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Clinical pharmaceutical service as a care strategy in intensive care: observational study

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Abstract

Objective: The present study aims to describe Pharmacotherapeutic Problems (PF) and Pharmaceutical Interventions (PI), as well as analyze the relationships between the number of pharmaceutical interventions and variables related to the patient, in order to explore the contribution of the pharmaceutical service to therapy care in intensive settings. **Method:** This is an analytical-descriptive, retrospective study, referring to data obtained through the pharmaceutical interventions form, filled out by residents during multidisciplinary rounds in the Adult Intensive Care Unit (ICU) of a large hospital in the city of Rio de Janeiro. These data were collected between August and December 2021. In addition to the analysis of the sample characteristics, pharmacotherapeutic problems, pharmaceutical interventions, team acceptability, direction of interventions and analysis of the correlation between the number of pharmaceutical interventions and variables such as sex, age, reasons for admission to the ICU and clinical outcome. **Results:** 116 forms were included and analyzed. The approximate average age of participants was 62 years, with 56% of patients being female and 85.3% having some comorbidity. 345 pharmaceutical interventions related to previously identified pharmacotherapeutic problems were carried out, directed to the multidisciplinary team, of which 93.1% were accepted. The most frequent intervention was "adequacy of the prescribed infusion rate" (135/39.4%). Statistical significance was found between the number of pharmacotherapy interventions for patients admitted to the ICU postoperatively and the clinical outcome. **Conclusion:** The large number of pharmacotherapeutic problems identified, the interventions carried out, the number of participating teams and the correlation between the variables analyzed suggest that the role of the pharmacist in multidisciplinary teams in intensive care brought benefits to the patients participating in the study. The high acceptance rate highlights the relevance of the clinical pharmacist in promoting rational and safe pharmacotherapy and assistance in the care of critically ill patients.

Keywords: Clinical Pharmacy Service. Outcome and Process Assessment Health Care. Intensive Care Unit.

Serviço farmacêutico clínico como estratégia de cuidado em terapia intensiva: estudo observacional

Resumo

Objetivo: O presente estudo tem como objetivo descrever os Problemas Farmacoterapêuticos (PF) e Intervenções Farmacêuticas (IF), bem como analisar as relações entre o número de intervenções farmacêuticas e variáveis relacionadas ao paciente, a fim de explorar a contribuição do serviço farmacêutico no cuidado em terapia intensiva. **Método:** Trata-se de um estudo analítico-descritivo, retrospectivo, com dados coletados, entre agosto e dezembro de 2021, em formulário de intervenções farmacêuticas, preenchidos pelos residentes durante os *rounds* multidisciplinares na Unidade de Terapia Intensiva Adulto (UTI) de um hospital de grande porte do município do Rio de Janeiro. Além da análise das características da amostra, foram descritos os problemas farmacoterapêuticos, intervenções farmacêuticas, aceitabilidade da equipe, direcionamento das intervenções e a análise da correlação entre o número de intervenções farmacêuticas e variáveis como sexo, idade, os motivos de internação na UTI e desfecho clínico. **Resultados:** Foram analisados formulários de 116 pacientes. A idade média aproximada dos participantes foi de 62 anos, sendo 56% do sexo feminino. A maioria (85,3%) apresentava pelo menos uma comorbidade. Foram realizadas 345 intervenções farmacêuticas relacionadas a problemas farmacoterapêuticos previamente identificados, direcionadas à equipe multidisciplinar, das quais 93,1% foram aceitas. A intervenção mais frequente foi a "adequação da taxa de infusão prescrita" (135/39,4%). Foi encontrada significância estatística entre a quantidade de intervenções na farmacoterapia de pacientes que ingressaram na UTI no pós-operatório e o desfecho clínico. **Conclusão:** A grande quantidade de problemas farmacoterapêuticos identificados, as intervenções realizadas, o número de equipes participantes e a correlação entre as variáveis analisadas sugerem que a atuação do farmacêutico nas equipes multiprofissionais em terapia intensiva trouxe benefício para os pacientes participantes do estudo. A alta taxa de aceitação evidencia a relevância do farmacêutico clínico na promoção de uma farmacoterapia racional e segura e auxílio no cuidado do paciente crítico.

Palavras-chave: Serviço de Farmácia Clínica. Avaliação de Processos e Resultados em Cuidados de Saúde. Unidade de Terapia Intensiva.

Introduction

Intensive care patients are among the most vulnerable to Pharmacotherapeutic Problems (PP) , mainly due to their exposure to more complex therapeutic regimens[1,2]. According to the report by the American Institute of Medicine, "To Err is Human: Building a Safer Health System" (2000), that year almost 7,500 deaths were related to medication errors in hospitals and more than 10,000 deaths in outpatients could have been avoided[3].

The pharmaceutical care process involves recognizing the demand, identifying problems, outlining the care that includes interventions and evaluating the documented results[4]. The clinical pharmacist's role in Intensive Care Units (ICU) contributes to the optimization of pharmacotherapy by providing resources such as pharmaceutical guidance, identification of pharmacotherapeutic problems and Pharmaceutical Interventions (PI) aimed at the multidisciplinary team[2,5]. The care provided by this professional has been shown to reduce risks related to the use of medications, providing quality pharmaceutical care, and contributing to patient safety through effective management mechanisms for patients and institutions[6–8].

The rounds are organizational tools structured in sessions made up of various health professionals who propose conducts and care plans aimed at the patient's recovery and meet the principle of integrality, as laid down in the guidelines of the Unified Health System (Sistema Único de Saúde, SUS)[9]. In the provision of (PS) as part of the multi-professional team, it is necessary to evaluate and make clinical decisions in relation to the patient, proposing pharmaceutical interventions based on the best evidence and within the legal limits of their work[4].

Given that these interventions are important in critical situations such as ICU admission and stay, the contribution of studies that document and evaluate activities carried out by pharmacists in ICUs in Brazil would make it possible to analyze the repercussions of this work on patient care and safety[2,5]. In this context, this study aims to describe PP and PI, as well as to analyze the relationships between the number of PI and patient-related variables, the reasons for ICU admission and outcome (discharge or death), in order to explore the contribution of the PS in intensive care.

Methods

Study type, setting and participants

This is an analytical-descriptive, cross-sectional study of data obtained from adult patients admitted to the Intensive Care Unit (ICU) of a large public hospital in the city of Rio de Janeiro, with 243 beds, 12 of which were specific to intensive care.

The hospital was part of the Training Units (TU) associated with the Hospital Pharmacy Residency program at the Fluminense Federal University (Universidade Federal Fluminense, UFF), and treated medium and high complexity patients who had been regulated by SISREG (Regulation System/SUS), especially cancer surgeries, hematology, ophthalmology, orthopedics, and intensive care. The Clinical Pharmacy Service had been implemented by the residents, but there was no exclusive pharmacist to monitor patients and prescriptions were not computerized.

The multiprofessional rounds at this hospital took place from Monday to Friday and were made up of physicians, nurses, physiotherapists, nutritionists, pharmacists, and other health professionals (social workers, speech therapists and dental surgeons). Before the session began, the residents received the prescriptions and analyzed them in conjunction with the medical records, prioritizing patient safety, effectiveness of pharmacotherapy and improvement of the clinical outcome, then at an agreed time they went to the ICU to begin the session. During this process, the resident pharmacist was consulted by other professionals on matters related to pharmacotherapy and assisted in decisions and conducts that were within their skills, as well as identifying pharmacotherapeutic problems, carrying out the necessary pharmaceutical interventions and recording them on a form. If the need for intervention was identified outside of the rounds, the resident pharmacist would contact the team by telephone in order to ensure the rational use of medications and patient safety.

Data collection

Data collection was carried out between August and December 2021 on "pharmaceutical interventions " forms for patients of both genders, under intensive care, aged 18 or over, completed during the multiprofessional round, or by telephone contact, already standardized in the hospital's Clinical Pharmacy Service. Incorrectly completed forms were excluded. The correct form was that which had all the data clearly expressed, with no missing or incomprehensible information.

The method for classifying pharmaceutical interventions was based on the definitions in the Manual for Pharmaceutical Care, proposed at the Granada Consensus in 2005[10] and in the study by Milani, Araujo and Polisel (2018), simplified to adapt to the hospital's reality.

The "pharmaceutical interventions form" had information in its header that allowed the sample to be characterized (reason for hospitalization, whether or not there were comorbidities, age and gender), in the body of the form there were the types of pharmacotherapeutic problems and their possible interventions as described in **Figure 1,** whether or not they were accepted and the team to which these interventions were directed (medicine, nursing, physiotherapy, nutrition or others). All the forms filled in for interventions carried out in the adult ICU during the period in question were analyzed. The variables analyzed were: (a) number of PI; (b) gender; (c) age; (d) reasons for ICU admission and (e) outcome: discharge or death.

Data analysis and hypothesis proposal

The data obtained was recorded in spreadsheets and processed using descriptive and exploratory statistical analysis, with the results displayed in graphs and/or tables in Microsoft Excel® and IBM® SPSS Statistics. Categorical and absolute frequencies were analyzed for reason for admission, presence of comorbidities, gender, clinical outcome, distribution of PP, PI, team acceptability and direction of interventions. Measures of central tendency and dispersion, mean and standard deviation, for age and length of stay.

Correlation tests were also carried out between the number of PI and patient-related variables such as gender and age, outcome (discharge or death) and the reasons for admission to the ICU (post-operative or other) and outcome (discharge or death), using Student's t-test to test the hypotheses. The Student's t-test was used because it is an appropriate statistical tool for comparing the means between two groups of data, determining whether they are significantly different from each other, which is one of the aims of our research.

Figure 1. Theoretical references used to assess pharmacotherapeutic problems and carry out pharmaceutical interventions.

Categories	Pharmacotherapeutic Problems (PP)	Pharmaceutical Interventions (PIs)
Indication	Problems related to the prescription or indication of the medication, the existence of an allergy or adverse reaction, analyzing the clinical situation and/or unnecessary medication[1].	Intervention in the therapeutic regimen; suggesting the inclusion of medication; suggesting the substitution of one medication for another, or a more suitable alternative for the patient's clinical condition[4,1].
Dose	Prescriptions with overdose, underdose, lack of dose adjustment and serum dosage, with information based on the available literature, taking into account the patient's age, weight, body surface area and renal and hepatic function[2,5]. Problems related to the duration and dosage of treatment, as well as the prescribed infusion rate[1,2].	Adjustment, adaptation, increase, reduction, or dose individualization[2,5]. Interventions related to the frequency of medication administration, duration of treatment, suggestion of discontinuation or prolongation of treatment. Adjusting the infusion rate[1,2,5].
Medication interaction	Prescribed medications that may cause harm to the patient due to drug-drug or drug-food interactions[1,2].	Advice on the management of medication interactions with clinical relevance. Whether between drugs or between drugs and food provided by Micromedex®[2,5].
Administration Route	Problems related to the type of administration route considering the patient's clinical condition or route not recommended in the literature due to the drug's pharmacokinetic characteristics[1,2].	Suggest changing the route of administration, taking into account the characteristics of the drug and the patient's clinical conditions[1,2].
Pharmaceutical form	Pharmaceutical form unsuitable for the patient's clinical condition (older adults, difficulty swallowing, presence of nasogastric or nasoenteric tubes, etc.); pharmaceutical form prescribed in disagreement with the hospital's standardization or unavailability of stock at the time[1].	Suggested replacement or adaptation of pharmaceutical form / presentation[1,2].
Preparation and administration	Errors in dilution, reconstitution, stability, speed, time and rate of infusion, physical-chemical incompatibilities between drugs and drug/diluent, as well as the stability of prescribed drugs, according to dilution. Incorrect medication handling[1,2].	Suggesting changes to the preparation with the nursing team due to incorrect handling of medications. Active guidance with the teams on good handling practices (especially for injectables) and correct storage. Suggested team training[1,2,5].
Special prescriptions and requests	Problems which, due to improper prescription, lack of stock or lack of justification, can cause harm to the patient. Problems not related to the medications themselves, but to prescriptions and special requests[1].	Requesting or advising on how to fill in the specific justification for prescribed antimicrobials or high-cost medications that have not been administered due to the absence of these documents, in accordance with the institution's rules[1,3].
Others	General problems related to pharmacotherapy[6] (open field).	Pharmaceutical guidance for the multidisciplinary team that contributes to the patient's improvement and quality of life[6].

Fonte: [1]Milani, Araujo e Polisel, 2018; [2]Ribeiro e colaboradores, 2015; [3]Pilau, Hegele e Heineck, 2014; [4]Medeiros e Moraes, 2014; [5]Silva, 2009; [6]Bovo e colaboradores, 2009.

Based on the theoretical framework[2,6] and the objectives, four hypotheses are proposed. The literature does not categorically show significant relationships between the number of pharmaceutical interventions and demographic and clinical variables[2,6]. Therefore, our hypotheses suggest that there is no significant relationship: Hypothesis 1. There will be no significant differences in the number of pharmaceutical interventions and the "gender" variable. Hypothesis 2. There will be no significant differences in the number of pharmaceutical interventions and the "age" variable. Hypothesis 3. There will be no significant differences in the number of pharmaceutical interventions and the clinical outcome (discharge or death) of the patients. Hypothesis 4: There will be no significant differences in the number of pharmaceutical interventions or the reason for patients' hospitalization, considering "post-operative" and others.

This study was approved by the UFF Research Ethics Committee (CAAE 58458722.4.0000.5243).

Results

Descriptive analysis

Of the 126 forms for patients followed up in the adult ICU, ten were excluded due to incorrect completion. In the sample of 116 patients, the approximate mean age was 62.3 years (range 21-90 years; SD=14.2). Of these, 66.4% were aged 60 or over. Fifty-six percent were female.

As for associated diseases, 85.3% of patients had some comorbidity. The mean length of stay was 8.78 days (range 1 to 126 days; SD=±17.39). Approximately 21% of the patients died and 79% were discharged to the wards. PP were identified for 67.2% of patients. Among the 27 reasons for admission, the most common reasons for ICU admission were: "postoperative" (62.9%), "Covid-19" (16.9%), "oncological complications" (6%) and "lowered level of consciousness" (6%).

A total of 345 PI were carried out based on previously identified PP (a mean of approximately 3 PP per patient). Only 7.3% of the interventions were refused. In terms of targeting, 91.6% were related to the medical team and 8.4% to the nursing, nutrition, dentistry, and physiotherapy teams. Of particular note were the 2 interventions carried out with the nutrition team, "Advice on managing drug-nutrient interactions", 1 intervention "Medication suggestion for untreated clinical condition" for the dentistry team and 2 pharmaceutical guidance interventions with the physiotherapy team recorded in the open field.

"Dose" followed by "Prescriptions and Special Requests" and "Indication" were the categories of pharmacotherapeutic problems most observed in the study, according to **Figure 2**.

Among the most common interventions were "adjusting the prescribed infusion rate" (135/39.1%), followed by "Request/ Guidance on filling in the justification for antimicrobials that were overdue or not taken" (38/11%) and "Guidance on stock availability" (30/8.7%) **(Table 1).**

Hypothesis analysis

Table 2 shows the relationship between the dependent variable number of pharmaceutical interventions and the independent variables gender (t=-0.194; p=0.846) and age (t=-0.557; 0.579). No significant differences were observed in any of the variables. Therefore, hypotheses 1 and 2 were accepted.

Table 3 shows the relationship between the dependent variable number of pharmaceutical interventions and the independent variables outcome (t=2.391; p=0.024) and reason for admission to the ICU (t=-2.382; p=0.021). Therefore, hypotheses 3 and 4 were rejected.

Figure 2. Numerical distribution of pharmacotherapeutic problems (PP) identified by category, in the ICU of a large public hospital, Rio de Janeiro, 2021.

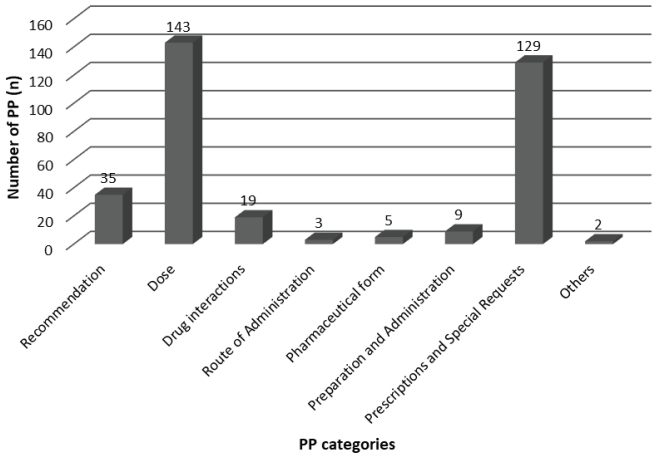

Table 1. Pharmaceutical interventions carried out in the ICU of a large public hospital, Rio de Janeiro, 2021

Pharmaceutical Interventions	n	(%)
Suggested medication for an untreated medical condition	5	1.4
Recommendation to discontinue a medication in the event of therapeutic duplication	0	0.0
Suggestion of a more suitable or available therapeutic alternative	9	2.6
Suggested discontinuation of medication in case of known/reported allergic reaction	2	0.6
Guidance on continuing medication treatment	2	0.6
Suggested indication for the patient's routine medication	1	0.3
Medication Reconciliation	1	0.3
Suggested indication of medication for prophylactic measures	15	4.3
Suggested dose change in case of overdose	1	0.3
Suggested dose change in case of underdose	0	0.0
Suggested dose adjustment according to altered kidney or liver function	5	1.4
Suggested serum drug dosage	0	0.0
Suggestion to change the dose interval according to what is recommended in the literature or duration of treatment	2	0.6
Adequacy of the prescribed infusion rate	135	39.1
Recommendations based on the identification of drug-drug interactions	15	4.3
Recommendations based on the identification of drug-nutrient interactions	4	1.2
Recommendation to change the route of administration in case of incompatibility or according to the patient's clinical case	3	0.9
Suggested adaptation to standardized or currently available pharmaceutical form	2	0.6
Suggesting the right pharmaceutical form according to the patient's needs	3	0.9
Recommendation to change or suspend dilutions not recommended due to lack of stability or physicochemical incompatibility	1	0.3
Suggested changes or suspension of dilutions not recommended due to lack of stock	0	0.0
Recommendation in case of incorrect storage	0	0.0
Guidance on good medication handling practices	3	0.9
Guidance on administering the medication	5	1.4
Request/Guidance for filling in high-cost justification that was overdue or not carried out	8	2.3
Request/Guidance on filling in the justification for antimicrobials that were expired or not carried out	38	11.0
Guidance on stock availability	30	8.7
Guidance on the standardization of medications	10	2.9
Request/Guidance on correcting medication prescriptions	43	12.5
Others	2	0.6
TOTAL	**345**	**100**

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Table 2. t-Student for dependent variable number of pharmaceutical interventions and independent variables gender and age, and descriptive analysis of interventions according to gender and age, Rio de Janeiro, 2021.

	Gender						Age (years)					
Pharmaceutical Interventions	**tt**	***pp***		**N**	**M**	**SD**	**tt**	***p***		**N**	**M**	**SD**
	-0.194	00.846	Female	65	2.86	5.59	--0.557	0.579	≥60	77	3.08	5.69
			Male	51	3.08	6.40			≤60	39	2.72	6.48
			Total	116	2.96	5.94				116	2.96	5.94

Captions. N: sample; M: Mean; SD: Standard Deviation, * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

Table 3. : t-Student for dependent variable number of pharmaceutical interventions and independent variables outcome and reason for ICU admission, and descriptive analysis of interventions according to outcome and reason for ICU admission, Rio de Janeiro, 2021

	Outcome						Reasons for ICU admission					
Intervenções Farmacêuticas	**Tt**	***pp***		**NN**	**MM**	**SDP**	**tt**	***p***		**N**	**M**	**DP**
	2.391	0.024	Death	24	6.21	8.01	-2.382	0.021	Postoperative	74	1.74	2.64
			Discharge	92	2.11	4.99			Others	42	5.10	8.90
			Total	116	2.96	5.94				116	2.96	5.94

Captions. N: sample; M: Mean; SD: Standard Deviation, * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

Discussion

Due to the complexity of the conditions referred to the ICU, the presence of a multidisciplinary team is necessary and fundamental. This model is more effective and efficient for critically ill patients in terms of length of stay, cost reduction and mortality[2,6]. The integration of the clinical pharmacist into the multi-professional care team is linked to the reduction of complex problems related to pharmacotherapy[11].

The characterization of the sample helps guide the strategies and planning of intensive care and is related to the hospital's care profile[12]. Among the main reasons for admission to the ICU at the study site were post-surgery, mostly related to oncological surgeries and complications from breast cancer, which would explain the higher prevalence of women (56%) compared to men.

The mean age of 62 years found corroborates the review by Pilau, Helege and Heineck (2014); of the articles included, three were close in age to the results of this study[7]. In relation to the presence of comorbidities, 85.3% had some associated disease, which may be linked to the increased use of medication[2]. The ageing of the population is associated with an increase in morbidity, requiring greater monitoring and the need for follow-up in intensive care[7,13].

Some studies in this area do not present the mean length of stay[2,6-8,22]. Fideles et al. (2015) evaluated three years of activities carried out by clinical pharmacists in intensive care and found a mean time of 6.7 days, which is shorter than the 8.78 days found in this study[14]. Covid-19 was the second main reason for hospitalization (16.9%) and has a profile of longer hospital stays[15]. This may be one explanation for the slightly longer mean length of stay, as in a study that evaluated pharmaceutical interventions only in patients with Covid-19[16]. The range was from 1 to 126 days (sd=±17.39), the patient whose hospitalization time was 126 days was due to Covid-19, this maximum peak possibly influenced the result of the mean described.

PP related to dosage, special prescriptions and requests and the indication of medications were the most prevalent in this study. These problems may be associated with the profile of the hospital, the reason for admission, therapeutic choices, and the lack of computerized prescriptions[1,12,17,18]. Among the 345 PI, the "adequacy of the prescribed infusion rate", included in the "dose" pharmacotherapeutic problem category, was the most prevalent. A study by Cardinal and Fernandes (2014) also found a higher prevalence of interventions related to dose adjustment and duration and frequency of medication, as did Medeiros and Moraes (2014), whose higher prevalence of interventions in dilution management and infusion time, corroborating the data in this study[17,19].

As for the acceptance of the interventions by the teams, 93.1% were accepted, of which 91.6% went to the medical team and 8.4% to the nursing, nutrition, physiotherapy, and dentistry teams. Participation in the rounds is an important part of the process of integration and quality of multi-professional care[7,11]. Of particular note were the interventions carried out with the nutrition team, where "Advice on managing drug-nutrient interactions" was given in cases of enteral nutrition and oral medication. The intervention of "Suggesting medication for an untreated clinical condition" for the dental team, which although not part of the multidisciplinary team that accompanies the rounds on a daily basis, was contacted for support on a specific case. And finally, the two interventions carried out with the physiotherapy team, recorded in the open field, were for pharmaceutical guidance in order to help them in the best context of action in relation to the action of the medications in use by the patients.

The study's high acceptance rates show that the recommendations are clinically relevant[7,20]. On the other hand, the hypotheses tested presented different results: no relationship was observed between the number of interventions and the characteristics of gender and age. Statistical significance was found in the other groups analyzed, suggesting a greater number of interventions in the pharmacotherapy of patients who entered the ICU in the postoperative period[21]. There was a relationship between the number of interventions and the patient's clinical outcome, indicating that more interventions were carried out in the pharmacotherapy of patients who were discharged, corroborating the review data that indicates a significant reduction in the likelihood of mortality in patients who had pharmacists as part of the multiprofessional teams in intensive care[11].

This study presents the theoretical framework for each category of pharmacotherapeutic problem, with its possible interventions, which makes it easier to understand and reproduce in other study scenarios, but it does have some limitations. As this is a single-center study, the results of this research cannot be extrapolated to other services. In relation to the form, the data expressed does not show the type of comorbidity or the reason for refusing the interventions, which limited some analyses. Although the types of intervention are similar to those of Milani, Araujo and Poliseu (2018)[6], the categories of PP and the form of analysis are different. Other studies in the area, such as those by Barros and Araujo (2021), Cardoso et al. (2022) and Dias et al. (2019) have different categories, forms, and ways of analyzing the results[8,22,23], so there is no possibility of directly comparing them. We therefore suggest validating an evaluation method and instrument that can be adapted to different practice scenarios, with a view to comparing the results of studies in this area.

Conclusion

The large number of PP identified, interventions carried out, participating teams and the correlation between the variables analyzed reaffirm the importance of the pharmacist's role in multi-professional teams in intensive care.

The high acceptance rate highlights the importance of clinical pharmacists in optimizing pharmacotherapy, directly helping to care for critically ill patients in terms of clinical improvement and safety.

There is a need for more studies in this area, especially focusing on the pharmacist as an integral part of the multi-professional team, helping with clinical outcomes and patient safety.

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Collaborators

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Conflict of interest declaration

The authors declare no conflicts of interest.

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