 3).

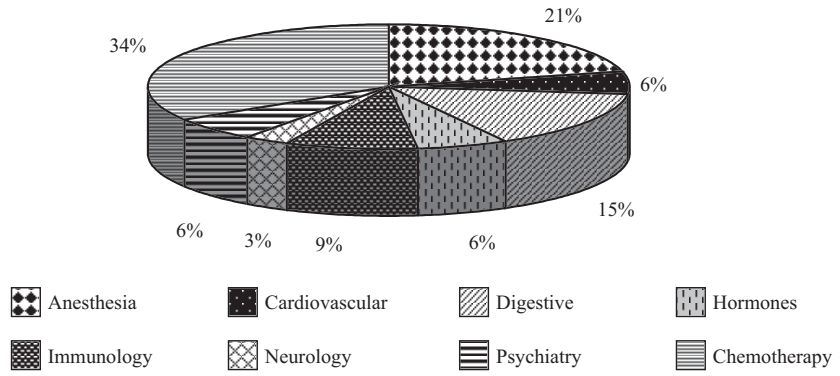

Figure 3 – Drugs used by patients submitted to bone marrow transplantation according to Alpha therapeutic classification – São Paulo, 2005.

72.7% (n=24) of the agents used by the sample had potential for interaction, i.e. characteristics that favored the occurrence of DI (Table 2).

Table 2 – Distribution of the drugs used by patients submitted to bone marrow transplantation according to their potential interaction – São Paulo, 2005.

Potential interaction	Drugs	
	N	%
Yes Allopurinol, naproxen, morphine, fentanyl, furosemide, omeprazole, atenolol, ondansetron, metoclopramide, ranitidine, hydrocortisone, dexamethasone, cyclosporine, phenytoin, diazepam, sertraline, fluconazole, levofloxacin, sulphametoxazole + trimethoprim, teicoplanin, vancomycin, ciprofloxacin, cyclophosphamide and melphalan.	24	72.7
No Metamizole, paracetamol, diphenhydramine, dimenhydrinate, cefepime, hydroxyzine, acyclovir, meropenem	9	27.3
Total	**33**	**100.0**

Among the drugs with potential of interaction (N=24), 79.2% (n=19) were classified as precipitators (allopurinol, antiemetic drugs, corticosteroids, diazepam, durosemide, phenytoin, naproxen, antineoplasic chemotherapy drugs and antimicrobials, ranitidine, omeprazole and sertraline) and 20.8% (n=5) as objects (morphine, fentanyl, atenolol, cyclosporine and melphalan). Among these, 16.7% (n=4) presented characteristics of both precipitators and objects (vancomycin, cyclophosphamide, metoclopramide and phenytoin).

In the analysis of potentially interactive drugs (N=24), 66.8% (N=16) had characteristics that affected the hepatic metabolism, either inhibiting (46.0%) or stimulating (20.8%) (Table 3).

Table 3 - Distribution of potentially interactive drugs used by patients submitted to bone marrow transplantation, according to pharmacological characteristics – São Paulo, 2005

Pharmacological characteristics	Drugs	
	N	%
Enzymatic inhibitors Allopurinol, omeprazole, ciprofloxacin, diazepam, fluconazole, sertraline, levofloxacin, metoclopramide, ondansetron, ranitidine and sulphametoxazole + trimethoprim.	11	46.0
Enzymatic inductors dexamethasone, hydrocortisone, omeprazole, phenytoin and cyclophosphamide	5	20.8
Close connection with plasmatic proteins naproxen, teicoplanin	2	8.3
Affects kidney clearance furosemide, vancomycin	2	8.3
Central Nerve System Action morphine, fentanyl	2	8.3
Narrow therapeutic index atenolol, cyclosporine	2	8.3
Total	**24**	**100.0**

Among the antimicrobial chemotherapy drugs, 66.7% (n=6) presented potentially interactive characteristics (sulphametoxazole + trimethoprim, teicoplanin, vancomycin, levofloxacin, ciprofloxacin), while 33.3% (n=3) did not (cefepime, acyclovir, meropenem).

As for the pharmacological characteristics of the antimicrobials that could trigger DI, 66.6% were enzymatic inhibitors (ciprofloxacin, fluconazole, levofloxacin, sulphametoxazole + trimethoprim).

Among the antimicrobials, fluconazole was highlighted as the drug with the highest amount of combinations (85.7%), capable of combining with five distinct drugs. Ciprofloxacin combined with three different drugs, although it occurred in a single patient. As for fluconazole, of the total number of patients (n=32) using it, 93.7% (n=30) presented DI-resulting combinations. It was also observed that half of the sample (n=35) was exposed to potentially interactive combinations (Table 4).

Table 4 – Distribution of patients submitted to bone marrow transplantation, according to exposure to existing combinations between potentially interactive antimicrobials and other drugs – São Paulo, 2005.

Antimicrobial drug combinations	Patients (n=35) N	%
Fluconazole + diazepam + omeprazole	8	22.9
Fluconazole + dexamethasone + omeprazole	4	11.4
Fluconazole + cyclosporine + omeprazole	4	11.4
Fluconazole + cyclosporine + phenytoin + dexamethasone + omeprazole	3	8.5
Fluconazole + omeprazole	3	8.5
Fluconazole + diazepam + cyclosporine + omeprazole	2	5.7
Fluconazole + diazepam + dexamethasone + omeprazole	2	5.7
Fluconazole + diazepam + cyclosporine + dexamethasone + sertraline + omeprazole	1	2.9
Fluconazole + dexamethasone + omeprazole + cyclosporine	1	2.9
Fluconazole + cyclophosphamide	1	2.9
Fluconazole + sertraline	1	2.9
Subtotal 1 (Fluconazole)	**30**	
Sulphametoxazole + trimethoprim + cyclosporine	2	5.7
Sulphametoxazole + trimethoprim + phenytoin	2	5.7
Subtotal 2 (Sulphametoxazole + trimethoprim)	**4**	
Ciprofloxacin + dexamethasone + diazepam + cyclophosphamide	1	2.9
Subtotal 3 (Ciprofloxacin)	**1**	
Total (1+2+3)	**35**	**100.0**

Fluconazole presented 7 distinct combinations (fluconazole + omeprazole, fluconazole+diazepam, fluconazole + cyclosporine, fluconazole + dexamethasone, fluconazole + phenytoin, fluconazole + sertraline, e fluconazole + cyclophosphamide), with 40.0% of the sample receiving fluconazole + omeprazole and 18.5% receiving fluconazole + diazepam (Table 5).

Table 5 – Distribution of patients submitted to bone marrow transplantation according to exposure to potentially interactive combinations of fluconazole – São Paulo, 2005

Potentially interactive combination	Patients N	%
Fluconazole + omeprazole	28	40.0
Fluconazole + diazepam	13	18.5
Fluconazole + cyclosporine	11	15.7
Fluconazole + dexamethasone	10	14.2
Fluconazole + phenytoin	3	4.2
Fluconazole + sertraline	2	2.8
Fluconazole + cyclophosphamide	1	1.4

For ciprofloxacin, the following combinations were identified: ciprofloxacin + cyclosporine (1.4%), ciprofloxacin + ciclophosphamide (1.4%), ciprofloxacin + diazepam (1.4%) and ciprofloxacin + dexamethasone (1.4%).

For sulphametoxazole + trimethoprim, 2 potentially interactive combinations were verified: sulphametoxazole + trimethoprim + cyclosporine (2.9%) and sulphametoxazole + trimethoprim + phenytoin (2.9%).

DISCUSSION

As for the scheduling profile of the drug administration times, the results obtained in the present study were similar to another study involving onco-hematologic patients, where it was observed that 74.4% of the administered doses were concentrated at 10 AM and 10 PM[13]. This concentration of several drugs at certain times is often related to the norms of the institution, as well as to nursing teams' work habits, which do not schedule medication at specific times so as to avoid forgetfulness or interference in the drug administration activity.

The average amount of drugs administered at 7 AM (0.23), 1 PM (0.24) and 7 PM (1.53), which correspond to the moment when shifts are changed, was lower, as well as at 3 PM (0.17) and 4 PM (0.24) (Table 3), which represent visiting times by family members. This allows us to infer that the nursing team avoided using certain times in this study, repeating a practice that is common in several services, aiming to meet institutional routines instead of patients' needs[13]. Besides, it is worth noting that simultaneous drug scheduling represents a risk factor of harmful DI for the patient, especially when these agents present a potential for interaction[10].

Regarding the pharmacologic profile, despite the occurrence of polypharmacy (7.97 drugs per patient, on the average) the identified classes were compatible with the therapeutic necessities of the patients, since the drugs introduced in the conditioning phase were aimed at avoiding, reducing or relieving frequent problems, such as nausea, vomiting, pain, bleeding and mucositis, consequences of antineoplastic chemotherapy[1-2,4].

The agents working on the digestive system are considered essential and administered in high dosages for the prevention and relief of nausea, vomiting and epigastric pain. The analgesic class, despite its low frequency, is important for controlling pain related to mucositis and fever control, commonly associated to neutropenia or tumor-related fevers. Besides, when the patients feel no pain, they present better food acceptance and higher tolerance to orally-administered drugs.

The broad utilization of the chemotherapy class is justified by the need to prevent and treat viral, bacterial, fungal and helmintic infections, frequent in patients submitted to BMT. Antimicrobials with higher frequencies were recommended by specialists, in accordance with the protocols from the *Centers for Disease Control and Prevention* (2000)[5,14]. Therefore, aciclovir, used by all patients (N=70) is the first antiviral choice for the prophylaxis of opportunist infections (simple herpes and varicella-zoster viruses), typical of the BMT conditioning phase[2,5,14].

At the clinic, fungal infections in patients submitted to BMT are mainly caused by *Cândida spp* and *Aspergillus spp*[2,6,15], and are related to factors like prolonged use and pancytopenia, use of wide-spectrum antibiotics, central venous access, chemotherapy, radiotherapy and immunosuppressant protocols for prevention of graft versus host disease. For these cases, fluconazole has been shown to significantly prevent and treat infections, besides being the antifungal drug of choice for BMT patients and the only one used in the present study[16]. One study that investigated candidemia related to the central catheter in patients submitted to allogenic BMT showed that several types of fungi were susceptible to fluconazole[17].

Despite clinical indications being adequate and fully justified by the patients' needs, an expressive share of the drugs (72.7%) presented potentially interactive characteristics, a factor that favored the occurrence of DI and could jeopardize the therapeutic success, depending on the combination adopted.

Among the drugs with interactive potentials, most (79.2%) were classified as precipitators, i.e. acting mainly through processes of enzymatic inhibition and induction and capable of affecting the pharmacological responses to the object drugs[7-8]. Among the precipitators, enzymatic inhibitors stood out (45.8%).

When the antimicrobial chemotherapy drugs were analyzed, 66.7% of them also presented precipitator characteristics and, except for vancomycin and teicoplanin, all others were enzymatic inhibitors, which could inhibit the metabolism of an object agent, increasing its serum level as well as its toxicity[7-9,12].

Therefore, the analysis of potentially interactive combinations of this therapeutic class included fluconazole, ciprofloxacin, levofloxacin and sulphametoxazole + trimethoprim, since vancomycin and teicoplanin, although potentially interactive, did not present combinations that could result in DI.

Half the patients (n=35) were exposed to combinations that could result in potential DI, regardless of the antimicrobial drug involved. Fluconazole combined with up to five agents who also presented interactive potentials, although only one patient was exposed to this situation. The combination with three agents occurred in 26.7% of the patients receiving antifungal drugs. These multiple associations could reflect in important adverse reactions, but difficult to correlate with the therapy, since the DI analysis, in literature and in computer programs, is done by matching two drugs at a time.

For fluconazole, some of the potentially interactive combinations (fluconazole + omeprazole, fluconazole + cyclophosphamide) could alter the absorption pattern, affecting the bioavailability of the azolic antimicrobial. In these cases, the simultaneous scheduling of medication should be avoided, since fluconazole dissolution may be reduced in the presence of a higher gastric pH[7-8].The potential clinical implications, in a situation where azolics are chronically co-administered with agents that affect their absorption include the decrease of effective serum levels and, consequently, reduced therapeutic efficiency. In BMT patients, due to the high risk of fungal infections, this alteration in bioavailability would certainly increase morbidity and mortality rate.

The other identified combinations could affect the metabolization standard of the object agent. Fluconazole is an enzymatic inhibitor (CYP_{450}) of the isoenzymes CYP2C8/9, CYP2C19 and CYP3A4, responsible for the biotransformation of several drugs. Co-administering this inhibitor with drugs used by the sample in this study, from the perspective of clinical implications, could result in increased serum levels of the combined agent with fluconazol, increasing the toxicity potential[7-8].

In daily practice, patients submitted to BMT used sulphametoxazole + trimethoprim since the start of their conditioning as prophylaxis for *Pneumocistis carinii*, with the therapy being interrupted on day -1 (the day before the infusion of bone marrow). However, cyclosporine is also introduced on day -1, a situation that certainly predisposes to the occurrence of DI among these agents. This combination can affect metabolism and result in increased nephrotoxicity and reduced serum levels of cyclosporine, increasing the risk of rejecting the graft[12]. The process of enzymatic inhibition triggered by sulphametoxazole + trimethoprim is slow and, even with its suspension on day -1, the consequent effects of this combination should be carefully monitored, especially in patients with risk factors for nephrotoxicity. In practice, it is necessary to establish the dose adjustment according to the serum levels of cyclosporine in order to assure therapeutic success, whenever there is a combined regimen[8-9, 12].

CONCLUSIONS

The present study allowed for the following conclusions: patients, in general, had their medication scheduled at "standard" times, i.e 10 AM (100%), 6 PM (95.7%) and 10 PM (100%) in the different work shifts of the nursing team; most drugs (72.7%) used by the patients presented potential for interaction, with the precipitators (79.2%) being worth noting, since they are able to affect the hepatic metabolism (66.8%); half the sample was exposed to co-administering potentially interactive antimicrobials, with fluconazole being the most commonly involved agent (85.7%), responsible for the exposure of 40% of the patients to the combination fluconazole+omeprazole.

Therefore, co-administering potentially interactive medication was frequent for BMT patients, a condition that, associated to complex polypharmacy and the simultaneous scheduling of administration times for these agents, could predispose the patient to undesirable events, affecting the safety of the therapy.

The authors believe that the nurse plays a fundamental role in the prevention of problems related to the necessary therapeutic combinations, like those verified in the present study. The nurse can: seek out detailed information (pharmacokinetic characteristic, adverse effects and interactions) about the drugs, avoid simultaneous scheduling of potentially interactive drugs and monitor the patients' response to the therapy, communicating each and every alteration to the clinician.

In BMT patients, whose clinical condition is critical, especially in the conditioning stage, and whose alteration of medication bioavailability, often caused by co-administering agents, can represent therapeutic success or failure, it is indispensable for nurses to acknowledge the importance of including, in the patients' daily prescription, nursing interventions directed at the pharmacological therapy.

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Correspondence addressed to: Rosimeire Barbosa Fonseca
Rua Visconde de Balsemão, 191 - Apto 64b Vila Mafra
CEP 03414-080 - São Paulo, SP, Brazil