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Characterization of pharmaceutical recommendations in the management of mandatory occult fluids in critically ill patients

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Abstract

Objective: The present study aimed to characterize pharmaceutical recommendations (PR) Focused on the management of mandatory occult fluids in critically ill patients. **Methods:** Observational, descriptive, and cross-sectional study developed in a university hospital from April to December 2024. The PRs related to the management of mandatory occult fluids performed in the analyzed unit between January 2023 and June 2024 were characterized. The demographic profile of the patients targeted by the PRs was described, as well as the main groups of medications involved and the volume of mandatory occult fluids saved. Data were collected from the PR database of the institution's clinical pharmacy unit and subsequently analyzed through descriptive measures, where numerical variables were presented as mean and standard deviation and categorical variables were exposed as frequency. The project was developed in full compliance with the ethical principles established in resolution 466/12 of the National Health Council. **Results:** The sample consisted of 90 patients, predominantly men with a mean age of 59.77 years. A total of 5,112 RFs were performed, of which 163 (3.19%) were related to mandatory occult fluid management, representing an average of 1.81 PRs per patient. The main group of drugs involved in the recommendations were anti-infectives for systemic use (61.35%), which was also the group of drugs that obtained the largest amount of volume saved (53.81%). A total of 150.584 L of fluids were avoided by performing PRs related to fluid management, representing a saving of 1.655 L per patient. **Conclusion:** The findings demonstrate the potential that pharmacists have in managing mandatory hidden fluids in critically ill patients, since their recommendations help prevent unnecessary fluid overload that could lead to unfavorable outcomes in this group of individuals.

Key words: fluid therapy, intensive care unit, pharmacist, clinical pharmacy.

Caracterização das recomendações farmacêuticas no gerenciamento de fluidos ocultos obrigatórios em pacientes críticos

Resumo

Objetivo: O presente estudo objetivou caracterizar as recomendações farmacêuticas (RF) voltadas ao gerenciamento de fluidos ocultos obrigatórios em pacientes críticos. **Métodos:** Estudo de caráter observacional, descritivo e transversal desenvolvido em um hospital universitário no período de abril a dezembro de 2024. Caracterizaram-se as RF relacionadas ao gerenciamento de fluidos ocultos obrigatórios realizadas na unidade analisada no período entre janeiro de 2023 e junho de 2024. Descreveu-se o perfil demográfico dos pacientes alvo das RF, bem como os principais grupos de medicamentos envolvidos e volume de fluidos ocultos obrigatórios economizados. Os dados foram coletados a partir do banco de dados de RF da unidade de farmácia clínica da instituição, sendo posteriormente analisados através de medidas descritivas, onde as variáveis numéricas foram apresentadas como média e desvio-padrão e as variáveis categóricas foram expostas como frequência. O projeto foi desenvolvido obedecendo integralmente os princípios éticos estabelecidos na resolução 466/12 do Conselho Nacional de Saúde (CNS). **Resultados:** A amostra foi composta por 90 pacientes, com predominância de homens com idade média de 59,77 anos. Realizou-se 5112 RF, sendo 163 (3,19%) relacionadas a gerenciamento de fluidos ocultos obrigatórios, representando uma média de 1,81 RF por paciente. O principal grupo de fármacos envolvido nas recomendações foram os anti-infecciosos para uso sistêmico (61,35%), sendo também o grupo de fármacos que obteve a maior quantidade de volume poupado (53,81%). Um total de 150,584 L de líquidos teve sua administração evitada através da realização das RF relacionadas ao gerenciamento de fluidos, representando uma economia de 1,655 L por paciente. **Conclusão:** Os achados demonstram o potencial que o farmacêutico possui no gerenciamento de fluidos ocultos obrigatórios em pacientes críticos, uma vez que suas recomendações auxiliam na prevenção de uma sobrecarga hídrica desnecessária que poderia levar a desfechos desfavoráveis nesse grupo de indivíduos.

Palavras-chave: fluidoterapia, unidade de terapia intensiva, farmacêutico, farmácia clínica.



Introduction

The use of fluids in Intensive Care Units (ICUs) represents the most commonly performed intervention in critically ill patients, and it can trigger either beneficial or adverse effects depending on how it is administered¹. Fluid overload is associated with adverse clinical outcomes, such as prolonged mechanical ventilation, extended ICU and hospital stays, higher incidence of organ dysfunction, and increased mortality. This excess of fluids can lead to intra-abdominal hypertension and renal venous congestion, promoting the development of acute kidney injury and impairing the recovery of renal function. Additionally, the extravasation of fluids into the interstitial space contributes to pulmonary and tissue edema, reducing lung compliance, compromising oxygenation, and increasing the need for ventilatory support²⁻⁴.

In this context, the management and optimization of fluid balance have emerged as central elements in the care of critically ill patients². Fluid management, also known as fluid stewardship, represents a targeted strategy aimed at promoting the rational use of intravenous fluids, contributing to the prevention of the detrimental effects that fluid overload can have on patient clinical outcomes³.

Less obvious sources of fluid administration, referred to as hidden fluids, correspond to the portion of volume delivered as part of routine care that is not specifically prescribed⁴. These sources can be divided into mandatory fluids, represented by drug diluents, and discretionary fluids, represented by intravenous maintenance fluids, resuscitation boluses, nutrition, and blood products⁵.

Hidden fluids are frequently overlooked in the hospital environment and are often not properly accounted for when evaluating the patient's administered fluid volume and its impact on daily fluid balance³. However, literature data indicate that intravenous drug diluents, one of the main sources of hidden fluids, may represent the largest source of volume administered to the patient, particularly when used intermittently⁶.

The presence of a multidisciplinary team is an essential part of best practice models for critical care, with the pharmacist being one of its key components⁷⁻⁸. According to the Society of Critical Care Medicine in the United States, the presence of this health professional in intensive care is essential to ensure safer and more rational medication use, reducing patient harm and improving clinical outcomes⁹.

Among the activities performed by the pharmacist is the clinical review of pharmacotherapy¹⁰. This review allows the identification and recommendation of points for optimization of the patient's pharmacotherapy regarding the necessity, effectiveness, and safety of prescribed medications¹¹. Given this role of the pharmacist in managing patient pharmacotherapy, it follows that they can also contribute effectively to the management of fluids administered to critically ill patients³.

International studies, such as that by Hawkins *et al.* (2022)¹² conducted in the United States, have highlighted the significant contribution of pharmacists in the field of fluid management, demonstrating the positive impact of these practices on the management and safety of intravenous fluid use in hospital settings. This impact was measured based on the percentage of recommendations related to fluid administration, which reached nearly 20% of the total recommendations made in the unit under study, emphasizing the need for future research to evaluate the effect of fluid stewardship programs on patient outcomes¹².

However, in Brazil, studies directly addressing the role of pharmacists in this context remain scarce. The national literature lacks more robust research analyzing and demonstrating the contribution of this professional category in the implementation and improvement of fluid stewardship programs, characterizing and quantifying the recommendations made by pharmacists in Brazil regarding the management of mandatory hidden fluids. This gap represents a limitation to the expansion of this practice within the Brazilian healthcare system.

Based on the above, it is highly relevant to evaluate the contribution of pharmacists in fluid management in an ICU through the recommendations provided to prescribing professionals, aiming to optimize patient pharmacotherapy and support the implementation and strengthening of fluid stewardship programs in Brazil. Accordingly, the present study was designed to characterize the recommendations made by pharmacists focused on the management of mandatory hidden fluids in critically ill patients, aiming to prevent unnecessary fluid administration to this patient population.

Methods

Study Setting

The study was conducted at the Walter Cantídio University Hospital (HUWC), affiliated with the Federal University of Ceará. HUWC is part of the Brazilian Unified Health System (SUS) and plays an important role in healthcare delivery in the state of Ceará. The hospital offers services divided into clinical and surgical specialties, in addition to non-medical specialties such as outpatient and clinical pharmacy. It has two ICUs—one surgical and one medical—each with eight beds and a multidisciplinary team including physicians, nurses, nursing technicians, physiotherapists, speech therapists, nutritionists, social workers, and pharmacists.

Clinical pharmacists allocated to the two ICUs perform daily clinical reviews of the pharmacotherapy of hospitalized patients from Monday to Friday, assessing the necessity, effectiveness, safety, convenience, and administration process of the prescribed medications. Based on this review, recommendations are made to other members of the multidisciplinary team regarding the rational use of medications during multiprofessional rounds or case discussions with the prescriber. The pharmaceutical recommendations are subsequently recorded by the responsible pharmacist in the clinical pharmacy unit database using an electronic spreadsheet in Microsoft Office Excel 2016.

Study Design

This is an observational, descriptive, and cross-sectional study that characterized pharmacist recommendations focused on the management of mandatory hidden fluids in hospitalized patients in an intensive care unit. Data were collected from records of pharmaceutical recommendations made between January 2023 and June 2024 in the institution's medical ICU.

Patients aged 18 years or older who were admitted to the medical ICU at HUWC during the study period and who received any type of pharmacist recommendation related to the management of mandatory fluids were included in the study.

The variables studied were:

- Patient demographic data: sex, age.
- Total number of pharmacist recommendations made in the medical ICU at HUWC during the study period.
- Pharmacist recommendations related to the management of mandatory hidden fluids made in the medical ICU at HUWC during the study period.
- Main classes of medications targeted by recommendations for mandatory hidden fluid management in the medical ICU at HUWC during the study period.
- Acceptance of pharmacist recommendations regarding the management of mandatory hidden fluids by the prescribing professionals in the unit.
- Total volume of mandatory hidden fluids not administered to patients as a result of pharmacist recommendations during the study period, as well as its stratification by patient and medication group.

Data Collection

Pharmacist recommendations made in the medical ICU at HUWC between January 2023 and June 2024 were included in the study. Recommendations outside this period or incomplete recommendations—such as those missing medication name, previously used diluent volume, suggested diluent volume, or patient data including age and sex—were excluded.

The data used in the study were collected from the clinical pharmacy unit's pharmacist recommendation database at HUWC, stored in an electronic spreadsheet using Microsoft Office Excel® 2016.

Medications targeted by recommendations for mandatory hidden fluid management were classified according to the Anatomical Therapeutic Chemical (ATC) classification system, level 1 corresponding to the anatomical group and level 2 to the therapeutic group¹³.

The total volume of mandatory hidden fluids not administered to patients targeted by the recommendations was calculated by summing the differences between the volume (in mL) of the drug diluent prescribed by the attending physician before and after the pharmacist recommendation. The total volume spared was then divided by the number of patients included in the study and also stratified by the involved medication groups.

Statistical Analysis

Collected data were tabulated in Microsoft Office Excel® 2016 for subsequent statistical analysis. Descriptive statistical analysis was performed, with numerical variables presented as mean $\pm$ standard deviation and categorical variables expressed as frequencies.

Ethical Aspects

The project was approved by the Ethics Committee of the Walter Cantídio University Hospital (CEP-HUWC) under opinion number 5,409,579 and CAAE number 56178022.9.0000.5045. The research was conducted in full compliance with the ethical principles established in Resolution 466/12 of the National Health Council (CNS).

Results

During the analyzed period, 230 patients received some type of pharmacist recommendation, of whom 90 (39.13%) were targeted by recommendations related to mandatory hidden fluids. Male individuals were predominant (51.11%; $n=46$), with a mean age of 59.77 years (SD: 14.89). A total of 5,112 pharmacist recommendations (PRs) were made for patients admitted to the ICU under study during this period, of which 163 (3.19%) were related to the management of mandatory hidden fluids, representing an average of 1.81 PR per patient. The acceptance rate of these recommendations was 83.44% ($n=136$).

A total of 35 medications were involved in PRs related to the management of mandatory hidden fluids, with a predominance of recommendations concerning drugs from the systemic anti-infectives group (61.35%; $n=100$), nervous system (13.50%; $n=22$), and systemic hormonal preparations excluding sex hormones and insulins (8.59%; $n=14$). Within the first group, the most frequently recommended medications were Polymyxin (22.70%; $n=37$), followed by Vancomycin (15.95%; $n=26$) and Amikacin (9.20%; $n=15$). Among nervous system drugs, the most common were Midazolam (6.13%; $n=10$), Fentanyl (1.84%; $n=3$), and Phenytoin (1.84%; $n=3$). Hydrocortisone (7.36%; $n=12$), Dexamethasone (0.61%; $n=1$), and Methylprednisolone (0.61%; $n=1$) corresponded to the systemic hormonal preparations group, as shown in Table 1.

Regarding the volume of mandatory hidden fluids spared during the period, a total of 150.584 L of fluids were not administered as a result of PRs corresponding to volume adjustments. When analyzing the average volume savings per patient involved in the recommendations, an average of 1.655 L of fluids was spared per individual. Among the accepted recommendations, the highest volume spared for a single patient during hospitalization was 9.360 L, and the lowest volume spared was 0.150 L.

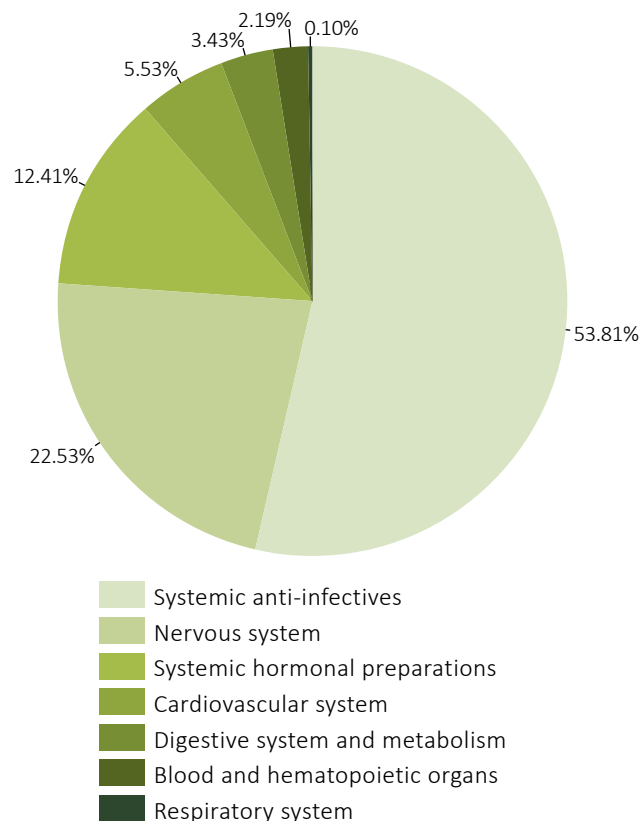
In terms of the stratification of total fluid volume spared by medication groups according to the Anatomical Therapeutic Chemical (ATC) classification, there was a predominance of savings related to diluents of drugs belonging to the systemic anti-infectives, nervous system, and systemic hormonal preparations excluding sex hormones and insulins.

Systemic anti-infectives accounted for a savings of 81.030 L (53.81% of the total volume spared), predominantly for Polymyxin (40.120 L) and Vancomycin (12.300 L). Nervous system drugs accounted for 33.926 L (22.53% of the total spared), with the highest volume spared for Phenytoin (14.720 L) and Midazolam (11.952 L). Systemic hormonal preparations excluding sex hormones and insulins accounted for 18.680 L (12.41% of the total spared), predominantly for Hydrocortisone (10.350 L). The complete distribution of non-administered fluid volumes by each analyzed group is illustrated in Figure 1.

Table 1. Classification of the main medications targeted by recommendations for the management of hidden fluids in the clinical intensive care unit.

Medications	Recommendations N (%)
Systemic anti-infectives	100 (61.35%)
Polymyxin B	37 (22.70%)
Vancomycin	26 (15.95%)
Amikacin	15 (9.20%)
Nervous system	22 (13.50%)
Midazolam	10 (6.13%)
Fentanyl	3 (1.84%)
Phenytoin	3 (1.84%)
Systemic hormonal preparations, excluding sex hormones and insulins	14 (8.59%)
Hydrocortisone	12 (7.36%)
Dexamethasone	1 (0.61%)
Methylprednisolone	1 (0.61%)
Blood and hematopoietic organs	12 (7.36%)
Tranexamic acid	3 (1.84%)
Sodium glycerophosphate	3 (1.84%)
Potassium chloride	3 (1.84%)
Cardiovascular system	8 (4.91%)
Norepinephrine	5 (3.07%)
Dobutamine	3 (1.84%)
Digestive system and metabolism	6 (3.68%)
Bromopride	2 (1.23%)
Omeprazole	2 (1.23%)
Scopolamine	1 (0.61%)
Respiratory system	1 (0.61%)
Acetylcysteine	1 (0.61%)

Figure 1. Stratification of spared fluid volume by drug groups according to the Anatomical Therapeutic Chemical (ATC) Classification in the clinical intensive care unit.



systemic hormonal preparations groups, corresponding to the same medication groups with the highest number of pharmacist recommendations.

Bashir et al. (2017)⁵ identified antimicrobials as the main sources of hidden fluids, followed by electrolytes and anti-ulcer agents.⁵ Similar results were obtained by Gamble et al. (2022)³, who identified antimicrobials, vitamins, electrolytes, and medications for pain, agitation, and delirium as the main sources of volume.³ These findings are consistent with the scenario identified in the present study regarding the category recognized as the main source of mandatory hidden fluids and also highlight other classes of medications with the potential to act as key agents in recommendations related to the management of mandatory hidden fluids due to their large volumes and high frequency of administration³.

This study has limitations, including a small patient sample and the inability to establish the influence of pharmacist recommendations related to the management of mandatory hidden fluids on clinical outcomes. Therefore, further studies are needed to better understand the impact of pharmacist recommendations on the management of mandatory fluids administered to ICU patients.

Nonetheless, the results of the present study demonstrate the significant contribution of pharmacists in managing fluids administered to critically ill patients. Therefore, the presence of these professionals in multidisciplinary ICU teams is of great importance to increasingly prevent unnecessary fluid overload from sources often overlooked by the care team.

Discussion

An average of 1.81 pharmacist recommendations per patient related to the management of hidden fluids was observed during the study period, with an associated acceptance rate of 83.44%. When comparing studies that evaluated the rate of pharmacist recommendations related to fluid therapy, results similar to those found by Hawkins et al. (2022)¹² and Cerqueira et al. (2024)¹⁴ were observed, with averages of 1.54 and 2.4 recommendations per patient, respectively. However, both studies present a bias in relation to the present study, as they assessed recommendations related to other sources of volume and not exclusively mandatory hidden fluids^{12,14}.

Regarding the medications involved in PRs related to hidden fluid management, this study identified a predominance of drugs from the systemic anti-infectives group, followed by agents acting on the nervous system and systemic hormonal preparations.

When stratifying the volume of fluid spared by medication groups, a predominance of fluids spared was observed for drug diluents belonging to the systemic anti-infectives, nervous system, and

Conclusion

The results of the present study demonstrate an important rate of pharmacist recommendations per patient for the management of mandatory hidden fluids during the study period, comparable to those of previous studies, with a high degree of acceptance by prescribers. Data were also obtained regarding the main drugs targeted by these recommendations, with particular emphasis on medications belonging to the anti-infective category as the principal agents involved in fluid-sparing recommendations. Thus, the findings highlight the potential role of pharmacists in the management of mandatory hidden fluids in critically ill patients, aiming to reduce unnecessary fluid administration in this patient population.

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Contributors

ALO contributed to the conception, development, and review of the project. SJA contributed to the writing and review of the project. OAB contributed to the writing and review of the project. LCO contributed to the writing and review of the project. NJA and LAM contributed to the conception, development, and review of the project.

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Conflict of Interest Statement

The authors declare no conflict of interest regarding this article.

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