

## **Original Article**

# Deprescribing medicines in an intensive care unit of a university hospital from Ceará

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## Abstract

Objectives: To evaluate the pharmaceutical deprescription recommendations made to patients hospitalized in an adult clinical Intensive Care Unit (ICU). Methods: This is a cross-sectional, descriptive, and quantitative study developed with pharmaceutical recommendations for drug deprescription, in the adult ICU of a university hospital in Fortaleza- CE, from 2017 to 2018. Data from patients and recommendations were collected from patient records. The acceptability of the recommendations was measured from the visualization of the suggested alteration in 24 hours. The drugs included in the recommendations were categorized according to the Anatomical Therapeutic Chemical (ATC) and Potentially Dangerous Drug (MPP) classifications. The data were compiled and analyzed using the Microsoft Office Excel® 2013 software. Results: A total of 388 recommendations were made for the non-prescription of medications to 210 adult patients who were mostly male (58%) and with a mean age of 56 years. ± 16.8. The acceptability of the recommendations was 93.3% (n=362) and the average number of medications not prescribed per patient was 1.7 ± 0.7, all of which were abruptly discontinued. Problems related to deprescription were mainly prescription of unnecessary drugs (77.6%) contraindicated drugs (8.0%) and therapeutic duplicity (5.1%). The most frequent therapeutic classes are antibacterials for systemic use (11.3%), ophthalmic (20.8%) and medicines for functional gastrointestinal disorders (9.5%). The main drugs not prescribed were hypromellose eye drops + dextran (9.6%), bromopride (6.9%) and injectable potassium chloride (5.8%), the latter being considered an MPP. The class most associated with non-acceptance of deprescription other than corticosteroids is systemic use (23.1%). Conclusion: This study showed a high level of acceptance of deprescription recommendations, especially among antibacterials for systemic use. Injectable potassium chloride, considered an MPP, ranked third overall in terms of non-prescription. Future studies should evaluate the impact of deprescription recommendations on morbidity and mortality in the ICU and on the reduction of hospital costs.

Keywords: Drug Therapy, Pharmaceutical Care, Intensive Care Units.

#### Desprescrição de medicamento em unidade de terapia intensiva de um hospital universitário do Ceará

## Resumo

Objetivos: Avaliar as recomendações farmacêuticas de desprescrição realizadas aos pacientes internados em uma Unidade de Terapia Intensiva (UTI) clínica adulto. Métodos: Trata-se de um estudo transversal, descritivo e quantitativo desenvolvido com as recomendações farmacêuticas de desprescrição de medicamentos, na UTI adulto de um hospital universitário em Fortaleza – CE, de 2017 a 2018. Os dados dos pacientes e das recomendações foram coletados a partir de prontuários de pacientes. A aceitabilidade das recomendações foi mensurada a partir da visualização da alteração sugerida em 24 horas. Os medicamentos envolvidos nas recomendações foram categorizados de acordo com a classificação Anatomical Therapeutic Chemical (ATC) e com a de Medicamentos Potencialmente Perigosos (MPP). Os dados foram compilados e analisados usando o software Microsoft Office Excel® 2013. Resultados: Realizou-se um total de 388 recomendações de desprescrição de medicamentos a 210 pacientes adultos que eram majoritariamente do gênero masculino (58%) e com idade média de 56 anos ± 16,8. A aceitabilidade das recomendações foi de 93,3% (n=362) e a média de medicamentos desprescritos por paciente foi de 1,7  $\pm$  0,7, sendo todos interrompidos de forma abrupta. Os problemas relacionados com as desprescrições foram principalmente, prescrição de medicamentos não necessários (77,6%) medicamentos contraindicados (8,0%) e duplicidade terapêutica (5,1%). As classes terapêuticas mais prevalentes foram os antibacterianos para uso sistêmico (11,3%), oftalmológicos (20,8%) e medicamentos para distúrbios gastrointestinais funcionais (9,5%). Os principais medicamentos desprescritos foram o colírio hipromelose + dextrano (9,6%), bromoprida (6,9%) e cloreto de potássio injetável (5,8%), sendo esse último considerado um MPP. A classe mais associada a não aceitação da desprescrição foi a dos corticosteroides para uso sistêmico (23,1%). Conclusão: Este estudo mostrou um elevado nível de aceitação das recomendações de desprescrição, especialmente entre os antibacterianos para uso sistêmico. O cloreto de potássio injetável, considerado um MPP, ocupou o terceiro lugar geral de desprescrição. Futuros estudos devem avaliar o impacto das recomendações de desprescrição na morbimortalidade na UTI e na redução de custos hospitalares.

Palavras-chave: Farmacoterapia, Cuidado farmacêutico, Unidades de Terapia Intensiva.





### Introduction

The complexity of the care offered in Intensive Care Units (ICUs) is largely related to the pharmacotherapy used<sup>1</sup>. The presence of patients in serious conditions, polymedicated, using Potentially Dangerous Medications (PDMs) and with a high frequency of changes in their therapy facilitates the occurrence of adverse events and makes this environment especially conducive to errors<sup>2-3</sup>.

A number of studies indicate that critically-ill patients accumulate a mean of 1.7 errors every day and that medication errors are the most common ones, probably due to the high number of medications, with an estimated mean of 8 to 14.51 drugs per prescription<sup>4</sup>. These errors represent 78% of the serious medical errors in ICUs and affect between 9.4% and 64% of the prescriptions.<sup>5-7</sup>

Bearing in mind this complexity, optimization of pharmacotherapy and deprescription of any unnecessary medication is fundamental to prevent the occurrence of Drug-Related Problems (DRPs)<sup>8</sup>. Drug deprescription, understood as the intentional process of withdrawing an inappropriate or unnecessary medication supervised by a health professional, can reduce medication errors, adverse reactions, drug interactions and incompatibilities and hospital costs<sup>9,10</sup>.

In the literature, there is diverse evidence about the benefits of deprescribing certain medications, such as antihypertensives, antipsychotics, benzodiazepines, hypoglycemic agents and gastric protectors, especially in primary care<sup>11-15</sup>. However, there are countless professional and cultural barriers that hinder this process, as it usually depends on clinical judgment and retrospective studies of low evidence<sup>16-17</sup>.

In a systematic review that evaluated the impact of deprescription in primary care, it was indicated that the most successful deprescription recommendations were carried out with intense collaboration with pharmaceutical professionals and continuing education<sup>16</sup>. As members of a multiprofessional team, pharmacists are key players in the drug deprescription process and in the construction of the idea that deprescription is a therapeutic intervention similar to initiation of a clinically appropriate therapy<sup>18,19</sup>.

Despite the existence of recent studies in the international literature on drug deprescription, there is still an incipient approach to this topic in ICU settings, especially at the national level. In Brazil, deprescription is still a little discussed topic among health professionals. In this sense, the objective of the current study was to assess the deprescription pharmaceutic recommendations for the patients hospitalized in a clinical ICU for adults in Brazil.

# Methods

This is a cross-sectional, descriptive and quantitative study developed between January 2017 and December 2018 based on the pharmaceutical recommendations for drug deprescriptions carried out in the ICU for adults of a university hospital from Fortaleza - CE. The study was carried out in accordance with the regulatory guidelines and standards for research involving human beings and was approved by the hospital's Ethics and Research Committee under opinion No. 2,699,465 and CAAE No. 74283417.4.0000.5045. A scheme of the study methodological flow is shown in Figure 1.

**Figure 1.** Methodological flow corresponding to the study of pharmaceutical recommendations regarding medication deprescriptions in an Intensive Care Unit for adults, Fortaleza – CE (2017-2018).



1- Anatomical Therapeutic Chemical; 2- Potentially Dangerous Medications.

The university hospital under study offers high-complexity health assistance and is part of the Unified Health System (*Sistema Único de Saúde*, SUS). The ICU under study consists of eight active beds and serves clinical patients. It has a closed clinical medical staff and a multiprofessional team comprised by physicians on duty and day laborers, nurses and nursing technicians, physiotherapists, pharmacists and nutritionists. Residents in the Medicine, Nursing, Pharmacy and Physiotherapy areas are also part of the care team. During the data collection period, the institution under study did not have a prescription and/or electronic evolution system.

The pharmaceutical recommendations were made by the ICU Clinical Pharmacy team, comprised by a staff pharmacist and by three resident pharmacists. The recommendations were forwarded to the medical professional during the patient's ICU admission and conducted on patients undergoing pharmacotherapy monitoring. The recommendations were transmitted verbally based on the drug prescriptions corresponding to patients admitted any day of the week and aged at least 16 years old. A pharmacist evaluated the prescriptions from Monday to Friday, by validating the 24-hour medical prescription. Any medications added during weekends or on holidays were included in the pharmaceutical analysis on the first following working day. Acceptance of the recommendations was confirmed from the verification of the change suggested in the prescriptions within 24 hours.

The data corresponding to the patients and to the recommendations made were collected in an exclusive form based on the medical charts and of the second copies of the prescriptions filed in the Pharmacy sector. The demographic and clinical variables collected from the patients included age, gender and medications involved in the recommendations. The classification of the associated DRPs was carried out according to the standardization of the hospital's clinical pharmacy unit, which is based on the Second Consensus of Granada (Table 1)<sup>20</sup>.





Table 1. Definition of the Drug-Related Problems (DRPs) evaluated in the medical prescriptions and which justified the deprescrip	tion
pharmaceutical recommendations in an Intensive Care Unit for adults, Fortaleza – CE (2017-2018).	

DRP <sup>1</sup>	Definition
Unnecessary medication prescribed	Medication prescribed without indication and/or without scientific evidence of therapeutic benefit in the hospital or medical prescription.
Contraindication	The medication prescribed is contraindicated due to side effect, ADR2, age group, comorbidity, others.
Therapeutic duplicity	The same item was prescribed twice, or two medications with the same indication.
ADR <sup>2</sup>	Adverse reaction suspected to be related to use of the medication.
Inadequate treatment time	Inadequately specified treatment time (less than or greater than recommended) in the hospital or medical prescription.
Overdose	Medication in a higher dose than recommended due to inappropriate use or inadequate prescription of dose, dosage, others.
Drug-drug interaction	Drug-drug interaction.
Inadequate selection	The drug prescribed, although necessary, is not the best therapeutic option.
Unavailability (lack)	Medication unavailable because it is out of stock at the institution (hospital, outpatient pharmacy or health center).
Unavailability (lack)	Medication unavailable because it is out of stock at the institution (hospital, outpatient pharmacy or health center).

1- The classification of the associated DRP was carried out according to the standardization of the clinical pharmacy unit of the hospital, which is based on the Second Consensus of Granada20. 2- Adverse Drug Reaction.

The medications involved in the recommendations were categorized according to the second level of the *Anatomical Therapeutic Chemical* (ATC) classification, in which drugs are divided into different groups according to the organ or system where they act, as well as to their chemical, pharmacological and therapeutic properties<sup>21</sup>. Identification of the PDMs, established by the Institute for Safe Medication Practices (ISMP) - a non-governmental, independent and not-for-profit organization that works to promote safe practices in the use of medications and health products in Brazil - was also carried out<sup>22</sup>. For the most prevalent medications, the reason for recommending deprescription was established, according to the literature and to clinical guidelines<sup>23-36</sup>. The pharmaceutical recommendations recorded with lack of information and medical approval were excluded from the study.

The data were introduced and analyzed in Excel<sup>\*</sup> (version 2016). Descriptive statistical analysis was used, where the numerical variables were presented as mean, standard deviation, absolute and relative frequency, and the categorical variables were displayed in terms of frequency.

# Results

During the study period, deprescription recommendations were made for 210 patients who were mostly male (58%; n=122) and with a mean age of 56 years old  $\pm$  16.8 (variation: 16-89 years old). A total of 390 deprescription recommendations were made to the medical team, of which two were excluded due to lack of data about their acceptance or not. Most of the recommendations included (67%; n=262) were carried out in 2018 and their acceptability was 93.3% (n=362), with a mean number of medications deprescribed per patient equal to  $1.7 \pm 0.7$  (Table 2).

The problems associated with the recommendations mainly included prescription of unnecessary medications (77.6%; n=301), prescription of contraindicated medications (8.0%; n=31), therapeutic duplicity (5.1%; n= 20), emergence of adverse drug reactions (4.9%; n=19) and inadequate treatment time (2.1%; n=8) (Table 2). In the universe of the unaccepted recommendations (n=26), the most frequently associated problem corresponded to prescription of unnecessary medications (92.3%; n=24).

According to the ATC level 2 classification, the most prevalent therapeutic classes in the recommendations were antibacterials



for systemic use (11.3%; n=44), ophthalmic drugs (20.8%; n=42), medications for functional gastrointestinal disorders (9.5%; n=37), blood substitutes and perfusion solutions (9.3%; n=36) and corticosteroids for systemic use (5.9%; n=23) (Table 3). The class that was most frequently associated with deprescription non-acceptance was corticosteroids for systemic use (23.1%; n=6). Among the recommendations, 18.0% (n=70) involved PDMs, with potassium chloride (34.3%; n=24), magnesium sulfate (17.1%, n=12) and unfractionated heparin (11.4%, n=8) as the most prevalent.

**Table 2.** Demographic data of the patients and those related to the medications involved in the pharmaceutical deprescription recommendations made in an Intensive Care Unit for adults, Fortaleza - CE (2017-2018).

Sociodemographic data	n (%)
Male gender	122 (58)
Age (Mean - Standard Deviation)	56.0 - 16.8
Drug deprescription	n (%)
Deprescription recommendations	388
Acceptability of the recommendations	362 (93.3%)
Deprescription per patient (Mean - Standard Deviation)	1.7-0.7
Potentially Dangerous Medications (PDMs)	70 (18.0%)
Problems related to the deprescription recommendations (DRPs) <sup>1</sup>	n (%)
Unnecessary medication prescribed	302 (77.8)
Contraindication	32 (8.3)
Therapeutic duplicity	20 (5.1)
Adverse drug reaction	18 (4.6)
Inadequate treatment time	8 (2.1)
Overdose	4 (1.0)
Drug-drug interaction	2 (0.5)
Unavailability in the institution	1 (0.3)
Inadequate selection	1 (0.3)

1- The classification of the associated DRP was carried out according to the standardization of the hospital's clinical pharmacy unit, which is based on the Second Consensus of Granada $^{\rm 20}$ .

In relation to the deprescribed medications, a total of 93 different drugs were observed, all abruptly interrupted. The most prevalent were hypromellose + dextran (9.6%, n=35), bromopride (6.9%, n= 25), potassium chloride (5,8%, n= 21), chlorexidine 0.12% (5.0, n=18) and thiamine (4.1%, n=15). The reasons for the most frequent drug deprescription recommendations are presented in Table 4.



**Table 3.** Acceptance percentage corresponding to the drug deprescription recommendations by therapeutic class made in an Intensive Care Unit for adults, Fortaleza – CE (2017-2018).

ATC Classification <sup>1</sup>	Total n (%)	DRP (n)	n (%)
		Unnecessary medication prescribed (29)	28 (96.5)
101 Antibastarial drugs for systemis use	44 (11 2)	Adverse drug reaction (6)	5 (83.3)
JUI - Antibacteriai drugs for systemic use	44 (11.3)	Inadequate treatment time (5)	5 (100)
		Overdose (4)	4 (100)
CO1 Ophthalmalagia druga	12 (10.0)	Unnecessary medication prescribed (41)	38 (92,7))
SOI - Ophthalmologic drugs	42 (10.8)	Therapeutic duplicity (1)	1 (100)
A03 - Medications for functional gastrointestinal disorders	37 (9.5)	Unnecessary medication prescribed (3)	0 (0)
		Unnecessary medication prescribed (34)	30 (88.2)
B05 - Blood substitutes and perfusion solutions	36 (9.3)	Drug-drug interaction (1)	1 (100)
		Therapeutic duplicity (1)	1 (100)
102 Cartianatoraida far austaria una	22 (5.0)	Unnecessary medication prescribed (22)	16 (72.7)
HUZ - Corticosterolas for systemic use	23 (5.9)	Therapeutic duplicity (1)	1 (100)
	22 (5.0)	Unnecessary medication prescribed (21)	21 (100)
All - Vitamins	23 (5.9)	Therapeutic duplicity (2)	2 (100)
	18 (4.6)	Unnecessary medication prescribed (16)	16 (100)
AUI - Stomatological preparations		Therapeutic duplicity (2)	2 (100)
		Unnecessary medication prescribed (13)	13 (100)
J02 - Antimycotics for systemic use	16 (4.1)	Contraindication (1)	1 (100)
		Therapeutic duplicity (2)	2 (100)
		Unnecessary medication prescribed (13)	12 (92.3)
A12 - Mineral supplements	15 (3.9)	Contraindication (1)	1 (100)
		Therapeutic duplicity (1)	1 (100)
		Unnecessary medication prescribed (8)	7 (87.5)
N05 - Psycholeptic drugs	12 (3.1)	Contraindication (2)	2 (100)
		Adverse drug reaction (2)	2 (100)
		Contraindication (7)	7 (100)
P01 Antithromhotic agents	11 (2.8)	Unnecessary medication prescribed (2)	2 (100)
BOT - Altitutolipotic agents		Therapeutic duplicity (1)	1 (100)
		Inadequate selection (1)	1 (100)
		Unnecessary medication prescribed (4)	4 (100)
NO2 Analgasias	10 (2.6)	Contraindication (4)	4 (100)
NUZ - Analgesics		Adverse drug reaction (1)	1 (100)
		Drug-drug interaction (1)	1 (100)
Others <sup>1</sup>	101	-	-
Total	388	-	-

1- Therapeutic classes with percentage frequency less than 1 according to the second level of the Anatomical Therapeutic Chemical classification (ATC)<sup>21</sup>.

# Discussion

From the researched literature, it is perceived that, to the present day, this is the first study that evaluates drug deprescription in the ICU environment in Brazil, as the existing studies are aimed at the aged population in primary care<sup>37,38</sup>. Additionally, the deprescription recommendations were made by clinical pharmacists as a strategy to optimize pharmacotherapy and prevent negative drug-related outcomes. Thus, this study reinforces the importance of the technical evaluation of medical prescriptions by clinical pharmacists and their important role in deprescribing medications, as well as in defining the patients' therapeutic plan together with the multiprofessional team.

Lee *et al.* (2019) point out that the participation of clinical pharmacists in multiprofessional teams can improve patient outcomes and reduce mortality rates, ICU hospitalization times and adverse drug events<sup>39</sup>. In critically-ill patients, where the

patients' complexity requires a careful clinical evaluation and a delicate management of drug therapy, there is evidence of the benefit of the pharmacists' presence in improving care and reducing costs<sup>40,41</sup>.

In this study, acceptance over 90% of the pharmaceutical deprescription recommendations was observed, which may indicate the presence of a consolidated clinical pharmaceutical service and a relationship of trust between physicians and clinical pharmacists. Similar results were reported in a Thai study in ICU, where 99.2% of the general recommendations were accepted and 90.8% were changed within 24 hours, with the recommendation to discontinue therapy as the second most frequent<sup>42</sup>. In the study by Fideles *et al.* (2015), carried out in the same locus as the current research, the accepted recommendations for discontinuing therapy were among the ten most frequent recommendations and showed important growth in the percentage between the first and last period of analysis<sup>43</sup>.





#### Table 4. Reasons for the deprescription recommendations made in an Intensive Care Unit for adults, Fortaleza – CE (2017-2018).

Medication	n (%)	Reason for deprescription based on clinical guidelines
Hypromellose + Dextran	37 (9.5)	Absence of risk factors for eye injury, absence of sedation, presence of blinking reflexes and healthy eye surface <sup>23</sup> .
Bromopride	27 (7.0)	Absence or improvement of the symptoms that led to its prescription, such as nausea, vomiting and paralytic bowel, presence of diarrhea and/or appearance of adverse reactions <sup>24</sup> .
Potassium chloride	24 (6.2)	Normal or elevated serum potassium values after electrolyte replacement, absence of major potassium-depleting agents, and/or risk of hyperkalemia <sup>25</sup> .
Hydrocortisone	19 (4.9)	Reversed septic shock, with hemodynamic stabilization and clinical improvement after acute corticosteroid therapy(up to 3 weeks) and/or increased risk of fluid retention, development of infections and rise in blood pressure and blood glucose <sup>26</sup> .
Chlorexidine	18 (4.6)	Absence of MVAP <sup>1</sup> risk, patients breathing room air and with normal level of consciousness and/or onset of adverse reactions <sup>27</sup> .
Thiamine	15 (3.9)	Absence of vitamin deficiency, achievement of the therapeutic target after replacement, reversal/ improvement of the shock condition <sup>28</sup> .
Meropenem	12 (3.1)	Treatment time finished, clinical improvement of the patient, absence of infection signs and symptoms, need to replace the antibiotic therapy, increased risk of bacterial resistance and/or appearance of adverse reaction <sup>529,30</sup> .
Magnesium sulphate	12 (3.1)	Normal or elevated serum magnesium values after electrolyte replacement, absence of major magnesium-depleting agents, and hypermagnesemia risk <sup>25</sup> .
Vancomycin	11 (2.8)	Treatment time finished, clinical improvement of the patient, absence of infection signs and symptoms, need to replace the antibiotic therapy, increased risk of bacterial resistance and/or appearance of adverse reactions, such as red neck syndrome and renal failure <sup>29,30</sup> .
Drinking water	9 (2.3)	Normal serum sodium values after free water supply, positive water balance and/or risk of fluid retention <sup>31</sup> .
Lactulose	9 (2.3)	Normal bowel transit, presence of diarrhea, absence of any constipating agent, reversal of encephalopathy <sup>32,33</sup> .
Heparin	8 (2.1)	Absence of risk factors for venous thromboembolism, presence of active bleeding, thrombocytopenia, prolonged APTT2 and/or performance of a surgical procedure <sup>34</sup> .
Dipyrone	7 (1.8)	Absence of pain or fever, use of other analgesics, masking possible infection, presence of allergic reaction and/or appearance of adverse reactions <sup>35</sup> .
Omeprazole	7 (1.8)	Absence of risk factors for gastric ulcer, presence of drug interaction and/or appearance of adverse reactions <sup>36</sup> .
Total	388 (100%)	

MVAP<sup>1</sup>: Mechanical Ventilation-Associated Pneumonia. APTT<sup>2</sup>: Activated Partial Thromboplastin Time.

According to the literature, the acceptance rates of pharmaceutical recommendations by physicians represent a good indicator of the quality of the clinical pharmacy service. The prioritization of high-risk recommendations and the presence of efficient communication between professionals improve the rates of recommendations accepted by the medical team<sup>44</sup>. In addition to that, a number of studies indicate that the pharmaceutical recommendations transmitted to resident physicians are associated with higher acceptance rates, probably due to their greater availability and openness to discussions, an important factor in a university hospital, such as the one in this study<sup>45</sup>.

Our findings indicate that the prescription of unnecessary medications (without indication and/or without scientific evidence of therapeutic benefit) was the most prevalent reason for deprescribtion recommendations. Although limited, a systematic review shows that the use of unnecessary medications in older adults, a population segment of similar age to this study, varies from 40% to 50% and that this can cause irreversible harms to the patients, such as cognitive decline and/or premature death<sup>46</sup>. The literature also shows that, in the process of identifying unnecessary medications, the definition of clear clinical criteria, such as through algorithms, and the presence of a clinical pharmacist are fundamental<sup>46</sup>.

According to the ATC classification, antimicrobials for systemic use were the most involved in the pharmaceutical recommendations,

especially meropenem and vancomycin, a result that is similar to the one found in other studies<sup>42,43</sup>. IN-hospital infections by multi-drug resistant microorganisms are frequent problems in ICUs and require the use of broad-spectrum antimicrobials, such as carbapenems and glycopeptides<sup>29</sup>. Proper use of antimicrobial agents and their deprescription, when necessary, with continuous application of harmacokinetics principles and assessment of bacterial resistance, is fundamental to reduce the toxicity risk and guide actions to prevent and control bacterial resistance<sup>29,30,48</sup>.

The therapeutic class most associated with deprescription non-acceptance corresponded to corticosteroids for systemic use, with emphasis on hydrocortisone, frequently prescribed for reversing septic shock together with vasoactive drugs<sup>49</sup>. In the presence of reversed septic shock and hemodynamic stabilization, discontinuation in the use of systemic corticosteroids is recommended in order to avoid the development of metabolic adverse reactions and superinfections<sup>26,49</sup>. In this study, the high non-acceptance rate can be related to uncertainties about the benefit of this therapy in reducing mortality and about the definition of doses and treatment length in time<sup>50</sup>.

With regard to the medications, it was observed that hypromellose/ dextran eye drops, belonging to the ophthalmological class, were the most prevalent in the deprescriptions. These eye drops are widely used as prophylaxis for corneal ulcers in sedated patients in ICUs, and their deprescription is recommended





when the patients are not sedated and present spontaneous eye opening<sup>23</sup>. In addition to that, most ophthalmic formulations contain preservative substances such as benzalkonium chloride (BZC), which can cause allergic eyelid dermatitis as an adverse effect<sup>51</sup>. Secondly, there was deprescription of bromopride, usually prescribed as an antiemetic and prokinetic agent, here deprescribed in the presence of significant improvement in nausea, vomiting and gastric residue<sup>24</sup>.

Among the PDMs, injectable potassium chloride was the most deprescribed medication, ranking third overall in terms of deprescription. When compared to other drugs, PDMs have a higher risk of causing serious harms to the patients if used incorrectly. In this case, the deprescription of potassium chloride prevents the occurrence of adverse events, mainly at the cardiovascular level. The presence of PDMs in medical prescriptions is a reason for double-checks and signals the patients that should be monitored as a priority. Therefore, these medications are potentially subjected to increased surveillance by clinical pharmacists, being the target of pharmaceutical recommendations<sup>52</sup>.

As explained, our study presents valuable and important information about drug deprescription in ICUs that can be taken into account for patient safety measures, as well as for the methodological adequacy of similar studies. However, it does have some limitations, such as the following: the sample size can be considered small; it is not a multicenter study; and absence of clinical data in some records, hindering a more accurate analysis and identification of possible associated factors. Thus, these data cannot be extrapolated to other centers, although they can be used as a guide. It is worth noting that the scarcity of clinical reports on the issue of drug deprescription in ICUs made it difficult to compare the results found with the literature.

Future studies should evaluate the impact of deprescription recommendations on morbidity and mortality in ICUs and on the reduction of hospital costs, as well as the presence of clinical pharmacists leading these recommendations. In addition to that, it should be encouraged to develop evidence-based algorithms to facilitate the deprescription process, identification of adverse symptoms and contraindications in the ICU environment<sup>53</sup>.

# Conclusion

This study evaluated the drug deprescription recommendations made by a clinical pharmacist to critically-ill patients and showed a high acceptance level of the recommendations by the medical professionals, which may indicate the presence of a consolidated clinical pharmaceutical service. The most frequent problem related to deprescription was 'prescription of unnecessary medications', with antibacterials for systemic use and hypromellose/dextran eye drops as the most prevalent therapeutic class and medication in the derescriptions, respectively. Among the PDMs, injectable potassium chloride ranked third overall in terms of derescription, preventing the occurrence of potentially fatal adverse events. Given this scenario, this study reinforces the importance of clinical pharmacists reviewing medical prescriptions and their role in deprescribing medications in ICU environments.

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#### Collaborators

AVMO, RVC, JMAN and HRS carried out the conception, design and guidance of the study. RNB, AMC, LMM and CCA carried out data collection and review. AVMO, RVC and EFC wrote the article. JMAN, CCA, and HRS critically reviewed the article. All the authors approved the final version to be published, are responsible for all information in the paper and guarantee accuracy and integrity of any of its parts.

#### **Conflict of interest statement**

The authors declare the absence of conflicts of interest in relation to this article.

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