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Pharmaceutical Intervention: description of the role of the clinical pharmacist in intensive care units

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Abstract

Objective: To describe and analyze the profile of pharmaceutical interventions by identifying and classifying drug-related problems (DRP) and carrying out pharmaceutical interventions in order to highlight the importance of the intensivist clinical pharmacist. **Methodology:** Cross-sectional, descriptive and retrospective study of the results of the pharmacotherapeutic monitoring service aimed at critically ill patients admitted to the Cardiological and General ICUs of a state public hospital. Data were collected from September 1, 2020 to March 30, 2021, through an institutional pharmacotherapeutic follow-up report and the DRPs identified, quantified and classified according to the Pharmaceutical Care Network Europe. The drugs involved in the problems were categorized using the Anatomical Therapeutic Chemical. **Results:** A total of 331 patients were followed up during the study period, with the identification of 181 MRPs. Of these, most were related to adverse event (possibly) representing (34.8%) and unavailability or inadequacy of pharmaceutical presentation (29.8%). The main causes of DRP identified were inadequate pharmaceutical form (19.3%) and unavailable prescribed medication (19.3%). Most of the problems (24%) were related to the class of drugs that act on the nervous system and the class of general anti-infectives for systemic use (23%). Of the recommendations made for the optimization of pharmacotherapy, 98.3% were accepted, with the suggestion of changing the pharmaceutical form prevailing (22.1%). **Conclusion:** The high acceptability of the interventions suggested by the intensivist clinical pharmacist reinforces the importance and need for the clinical services provided by this health professional.

Key words: intensive care units; critical care; clinical pharmacy; pharmaceutical care; drug-related problems; prescription drug monitoring.

Intervenção Farmacêutica: descrição do papel do farmacêutico clínico em unidades de terapia intensiva

Resumo

Objetivo: Descrever e analisar o perfil de intervenções farmacêuticas através da identificação e classificação dos problemas relacionados a medicamentos (PRM) e realização de intervenções farmacêuticas visando evidenciar a importância do farmacêutico clínico intensivista. **Metodologia:** Estudo transversal, descritivo e retrospectivo dos resultados do serviço de acompanhamento farmacoterapêutico direcionado aos pacientes críticos internados nas UTI's Cardiológica e Geral de um hospital público estadual. Os dados foram coletados, no período de 01 de setembro de 2020 a 30 de março de 2021, por meio de relatório de acompanhamento farmacoterapêutico institucional e os PRM identificados, quantificados e classificados conforme a *Pharmaceutical Care Network Europe*. Os medicamentos envolvidos nos problemas foram categorizados utilizando o *Anatomical Therapeutic Chemical*. **Resultados:** Um total de 331 pacientes foram acompanhados no período do estudo, com identificação de 181 PRM. Destes, a maior parte foi relacionada à evento adverso (possivelmente) representando (34,8%) e indisponibilidade ou inadequação de apresentação farmacêutica (29,8%). As principais causas dos PRM identificados foram forma farmacêutica inadequada (19,3%) e medicamento prescrito não disponível (19,3%). A maior parte dos problemas (24%) relacionava-se à classe dos medicamentos que atuam no sistema nervoso e à classe dos anti-infecciosos gerais para uso sistêmico (23%). Das recomendações realizadas para a otimização da farmacoterapia, 98,3% foram aceitas sendo prevalente a sugestão de alteração da forma farmacêutica (22,1%). **Conclusão:** A alta aceitabilidade das intervenções sugeridas pelo farmacêutico clínico intensivista reforça a importância e necessidade dos serviços clínicos prestados por este profissional da saúde.

Palavras-chave: unidade de terapia intensiva, cuidados intensivos, farmácia clínica, cuidados farmacêuticos, problemas relacionados aos medicamentos; monitoramento de prescrição.

Introduction

According to Pharmaceutical Care Network Europe (PCNE), Drug-Related Problems (DRPs) can be defined as any event that interferes with the patient's pharmacotherapy and, consequently, leads to or may lead to undesirable clinical outcomes[1]. The Intensive Care Unit (ICU) offers assistance to patients in critical clinical conditions, and is the place where the highest number of DRPs occurs. Most critically-ill patients are more prone to DRPs due to the clinical nature of their diseases, complex and high-risk pharmacotherapy, polypharmacy, limited availability of venous access and frequent changes in pharmacotherapy due to their hemodynamic instability[2,3,4]. Thus, adverse events and their consequences have more severe dimensions in patients under intensive care and are often related to fatal outcomes and/or need for additional life support measures resulting in increased hospitalization times[2,3].

The clinical pharmacist plays an essential role within the multiprofessional team, promoting advanced pharmacotherapy in intensive care and better care quality for critically-ill patients by ensuring effectiveness and safety of the pharmacological treatment, resulting in a reduction of the mortality rate and hospitalization times for these patients. The following can be mentioned among the activities performed by this professional: follow-up and monitoring of the medical prescription with regard to the therapeutic indication of the prescribed medication, dose, dosage, administration route, dilution, incompatibilities and drug interactions, standardization of infusion solutions, elaboration of protocols, participation in multidisciplinary rounds, integration with the team and pharmacotherapy optimization, ensuring safety and effectiveness of the pharmacological treatment, in order to prevent the occurrence of DRPs[2,3,4,8].

Any planned action included in the pharmacotherapy follow-up process that requires recording, being carried out together with health professionals and patients and with the objective of solving or preventing negative clinical results arising from medication use, is defined as a pharmaceutical intervention. During the COVID-19 pandemic, the role of the intensive care clinical pharmacist evolved due to the new institutional responsibilities, the need to implement actions for safer practices, training new professionals called upon for reinforcement, monitoring of literature and clinical research initiatives and, finally, contributing to the development of new therapeutic strategies, thus certifying the importance of this professional in promoting rational use of medications, as well as promoting safety and efficacy of the pharmacological treatments[11].

Although the benefits of including a clinical pharmacist in the ICU are well established in the international literature, dissemination of Brazilian studies involving the practice, detailing of interventions of the clinical pharmaceutical service in this hospital sector and the relevance of this professional is still scarce. In this context, this study aims at describing the results obtained by the performance of the intensive care clinical pharmacist, through the identification and classification of DRPs, the implementation of interventions aimed at resolving them and, thus, highlight the importance of this professional in the Cardiology and General ICUs for adults of a public teaching hospital in the city of Joinville, Santa Catarina.

Methods

A cross-sectional, descriptive and retrospective study referring to the pharmacotherapy follow-up service directed to critically-ill patients hospitalized in the Cardiology and General ICUs of a state public hospital located in Joinville - Santa Catarina, a reference in Cardiology; cardiovascular, general and vascular surgery; Psychiatry, and infectious diseases. The project was approved by the Research Ethics Committee of the Hans Dieter Schmidt Regional Hospital on September 28th, 2021, under CAAE number: 52108521.0.0000.5363, with permission to waive the Free and Informed Consent Form.

The study locus is considered a large-size teaching hospital of medium and high complexity, with a closed clinical staff, which has nearly 250 beds, of which 10 are in the Cardiology ICU and 10 are in the General ICU. Data collection took place between September 1st, 2020, and March 30th, 2021.

The study included patients hospitalized for more than 24 hours in the Cardiology and General ICUs included in the pharmacotherapy follow-up service and the exclusion criteria selected corresponded to patients who had not been followed-up by the clinical pharmacist during their hospitalization period, those who stayed for less than 24 hours in the ICUs or those who had incomplete follow-up forms, thus precluding data analysis.

The pharmacotherapy follow-up service was performed by resident pharmacists in intensive care every weekday and during the weekends, when they were on duty at the institution. The patients were included in the follow-up based on hospitalization time and according to the availability of resident pharmacists. The pharmacists used the institutional pharmacotherapy follow-up spreadsheet, developed based on the PW (*PharmacotherapyWorkup*) methodology, created by Cipolle *et al.* (2012).

In line with the PW method, the therapeutic follow-up involved full and daily evaluation of the patient's clinical and laboratory parameters, as well as the medical prescriptions (evaluating indication, dose, frequency, dosage, administration route, drug interaction, dilution and compatibility, among others). Each DRP identified resulted in a specific and individualized intervention with the multiprofessional team aiming at its resolution. As a first step, these interventions were performed verbally (through a discussion of the problem identified in a timely manner with the physician responsible for the patient or during the multiprofessional rounds), with subsequent recording of the evolution in the electronic medical chart.

Based on the PCNE DRP classification, the problems were grouped according to treatment effectiveness, treatment safety and other aspects. The categories of causes were drug selection, pharmaceutical form, dose selection, treatment length in time and drug dispensation, while the intervention plan was classified at the prescriber or medication levels. In relation to acceptability of the interventions performed, they were grouped into accepted intervention and non-accepted intervention, while the DRP status was separated into resolved, partially resolved and unresolved.

Diverse information on the demographic profile (gender, age and clinical outcome), DRPs identified and classified according to PCNE, and pharmaceutical interventions carried out and with their evolution recorded in the patient's electronic medical chart from the Hospital's Health Management System (*Sistema de Gestão em Saúde*, SGS) were analyzed by issuing a retroactive

months report containing the date, the number of the medical record and the description of the intervention for later evaluation. The medications involved in the DRPs identified were classified according to the Anatomical Therapeutic Chemical (ATC) model, taking into account the categorization according to the main anatomical/pharmacological groups.

The secondary data, obtained from the SGS report, were tabulated in Microsoft Excel® spreadsheet format and the analysis was performed using the same program, in which descriptive statistics techniques were applied. The results were presented in frequency distribution tables, charts and graphs.

Results

During the period from September 2020 to March 2021, the clinical pharmacy team carried out the pharmacotherapy follow-up of 331 patients hospitalized in the ICUs, analyzed 2,658 medical prescriptions and performed 234 pharmaceutical interventions.

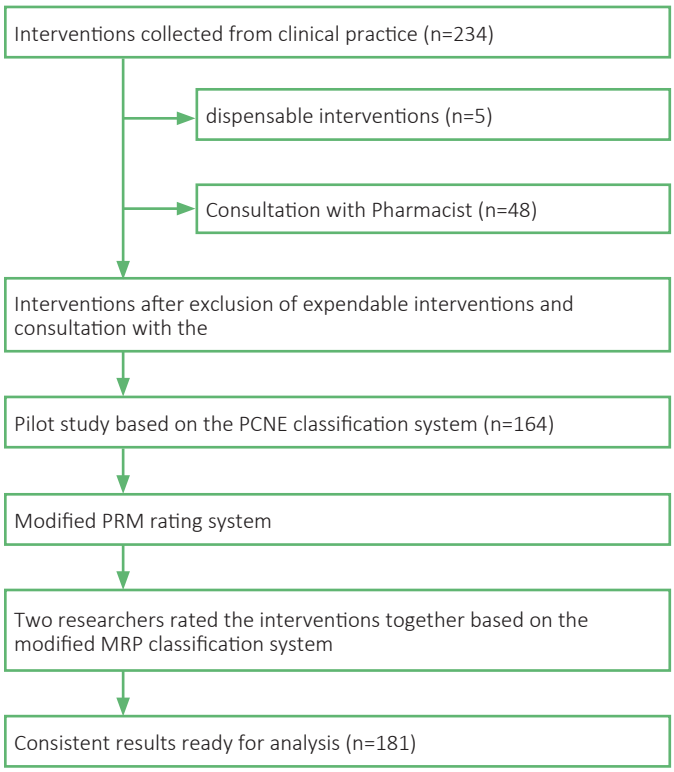
The mean age of the population of patients admitted to the Cardiology ICU was 60.9 ± 11.5 years old, 64.2% of whom were male (n=115), while the mean age of the patients admitted to the General ICU was 56.3 ± 16.1 years old, with 57.9% male subjects (n=88). The age group corresponding to most of the patients allocated to the Cardiology ICU was > 60 years old (55.9%), while for the General ICU it was from 18 to 60 years old (54.6%). The mean age in the ICUs under study (Cardiology and General) was 58.3 years old and it was verified that 61.3% of the hospitalized patients were male. The main clinical outcome of the patients hospitalized in the ICUs was discharge to the ward (75.5%) (Table 1).

Table 1. Characterization of the patients followed-up by the pharmacist throughout the study period, according to hospitalization unit

Characterization of the patients (n=179)	n	Proportion (%)
CARDIOLOGY ICU		
Age group, years old		
18-60	79	44.1
> 60	100	55.9
Gender		
Male	115	64.2
Female	64	35.8
Outcome		
Discharge from the ICU	147	82.1
Death	32	17.9
Transfer	0	0
GENERAL ICU		
Age group, years old		
18-60	83	54.6
> 60	69	45.4
Gender		
Male	88	57.9
Female	64	42.1
Outcome		
Discharge from the ICU	103	67.8
Death	46	30.2
Transfer	3	2

In the period, 234 interventions were collected through the SGS pharmaceutical evolution report and analyzed by the clinical pharmacist, and they were divided into dispensable interventions (n=5), defined as recommendations related to documentation or non-clinical issues, consultation with the pharmacist by the multidisciplinary team (n=48) and interventions related to DRPs (n=181) found in the 2,658 prescriptions analyzed. Classification of the pharmaceutical interventions was carried out jointly by two researchers based on the modified DRP classification system (modified PCNE) aiming to include the 181 interventions found as described in the flowchart presented in Figure 1.

Figure 1. The flowchart for classifying drug-related problems during pharmaceutical



A flowchart was used to show the PRM classification process using a modified PRM classification system (modified PCNE). The expendable interventions (n=5) and consultation with the pharmacist (n=48) were interventions that had no clinical relevance

The result of the data analysis for the DRPs and the related causes are described in Table 2. Among the 181 DRPs identified, the main problems were “P2.1 (Possible) ongoing adverse event” (34.8%), “P3.3 Unavailability or inadequacy of pharmaceutical form” (29.8%) and “P3.2 Unspecified problem” (14.4%). The results of the classification of medications according to the Anatomical Therapeutic Chemical (ATC) model indicated that the 3 main organic systems related to DRPs were “N - Nervous system” (24%), “J- General anti-infectives for systemic use” (23%), “B - Blood and hematopoietic organs” (15%) and “A - Digestive system and metabolism” (14%), as shown in Figure 2.

Among the 181 interventions proposed by the intensive care clinical pharmacists to solve the DRPs, nearly 68.5% (n=124) were made at the medication level, mainly including “I3.3 Formulation changed” (22.1%), “I3.4 Instructions for use changed”(13.3%) and “I3.2 Dosage changed” (12.7%), according to Table 3. The

interventions at the prescriber level represented 31.5% (n=57), of which 52.2% were discussed with the prescriber in order to find the best clinical decision together and 28.1% were proposed to him based on knowledge of the pharmacokinetic and pharmacodynamic parameters. No intervention was proposed at the patient level because, as they were critically-ill subjects admitted to the ICUs, most of them were sedated, mechanically ventilated or unable to communicate.

The analysis of 181 causes of DRPs showed that "C1 Drug selection'' caused the highest proportion of DRPs (30.4%), followed by "C3 Dose selection'' (29.8%), "C2 Pharmaceutical form'' (19.3%) and "C5 Dispensation'' (19.3%). The main subcategory of causes of DRPs was "C2.1 Inadequate pharmaceutical form (for this patient)'' and "C5.1 Prescribed medication not available''.

Table 2. Number of Drug-Related Problems (DRPs) and reasons for all the medications during the pharmaceutical interventions

Description	All medications	
Problem	**n**	**Proportion (%)**
P1 Treatment effectiveness	**31**	**17.1**
P1.2 Less than optimized effect	15	8.4
P1.3 Untreated symptoms or indication	16	8.8
P2 Treatment safety	**63**	**34.8**
P2.1 (Possible) ongoing adverse event	63	34.8
P3 Others	**87**	**48.1**
P3.1 Unnecessary treatment	7	3.8
P3.2 Unspecified problem	26	14.4
P3.3 Unavailable or inadequate pharmaceutical form	54	29.8
Total	**181**	**100**
Cause	**n**	**Proportion (%)**
C1 Drug selection	**55**	**30.4**
C1.1 Inappropriate medication according to guidelines/protocols	2	1.1
C1.2 Medication lacking therapeutic indication	6	3.3
C1.3 Inadequate combination of medications, or of medications and herbal medicines, or of medications and dietary supplements	1	0.6
C1.4 Inadequate duplicity of therapeutic group or active ingredient	30	16.6
C1.5 Absence of treatment or incomplete treatment despite therapeutic indication	16	8.8
C2 Pharmaceutical form	**35**	**19.3**
C2.1 Inadequate pharmaceutical form (for this patient)	35	19.3
C3 Dose selection	**54**	**29.8**
C3.1 Subtherapeutic dose	2	1.1
C3.2 Overdose	21	11.6
C3.3 Not frequent or sufficient dosage	7	3.9
C3.4 Too frequent a dosage	10	5.5
C3.5 Incorrect, confusing or absent dosage instructions	14	7.8
C4 Treatment length in time	**2**	**1.2**
C4.2 Too long a treatment	2	1.1
C5 Dispensing	**35**	**19.3**
C5.1 Medication prescribed not available	35	19.3
Total	**181**	**100**

Figure 2. Classification of the medications involved in the DRPs according to the Anatomical Therapeutic Chemical (ATC) classification.

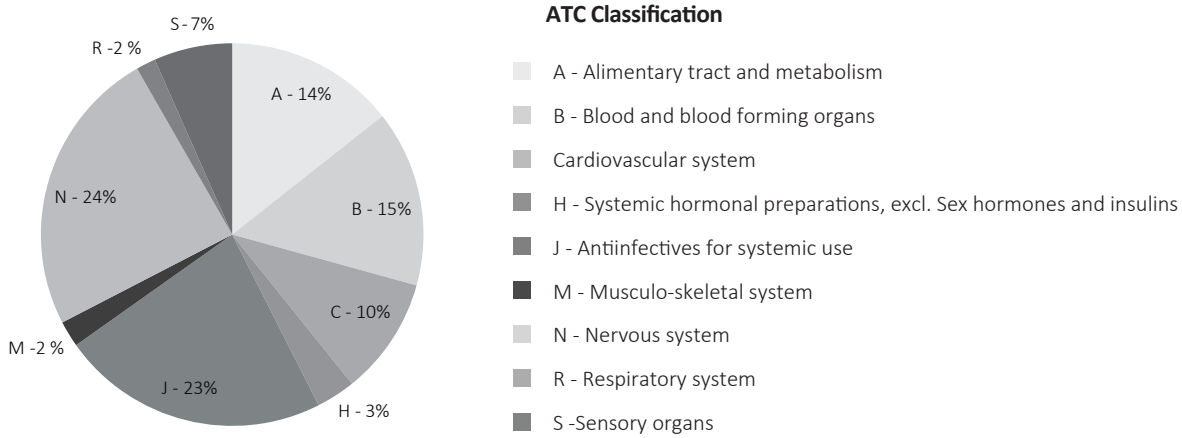


Table 3. Pharmaceutical intervention plan (main domain) and acceptability of the interventions performed by the clinical pharmacists

Intervention plan	n	Proportion (%)
I1 At the prescriber level	**57**	**31.5**
I1.1 Informed to the prescriber	11	6.1
I1.3 Intervention proposed to the prescriber	16	8.8
I1.4 Intervention discussed with the prescriber	30	16.6
I3 At the medication level	**124**	**68.5**
I3.1 Medication changed	8	4.4
I3.2 Dose changed	23	12.7
I3.3 Pharmaceutical form changed	40	22.1
I3.4 Use recommendation changed	24	13.3
I3.5 Medication discontinued or suspended	16	8.8
I3.6 Medication initiated	13	7.2
Acceptability	**n**	**Proportion (%)**
A1 Intervention accepted	**178**	**98.4**
A1.1 Intervention accepted and fully implemented	169	93.4
A1.2 Intervention accepted and partially implemented	2	1.1
A1.3 Intervention accepted but not implemented	7	3.9
A2 Intervention not accepted	**3**	**1.6**
A2.1 Intervention not accepted: not viable	1	0.5
A2.3 Intervention not accepted: other reason (specific)	2	1.1

Based on the results obtained from the pharmaceutical interventions that were carried out, the main cause related to unspecified problems (P3.2) was "C5.1 Prescribed medication not available'' (n=33). In relation to (Possible) ongoing adverse event occurring (P2.1) the main causes were "C3.2 Overdose'' (n=21) and "C1.4 Inadequate duplicity of therapeutic group or active ingredient'' (n=19). Regarding untreated symptoms or indication (P1.3) the main cause was "C1.5 Absence of treatment or incomplete treatment despite therapeutic indication'' (n=16).

A total of 181 pharmaceutical interventions were proposed to the medical team with the objective of solving the DRPs found, with an acceptance rate of 98.4% (n=178), where "A1.1 Intervention accepted and fully implemented" (93.4%) was the main subclassification, followed by "A1.3 Intervention accepted but not implemented" (3.9%), according to Table 3. In relation to the DRP status, 95.6% were fully resolved and 3.9% did not show resolution, the main reason being lack of consensus between the pharmacist and the prescribing physician (3.6%).

During the study period, 48 records were related to consultations with the pharmacist, through which recommendations related to drug therapy were suggested to the multiprofessional team. The main recommendations/guidelines made by the clinical pharmacist were related to Y-mismatch of the medications (37.5%), dilution (33.3%) and dose confirmation (12.5%).

Discussion

Studies that show the results of the performance of clinical pharmaceutical services in the care of critically-ill patients and/or that are based on the classification of the DRPs according to PCNE are still scarce in the literature. The vulnerability of ICU patients, their critical condition and the pharmacotherapy reinforce the need for daily pharmacotherapy follow-up, turning this into a priority scenario for the clinical pharmacist to assess health problems and medications in use.

The multiprofessional residency program enabled inclusion of the pharmacist in the Cardiology and General ICUs, as well as the implementation of clinical activities. Daily pharmacotherapy follow-up of critically-ill patients admitted to hospital ICUs is grounded on the use of spreadsheets and tables specifically prepared for this purpose, based on the monitoring of the medications used according to therapeutic indication, time of use, including antimicrobial therapy and treatment of other pathologies and comorbidities, dose, dosage, drug interactions, etc., aiming at identification of the DRPs so that they can be prevented/solved, providing a safe and effective pharmacological treatment. The tools used have fields for recording the diverse information considered indispensable for the performance of pharmacotherapy follow-up, such as type of diet, level of consciousness, laboratory tests, presence of prophylaxis for critically-ill patients, sedation and/or analgesia, drug reconciliation and blood glucose control, among others.

In the ICUs under study (Cardiology and General), specifically, it was verified that 61.3% of the patients were male and that the mean age was 58.3 years old, reflecting the global reality of Brazilian public ICUs, in which 53.48% of the patients are male and the mean age is 58.4 years old[1]. The mean age in the Cardiology ICU was 60.9 ± 11.5 years old and 64.2% of these patients were male, similarly to the epidemiological profile described by Bosso *et al.* (2013)[16]. The high number of medications used (most of the patients on polypharmacy – use of 5 or more drugs – and excessive polypharmacy – 10 or more drugs) due to the clinical criticality found in these patients, the high prevalence of chronic diseases in aged patients and the significant rate of evolution to death (23.6%) reasserts the clinical and therapeutic complexity of these patients.

Most of the DRPs identified were related to a (possible) ongoing adverse event occurring due to use of the medications (34.8%), being directly related to overdose and inadequate duplicity of the therapeutic group or active ingredient. This was also the main problem identified by a clinical pharmacy service in a reference Surgical ICU with an adult profile from China (31%), in an ICU for adults in Brazil (37.7%)[2] and in a respiratory unit from China (34.1%)[13]. The second main DRP was related to unavailability or inadequacy of the pharmaceutical form, classified from the modified PCNE, and such unavailability may be correlated with shortage of medications due to the increase in global consumption and/or with shortage due to lack of raw materials and production difficulties as a result of the COVID-19 pandemic, which especially impacted public institutions.

The main organic system related to the DRPs was the nervous system (24%), covering medications such as analgesics, anesthetics, antiepileptics and psycholeptics. When compared to other studies, the nervous system was only related to 14.4%[6] and 10%[7], not being the main organic system involved in DRPs in both studies. This difference can be explained by the COVID-19 pandemic that caused an increase in the use of analgesics and sedatives due to the large number of critically-ill patients dependent on mechanical ventilation; and the need to increase the concentrations of the fentanyl and midazolam solutions to achieve an adequate sedation level in these patients can be cited as an example. Antimicrobials for systemic use were the second main group related to DRPs (23%)

according to ATC, reflecting the reality of most ICUs, as critically-ill patients are more susceptible to infections by microorganisms due to the presence of pathophysiological changes. In other studies, nearly 81.3%[12], 59.5%[5], 53%[3] and 42.6%[1] of the DRPs were related to antimicrobials for systemic use. However, in all the studies, this pharmacological class was classified as the main group causing problems, differing from the result found in this study, which can be related to the period of the studies consulted, which were conducted before the COVID-19 pandemic, when there was no increase and/or excessive use of analgesics and sedatives.

The main cause related to the DRPs was drug selection, mainly related to therapeutic duplicity (16.6%) and to absence of treatment or incomplete treatment (8.8%), showing certain similarity with the results found in other studies carried out in ICUs for adults[5,13,14]. The main therapeutic duplicity identified was concomitant use of quetiapine and risperidone (atypical antipsychotics), mainly used to reduce psychomotor agitation in patients under weaning from mechanical ventilation and/or treatment for *delirium*. Absence of treatment or incomplete treatment was mainly linked to prophylaxis of venous and/or pulmonary thromboembolism, stress ulcer and corneal injury, widely recommended for critically-ill patients, as well as to absence of drug reconciliation, with antidepressants/anxiolytics as the main classes of related medications.

Other causes of DRPs considered extremely relevant in our study were inadequate pharmaceutical form (19.3%), overdose (11.6%) and very frequent dosage (5.5%), which is in agreement with what was observed in other studies[2,5,13]. Inadequacy of the pharmaceutical form was, in a greater proportion, related to the prescription of tablets with the recommendation of administration via tubes, when they presented contraindication to administration by this route or when it was possible to use the oral solution, in order to avoid a reduction in bioavailability of the drug. Finally, the main DRPs as a consequence of overdose were related to the absence of dose and dosage adjustment of antimicrobials in patients with renal failure.

In order to resolve the DRPs identified, interventions were carried out with the multiprofessional team of the ICUs. All the pharmaceutical interventions were performed together with the physicians due to the need to change the prescription in view of the identification of the DRPs and their complexity. The acceptance rate for the pharmaceutical interventions was extremely significant (98.3%), which can be a reflection of the inclusion of the pharmacist into the multiprofessional team and of the relevance and impact of the interventions proposed by the clinical staff. When compared to other studies, the acceptance rate was similar to those of two hospitals in China (97%[5] and 96.2%[13]) and of one university hospital in Switzerland (97.8%[14]), and higher than the rates shown in Brazilian hospitals (92.7%[3] and 81.7%[18]).

Possible failures in recording of the outcomes of the pharmaceutical interventions, non-follow-up of the patient by the clinical pharmacist, and the fact that the research was conducted in a single center may confer limitations to the study; therefore, the DRP patterns may not be generalizable to other inpatient sectors or hospitals in Brazil. Our research exclusively evaluated the impact of clinical pharmacists on the identification and resolution of DRPs related to the pharmacotherapy of critically-ill patients. Further studies are required to establish the relationship between the DRPs and the patients' clinical outcomes.

Conclusion

ICU patients are in critical conditions, which results in polypharmacy, which is directly related to the occurrence of various DRPs. The intensive care clinical pharmacist is a fundamental component of the multiprofessional team, with the ability to conduct the pharmacotherapy follow-up of critically-ill patients, enabling identification and resolution of the DRPs found and contributing to efficacy and safety of the pharmacological treatment. The high acceptability rate of the pharmaceutical interventions shows the importance and relevance of this professional in ensuring better quality of care for critically-ill patients.

Given the results obtained, the importance of pharmaceutical interventions aimed at the resolution of DRPs in critically-ill patients is noticed. The interventions were widely accepted and implemented by the prescribing professionals, evidencing the importance of the clinical pharmacist within the ICU, as well as his effective participation in the multiprofessional team, directly contributing to rational use of medications aiming at better patient care.

Collaborators

SLC and CN were in charge of conceiving and designing the project, as well as of data analysis and interpretation, and were also responsible for writing the article and for the relevant critical review of the intellectual content.

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Conflict of interest statement

Os autores declaram inexistência de conflitos de interesses em relação a este artigo.

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