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Prevalence of the use of medications requiring renal adjustment in critical care units of a public hospital

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Abstract

Objective: To evaluate, among the most prescribed medications in the Intensive Care Units (ICU) of a public teaching hospital, those that require dose adjustment according to renal function, and to present the role of the pharmacist in this care setting. **Methods:** A cross-sectional observational study was conducted, with data collected from medication prescriptions through reports generated by the institution's Hospital Information System from 2015 to 2019. Step 1: Based on the list of all medications prescribed during this period in two ICUs of the institution, the prevalence of prescription was calculated. For the 100 most used medications, a search was conducted on the Uptodate platform regarding the need for dose adjustment based on renal function. The data were compiled into a Microsoft Excel spreadsheet. Step 2: The compiled data were presented to five clinical pharmacists from the institution, who assessed the severity and likelihood of occurrence of potential non-adjustment of doses for the 10 most prevalent medications that require it, using the Hazard Score Matrix. **Results:** Of the 100 most prevalent, a total of 34 medications were identified that require dose adjustment, with the most predominant classes being antimicrobials (41.2%), followed by those related to the cardiovascular system (20.6%) and the central nervous system (17.6%). The medications that scored highest when evaluated by the Hazard Score Matrix were morphine and regular insulin, followed by enoxaparin and potassium chloride. It was noted that dose adjustment is necessary not only to reduce adverse reactions or nephrotoxicity but also to ensure therapeutic effectiveness. **Conclusion:** This study emphasized the importance of adjusting medication doses in critically ill patients with renal dysfunction. Many frequently prescribed medications require dose modifications to ensure safety and effectiveness, particularly those classified as 'high-alert' due to their narrow therapeutic range. Collaboration between physicians and pharmacists is essential for minimizing risks in this context. Additionally, the use of risk analysis tools, such as HFMEA, facilitates the implementation of preventive interventions and dose adjustment protocols.

Key words: renal elimination; evidence-based pharmacy practice; pharmacy service, hospital.

Prevalência do uso de medicamentos que necessitam de ajuste renal em unidades críticas de um hospital público

Resumo

Objetivo: Avaliar, dentre os medicamentos mais prevalentemente prescritos nas Unidades de Terapia Intensiva (UTI) de um hospital público de ensino, aqueles que demandam ajuste de dose conforme função renal e apresentar o papel do farmacêutico nesse cenário assistencial. **Métodos:** Foi realizado um estudo observacional transversal, sendo coletados dados das prescrições de medicamentos por meio de relatórios gerados pelo Sistema de Informação Hospitalar da instituição, no período de 2015 a 2019. Etapa 1: A partir da lista de todos os medicamentos prescritos no período em duas UTIs da instituição, realizou-se o cálculo de prevalência de prescrição. Para os 100 medicamentos com maior prevalência de utilização, foi realizada busca na plataforma *Uptodate* sobre a necessidade de ajuste de dose pela função renal. Os dados foram compilados em planilha do Microsoft Excel. Etapa 2: os dados compilados foram apresentados para cinco farmacêuticos clínicos da instituição que avaliaram a gravidade e probabilidade de ocorrência do eventual não ajuste de dose dos 10 medicamentos mais prevalentes que o requerem, utilizando a *Hazard Score Matrix*. **Resultados:** Dos 100 mais prevalentes, obteve-se um total de 34 medicamentos que necessitam de ajuste de dose, sendo as classes mais predominantes a dos antimicrobianos (41,2%), seguida daqueles relacionados ao sistema cardiovascular (20,6%) e daqueles relacionados ao sistema nervoso central (17,6%). Os medicamentos que apresentaram maior escore quando avaliados pela *Hazard Score Matrix* foram morfina e insulina regular, seguidos de enoxaparina e cloreto de potássio. Observou-se que o ajuste de dose é necessário não apenas para reduzir quadros de reações adversas ou nefrotoxicidade, mas também para garantir a efetividade terapêutica. **Conclusão:** Este estudo destacou a importância do ajuste das doses de medicamentos em pacientes críticos com disfunção renal. Muitos dos medicamentos frequentemente prescritos necessitam de alterações nas doses para garantir segurança e efetividade, especialmente aqueles classificados como de "alta vigilância" ou "potencialmente perigosos", devido à sua faixa terapêutica estreita. A colaboração entre médicos e farmacêuticos é fundamental para a minimização de riscos nesse contexto. Ademais, a utilização de ferramentas de análise de risco, como o HFMEA, facilita a implementação de intervenções preventivas e protocolos de ajuste de dose.

Palavras-chave: eliminação renal; prática farmacêutica baseada em evidências; serviço de farmácia hospitalar.

Introduction

Renal insufficiency is a common condition among patients admitted to intensive care units (ICUs), presenting a significant challenge to clinical practice, especially regarding medication dose adjustment. Critically ill patients often exhibit acute or chronic changes in renal function, which demands heightened attention from healthcare professionals in pharmacotherapy management. Inadequate medication adjustment can lead to serious adverse effects, including toxicity or therapeutic failure, compromising patient safety and recovery[1].

The role of the clinical pharmacist in managing pharmacotherapy for patients with renal insufficiency is crucial to ensure the safety and efficacy of drug treatment. The presence of this professional in the multidisciplinary team enables continuous renal function evaluation, the identification of medications requiring dose adjustments, and the monitoring of potential toxicities. Studies show that clinical pharmacist interventions in ICUs significantly reduce the occurrence of drug-related adverse events, especially in patients with renal impairment. Furthermore, pharmacists contribute to the individualization of treatment, collaborating with doctors and nurses to optimize doses and adjust complex therapies. Personalizing treatment according to the dynamic changes in renal function in critically ill patients allows for a safer and more effective approach, preventing both underdosing and drug accumulation toxicity[2,3].

However, for the clinical pharmacist's performance in the ICU to be optimized, the potential risks of pharmacotherapy must be mapped in advance. This enables the pharmacist to be more assertive in identifying pharmacotherapy-related problems that present a higher risk of adverse events to patients. Tools such as HFMEA (Health Care Failure Mode and Effect Analysis) have proven to be an effective approach in identifying potential risks associated with healthcare. Moreover, the ICU environment provides a suitable setting for the use of this tool, which can highlight for the care team and pharmacists the highest risks associated with the use of medications requiring dose adjustments based on renal function[4].

Thus, this study aimed to investigate the demand for dose adjustment of the most frequently prescribed medications, according to renal function, in critically ill patients, based on the risk score calculated from the perspective of clinical pharmacists.

Methods

A cross-sectional observational study was conducted following the guidelines of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE statement) and approved by the institution's Research Ethics Committee (49543321.6.0000.0096).

The study considered all medication prescriptions from 2015 to 2019 for patients hospitalized in two ICUs of a public teaching hospital located in the southern region of the country. Together, the study units have a total of 26 beds and apply the following hospitalization criteria: age over 18 years; the presence of severe health conditions; the need for continuous monitoring; and/or the requirement for advanced life support. Patients admitted to the study units may come from within the hospital (wards or emergency department) or externally (from other institutions in the municipality via a regulatory center). These units were selected for the present study due to the high prevalence of critically ill patients with renal insufficiency or organ dysfunction, as inadequate dose adjustment in such conditions may increase the risk of toxicity or therapeutic ineffectiveness.

To retrieve prescriptions, the institution's Hospital Information System (SIH) was used. The prescription data were processed in a Microsoft Excel spreadsheet to establish the most prevalently prescribed medications in the study units, using the following formula: Prevalence (%) = ("prescriptions.day"/"patients.day") x 100[5–7].

From the top 100 most prevalent medications, research was conducted on the UpToDate platform, the same used in the routine of the institution's professionals, to determine the list of medications that require dose adjustments according to the patient's renal function. For those identified as requiring dose adjustment according to the literature used, a relevance evaluation of the adjustment was performed through a risk analysis.

The risk analysis was conducted using HFMEA, a method applied in healthcare services to identify and prevent potential failures in processes before they cause harm to patients. It proactively analyzes failure modes (possible errors) in care processes and evaluates their effects (impact on the patient). The method involves mapping the process, identifying risks, prioritizing the most critical failures, and developing corrective actions to minimize the probability of errors, promoting safety and quality of care[8]. In this study, the failure mode was defined as: "the most prevalently prescribed medications in ICUs that require dose adjustments based on renal function."

In this context, to identify failure modes related to the use of medications requiring dose adjustments based on renal function, the HSM (Hazard Score Matrix) was used. HSM is a tool used to prioritize identified failure modes based on the risk level they represent to patient safety, evaluating each potential failure in two main criteria: severity and probability[8]. The severity and probability scores can range from 1 to 4 and are presented in Table 1. To prioritize the failure modes, the multiplication of severity and probability scores for each situation is performed, ranking them from "1" (Remote and Minor) to "16" (Frequent and Catastrophic), as shown in Table 2.

To identify risks in the use of medications requiring dose adjustments according to renal function, the study selected pharmacists with a minimum of three years of experience in clinical pharmacy and previous work in ICUs. The selected pharmacists independently evaluated each medication defined within the failure mode and assigned probability and severity scores according to Table 1. Based on the responses obtained, the median probability and severity were calculated, which were multiplied to obtain the HSM score (Table 2).

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Table 1. Interpretation of Values Used in the Risk Scoring Matrix (HSM)

Indicated Number	Correspondence for Severity	Correspondence for Probability
1	Minor: no injury and no increase in hospital length of stay or level of care	Remote: unlikely to occur (at some point in 5 to 30 years)
2	Moderate: increase in hospital length of stay or level of care for 1 or 2 patients	Uncommon: possible to occur (at some point in 2 to 5 years)
3	Major: permanent decrease in bodily function (sensory, motor, physiological, or intellectual), disfigurement, need for surgical intervention, increase in hospital length of stay or level of care for 3 or more patients	Occasional: likely to occur (several times in 1 to 2 years)
4	Catastrophic: death or permanent major loss of function (sensory, motor, physiological, or intellectual)	Frequent: likely to occur immediately or within a short period (may occur several times in a year)

SOURCE: Adapted from DE ROSIER et al. (2002).

Table 2. Risk Score after Analysis of Severity and Probability

		Severity			
		Catastrophic	Major	Moderate	Minor
Probability	**Frequent**	16	12	8	4
	Occasional	12	9	6	3
	Uncommon	8	6	4	2
	Remote	4	3	2	1

SOURCE: Adapted from DE ROSIER et al. (2002).

Results

During the evaluated period, 422 medications were prescribed in both units. Of these, the 100 most prevalently prescribed medications were identified and are presented in Table 3. For these 100 medications, it was found that 34 of them require dose adjustment according to renal function. The UpToDate platform references used to assess the need for dose adjustment for each medication based on renal function are provided in Appendix 1.

According to Table 3, the medication with the highest prescription prevalence was dipyrone, with 95.4% of hospitalized patients in the study units having at least one prescription of this medication daily. Medications like omeprazole, used for stress ulcer prophylaxis, and enoxaparin, used for venous thromboembolism prophylaxis, had lower prescription prevalences compared to dipyrone, at 62.3% and 47.0%, respectively.

Among the medications requiring dose adjustment based on renal function (Table 3), the therapeutic class with the highest prescription prevalence was antimicrobials (n=14, 41.2%), followed by medications related to the Cardiovascular System and Central Nervous System/Pain with 7 (20.6%) and 6 (17.6%) medications, respectively.

Table 3. One Hundred Most Prescribed Medications in Intensive Care Units from 2015 to 2019, with Corresponding Assessment of Dose Adjustment Needs Based on Renal Function. (Continua)

Active Ingredient	Prevalence (%)	Dose Adjustment?
Dipyrone	95.43	No
Sodium Chloride	81.28	No
Glucose	78.71	No
Omeprazole	62.25	No
Bromopride	56.16	No
Enoxaparin	46.95	Yes
Morphine	40.36	Yes
Regular Insulin	39.26	Yes
Ondansetron	37.92	No
Norepinephrine	32.58	No
Furosemide	32.47	Yes
Heparin	31.50	No
Ranitidine	29.71	Yes
Fentanyl	27.01	Yes
Midazolam	22.31	No
Haloperidol	17.86	No
Hydroelectrolyte Solution	17.70	No
Ceftriaxone	17.39	Yes
Hydrocortisone	17.12	No
Atropine	16.07	No
Ipratropium	16.07	No
Meropenem	15.93	Yes
Thiamine	15.73	No
Amlodipine	15.29	No
Acetaminophen	14.20	No
Propofol	14.13	No
Potassium Chloride	13.88	Yes
Fenoterol	13.3	No
Acetylsalicylic Acid	13.00	No
Prednisone	12.4	No
Clonidine	12.36	Yes
Lactulose	12.29	No
Metoclopramide	12.04	Yes
Levothyroxine	11.95	No
Diazepam	11.91	No
Scopolamine	11.85	No
Zinc Oxide	11.85	No
SMZ+TMP	11.54	Yes
Terbutaline	11.14	No
Tramadol	9.99	Yes
Carvedilol	9.91	No
Methylprednisolone	9.76	No
Amiodarone	9.35	No
Piperac+Tazo	9.23	Yes
Yesvastatin	9.21	No
Vancomycin	9.05	Yes
Azithromycin	8.95	No
Risperidone	8.81	Yes
Phenytoin	8.61	No
Salbutamol	8.45	No
Enalapril	8.35	Yes
Folic Acid	8.19	No
Isophane Insulin	7.56	No
Atorvastatin	7.41	No
Levomepromazine	6.49	No
Spironolactone	6.34	Yes
Symethicone	6.30	No
Nitroglycerin	6.12	No
Fluoxetine	5.95	No

Table 3. One Hundred Most Prescribed Medications in Intensive Care Units from 2015 to 2019, with Corresponding Assessment of Dose Adjustment Needs Based on Renal Function. (Concluded)

Active Ingredient	Prevalence (%)	Dose Adjustment?
Vasopressin	5.91	No
Nystatina	5.82	No
Calcium Gluconate	5.74	No
Phytonadione	5.57	No
Fluconazole	5.52	Yes
Dexamethasone	5.28	No
Cyanocobalamin	5.21	No
Metronidazole	5.14	Yes
Valproic Acid	4.95	No
Gabapentin	4.85	Yes
Losartan	4.83	No
Mineral Oil	4.32	No
Cefepime	3.66	Yes
Amitriptyline	3.62	No
Soidum Bicarbonate	3.32	No
Clopidogrel	3.30	No
Acyclovir	3.27	Yes
Atenolol	3.11	Yes
Clonazepam	3.03	Yes
Sodium Phosphate	2.92	No
Magnesium Sulfate	2.81	Yes
Polymyxin B Sulfate	2.67	Yes
Colagenase	2.62	No
Oseltamivir	2.60	Yes
Epinephrine	2.45	No
Glycerin	2.42	No
Phenobarbital	2.41	Yes
Dobutamine	2.37	No
Hydralazine	2.25	No
Clindamycin	2.24	No
Hydrochlorothiazide	2.22	Yes
Dexchlorpheniramine	2.20	No
Acetylcisteine	2.15	No
Tranexamic Acid	2.05	Yes
Lamivudine	2.04	Yes
Clarithromycin	2.00	Yes
Ascorbic Acid	1.99	No
Carbamazepine	1.92	No
Diphenhyftamine	1.90	No
Mucopolysaccharide polysulphate	1.88	No
RHZE	1.85	Yes

RHZE: Rifampicin + Isoniazid + Pyrazinamide + Ethambutol; SMZ+TMP: Sulfamethoxazole+Trimethoprim; Piperac+Tazo: Piperacilin+Tazobactam.

Table 4 presents the top ten most prescribed medications requiring dose adjustment according to renal function, in descending order of prevalence, along with the data from the HSM assessment conducted by the hospital's clinical pharmacists. Morphine and regular insulin, both classified as high-risk medications, were rated with the maximum risk score (HSM=16) by pharmacists, due to the catastrophic severity of an adverse event and the high likelihood of occurrence. At the other end of the spectrum, ceftriaxone and meropenem, both classified as antibiotics, were rated with the minimum risk score (HSM=1), due to the lower severity and the remote probability of an adverse event occurring from failure to adjust the dose based on renal function.

Depending on the medication, UpToDate recommends different protocols for dose adjustment. Table 5 presents the guidelines for the ten most prevalent medications mentioned above.

Discussão

In a sample of the 100 most frequently prescribed medications in critical care units of a public teaching hospital, 34 were identified as requiring dose adjustment based on the patient's renal function. Of these, the ten most prevalent were reviewed in the literature to assess possible adverse effects related to the lack of dose adjustment and other treatment-related consequences. Additionally, five clinical pharmacists with prior ICU experience independently assessed the severity and likelihood scores for the potential failure to adjust the doses of these ten medications, using the HSM (Hazard Score Matrix).

Among the medications requiring dose adjustment according to renal function, enoxaparin was the most prescribed, with an occasional probability of catastrophic adverse events, scoring 12 in the HSM analysis. In this case, monitoring for possible bleeding, sudden abdominal pain (due to abdominal hematomas), acute drops in hemoglobin levels, altered consciousness, and hypotension[9] is crucial.

With a similar score, potassium chloride is generally prescribed for hypokalemia to prevent rhabdomyolysis and ventricular arrhythmias[10]. However, inappropriate administration in cases of redistributive hypokalemia may lead to rebound hyperkalemia and cardiotoxicity, making it important to monitor physiological effects through ECG and muscle strength[11].

Table 4. Ten Most Prevalently Prescribed Medications Requiring Dose Adjustment Based on Renal Function and Their Hazard Score Matrix Evaluations.

Drug	Prevalence (%)	F1		F2		F3		F4		F5		MED S	MED P	SCORE
		S	P	S	P	S	P	S	P	S	P			
Enoxaparin	46.95	3	4	3	4	3	4	3	3	3	3	3	4	12
Morphine	40.36	4	4	4	4	4	4	2	2	2	2	4	4	16
Regular Insulin	39.26	3	4	3	4	4	3	4	2	4	4	4	4	16
Furosemide	32.47	2	2	2	3	2	3	2	3	2	2	2	3	6
Fentanyl	27.01	2	3	3	3	2	4	2	3	3	3	2	3	6
Ceftriaxone	17.39	1	1	1	2	1	1	1	1	1	1	1	1	1
Meropenem	15.93	1	1	1	2	1	1	3	3	1	1	1	1	1
Potassium Chloride	13.88	4	3	4	3	4	3	4	2	4	4	4	3	12
Clonidine	12.36	2	1	2	1	2	1	2	1	2	2	2	1	2
Metoclopramide	12,04	1	1	1	1	2	3	2	3	1	2	1	2	2

F1- pharmacist 1; F2- pharmacist 2; F3- pharmacist 3; F4- pharmacist 4; F5- pharmacist 5; S- severity; P- probability; MED S- median severity; MED P- median probability.

Table 5. Dose Adjustment Recommendations for the Ten Most Prevalent Medications

MEDICAMENTO	Recomendações
Enoxaparin	**For treatment:** **CrCl > 50 mL/min:** no adjustment needed **CrCl between 30 and 50 mL/min:** No adjustment needed. Monitor for possible bleeding. **CrCl < 30 mL/min:** 1 mg/kg once daily. **For prophylaxis of venous thromboembolism in moderate-to-high-risk trauma patients**: **CrCl between 50 and 60 mL/min:** administer 30 mg every 12 hours, subcutaneously. **CrCl between 30 and 50 mL/min:** administer 30 mg every 12 hours, subcutaneously. **CrCl < 30 mL/min:** consider an alternative pharmacological prophylaxis, such as heparin. **For venous thromboembolism prophylaxis (excluding trauma patients):** **CrCl < 30 mL/min:** 20 to 30 mg once daily.
Morphine	**CrCl between 30 and 60 mL/min:** Consider changing opioid or reduce to 50-75% of initial dose and extend administration intervals. **CrCl between 15 and 30 mL/min:** Avoid use; or reduce to 25-50% of initial dose. **CrCl < 15 mL/min:** Completely avoid use.
Regular Insulin	**CrCl between 10 and 50 mL/min:** Administer 75% of the usual dose. Monitor glucose levels closely. **CrCl < 10 mL/min:** Administer 50% of the usual dose. Monitor glucose levels closely.
Furosemide	Dose adjustment is recommended when CrCl is below 30 mL/min. For oral administration, higher doses may be needed due to reduced tubular secretion. For continuous infusion, start with 20 mg/hour; if diuresis is ineffective, repeat bolus dose and increase infusion to 40 mg/hour.
Fentanyl	Adjustments recommended for transdermal formulation. **CrCl between 10 and 50 mL/min:** Reduce to 75% of the usual dose. **CrCl < 10 mL/min:** Reduce to 50% of the usual dose. For intravenous formulation, use small doses and titrate based on analgesic response and adverse effects.
Ceftriaxone	**CrCl > 130 mL/min:** Administer 2 grams twice daily to ensure therapeutic effectiveness. **CrCl < 15 mL/min:** Closely monitor plasma concentration if daily dose exceeds 2 grams, especially with concurrent liver dysfunction.
Meropenem	For recommended use of 1 gram or 2 grams every 8 hours: **CrCl between 25 and 50 mL/min:** Reduce administration frequency from every 8 hours (usual) to every 12 hours. **CrCl between 10 and 25 mL/min:** Reduce to 50% of the usual dose, every 12 hours. CrCl < 10 mL/min: Reduce to 50% of the current dose, every 24 hours.
Potassium Chloride	**CrCl between 30 and 60 mL/min:** Use cautiously, monitoring potassium levels. **CrCl < 30 mL/min:** Reduce initial IV dose by at least 50% and proceed with caution. For oral administration, start with the lower end of the dosage range, especially when using medications that increase potassium levels.
Clonidine	**CrCl < 30 mL/min:** Start treatment with a reduced dose, increasing cautiously based on blood pressure and heart rate monitoring.
Metoclopramide	**CrCl between 10 and 60 mL/min:** Reduce dose to 50% of the usual daily dose. **CrCl < 10 mL/min:** Reduce dose to 33% (or less) of the usual daily dose.

CrCl- creatinine clearance; mg- milligram; mL- milliliter.

Morphine and regular insulin received the maximum score of 16 in the HSM analysis, indicating a high probability of immediate or short-term catastrophic events if dose adjustments are not made. Although morphine clearance is similar between patients with normal and impaired renal function, glucuronide metabolites accumulate significantly in patients with reduced kidney function, with M6G being a major contributor to toxicity[12]. Regular insulin dose adjustment is necessary due to altered clearance in renal dysfunction, and rapid-acting insulins are recommended, as they present a lower risk of hypoglycemia in renal insufficiency[13].

The interruption of sodium reabsorption and the increase in hypoxic injury are likely factors contributing to the worsening of acute renal failure in patients using furosemide[14]. This drug received a score of 6 in the analysis of severity and probability, suggesting that problems arising from inadequate dose adjustment are uncommon but have greater severity. The same is true for fentanyl, which, compared to other opioids, is considered a drug with a lower likelihood of causing toxic harm in renal failure, due to the rapid redistribution of its metabolites, which have no pharmacological or toxicological activity and are quickly excreted[15,16]. Nonetheless, dose titration is recommended based on analgesic response and adverse effects, especially if in continuous infusion[17-19], along with careful monitoring of drug accumulation in the body and well-defined adjustments for transdermal formulation, as it is a highly lipophilic drug[20].

Unlike other prescribed medications, dose adjustments for ceftriaxone and meropenem are also necessary due to their impact on treatment effectiveness. Both received a minimum score of 1 in the HSM assessment, indicating a remote probability of adverse events of lesser severity when dose adjustment is not performed. However, it is important to note that the matrix used considered only the interference in the occurrence of adverse events. Ceftriaxone, due to its mixed excretion through biliary and renal clearance, experiences minimal changes in its pharmacokinetics in cases of renal dysfunction, owing to compensatory mechanisms[21]. On the other hand, the excretion of meropenem occurs predominantly via the renal route, which may reduce by over 60% in patients with impaired renal function and in critical conditions, as analyzed in the present study[21-23].

Seldom used in antihypertensive pharmacotherapy, despite belonging to the antihypertensive[24] class, clonidine requires dose adjustments justified by its high renal elimination (40 to 60%) and possible alterations in its response in patients with severe renal insufficiency[25]. According to the HSM assessment, it received a score of 2, indicating that it is not a medication that frequently presents issues related to dose adjustment in the hospital context, similar to metoclopramide. Regarding the antiemetic, the low occurrence of adverse events may be related to its excretion through other pathways; its renal clearance accounts for about 21% or less of the total plasma clearance[26]. Nevertheless, the literature recommends dose adjustments, which may be particularly important in patients with a history of Parkinson's disease, as the accumulation of this medication in the body can cause extrapyramidal effects, such as dystonia, akathisia, and parkinsonian manifestations[26-27].

Despite the extensive literature on dose adjustment of medications based on the patient's renal function, discrepancies have been identified between the information presented in scientific articles on UpToDate and the assessment conducted by clinical pharmacists. One justification for this is that the HSM considers only the severity and likelihood of problems arising from the lack of dose adjustment. In some cases, such as meropenem and ceftriaxone, as previously mentioned, such adjustments in pharmacotherapy are necessary to ensure treatment effectiveness. Furthermore, despite the clinical perception of pharmacists and the recommendations from the database used in the institution, in some instances, there were no justifications or sufficient current literature to support the need for dose adjustment. This was the case for morphine, which received a score of 9 in the HSM and has a well-established adjustment description in UpToDate, but no studies were identified to justify this decision.

Regarding patients with altered renal function, Sukkha and collaborators[28] evaluated medical records and pharmaceutical interventions conducted over approximately one year with 158 patients hospitalized in a tertiary hospital in Thailand, who had a creatinine clearance of less than 60 mL/min or acute renal failure upon admission and were using antimicrobials. In this evaluation, 190 recommendations were suggested by pharmacists, including dose reductions or increases, directly impacting the pharmacoeconomics of the hospital, with an estimated cost-saving of approximately 42 euros per intervention.

On the other hand, a cross-sectional observational study conducted in Pakistan aimed to evaluate pharmacists' knowledge and perceptions regarding renal dose adjustment in patients with chronic kidney disease using the Renal Dosing Questionnaire-13 (RDQ-13). It was found that although approximately 96.3% (n = 270) of the participating professionals considered dose adjustment relevant for these patients, only 44.8% felt confident in determining the appropriate dose for patients. This demonstrates a fragility in access to information and a lack of standardized guidelines for such adjustments[29].

In addition, there is a challenge in determining renal function through estimated equations that rely on endogenous markers, which can be influenced by various factors such as diet, age, and underlying diseases[30]; and difficulties in determining creatinine clearance from a 24-hour urine sample indicate a gap in defining adjustment criteria without considering these variables, hindering appropriate clinical decision-making.

As limitations of this research, it is important to note that the profile of the patients whose prescriptions were analyzed was not assessed, nor was it determined whether there was a dose adjustment for the medications in question or subsequent clinical outcomes, as the central objective was solely to investigate the demand for dose adjustment based on the renal function of the most frequently prescribed medications. Data on dose adjustments for any type of dialysis were also not presented; and the analysis using the Hazard Score Matrix focused only on the occurrence of adverse events. Additionally, the data were obtained from prescriptions of patients hospitalized in critical units, which have particular characteristics, making it difficult to generalize the results. Thus, there is a justified need for the development of studies that also address non-critical patients and analyze the impact resulting from the lack of dose adjustment of medications.

Conclusão

This study highlighted the critical importance of dose adjustment for medications in patients under intensive care, especially considering the prevalence of renal dysfunction in this population. The results demonstrate that a significant number of commonly prescribed medications require adjustments to ensure therapeutic safety and efficacy, emphasizing the essential role of clinical pharmacists in identifying and preventing potential risks. The predominance of therapeutic classes such as antimicrobials and cardiovascular drugs among those requiring adjustment underscores the relevance of more precise pharmacological interventions in these areas. Additionally, the use of risk analysis tools, such as the HFMEA method and the Hazard Score Matrix, provides a structured approach for evaluating medications with a high potential for causing harm, indicating the need for robust protocols and targeted preventive actions.

These findings reinforce the need to integrate dose adjustment practices into the routine of ICUs, promoting greater safety and effectiveness in patient care. Collaboration between physicians and clinical pharmacists is essential to ensure a pharmacological management that minimizes risks and maximizes therapeutic outcomes, especially in scenarios of renal impairment. In this context, more in-depth studies are needed on the clinical, humanistic, and economic impact of pharmaceutical interventions related to medication dose adjustments.

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Contributors

Project conception (A.M.M, D.B, I.R, L.F). Data analysis, interpretation, and manuscript drafting (D.B, I.R, L.F). Final critical review of the manuscript (A.M.M, I.R). All authors approved the final version of the manuscript and are responsible for all the information contained within.

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Conflict of Interest Declaration

The authors declare no conflict of interest concerning this article.

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