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Identification of drugs-related problems and pharmacists' interventions in a hospital in Southern Brazil

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Abstract

Objectives: to identify, describe and analyze drug-related problems (DRPs) and pharmaceutical interventions (PIs) in medical prescriptions of a hospital and estimate their economic impact on the health institution. **Methods:** quantitative cross-sectional descriptive study carried out from August 2020 to September 2021 in a reference hospital in cardiovascular care. DRPs were classified using the *Pharmaceutical Care Network Europe* (PCNE) version 9.1 tool, the economic impact was measured using the *Clinical, Economics, Organization Impact* (CLEO) tool and drugs involved in DRPs were classified according to the *Anatomical Therapeutic Chemical* (ATC). Data were analyzed using an *Excel* 2007 **Results:** A total of 857 DRPs were identified in the prescriptions from 560 patients, an average of 1.5 DRP per patient. The main DRP found was in the safety domain, with 39.1% adverse drug event (possibly) occurring, whereas the most prevalent cause was related to posology instructions that could be wrong, unclear or missing (22.8%). The most frequent PI was drug suspension (25.8%) and the change in the administration instruction (25.7%), 85.9% of the PI were accepted and implemented causing a fully resolved problem outcome, and 41.8% of the PIs decreased the costs for the institution. **Conclusion:** It was possible to identify and carry out a considerable amount of DRPs and PIs. These PIs aimed reducing possible harm related to drugs, in addition to promoting, in most cases, a cost reduction for the institution. The presence of the pharmacist working with the rest of the multidisciplinary health team proved to be essential, both in promoting safety in pharmacotherapy and harm reduction to patients and in-hospital pharmacoeconomics.

Key words: clinical pharmacy; hospital pharmacy; pharmaceutical care; drug prescriptions.

Identificação de problemas relacionados a medicamentos e intervenções farmacêuticas realizadas em um hospital no Sul do Brasil

Resumo

Objetivos: identificar problemas relacionados a medicamentos (PRMs) e realizar intervenções farmacêuticas (IFs) em prescrições médicas de um hospital e estimar seu impacto econômico para a instituição de saúde. **Métodos:** Trata-se de um estudo quantitativo transversal de natureza descritiva realizado de agosto de 2020 até setembro de 2021 em um hospital referência em atendimento cardiovascular. Foram analisadas pelas farmacêuticas do serviço as prescrições atendidas pelo serviço de farmácia da instituição. Os PRMs identificados foram classificados utilizando a ferramenta *Pharmaceutical Care Network Europe* (PCNE) versão 9.1, o impacto econômico foi mensurado pela ferramenta *Clinical, Economics, Organization Impact* (CLEO), os medicamentos envolvidos foram classificados conforme o *Anatomical Therapeutic Chemical* (ATC) os dados foram analisados por meio de tabela de *Excel* 2007. **Resultados:** Ao todo 857 PRMs foram identificados nas prescrições de 560 pacientes, com uma média de 1,5 PRM por paciente. O principal PRM encontrado foi no domínio de segurança, sendo o de possível reação adversa ao medicamento (39,1%), enquanto que a causa mais prevalente foram instruções de posologia incorretas, pouco claras ou ausentes (22,8%). A IF mais realizada foi a suspensão do medicamento (25,8%) e de alteração de instrução de administração (25,7%), sendo que 85,9% das IFs foram aceitas e implementadas gerando desfecho de problema totalmente resolvido e 41,8% geraram diminuição de gasto para a instituição. **Conclusão:** Foi possível identificar e realizar uma quantidade considerável de PRMs e IFs. Essas IF relizadas tiveram o objetivo de reduzir possíveis danos relacionados aos medicamentos, além de promover, na grande maioria das vezes, uma redução de custos para a instituição. A presença do farmacêutico atuando junto ao restante da equipe multidisciplinar de saúde mostrou-se essencial, tanto na promoção de segurança na farmacoterapia e redução de danos aos pacientes quanto na farmacoeconomia hospitalar.

Palavras-chaves: farmácia clínica; farmácia hospitalar; cuidado farmacêutico; prescrições de medicamentos.

Introduction

The Hospital Pharmacy service has a complex assistance scheme that encompasses various activities, from managerial to clinical. Such activities are included within the definition of "Pharmaceutical Assistance", which deals with the promotion, protection and recovery of individual and collective health, with medications as essential products and aiming at their rational use[1]. In addition to that, this service requires high budgetary value, making it necessary for the pharmacist to be able to provide care in order to ensure quality and reduce costs and risks[2].

The Pharmacy service within a hospital unit is shaped according to each institution's care profile. The Brazilian Society of Hospital Pharmacy established the minimum standards for the functioning of hospital pharmacies[3]. In general, the service is basically structured in logistical activities, handling and/or production, intersectoral activities focused on the patient, such as clinical pharmacy, for example, and quality assurance[2]. Through a technical evaluation of the prescriptions before dispensing, when it is possible to identify avoidable errors during this process, the Clinical Pharmacy aims at ensuring proper use of medications[4], ensuring patient safety and care quality[5].

The WHO estimates that millions of patients suffer harms each year because of unsafe care techniques and, with this, billions of dollars are spent due to errors in health systems worldwide[6]. The WHO's third global Patient Safety Challenge, launched in 2017, has the theme of "Medication without Harms" and aims at reducing by up to 50% the serious and avoidable harms related to medications worldwide in 5 years from its launch[7]. Such errors can occur at different stages of the care process, from prescription to transcription, dispensing, administration and/or monitoring[8].

Drug-related problems (DRPs) are circumstances or events that occur involving some drug therapy that can, in a real or potential way, cause some undesirable outcome to the patient. Pharmaceutical interventions (PhIs) are defined as documented actions and are carried out with the patient and the other colleagues of the multidisciplinary team in health, in order to avoid or solve any problems that may or do interfere with the pharmacotherapeutic process[9].

In this context, the hospital environment is a place where there is greater propensity for adverse events due to the concomitant and varied use of medications, requiring greater attention to their proper use. In addition to harms to the patient, potential DRPs can result in an increase of hospitalization times and expenses related to health recovery[10]. Given the above, this study aims at analyzing DRPs and PhIs in medical prescriptions of hospitalized patients and at estimating their economic impact.

Methods

This descriptive, cross-sectional and quantitative study was carried out in a public hospital from southern Brazil, with data collection between August 2020 and September 2021. The research project was submitted to and approved by the institution's Ethics and Research Committee (*Comitê de Ética e Pesquisa*, CEP) as per opinion number 4,461,432. The institution offers reference care for the Clinical, Surgical and Outpatient specialties in the Cardiology and Vascular areas. The hospital has approximately 140 active beds in the institution.

The Pharmacy Service has two satellite pharmacy units to serve and supply the units, one located in the emergency sector and another serving three hospitalization units and the Coronary Unit.

The work process to meet the prescriptions in the Pharmacy Service takes place through the receipt of second copies of prescriptions from the patients hospitalized in the units, followed by a screening procedure performed exclusively by the pharmacist, who indicates the quantities of medications necessary to fill a given prescription for a 24-hour period. This process is crucial for performing the pharmacotherapy review, identifying DRPs and resolving them through PhIs that can be implemented through contacts with the Medical or Nursing teams.

After screening, the medications are separated, passed through the barcode reader for verification, packaged and identified with a label with the name of each patient to later be delivered to the units. The sample was selected by convenience, all prescriptions of patients seen at the pharmacy units of the hospital during the day were eligible for the study, and non-hospitalized patients were not included in order to eliminate the bias due to lack of recording in electronic medical charts and data loss.

The DRPs selected for the PhIs were categorized according to the Pharmaceutical Care Network Europe (PCNE) classification, version 9.1; each DRP was classified into large groups defining the problem, cause, intervention, acceptance and outcome and, for each large group, the classification has domains and subdomains[11] that were also quantified in the results. Through a specific tool, Clinical, Economics, Organization Impact (CLEO), it was possible to classify each PhI according to its economic impact: "it generated an increase in cost", "it did not change the cost", "it generated a reduction in costs" or "undetermined"[12]. For this variable, the unit value of the medication involved in the DRPs and the consequence of the PhI based on the outcome were taken into account; the value was consulted directly in the stock control and pharmaceutical supply system of the institution; and the values were not measured in Reais in the results, they were only presented in percentages according to the aforementioned classification. The medications involved in the DRPs were classified according to the Anatomical Therapeutic Chemical (ATC) model.

In order to complement the analysis, data such as age and gender were collected from the patients whose prescriptions were subjected to PhIs, preserving the identity and other clinical information pertinent to the medical record according to the research ethical precepts. The PhIs were recorded using a *Google Forms* form and the statistics were obtained by descriptive analysis; the data were compiled, organized and analyzed in *Excel* 2007 tables.

Results

During the analysis period, 857 DRPs were identified in 560 patients, representing a mean of 1.5 DRPs per patient, 58.4% men and 41.6% women, with a mean age of 63 ± 13.6 and 64 ± 12.5 years old, respectively. Among the DRPs found, the effectiveness domain was the most prevalent (50.6%), and drug treatment effect outside the expected was the most frequent for this domain, followed by the safety domain with 39.1% of occurrence (Table 1).

Table 1. DRPs identified according to the PCNE V9.1 classification.

Domain	Code	Problem	n (%)
Effectiveness	P1.1	Ineffective drug treatment	132 (15.4)
	P1.2	Drug treatment effect outside the expected	248 (28.9)
	P1.3	Untreated symptoms or indications	54 (6.3)
	P1	Total	434 (50.6)
Safety	P2.1	(Probable) Adverse drug reaction	335 (39.1)
	P2	Total	335 (39.1)
Other	P3.1	Unnecessary drug treatment	35 (4.1)
	P3.2	Problem/Complaint not resolved (cost-effectiveness)	53 (6.2)
	P3	Total	88 (10.3)
		Total	**857 (100)**

Key: Domain, code and problems identified in absolute numbers (n) and percentages (%), DRPs: Drug-Related Problems, PCNE: Pharmaceutical Care Network Europe.

Among the causes of the DRPs, the domain related to dose selection was the most frequent (46.7%), followed by drug selection (32.5%), dispensing (10.4%), pharmaceutical form (7%), treatment length in time (2.3%) and medication use and administration process (1.3%). Incorrect, unclear or missing dosage instructions were the main causes identified among the DRPs (Table 2).

All the interventions were performed at the medication level, and the most frequent were request for medication suspension (25.8%) and administration instructions changed (25.7%), respectively (Table 3).

Table 2. Causes of the DRPs according to the PCNE V9.1 classification

Domain	Code	Cause	n (%)
1 Drug selection	C1.1	Medication not matching protocol/therapeutic guide	46 (5.4)
	C1.2	No indication for the medication	23 (2.7)
	C1.3	Drug interaction, or interaction between the medication and food	11 (1.3)
	C1.4	Inadequate drug or therapeutic group duplicity	98 (11.4)
	C1.5	Incomplete or absent treatment for the existing indication	85 (9.9)
	C1.6	Excess of medications prescribed for the same indication	15 (1.8)
	C1	Total	278 (32.5)
2 Pharmaceutical form	C2.1	Inadequate pharmaceutical form (for this patient)	60 (7.0)
	C2	Total	60 (7.0)
3 Dose selection	C3.1	Insufficient medication dose	92 (10.7)
	C3.2	Excessive medication dose	94 (11.0)
	C3.3	Insufficient dosage frequency	3 (0.4)
	C3.4	Excessive dosage frequency	15 (1.8)
	C3.5	Incorrect, unclear or missing dosage instructions	195 (22.8)
	C3	Total	399 (46.7)
4 Treatment length in time	C4.2	Too long a treatment	20 (2.3)
	C4	Total	20 (2.3)
5 Dispensing	C5.1	Medication prescribed not available	89 (10.4)
	C5	Total	89 (10.4)
6 Medication use/ administration process	C6.1	Inadequate administration time or dose interval	10 (1.0)
	C6.4	Medication not administered	1 (0.1)
	C6	Total	11 (1.1)
		Total	**857 (100)**

Key: Domain, code and causes identified in absolute numbers (n) and percentages (%), DRPs: Drug-Related Problems, PCNE: Pharmaceutical Care Network Europe.

Table 3. PhIs according to the PCNE V9.1 classification

Domain	Code	Intervention	n (%)
3 At the medication level	I3.1	Medication changed to ...	60 (7.0)
	I3.2	Dosage changed to ...	177 (20.7)
	I3.3	Formulation/Form changed to ...	107 (12.5)
	I3.4	Administration instructions changed to ...	220 (25.7)
	I3.5	Medication temporarily or definitely suspended	221 (25.8)
	I3.6	Medication initiated	72 (8.3)
		Total	**857 (100)**

Key: Domain, code and interventions performed in absolute numbers (n) and percentages (%), PhIs: Pharmaceutical Interventions, PCNE: Pharmaceutical Care Network Europe.

Acceptance and the outcome of each DRM and PhI generated convergent results, which are presented in Tables 4 and 5. In most of the cases, the PhIs were accepted and fully implemented, generating the problem totally solved (85.9%) outcome. Subsequently, the PhIs proposed with unknown acceptance resulted in the unknown problem outcome in 9.9% of the cases. The PhIs that were accepted but not implemented generated the outcome described as problem not solved due to lack of cooperation from the prescribing professional (3.5%). Finally, the PhIs that were not accepted due to disagreement led to the outcome defined as problem not solved due to ineffectiveness of the PhI (0.7%).

The results obtained in relation to the economic impact of the PhIs implemented showed that 41.8% of the PhIs generate a reduction in costs, 21.8% do not increase or reduce costs, 19% have an indeterminate impact and 17.4% generate an increase in costs for the institution. Among the medications involved in the DRPs, according to the Anatomical Therapeutic Chemical (ATC) classification, it was indicated that the main organic systems involved in the DRPs were "A- Digestive system and metabolism" (22.9%), "B- Blood and hematopoietic organs" (21.9%), "C – Cardiovascular system" (17.7%) and "N – Nervous system" (17.4%).

Table 4. Acceptance according to the PCNE V9.1 classification

Domain	Code	Acceptance	n (%)
Intervention accepted	A1.1	Intervention accepted and fully implemented	736 (85.9)
	A1.3	Intervention accepted but not implemented	30 (3.5)
Intervention not accepted	A2.2	Intervention not accepted: disagreement	6 (0.7)
Other	A3.1	Intervention proposed, acceptance unknown	85 (9.9)
		Total	**857 (100)**

Key: Domain, code of the interventions accepted in absolute numbers (n) and percentages (%), PCNE: Pharmaceutical Care Network Europe.

Table 5. Outcomes according to the PCNE V9.1 classification

Domain	Code	Outcome	n (%)
0 Unknown	O0.1	Unknown outcome	85 (9.9)
1 Solved	O1.1	Problem totally solved	736 (85.9)
3 Not solved	O3.2	Problem not solved, lack of cooperation from the prescribing professional	30 (3.5)
	O3.3	Problem not solved, ineffective intervention	6 (0.7)
		Total	**857 (100)**

Key: Domain, code of the outcomes in absolute numbers (n) and percentages (%), PCNE: Pharmaceutical Care Network Europe.

Discussion

Based on the study results, it was possible to identify and describe a considerable number of DRPs and perform PhIs in patients admitted to a Cardiology care hospital, in addition to the fact that the PhIs performed mostly promoted cost reductions for the institution. The findings highlight the importance of the presence of the pharmaceutical service as part of care management in the promotion of safety within the health service[13].

The study presented a mean of 1.5 DRPs per patient. Similar studies conducted in other countries indicate close mean values, such as in Turkey, where a mean of 1.6 DRPs per patient was identified, China with 0.6, and Switzerland with 2.6[14,15,16]. It is worth noting that these other studies used different populations and data collection times.

In addition to that, the mean age of the study population, both for men and for women, was above 60 years old, characterizing a predominantly aged population. A number of studies conducted in populations with cardiovascular problems show that older adults over 60 years of age tend to present more DRPs because they have more comorbidities and chronic conditions and, consequently, are polymedicated[15]. Another important issue surveyed by previous studies is that the combination of comorbidity and polypharmacy can increase the chances of developing drug-related adverse events[14].

The literature suggests several types of DRP classifications that generally follow the same line and logic and can be adapted to each specific situation for use in pharmacy services[11,17,18]. The main DRPs found in this study were those in the field of effectiveness (50.6%), which can reflect causes such as unavailability of medication, insufficient dosage, incomplete treatment or inadequate pharmaceutical form for the patient's condition. The second main domain of the DRPs was safety with a possible risk of adverse reaction (39.1%); this data can be related to the causes linked to duplicity of medications, doses above the allowed, and incorrect dosage instructions.

In general, the literature presents varied results for classification of the DRPs according to the PCNE method. A study carried out in Portugal with 31 institutionalized aged patients identified possible risk of adverse reaction (49.5%) as the main DRP, as well as treatment effect outside the expected with 14.8%[19]. In turn, a study conducted in China, including 198 patients admitted to a Neurology care unit, showed that 43.8% of the DRPs were related to the safety domain, followed by 32.2% related to the effectiveness domain[20]. Another study carried out in Turkey, with a sample collected from 91 patients admitted to a Cardiology care unit, found the effectiveness domain as the most prevalent with 49.4%, followed by the safety domain with 34.1%, data that are very similar to those found in this study[14].

In relation to the causes of the DRPs, the domains most frequently found in the study were dose selection with 46.7% and drug selection with 32.5%. These data are similar to those found in international studies, in which the main cause of DRPs is linked to drug selection in the first place and, secondly, to the dose selection domain[14,20,21,22,23,24] .

The medication groups most involved in the DRPs were those acting on the digestive tract and metabolism, blood and hematopoietic organs, cardiovascular system and nervous system. It is necessary to take into account that the study institution is a reference hospital unit in Cardiology care; however, the collection period in question took place during the COVID pandemic, which interfered changing the profile of medication use in the patients treated, such as increasing the consumption of analgesics and anti-inflammatory drugs (nervous system group). Even so, medications that act on the blood and hematopoietic organs and cardiovascular system were found, thus characterizing the specialty of the study hospital. In addition to that, it is important to emphasize that these classes are mostly medications considered potentially dangerous and require greater attention throughout their use process[25].

Among the PhIs proposed, all were performed at the medication level, with requesting medication suspension (25.8%) and changing administration instructions (25.7%) as the most recurrent PhIs, followed by dose change (20.7%) and change in formulation or form (12.5%). Such PhIs reflect the reality of the service in question, as lack of medications is common in many situations and, for this reason, drug suspension was one of the most prevalent PhIs, which also raises questions about the real need for the prescribed medications involved in the PhIs. Other studies present varied data, but most identified the medication domain as the most common for the PhIs: in Malaysia with 42.2%, in Turkey with 44.2% and in Brazil with 44%[14,26,27].

The acceptance rate of the PhIs in this study was 85.9%, whereas such rates were also high in other studies. In China, for example, some studies presented rates above 90%[15,27,28]. These high rates reflect a good relationship of trust between pharmacists and the health care team comprised by physicians and nurses, who work together to resolve DRPs and promote rational use and patient safety. It is worth mentioning that the collaborative process between pharmacists and other health professionals through the performance of PhIs is a fundamental tool for the health system to become safer and more effective[29].

In relation to the economic impact generated by the PhIs with cardiovascular patients discussed in this study, 41.8% of them reduced the costs. Studies with a similar methodology show that, in Lebanon, 46% of the PhIs generated a cost reduction for the institution (hospitalized aged patients[30]) and that, in France, there was a cost reduction in around 44.3% of the PhIs (cancer patients[12]) and 55.2% in another study (hospitalized patients with cognitive disorders[31]). Although the methodological tool does not quantify absolute costs, it is possible to relatively dimension the economic impact generated by the PhIs, highlighting the role of the pharmacist included in this process.

It is considered that pharmacists should play a fundamental role in the process to ensure safe medication use. These professionals have specific knowledge about pharmacotherapy and, through a review during the general processes of prescription preparation, distribution, administration and monitoring of adverse events, can contribute to patient safety, promoting rational use of medications[13]. Thus, avoiding DRPs through PhIs would be one of the main duties of hospital pharmacists.

It is important to take into account that among the study limitations is the fact that the institution evaluated does not have a Clinical Pharmacy service specialized in carrying out this task, and that all the pharmacists in the service perform both the assistance and the clinical service roles. Even so, it was possible to obtain relevant data for the institution, as this is an unprecedented study in the in-hospital setting. The data in this study are a way to stimulate expansion of the Clinical Pharmacy service within the hospital, highlighting the importance of the pharmacist in order to minimize possible risks related to medication use.

Conclusion

A considerable number of the DRPs was identified and described in prescriptions of hospitalized patients, which needed to be subjected to some type of PhI. Such PhIs were aimed at reducing possible drug-related harms, in addition to promoting, in most cases, a cost reduction for the institution. Although there are still obstacles, health services should consider the presence of a clinical pharmacist with a watchful eye promoting rational use of medications, optimizing pharmacotherapy, included in a multiprofessional environment and contributing to the patient-centered care management process.

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Collaborators

IAS and HC prepared the project; IAS was in charge of data collection. IAS and HC also analyzed and interpreted the data, in addition to elaborating and critically reviewing the article. The authors assume full responsibility for the data published and guarantee accuracy and integrity of the article.

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Conflict of interest statement

The authors declare that there are no conflicts of interest in relation to this article.

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