

EVALUATION OF PHARMACEUTICAL CLINICAL INTERVENTIONS IN THE ICU OF A PUBLIC HOSPITAL OF SANTA CATARINA

ABSTRACT

Objectives: This study aimed to analyze the profile of pharmaceutical clinical interventions performed concurrently with the medical prescription evaluation service.

Methods: This is a cross-sectional, prospective and observational study conducted at the General Intensive Care Unit of a public hospital in Santa Catarina, Brazil, with 8 beds in full occupation. The study included 54 patients hospitalized from February to July 2017. Included in the study were medical prescriptions and pharmaceutical interventions recorded in the electronic medical record of patients of both genders of any race, origin, age and pathology. Medical prescriptions and pharmaceutical interventions that did not belong to the hospitalization unit studied and the study period were excluded from the study.

Results: A total of 499 medical prescriptions belonging to 54 patients (48%), male patients (68%), hypertensive patients (27%), diabetic patients (22%) and polytrauma patients (13%) were analyzed. Of the prescriptions analyzed, 91.1% had a need for pharmaceutical intervention with a total of 64.2% acceptance. The main drug-related problems were drug interaction (40%), potential adverse effect (28%) and need for dose adjustment (13%). The classes of drugs that most needed intervention were analgesics (23%), cardiovascular (14%) and antimicrobials (13%).

Conclusions: In assessing clinical pharmaceutical interventions as a benefit in addition to critical care in the Intensive Care Unit we emphasize the percentage of acceptance of pharmaceutical interventions (64%), mostly those involving increased risk for adverse effects and drug interactions, thus contributing to the prevention of complications.

Keywords: Adverse effects, interactions between drugs, ICU, Hospital Pharmacy.

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INTRODUCTION

Patients hospitalized in the ICU are considered at high risk for problems related to medications, because they are in critical condition and because of the complexity of their pharmacotherapy.¹ In addition, its clinical condition often requires the use of several drugs, generating extensive prescriptions and leading to greater possibility of developing adverse events.²

Medical prescription (PM) is one of the important steps in the process of supplying medicines to the patient, which involves a multidisciplinary team: doctors, pharmacists, nurses and others, in which each professional has his / her responsibility and duties.^{3,4} In this context, the pharmaceutical professional has co-responsibility in disease prevention, health promotion and recovery.⁵

Studies carried out in Brazil demonstrate the relevance of this professional's performance in a multidisciplinary team by presenting acceptance of the pharmaceutical interventions that contributed to the reduction of risks of adverse drug events.^{6,7} Also, it is emphasized that the performance of a multiprofessional team allows a multidimensional evaluation of the patient and an integrated planning of the care plan.^{8,9}

Clinical Pharmacy has been gaining space beyond hospital institutions in recent years. Among the pharmaceutical services performed within a clinical pharmacy process is the prescription analysis, which, in identifying real or potential problems, generates one or more pharmaceutical interventions. Pharmaceutical intervention (PI) should be performed through appropriate and documented planning with the user

and health professionals for the purpose of resolving or preventing disorders, becoming an integral part of the pharmacotherapeutic follow-up process for contributing to the reduction of medication administration errors, treatment effectiveness, leading to improvement of clinical results, raising patient safety and quality of life.^{5,9,11} Given the low diffusion of the practice of this modality of attribution and use of the knowledge of the pharmacist, the present study is justified, which aimed to analyze the profile of pharmaceutical clinical interventions performed concomitantly to the service of evaluation of medical prescription.

METHOD

This is a cross-sectional, prospective and observational study performed at the general ICU of a public hospital in Santa Catarina, which contains eight beds with full occupation. The Hospital is a reference in urgency and emergency, intensive treatment, neurosurgery, oncology, orthopedics, traumatology and burned in the North region of Santa Catarina. Being a national reference in the treatment of stroke. The study included patients who were admitted to the general ICU during the study period. Included in the study were medical prescriptions and pharmaceutical interventions recorded in the electronic medical record of patients of both sexes of any race, origin, age and pathology during the period from February to July 2017.

Data collection and analysis

Subjective and objective data were collected from MV2000® Hospital Management System, referring

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to the patient, prior to the delivery of prescriptions and interventions. Of the data used in the analysis of pharmacotherapy regarding the patient were: identification, reason for hospitalization, comorbidities, medications for prior use and continuous use, clinical changes during hospitalization, addictions, allergy, age, weight and results of laboratory tests. The following variables were considered: indication, dosage, dose, pharmaceutical form, dilution, route of administration, interactions, physicochemical incompatibility, stability.

Regarding the prescription analyzes, the variables collected were the necessary interventions, according to type, quantity, acceptance, and reason for non-acceptance.

The databases consulted during the prescription analysis to infer the need for intervention were: *Stabilis 4.0* (incompatibility interactions), *Pharmaceutical Handbook** (General Medicine Information), *Sanford Guide** (dosage adjustment for antibiotic medications), *Medscape**, *Drugs** and *Micromedex 2.0* (severity and relevance of interactions and degree of evidence).

From these databases and the data collected in the system, the profile of drug interactions and potential adverse events was raised, since the observation of its real expression was not the target of this study.

Data were analyzed using Microsoft® Excel Office 2010 using descriptive statistics to characterize the population investigated by means of frequency.

Ethics in Research Considerations

The research was approved by the research ethics committee of the University of the Region of Joinville - UNIVILLE under the opinion nº 2387930.

RESULTS

The study population consisted of 54 patients, being younger than 18 years (6%, n=3), from 18 to 63 years old (48%, n=26) and from 64 years old (46%; with more frequent males (68%, n=37). Clinical scenarios covered the following specialties: Stroke (26%; n=14), neoplasms (17%, n=9), polytrauma (13%, n=7), burns (6%, n=3) and others (39%; lower individual frequency; and the most frequent comorbidities were: hypertension (27%, n=22), diabetes mellitus (17%, n=14) and heart disease (6%, n=5).

Regarding the period of hospitalization, the majority (68%, n=37) remained in the ICU for more than 7 days, and 22% (n=7) of these remained between 31 and 165 days. However, the majority (70%; n=38) were discharged from the unit and the others died.

A total of 499 prescriptions were analyzed, of which 52% (n=233) were primary for the 24-hour period and 48% (n=216) were complementary; on average 16 drugs per day per patient. Of the total prescriptions analyzed, 91% (n=409) required intervention resulting in 664 registered IFs, as presented in Table 1.

Table 1. Types and frequencies of problems related to prescription drugs that resulted in pharmaceutical interventions performed at the general ICU of a public hospital in the North of Santa Catarina.

Type	N (%)	Note
Drug interaction	265 (40)	Sum of adverse effect
Potential adverse effect	183 (28)	With potential for clinical worsening
Need for dose adjustment	88 (13)	Dose erroneous, nonexistent or according to renal function, hepatic and age.
Physico-chemical incompatibility	57 (9)	Possibility of annulment of the action
Therapeutic duplicity	20 (3)	Repeating effect promoter
Need for replacement	16 (2)	Motivated by lack of the drug
Route of administration	10 (2)	Wrong route
Need for dilution justification	9 (1)	Volume correction
Duplicidade de itens	5 (0.7)	Same twice-prescribed drug
Indication	5 (0.7)	Unnecessary drug. Required but not prescribed drug
Posology	4 (0.6)	Pleasure error
Guidance to prescriber	1 (0.1)	Request for high cost drug request
Patient guidance	1 (0.1)	Clarification for improved adherence to treatment
Total	664 (100)	

This study presented a total of 956 drugs with IF, with 76 different active principles. Of these, the most frequent were fentanyl (9%), morphine (7%), heparin (7%), methadone (5%) and hydrocortisone (5%). When distributed by therapeutic class, the most frequent were analgesics (23%, n=219), cardiovascular (14%, n=134), antimicrobials (13%, n=127), anticoagulants 9%, n=81) and corticoids (8%, n=79), as demonstrated in Table 2.

Table 2. Distribution by therapeutic class of drugs that required pharmaceutical intervention in a general ICU of a public hospital in the North of Santa Catarina.

Therapeutic class	N (%)
Analgesic (opioids and nonopioids)	219 (23)
Cardiovascular	134 (14)
Antimicrobial	127 (13)
Anticoagulant	81 (9)
Corticoid	79 (8)
Antidepressant	52 (5)
Sedative	50 (5)
Anesthetic	43 (5)
Antiepileptic	43 (5)
Antiulcer	34 (4)
Antipsychotic	23 (2)
Antiemetic	14 (2)
Hypolipid	14 (2)
Thyroid hormone	13 (1)
Neuromuscular blocker	12 (1)
Electrolyte	4 (0.4)
Acetylcholinesterase inhibitor	4 (0.4)
Antianemic (human erythropoietin)	3 (0.3)
Immunosuppressant	2 (0.2)
Laxative	2 (0.2)
Enzyme (pancreatin)	1 (0.1)
Hypoglycemic (insulin)	1 (0.1)
Vitamin (complex B)	1 (0.1)
Total	956 (100)

Table 3 presents the drugs most involved in the most frequent FI, presented in Table 1, which together represented 81% of the IFs performed. However, it is emphasized that the less frequent interventions also presented a relevant potential for morbidity. Of the potential drug interactions that presented a frequency of less than 2% alone, they represented 57% (n=56) of the total number of possible interactions, being as relevant as those with a higher incidence in the face of potential risks. The same reasoning applies to 16 different drugs, which together represent 25% of the potential adverse effects, despite having an individual frequency of less than 4%. The same is true for dose adjustment needs, where 15 drugs accounted for 24% incidence. The related risks were dose toxicity above therapy or drug inefficacy when the dose was below therapy.

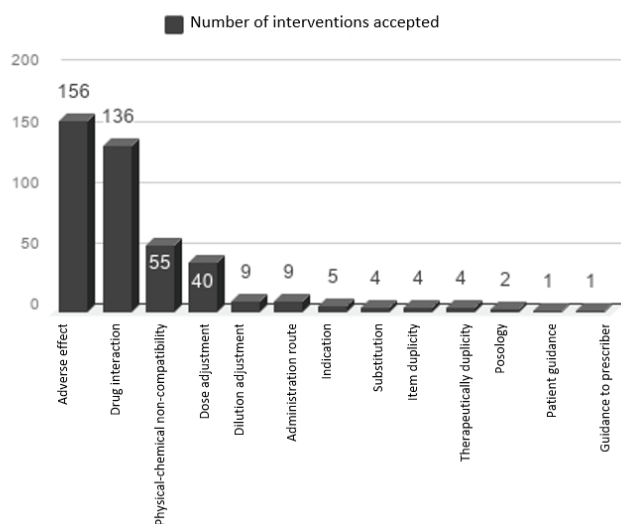
Table 3. More frequent pharmaceutical interventions and drugs more involved in a general ICU of a public hospital in the north of Santa Catarina.

Type of Intervention	Medications	%	Related risks
Communication of Risk of Interaction	Morphine x Fentanyl	15	Serotonergic syndrome
	Piperacillin x Heparin	8	Bleeding
	Sulfamethoxazole x Heparin	5	Bleeding
	Metoclopramide x Risperidone	5	Extrapyramidal reactions
	Levothyroxine x Heparin	4	Bleeding
	Amitriptyline x Methadone	2	QT interval widening
	Fentanyl x Propofol	2	Excessive sedation, coma, death
	Metoprolol x Verapamil	2	Bradycardia
	Another 56 distinct interactions with individual frequency < 2%	57	...
	Hazard Communication of Adverse Effect	Hydrocortisone	19
Amitriptyline		11	Delirium, constipation
Methadone		11	Delirium, constipation
Dexamethasone		10	Electrolyte and metabolic disturbance
Phenytoin		8	Metabolic Disorders
Prednisone		7	Electrolyte and metabolic disturbance
Morphine		6	Delirium, constipation
Fentanyl		4	Delirium, constipation
Another 16 different drugs with frequency < 4%		24	...
Dose adjustment		Metoclopramide	23
	Ranitidine	14	
	Heparin	14	
	Lorazepam	6	Dose above or below therapy with impaired renal or hepatic function; dose therapy over the elderly patient.
	Piperacillin + Tazobactam	6	Risk of toxicity or drug ineffectiveness.
	Ampicillin + Sulbactam	5	
	Midazolam	4	
	Risperidone	4	
	Another 15 different drugs with frequency < 3%	24	

Of the IFs performed in the general ICU, it was observed that the majority (64%, n=426) had acceptance, being considered accepted the interventions that promoted change in pharmacotherapy and were not accepted (36%; n=238) accepted by the prescriber did not promote changes in pharmacotherapy.

Among the most commonly accepted interventions were: potential adverse effects (37%, n=156), potential drug interactions (32%, n=136), physicochemical incompatibility (13%, n=55) and need for dose adjustment (9%, n=40), as shown in Figure 1.

Figure 1. Pharmaceutical clinical interventions accepted in the general ICU of a public hospital in the North of Santa Catarina



Of the IFs that were not accepted, 97% (n=230) were justified by the clinical condition of the patient with risk assessment and pharmacotherapy benefit. The reasons for not accepting the others were: a prescription copied from the previous day by another prescriber without change (1%; n=3), decided by the caller for not adjusting the dose of the drug by progressive improvement in renal function, although he still needed adjustment (0.8%; n=2), forgetfulness of the prescriber (0.4%; n=1), wrong / unnecessary intervention (0.4%; n=1) and material collection error leading to altered requiring the suspension of the drug (0.4%, n=1).

When the IFs were not accepted, the frequencies found were: potential drug interaction (54%; n=129), need for dose adjustment (20%; n=48), potential adverse effect (11%; n=27), therapeutic duplicity (7%, n=16), suggestion of substitution (5%, n=12), physical-chemical non-compatibility (0.8%, n=2), posology (0.8%, n=2), route of administration (0.4%, n=1) and item duplicity (0.4%; n=1).

Regarding the severity classification of the risks related to the types of IF performed, only drug interaction had a classification of degree of severity and level of evidence presented by the consulted databases. And, of the potential interactions noted, but not accepted, 57% (n=74) presented "greater" severity and the level of evidence classified as "reasonable" (Insufficient documentation, but pharmacology points to existence of interaction); 15% (n=19) "severe" with "good" evidence (Documentation is sufficient, but adequate controlled studies are lacking); 12% (n=15) "contraindicated" with "reasonable" evidence; 10% (n=13) "moderate" with "good" evidence; 3% (n=4) "minor" with "good" evidence and 3% (n=4) "monitor closely" with "good" evidence.

Despite the associated risks and the patients' clinical needs, it was decided to keep the medication, but with monitoring for the described risk, since drug therapy is usually necessary for clinical stabilization.

DISCUSSION

The present study had a population where most of the patients were male adults, but also a high number of elderly patients, which may be related to the types of specialties and the most frequent comorbidities found; and a large amount of drugs prescribed per day per patient. When it comes to an ICU, where patients are critical and present the most diverse clinical scenarios and morbidities, it is common to find many medications per prescription.

In a study involving prescription analysis performed at a Campo Grande-MS ICU in 2011, a similar population was also found where the patients had a mean age of 59 years, differing in sex, the majority of which were female (55%), average number of 14 prescription drugs.² And in another study carried out at an ICU in Curitiba-PR in 2012 the population was most of the male gender, with a mean age of 59 years and an average of 11 prescription drugs.¹²

The high quantity of prescription drugs directly implies greater potential for important drug interactions. In this study, 956 drugs were observed requiring pharmaceutical intervention, with the most frequent being: potential drug interactions, followed by potential adverse effects, need for dose adjustment and physicochemical incompatibility.

In a study carried out in Fortaleza-CE in 2013, although not in the same order of frequency, the types of PM interventions most found in the ICU were: dilution management (14%); dose adjustment (12%); management of adverse drug events (10%); and management interaction medication-drug (8%), results referring to 84% (n=699) of the accepted interventions performed with the medical staff.¹³

In a study carried out in an ICU of Recife-PE in 2013, results were found that compare with the current study, in relation to the most frequent types of interventions: adjustment in infusion time (38%); volume of infusion plus prescription (36%); enteral catheter (13%).⁹ It is possible that the results found for each study mentioned above are directly related to the type of routine of the pharmacy services of the studied sites.

The analysis of prescription is essential in the sense that it allows the anticipation of problems related to drugs that are very possibly avoidable. This contributes to ensuring the rational use of drugs within maximum parameters of efficacy and minimum toxicity, considering that the targets of care are patients with severe and little stable in the ICU. Thus, the prior detection of problems related to pharmacotherapy can prevent the occurrence of adverse events and consequent expenses resulting from the management of these.^{9,12} Therefore, prescription analysis has been presented as an important part of the pharmacotherapy follow-up process with a focus on patient safety.¹⁴⁻¹⁵

Although it was not possible to measure the impact of pharmaceutical interventions in the present study, it was found that the clinical pharmacy service can contribute to the prevention of drug-related problems with risk minimization, since the detailed PM analysis and pharmacotherapeutic follow-up by the pharmacist, resulted in the identification of a large number of IFs. Other studies have also shown that clinical pharmacy service is an important means to prevent problems and improve the quality of medication use. In one of these, the benefit of the pharmacist's involvement in clinical activities was highlighted, presenting a large number (n=933) of interventions performed in prescriptions of sectors with critical patients, among them ICU.¹² In another study, a total of up to 8.2 daily interventions per ICU patient.¹⁰ The present study had an average of 3 daily interventions per patient, with a minimum of 0 intervention and a maximum of 13 interventions, the largest number of interventions were for prescriptions with more than 25 prescribed drugs.

Of the IFs performed in this study, it was observed that the majority had acceptance resulting in a change in pharmacotherapy. And those not accepted, even if the majority (97%) of these were pertinent, did not result in a change in pharmacotherapy, they went through consideration of risk assessment and benefit by the prescriber who chose to maintain pharmacotherapy despite the associated risk, with clinical prevalence prevailing of the patient.

When quantifying acceptance of interventions generally, including partial acceptances in which the prescriber agreed that there was risk, but chose to maintain the prescription for the associated benefit, a high acceptance prevalence (98.8%) was obtained. A result close to that of this study was found with IF performed in a PIC-Recife ICU in 2013, with 98.2% acceptance.⁹ They also found a relatively high result of acceptance of the interventions (74.7%) in a study carried out in a Curitiba - PR ICU in 2012,¹² and another with 82.2% in a hospital in Belo Horizonte, MG in 2013.⁸

Even with partial acceptance, the interventions served as a warning to monitor the risks to the patient, especially when considering their severity, which assumed the following proportions: higher risk (57%), severe (15%) or moderate (10%) and contraindicated (12%), recommendation to monitor closely reached 3% and only 3% were of lower severity. With this, it can be said that the interventions contributed to add care to pharmacotherapy.

It is essential that the multiprofessional team be open to consider reflection on the potential for problems related to medications detected in prescription evaluation, since pharmacotherapy involves not only medical activities, but also those of other health professionals such as: care in administration the medication by the nurse; changes in the mental state accompanied by the psychologist that may be related to the drug effect; changes in nutritional status accompanied by the nutritionist who may be by the action of medications; the outcome of physical therapy work for withdrawal from mechanical ventilation may also be related to the medications used; among other professionals. And hospital pharmacy services should embrace and take care of this pharmacotherapy-based clinical care service to make it a daily routine, not only in the ICUs, but in all sectors of the hospital. In addition, it is necessary to work on variables that go beyond interprofessional human relations, which include infrastructure, team availability, time, specific knowledge about pharmacology.

Studies carried out to analyze the performance of the clinical pharmacist presented data demonstrating the impact of pharmaceutical clinical interventions as a benefit both in pharmacotherapy and in pharmacoeconomics.¹⁶⁻¹⁷ Together with the results of the present study, these data point out that the clinical pharmacy service in the monitoring of drug use has much to contribute with the health team, where the main beneficiary of the care will be the patient. The prevention of dangerous interactions and the triggering of adverse reactions contributes to the reduction of hospitalization time and, consequently, to the reduction of the expenses that a prolonged hospitalization can have.

The study had as a limitation to be performed only based on the interventions performed by the pharmacist Resident and pharmacist Preceptor of the multiprofessional intensive care residency program, which were responsible for the daily follow-up of the ICU medical prescriptions. The ideal would be to evaluate interventions performed by several pharmacists, but the clinical pharmacy is not yet a routine service of the hospital pharmacy service at the place of study, which would be fundamental to bring greater benefits to patients and the hospital.

CONCLUSION

When assessing clinical pharmaceutical interventions as a benefit in addition to the care of critical patients in the ICU, the percentage of acceptance of pharmaceutical interventions (64%) was overwhelmingly those involving increased risk for adverse effects and drug interactions, thus contributing to the prevention of complications. Therefore, the evaluation of prescription followed by pertinent pharmaceutical intervention can prevent errors related to pharmacotherapy, aggravating the patients' health and, consequently, may contribute to the reduction of the socioeconomic impact of prolonged hospitalizations.

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Contributors

DD, LPLW, EMP and FMF were responsible for the design and planning of the research project. DD was responsible for obtaining the survey data. DD, LPLW and EMP were responsible for data analysis and article writing. LPLW and EMP were responsible for reviewing the article. All authors approved the final version to be published.

Conflict of interest

The authors declare that there are no conflicts of interest

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