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Drug-related problems identified in the medication follow-up of patients hospitalized in a university hospital

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Abstract

Objective: To analyze the drug-related problems (DRPs) identified from the medication follow-up (MF) performed by pharmacy residents on hospitalized patients at a university hospital. **Methods:** A descriptive cross-sectional study was conducted between August and December 2024 at a high-complexity university hospital in the city of Rio de Janeiro. Data was obtained from the MF of patients in the medical and geriatric clinics, performed by pharmacy residents between January 2022 and December 2023. The identified DPRs were recorded on a specific MF form. Subsequently, they were compiled in an online Google Drive spreadsheet and coded according to the method of the French Society of Clinical Pharmacy. MF forms containing at least one identified DRP were included in the study, and those with errors in completion that compromised the final analysis were excluded. The drugs were coded according to the first level (main anatomical group) and fifth level (chemical substance) of the Anatomical Therapeutic Chemical (ATC) code. Descriptive statistical analysis of the data was performed in an online Google Drive spreadsheet. **Results:** Of the 469 patients monitored during this period, 183 had at least one DRP identified. A total of 339 DRPs were identified, at an average rate of 1.8 per patient, and were targeted for intervention in the AF. Following pharmaceutical intervention, 61.9% of DRPs were resolved. The main DRP was 'untreated indication' (45.1%), followed by 'inappropriate administration' (18.9%) and 'overdose' (14.7%). In terms of the ATC code, the majority of drugs belonged to the 'gastrointestinal tract and metabolism' group (30.4%), with omeprazole being the main representative (18.4%). The second most frequent group was 'nervous system' (19.5%), mainly represented by dipyrone (27.3%), followed by the 'blood and haematopoietic organs' group (17.4%), mainly represented by enoxaparin (50.8%). **Conclusions:** The data showed that AF is capable of identifying DRPs during hospitalisation, highlighting the contribution of pharmacists to the rational use of medication. The presented data may assist with institutional strategies aimed at DRPs at higher risk. Finally, it is suggested that studies evaluating the clinical outcomes of identified PRMs are conducted.

Keywords: clinical pharmaceutical services, pharmaceutical services, inpatients.

Problemas relacionados a medicamentos identificados no acompanhamento farmacoterapêutico de pacientes internados em um hospital universitário

Resumo

Objetivo: Analisar os problemas relacionados a medicamentos (PRM) identificados a partir do acompanhamento farmacoterapêutico (AF), realizado por residentes de farmácia, de pacientes hospitalizados em unidades de internação de um hospital universitário. **Métodos:** Estudo transversal descritivo, realizado entre agosto e dezembro de 2024, em um hospital universitário de alta complexidade da cidade do Rio de Janeiro. Os dados foram obtidos do AF de pacientes da clínica médica e geriatria, realizado por residentes de farmácia entre janeiro de 2022 e dezembro de 2023. Os PRM identificados foram registrados em formulário específico do AF. Posteriormente, foram compilados em planilha *online* do *Google Drive* e codificados conforme o método da Sociedade Francesa de Farmácia Clínica. Foram incluídos no estudo os formulários de AF que continham pelo menos um PRM identificado e excluídos aqueles com falhas no preenchimento que comprometessem a análise final. Os medicamentos foram codificados conforme o primeiro nível (grupo anatômico principal) e quinto nível (substância química) do código *Anatomical Therapeutic Chemical* (ATC). A análise da estatística descritiva dos dados foi realizada em planilha *online* do Google Drive. **Resultados:** De 469 pacientes acompanhados no período, 183 apresentaram pelo menos um PRM identificado. Um total de 339 PRM foram identificados, com média de 1,8 por paciente, e foram alvos de intervenção no AF.

Após intervenção farmacêutica, 61,9% dos PRM foram resolvidos. A "indicação não tratada" foi o principal PRM (45,1%), seguido da "administração inapropriada" (18,9%) e da "sobredose" e (14,7%). Considerando o código ATC, a maioria dos medicamentos fazia parte do grupo "trato alimentar e metabolismo" (30,4%), tendo o omeprazol como o seu principal representante (18,4%). O segundo grupo mais frequente foi o "sistema nervoso" (19,5%), representado principalmente pela dipirona (27,3%); seguido do "grupo sangue e órgãos hematopoiéticos" (17,4%), com a enoxaparina (50,8%) como o principal medicamento. **Conclusões:** Os dados mostraram que o AF é um serviço capaz de identificar PRM durante a internação e apontam para a contribuição do farmacêutico no uso racional de medicamentos. Os dados apresentados poderão auxiliar nas estratégias institucionais voltadas para os PRM de maior risco. Por fim, sugere-se estudos que avaliem os desfechos clínicos dos PRM identificados.

Palavras-chave: serviços clínicos farmacêuticos, cuidado farmacêutico, pacientes internados.

Introduction

Patient safety is understood as the reduction, to an acceptable minimum, of the risk of unnecessary harm associated with health care delivery[1]. This topic gained visibility and became a global concern in 1999 following the publication of the Institute of Medicine report *To Err is Human: Building a Safer Health System*[2]. That document highlighted the magnitude of adverse events (AEs) related to health care, defined as "incidents that result in harm to the patient"[3], including medication-related problems (MRPs)[2].

MRPs can be defined as "situations that arise during the medication use process that cause or may cause a negative outcome associated with medication use"[4]. MRPs include both medication errors (MEs) and adverse drug reactions (ADRs). MEs involve failures in the prescribing, dispensing, or administration processes, with or without harm to the patient[1], whereas an ADR is a harmful and unintended response to a medication that occurs at doses normally used for prophylaxis, treatment, or diagnosis[1].

Hospitalized patients, due to the use of multiple medications, are at high risk of experiencing MRPs, which may occur across different patient profiles[5,6]. In a systematic review of MRPs in hospitalized patients with type 2 diabetes mellitus, a prevalence ranging from 7% to 94% was observed across the 20 included studies[5]. Similarly, another systematic review involving hospitalized patients with chronic kidney disease reported a high prevalence of MRPs, ranging from 12% to 87%[6].

When they occur, MRPs have a multifaceted impact encompassing clinical, economic, and social dimensions. Clinically, they represent a significant cause of morbidity and mortality[7,8]. They may result in therapeutic ineffectiveness and adverse drug events (ADEs)[7,8] in 25% and 37% of cases, respectively[9]. From an economic perspective, MRPs lead to costs associated with prolonged treatments, hospital readmissions, and other expenditures[10,11], with a single hospitalization incurring an additional average cost of up to US$11,692[12]. From a social standpoint, MRPs may reduce patients' trust in health care professionals and health systems, potentially leading to reluctance to seek medical care[13,14].

Most MRPs are potentially preventable. Pharmacists are considered key members of the multidisciplinary health care team for their identification through clinical activities[15]. Their role in this context has been demonstrated in several studies conducted in both outpatient and hospital settings[16-18]. In two review studies involving 1,647 patients, pharmacists identified 3,301 MRPs and performed 3,533 clinical interventions, with a mean acceptance rate of 86.7% by the medical team and resolution of 80.3% of MRPs[19,20]. This resulted in an approximate 29% reduction in ADEs[19,20].

One activity aimed at identifying MRPs is pharmacotherapeutic follow-up (PTF)[21]. In this service, the pharmacist conducts a holistic assessment of the patient, which involves pharmacotherapy management through the analysis of health conditions, risk factors, and the patient's treatment, as well as the possible implementation of a set of managerial and educational interventions[21]. Unlike other services, PTF encompasses the perspective of continuity of care provided by the pharmacist through multiple patient encounters, characterizing it as a longitudinal work process[21]. Its primary objective is to prevent and resolve pharmacotherapy-related problems in order to achieve favorable clinical outcomes[21].

Despite the growing number of studies on MRPs, there remains a gap in the characterization of these problems and in the assessment of the effectiveness of PTF in high-complexity units that care for high-risk populations, such as older adults. Moreover, the literature lacks data demonstrating the contribution of training programs, such as health care residencies, to the sustainability and effectiveness of this service in university hospitals.

In this context, the aim of this study was to analyze the profile of MRPs identified during pharmacotherapeutic follow-up and the corresponding pharmaceutical interventions implemented to resolve them, performed by pharmacy residents among hospitalized patients in internal medicine and geriatrics units of a high-complexity university hospital.

Methods

Study design

This was a descriptive cross-sectional study conducted in the medical and geriatric inpatient units of the Clementino Fraga Filho University Hospital, Federal University of Rio de Janeiro. Data were obtained through pharmaceutical follow-up (PF) performed by pharmacy residents from January 2022 to December 2023.

Study setting and workflow

The study hospital, located in the city of Rio de Janeiro, is affiliated with the Brazilian Ministry of Health and the Unified Health System (Sistema Único de Saúde – SUS) and is a referral center for the treatment of several highly complex diseases.

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The hospital provides care for approximately 1,000 patients daily for outpatient visits and diagnostic procedures and maintains nearly 200 inpatient admissions per day. The medical and geriatric units have a total of 30 beds, of which 25 are allocated to the medical unit and 5 to the geriatric unit.

Pharmaceutical follow-up has been provided in these units since 2012 by pharmacists from the clinical pharmacy service. The team consists of two pharmacists specialized in hospital and clinical pharmacy and six multiprofessional pharmacy residents. This service is offered from Monday to Friday, on business days, between 7:00 a.m. and 4:00 p.m., from patient admission until hospital discharge or death.

For the implementation of pharmaceutical follow-up, a holistic assessment of the patient is performed, including a systematic and structured review of all prescribed medications with regard to the appropriateness of indication, dose, dosage regimen, route of administration, duration of therapy, therapeutic duplication, and monitoring of drug–drug interactions and adverse drug reactions (ADRs). Prescription analysis focuses particularly on the appropriateness of anticoagulant use for venous thromboembolism prophylaxis, albumin, antimicrobials, proton pump inhibitors, and medications administered via nasogastric or enteral tubes.

Laboratory tests are also monitored, especially electrolytes, complete blood count, biochemistry, microbiology, and coagulation parameters. Creatinine clearance is estimated using the 2021 CKD-EPI equation. Electronic medical records from the medical and multiprofessional teams are reviewed to better understand the patient's clinical condition.

In addition, blood pressure, heart rate, capillary blood glucose, bowel function, nausea/vomiting, and pain are monitored. During pharmaceutical follow-up, pharmacists provide bedside care to patients to clarify questions regarding their treatment and to collect information not recorded in the medical chart, such as the date of the last bowel movement, presence of pain, nausea, and vomiting.

To support prescription and laboratory analyses, the UpToDate, Medscape, and Micromedex databases, as well as institutional protocols and national and international clinical guidelines, are consulted.

When a drug-related problem (DRP) is identified during these analyses, a pharmaceutical intervention is performed by the pharmacy resident in collaboration with the medical and nursing teams and/or the patient in order to resolve it. For example, when an underdose-related DRP is identified in a prescription, the pharmacy resident contacts the medical team to suggest dose adjustment.

Data obtained during pharmaceutical follow-up (PF) were recorded in a form specifically developed for this purpose by pharmacists from the clinical pharmacy service. The following information was documented: patient name, medical record number, sex, age, date of admission to the inpatient unit, and hospitalization outcome (discharge or death). Data from prescription analyses were also recorded, such as medication indications; laboratory test results, such as patient renal function parameters; and clinical record data, such as the progression of the condition that led to hospitalization. Identified drug-related problems (DRPs) were likewise recorded on this form. The date of the pharmaceutical interventions performed to resolve the DRPs, as well as their acceptability, was also documented.

Upon admission to the hospital, the six pharmacy residents received training in pharmaceutical follow-up from the two pharmacists of the clinical pharmacy service. The training lasted five consecutive days, approximately two hours per day, and was conducted in person, combining theoretical and practical activities. Residents were instructed on how to perform prescription analyses, review laboratory test results, interpret electronic medical records, access clinical databases, carry out pharmaceutical interventions, and complete the data collection form. After this period, residents began conducting pharmaceutical follow-up independently and consulted the service pharmacists to clarify any questions as needed.

Each of the six pharmacy residents was responsible for five beds during the study period. After patient discharge or death, the completed form was properly archived in the clinical pharmacy service.

Data collection and DRP classification

Data collection was carried out between August and December 2024. In an online Google Drive spreadsheet created specifically for this study, the following information was entered, based on data extracted from the archived pharmaceutical follow-up forms: sex, date of birth, date of hospital admission and admission to the medical or geriatric ward, the identified DRP, the name of the medication involved, the intervention performed, and its acceptability. For the purposes of this study, a pharmaceutical intervention was defined as any record of these actions on the pharmaceutical follow-up form, and interventions were considered accepted when they resulted in concrete changes to the patient's electronic medication prescription.

DRPs were independently categorized by five pharmacy residents who were not involved in the pharmaceutical follow-up and were subsequently reviewed by the two pharmacists of the clinical pharmacy service. DRP categorization was based on the classification developed and validated by pharmacists from the French Society of Clinical Pharmacy[22]. The DRPs were translated and adapted into Brazilian Portuguese by the clinical pharmacy service pharmacists with the support of the Linguee text and document translation tool.

Some DRP types were adapted to facilitate readability and comprehension. For example, "subtherapeutic dosage" was adapted to "underdose" to avoid confusion with subtherapeutic serum drug levels. A new DRP category, "Medication availability/standardization," was created by the clinical pharmacy service pharmacists to reflect the local context, as prescriptions for medications that are standardized but unavailable in stock are very common in the studied unit. The original version, as well as the Portuguese translation and adaptation, are available in the supplementary material.

Inclusion and exclusion criteria

For this study, pharmaceutical follow-up forms containing at least one recorded DRP identified between January 2022 and December 2023 were included. Forms with incomplete or inadequate data that compromised data analysis—such as the absence of the name of the medication involved in the DRP or the type of DRP identified—were excluded.

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Data analysis

A descriptive statistical analysis was performed, with data presented as absolute and relative frequencies. The assumption of normality for the number of DRPs per patient was tested using the Shapiro–Wilk test. Median and interquartile range (IQR) were calculated when a non-normal distribution was observed ($p < 0.001$). Medications involved in the DRPs were coded according to the Anatomical Therapeutic Chemical (ATC) classification system, considering the first level (main anatomical group) and the fifth level (chemical substance).[17]

Ethical aspects

The study complied with all current ethical requirements established by the Brazilian National Health Council (Conselho Nacional de Saúde – CNS) Resolution No. 466/12. The study was approved by the institution's Research Ethics Committee under CAAE No. 82942524.7.0000.5257, with approval opinion No. 7,271,538.

Results

During the study period, 469 patients were followed by pharmacy residents. Of these, 286 patients (61%) were excluded from the analysis due to the absence of recorded DRPs in their pharmaceutical follow-up forms and/or incomplete data that compromised data analysis. A total of 183 patients (39.0%) had at least one DRP identified. Most patients with DRPs were female (64.5%) and older adults aged 60 years or older (62.3%).

Overall, 339 DRPs were identified during the study period. The Shapiro–Wilk test indicated a non-normal distribution ($W = 0.725$; $p < 0.001$); therefore, the median and IQR were calculated. The median number of DRPs per patient was 1.00 (IQR: 1.00–2.00), corresponding to a mean rate of 1.85 DRPs per patient. Of all identified DRPs, 210 (61.9%) were resolved following pharmaceutical interventions accepted by the medical or nursing teams. No pharmaceutical interventions directly involving patients were recorded during the study period.

The most frequent DRP identified was "untreated indication" (45.1%), followed by "inappropriate administration" (18.9%) and "overdose" (14.7%). No DRPs classified as "adverse drug reaction" were identified during the study period (Table 1).

The subtypes of each identified DRP and the most frequent medications involved in each subtype are presented in Table 2. The three most frequent medications were selected for presentation in Table 2; however, in some subtypes, more than three medications had the same frequency. Therefore, more than three medications are listed for certain subtypes. Examples of pharmaceutical interventions performed to resolve DRPs are shown in Table 3.

Regarding the total number of medications involved in the identified DRPs, the main groups were listed according to the first ATC level (main anatomical group). Most medications belonged to the "alimentary tract and metabolism" group (30.4%), followed by the "nervous system" (19.5%), "blood and blood-forming organs" (17.4%), "cardiovascular system" (12.4%), and "anti-infectives for systemic use" (8.3%) groups (Table 4).

Within these anatomical groups, the main medications involved, according to the fifth ATC level (chemical substance), were omeprazole (18.4%), dipyrone (27.3%), enoxaparin (50.8%), atenolol (16.7%), and piperacillin–tazobactam (14.3%) (Table 4).

Table 1. Type and frequency of drug-related problems (DRPs) identified during pharmaceutical follow-up of hospitalized patients in medical and geriatric wards at a university hospital in Rio de Janeiro, Brazil.

Type of DRP	DRP frequency, n (%)	DRPs resolved after pharmaceutical intervention, n (%)
Untreated indication	153 (45.1)	93 (27.4)
Inappropriate administration	64 (18.9)	46 (13.6)
Overdose	50 (14.7)	31 (9.1)
Subtherapeutic dose	23 (6.8)	13 (3.8)
Medication used without indication	20 (5.9)	11 (3.2)
Drug availability/standardization	13 (3.8)	6 (1.8)
Contraindicated / non-compliance with protocols	5 (1.5)	2 (0.6)
Drug interaction	5 (1.5)	5 (1.5)
Drug monitoring	4 (1.2)	1 (0.3)
Medication administration error	2 (0.6)	2 (0.6)
Adverse drug reaction	0	0
Total	**339 (100)**	**210 (61.9)**

Discussion

Pharmaceutical follow-up (PF) proved to be a relevant tool for identifying a considerable number of drug-related problems (DRPs) during hospital stay. Overall, 339 DRPs were identified in 39.0% of the patients followed. The effectiveness of this activity was demonstrated by both the DRP identification rate and the resolution rate, as 61.9% of the DRPs were resolved after interventions by pharmacy residents.

When integrated into a multidisciplinary team, clinical pharmacists are able to provide high-quality, coordinated, and patient-centered care. Part of this professional's routine includes developing a plan to initiate, modify, monitor, and/or discontinue drug therapy in collaboration with the multidisciplinary team.[23] Pharmaceutical follow-up is one of the pharmacist's activities that enables the development of such a plan, allowing for the identification of DRPs, the implementation of pharmaceutical interventions to resolve or prevent them, and, consequently, the promotion of safe and rational use of medications.[21]

Studies conducted in inpatient wards have also reported a significant number of DRPs. In a rheumatology ward of a teaching hospital in France, the clinical relevance of pharmaceutical interventions in prescription review was evaluated.[24] Using the same DRP classification adopted in the present study, 461 DRPs were identified in 1,313 prescriptions, and 67.2% were resolved after intervention.[24]

Table 2. Types, subtypes, and most frequent medications for each subtype of drug-related problem (DRP) identified during pharmaceutical follow-up of hospitalized patients in medical and geriatric wards at a university hospital in Rio de Janeiro, Brazil. The three most frequent medications are presented; in some subtypes, more than three medications had the same frequency and are also shown.

DRP and Subtypes (n; %)	Most frequent medications in subtypes (n)
Untreated indication (153; 45.1)	
Absence of prescription for a therapeutic indication (134; 87.6)	Lactulose (9), Metformin (9), Dipyrone (7)
Absence of prophylaxis or pre-medication (19; 12.4)	Enoxaparin (19)
Inappropriate administration (64; 18.9)	
Inadequate dosage (28; 18.3)	Ampicillin/sulbactam (2), Calcium carbonate (2), Dipyrone (2), Erythropoietin (2)
Most appropriate route of administration (22; 14.8)	Omeprazole (5), Dipyrone (3)
Incomplete information in prescription notes (6; 9.4)	Dipyrone (2), Vancomycin (2), Butylscopolamine (1), Morphine (1)
Inappropriate pharmaceutical form (5; 7.8)	Domperidone (1), Gabapentin (1), Metformin (1), Metoclopramide (1), Simethicone (1)
Inappropriate administration technique (3; 4.7)	Ferric hydroxide saccharate (2), Piperacillin/Tazobactam (1)
Overdose (50; 14.7)	
Supratherapeutic dose (43; 86)	Enoxaparin (5), Omeprazole (4), Atenolol (4)
Therapeutic duplication (same drug prescribed) (7; 14)	Clonidine (1), Diazepam (1), Spironolactone (1), Hydroxychloroquine (1), Lactulose (1), Omeprazole (1), Olanzapine (1)
Subtherapeutic dose (23; 6.8)	
Subtherapeutic dose (23; 100)	Bisoprolol (3), Cefepime (2), Dipyrone (2), Lactulose (2), Levothyroxine (2)
Medication used without indication (20; 5.9)	
Medication prescribed without justified indication (19; 95)	Omeprazole (3), Calcium carbonate (2), Enoxaparin (2), Lactulose (2)
Medication prescribed for prolonged period without risk of overdose (1; 5)	Hypromellose (1)
Drug availability/standardization (13; 3.8)	
Non-standardized medication (6; 46.2)	Cholecalciferol (2), Cyclobenzaprine (1), Codeine (1), Dapagliflozin (1), Pantoprazole (1)
Medication/formulation unavailable in stock (5; 38.5)	Clonazepam (1), Dipyrone (1), Lorazepam (1), Risperidone (1), Tacrolimus (1)
Patient using home medication, but standardized in hospital (2; 15.4)	Methadone (1), Sertraline (1)
Contraindicated / non-compliance with protocols (5; 1.5)	
Contraindication (5; 100)	Enoxaparin (2), Losartan (1), Mirtazapine (1), Morphine (1)
Drug interaction (5; 1.5)	
Drug-drug interaction (3; 60)	Calcium carbonate (2), Prednisone (1)
Drug-food/diet interaction (2; 40)	Calcium carbonate (1), Levothyroxine (1)
Drug monitoring (4; 1.2)	
Lack of laboratory monitoring (3; 75)	Folic acid (1), Cyanocobalamin (1), Ferric hydroxide saccharate (1)
Absence of serum dosage (1; 25)	Phenytoin (1)
Medication administration error (2; 0.6)	
Incompatibilidade físico-química entre medicamentos injetáveis (2; 100)	Fosfato de potássio (1), Ringer Lactato (1)

Similar findings have been reported in the Brazilian context. In a geriatric ward of a university hospital in São Paulo, a study analyzed pharmaceutical care practices and monitored clinical outcomes.[7] During the study period, 157 DRPs were identified in prescriptions of 53 hospitalized patients. DRPs were classified as "need/indication, adherence, safety, and effectiveness problems," and after pharmaceutical intervention, 80.9% of DRPs were resolved.[7]

These findings reinforce the importance of pharmaceutical follow-up for hospitalized patients in different inpatient units. Even when conducted by pharmacy residents—professionals undergoing in-service training—there is strong evidence that they have a high potential to identify DRPs.[25,26] Therefore, these professionals can be appropriately trained and effectively involved in the delivery of this activity.

Among the identified DRPs, "untreated indication" was the most frequent, which is consistent with findings from other studies on DRPs.[27,28] In a tertiary hospital in Ribeirão Preto, São Paulo, a study conducted between February 2016 and November 2019 aimed to identify DRPs in patients admitted to a neurology ward.[27]

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Table 3. Examples of pharmaceutical interventions performed and accepted to resolve each type of drug-related problem (DRP) identified during pharmaceutical follow-up of hospitalized patients in medical and geriatric wards at a university hospital in Rio de Janeiro, Brazil.

DRP	Example of DRP	Pharmaceutical intervention to resolve the DRP	Resolution
Untreated indication	Patient had not evacuated for 3 days according to nursing records. No prokinetic or laxative prescribed.	Suggested prescription of a laxative.	Lactulose added to the prescription by the medical team.
Inappropriate administration	Prescribed ampicillin/sulbactam 1.5 g IV every 12h, inconsistent with renal function (ClCr > 30 mL/min).	Suggested dose adjustment.	Dosage changed to every 8h.
Overdose	Prescribed enoxaparin 40 mg SC every 24h with impaired renal function (ClCr < 30 mL/min).	Suggested dose reduction.	Dose adjusted to 20 mg.
Subtherapeutic dose	At hospital discharge, bisoprolol 5 mg PO once daily prescribed. During hospitalization, HR controlled with 6.25 mg dose.	Suggested dose increase at discharge.	Dose adjusted to 6.25 mg.
Medication used without indication	Patient prescribed omeprazole 20 mg PO every 24h without clinical indication.	Suggested medication discontinuation.	Omeprazole discontinued by the medical team.
Drug availability/ standardization	Prescribed codeine 30 mg PO every 6h. Medication not standardized in the institution.	Suggested substitution with codeine/paracetamol 30 mg + 500 mg.	Medication substituted.
Contraindicated / non-compliance with protocols	Patient transitioning from enoxaparin to warfarin due to extensive common iliac artery thrombosis.	Suggested discontinuing enoxaparin due to two consecutive INR readings within therapeutic target.	Enoxaparin discontinued; warfarin maintained in prescription.
Drug interaction	Levothyroxine and calcium carbonate prescribed at the same time (5 a.m.). Levothyroxine therapeutic effect may be reduced.	Suggested changing calcium carbonate administration at least 4h apart from levothyroxine.	Levothyroxine maintained at 5 a.m.; calcium carbonate changed to 10 a.m.
Drug monitoring	Patient experiencing drowsiness. Taking phenytoin 100 mg PO every 12h for epilepsy.	Suggested serum phenytoin measurement for drug monitoring.	Serum measurement requested by medical team.
Medication administration error	Prescribed potassium phosphate to be added to Ringer's lactate solution. Risk of calcium salt precipitation.	Suggested adding potassium phosphate in normal saline.	Ringer's lactate replaced with normal saline.

ClCr- creatinine clearance; IV- intravenous; HR- heart rate; INR- international normalized ratio; SC- subcutaneous; PO- oral.

DRPs were classified as "need/indication, adherence, safety, and effectiveness problems," and the main cause of classification as a "need/indication problem," as well as the most frequent cause among all DRP types, was "untreated condition" (36.5%).[27]

In a hospital in Uganda, a prospective observational study involving hospitalized patients with acute or chronic kidney disease analyzed the prevalence, types, and associated factors of DRPs.[28] DRPs were categorized according to the Pharmaceutical Care Network Europe classification, and "untreated indication or symptoms" was the most frequently identified type, accounting for 35.6% of the 219 DRPs identified.[28]

This type of DRP is considered among the most clinically relevant due to its high frequency and its potential to cause patient harm, often severe.[29] It is estimated that up to 86% of medication omissions in prescriptions place patients at risk of some form of harm,[30] such as prolonged hospital stay, increased occurrence of emergency situations, and higher risk of death.[29]

The absence of a prescribed medication with a therapeutic indication was the most frequent subtype of the "untreated indication" DRP. This subtype has also been commonly reported in studies involving other patient profiles.[31,32] In a study conducted in a hospital in Pakistan, the prevalence and clinical significance of DRPs in patients with chronic kidney disease were evaluated.[31]

The absence of medications with a therapeutic indication was the second most common type, accounting for 37% of the identified DRPs, with antianemic and antihypertensive agents being the most frequently involved.[31] In Slovakia, a study conducted in hospitalized patients in a vascular surgery ward assessed the impact of pharmaceutical interventions on the prevalence of DRPs.[32] Of all identified DRPs, 40.3% were related to the absence of medications with a therapeutic indication, with atorvastatin being the most frequently involved drug.[32]

Unlike the studies mentioned above, lactulose was the main medication involved in the subtype "absence of prescription of a medication with a therapeutic indication" in the present study. This finding may be related to the specific focus of pharmaceutical follow-up on monitoring patients' bowel function. Lactulose is a medication primarily used to treat constipation. Although constipation is generally considered a benign condition, it may lead to potentially serious complications, such as fecal impaction, intestinal perforation, and fecal incontinence, which mainly affect older adults.[25]

When DRPs involve potentially high-alert medications, such as anticoagulants, the resulting harm may be even more severe.[33] In this study, enoxaparin was the only medication involved in the subtype "absence of prophylaxis or premedication" within the "untreated indication" DRP category. Parenteral anticoagulants are frequently used as prophylaxis in certain groups of hospitalized patients who present risk factors for venous thromboembolism (VTE), such as a history of VTE, advanced age, reduced mobility, active cancer, among others.[34]

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Table 4. Five most frequent anatomical groups according to the first level of the ATC (Anatomical Therapeutic Chemical) classification identified in drug-related problems (DRPs) and the respective drugs involved according to the fifth level of ATC. DRPs were identified during pharmaceutical follow-up of patients hospitalized in medical and geriatric wards at a university hospital in Rio de Janeiro, Brazil.

ATC	Group / Drug	n (%)
A	Alimentary tract and metabolism	103 (30.4)
A02BC01	Omeprazole	19 (18.4)
A12AA04	Calcium carbonate	15 (14.6)
A06AD11	Lactulose	14 (13.6)
-	Others	55 (53.4)
N	Nervous system	66 (19.5)
N02BB02	Metamizole (Dipyrone)	18 (27.3)
N05BA06	Lorazepam	7 (10.6)
N06AA09	Amitriptyline	4 (6.1)
N02BF01	Gabapentin	4 (6.1)
N02AX02	Tramadol	4 (6.1)
-	Others	29 (43.9)
B	Blood and hematopoietic organs	59 (17.4)
B01AB05	Enoxaparin	30 (50.8)
B03AC	Ferric hydroxide saccharate	5 (8.5)
B03AA07	Ferrous sulfate	4 (6.8)
-	Others	25 (59.5)
C	Cardiovascular system	42 (12.4)
C07AB03	Atenolol	7 (16.7)
C09CA01	Losartan	5 (11.9)
C10AA01	Simvastatin	5 (11.9)
-	Others	25 (59.5)
J	Antiinfectives for systemic use	28 (8.2)
J01CR05	Piperacillin + Tazobactam	4 (14.3)
J01CR02	Amoxicillin + Sulbactam	3 (10.7)
J01CR01	Ampicillin + Sulbactam	3 (10.7)
J01DE01	Cefepime	3 (10.7)
J01XA01	Vancomycin	3 (10.7)
-	Others	12 (42.9)
–	Outros ATC	41 (12,1)

Therefore, the absence of this medication class in prescriptions may result in thrombotic events during hospitalization, which can be fatal.[34] VTE prophylaxis is a mandatory assessment item in pharmaceutical follow-up, which may explain why enoxaparin was the only medication identified in this subtype.

"Inappropriate administration" was the second most common type of DRP identified in this study, and problems related to medication administration have been widely reported in the literature.[35,36] A recent systematic literature review aimed to identify medications associated with an increased risk of patient harm due to failures in the administration process.[36] The highest frequency of medication errors was observed during the preparation and administration phases, and all seven studies included in the review reported incidents that resulted in patient harm.[36]

The antibiotic ampicillin/sulbactam was the medication most frequently involved in the subtype "inappropriate dosage regimen" of the "untreated indication" DRP. Several antimicrobials require dose or dosing regimen adjustments in patients with kidney disease or those undergoing renal replacement therapy in order to avoid toxicity related to overdose, as well as treatment failure associated with underdosing and/or the potential development of bacterial resistance.[37] For these reasons, antibiotics are often among the medications most frequently involved in DRP studies.[38] In a study conducted at a Brazilian tertiary hospital, antimicrobials were the main medication group involved (36%) among 3,373 DRPs identified in hospitalized patients.[38] Similarly to the present study, an analysis of 698 DRPs identified in an intensive care unit of a tertiary hospital in Thailand showed that antibiotics were among the most frequently involved medications, with most cases related to overdose requiring dose or dosing regimen adjustment.[38]

In the medical and geriatric inpatient units of the study hospital, the use of feeding tubes is very common, and consequently medications are often administered via enteral tubes in patients who are temporarily unable to receive oral therapy. Therefore, pharmaceutical follow-up includes the assessment of medication suitability for administration via feeding tubes. In the subtype "most appropriate route of administration" within the "inappropriate administration" DRP category, the proton pump inhibitor (PPI) omeprazole was one of the medications involved. PPIs have also been reported in other DRP studies for various reasons, such as inappropriate timing of administration; inappropriate or unsafe route or site of administration; insufficient dilution volume; inappropriate diluent; unnecessary treatment; and therapeutic duplication.[31,32,38]

The administration of PPIs via feeding tubes has specific considerations. These medications are inactivated by gastric acid and are therefore formulated as enteric-coated granules to maintain their integrity until reaching the less acidic pH of the duodenum, where absorption occurs.[39] Consequently, crushing and dissolving these granules for tube administration is not recommended. However, enteric-coated granules may be preserved by dispersing them in an 8.4% sodium bicarbonate solution, allowing administration via feeding tubes without drug degradation and minimizing the risk of tube obstruction.[39] If this administration is not feasible and the patient already has peripheral venous access, switching the route of administration to the intravenous route may be more appropriate.[40]

"Overdose" was the third most frequently identified type of DRP, with the subtype "supratherapeutic dose" being the most common. Enoxaparin was the medication most frequently involved in this subtype. In a study conducted in the intensive care unit of the same hospital, the DRP "incorrect dose" was among the three most frequently identified, and enoxaparin was also the medication most commonly associated with dose adjustments.[18] In a university hospital in northeastern Brazil, an analysis of prescriptions for hospitalized adult patients identified "excessive dose" as the main type of DRP, with anticoagulants ranking among the potentially high-alert medications most frequently associated with DRPs.[41]

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According to the UpToDate database, this anticoagulant—both at prophylactic and therapeutic doses—requires dose adjustment based on renal function. Therefore, these findings reinforce the need for pharmacists to perform daily reviews of patients' laboratory tests to assess renal function and recommend appropriate dose adjustments, thereby preventing adverse medication events (AMEs), such as bleeding, as highlighted by UpToDate.

The subtype "therapeutic duplication," defined as the concomitant use of medications with the same mechanism of action or within the same pharmacological class without providing additional benefit,[42] within the "overdose" DRP category involved medications from different pharmacological classes. Antihypertensives, anxiolytics, and diuretics were among the duplicated medications, making it difficult to develop a targeted strategy for a specific drug class. One possible approach to reducing such duplications would be the implementation of alerts within electronic prescribing systems, as already occurs in some hospitals.[43] Depending on the number of medications in a prescription, duplication may go unnoticed by both the prescriber and the pharmacist responsible for prescription review.

Overall, the medications involved in DRPs were predominantly classified under the "alimentary tract and metabolism" group according to the first level of the ATC classification. Among these medications, omeprazole once again stood out, belonging to a group of drugs that are among the most frequently prescribed and often used irrationally.[44]

In a high-complexity hospital in southern Brazil, the inappropriate use of intravenous PPIs was evaluated and associated costs were estimated.[40] Appropriate PPI prescription was observed in only 23.4% of the 320 patients analyzed. Considering an approximate cost of US$1.00 per vial, an unnecessary expenditure of US$1,696.00 was estimated due to inappropriate intravenous PPI use during the six-month study period.[40] A drug utilization study conducted in a tertiary hospital in Spain found that 28.65% of hospitalized patients received a PPI prescription at admission, 82.62% during hospitalization, and 54.75% at discharge.[45] Moreover, inappropriate PPI indications were identified in 74.47%, 61.25%, and 80.24% of these cases, respectively.[45] These findings highlight that pharmaceutical follow-up of omeprazole use is essential to reduce its irrational use, as well as the associated costs both during and after hospitalization, since once initiated during hospital stay, this medication is highly likely to be continued at discharge.[46]

Following the "alimentary tract and metabolism" group, the "nervous system" group was the second most frequent, with dipyrone being the main medication involved. This finding is consistent with a study conducted in a university hospital in Natal, Rio Grande do Norte, which also identified analgesics and antipyretics among the drug groups most frequently associated with DRPs.[41] Pain can lead to both physical and psychological consequences, resulting in patient suffering, prolonged hospital stay, and increased risk of complications, and undertreatment of pain during hospitalization has been described in the literature.[47,48] Therefore, assessment of analgesic adequacy is essential to achieve better inpatient outcomes.

Finally, the data presented herein reinforce that, through their skills and in collaboration with other members of the multidisciplinary team, pharmacists should be actively involved in the development of protocols for appropriate medication use, given their unique perspective on prescribing practices and their ability to identify DRPs.[49,50] Moreover, pharmacists should also participate in the development of tools that enable monitoring of protocol implementation and in the training of healthcare professionals, thereby directly contributing to quality of care and the rational use of medications.[49,50]

To the best of our knowledge, this is the first study conducted at this institution to investigate drug-related problems (DRPs) identified in patients admitted to inpatient wards. The findings demonstrate the potential of pharmaceutical follow-up performed by pharmacy residents to identify DRPs and resolve them through pharmaceutical interventions. However, this study has some limitations. As a retrospective study based on the analysis of records documented by the pharmacy team, underdocumentation may have resulted in an underestimation of the number of DRPs identified during the study period. In addition, DRP identification was carried out by residents who, although able to identify a considerable number of DRPs, are professionals still in training in clinical pharmacy activities. Thus, it is possible that some DRPs were not identified and/or documented. Although residents received training in pharmaceutical follow-up, the form used to record pharmaceutical follow-up data was not pilot-tested. Furthermore, the residents involved in data collection were not the same individuals who conducted the pharmaceutical follow-up. The present study also did not assess whether patients whose pharmaceutical interventions were not accepted experienced any type of harm compared with patients whose interventions were accepted.

Conclusion

The present study demonstrated that pharmaceutical follow-up conducted by pharmacy residents was effective in identifying 339 DRPs in hospitalized patients admitted to medical and geriatric units. Moreover, the 61.9% DRP resolution rate following pharmaceutical interventions reinforces the central role of pharmacists in the prevention, identification, and resolution of DRPs. These findings highlight the potential of pharmaceutical follow-up as an essential clinical strategy in high-complexity units, particularly among older patients, and demonstrate the contribution of health residency programs to the improvement of pharmaceutical practice.

The applicability of these findings lies in the possibility of implementing institutional strategies focused on higher-risk DRPs to promote the safety of hospitalized patients. Prospectively, future studies should evaluate and compare clinical outcomes between patients whose DRPs were resolved and those whose DRPs remained unresolved after pharmaceutical intervention.

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Contributors

AFP: study conception, data analysis and interpretation, and manuscript drafting. MPM, HLM, RMN, LSA, SSG: data analysis and critical revision of the manuscript. IPM: data analysis and interpretation and critical revision of the manuscript.

CAT: critical revision of the intellectual content. All authors approved the final version of the manuscript and take responsibility for the accuracy and integrity of all aspects of the work.

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Conflict of interest statement

The authors declare no conflicts of interest related to this article.

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