Original Paper

Pharmaceutical recommendations in a university hospital transplant unit

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Abstract

Introduction: The transplanted patient has a complex pharmacotherapy, with the pharmacist having an important role in the multidisciplinary team. **Objective:** To analyze the pharmaceutical recommendations made during the hospitalization of the patients in kidney and liver transplant units. **Methods:** This was a cross-sectional study in which pharmaceutical recommendations from May 2017 to April 2018 were collected from the records contained in the database of the Clinical Pharmacy Unit of a University Hospital in Fortaleza, Brazil. The recommendations were categorized and analyzed based on the classification used in the institution. **Results:** There were 1241 pharmaceutical recommendations involving 325 patients and 1466 medications. The recommendations were more frequent during liver transplantation (54.2%, n = 672), with dose adjustments (18.2%, n = 122) and dilution / reconstitution (9.8%, n = 66) being the most predominant types. In kidney transplantation, recommendations for education about medication use (17.6%, n = 100) and treatment adherence strategies (17.6%, n = 100) were the most predominant. The most frequent therapeutic classes were systemic antibacterials (31.2%, n = 458) and immunosuppressants (25.1%, n = 368). The acceptance rate of recommendations for kidney and liver transplantation were 95.1% (n = 541) and 95.4% (n = 641), respectively. **Conclusions:** The present study showed a high frequency of pharmaceutical recommendations and these results demonstrate that the detection of drug-related problems generates pharmaceutical recommendations that can contribute to the reduction of negative drug-associated results and increase patient safety.

Keywords: Pharmaceutical Services, Patient Safety, Kidney transplantation, Liver transplantation.

Recomendações farmacêuticas em uma unidade de transplante de um hospital universitário

Resumo

Introdução: O paciente transplantado possui uma farmacoterapia complexa, tendo o farmacêutico um importante papel na equipe multidisciplinar. **Objetivo:** Analisar as recomendações farmacêuticas realizadas durante a hospitalização dos pacientes em uma unidade de transplante hepático e renal. **Métodos:** Trata-se de um estudo transversal no qual as recomendações farmacêuticas, realizadas no período de maio de 2017 a abril de 2018, foram coletadas a partir dos registros contidos do banco de dados da Unidade de Farmácia Clínica de um Hospital Universitário em Fortaleza, Brasil, sendo categorizadas e analisadas com base na classificação utilizada na instituição. **Resultados:** Foram realizadas 1241 recomendações farmacêuticas envolvendo 325 pacientes e 1466 medicamentos. As recomendações foram mais frequentes no transplante hepático (54,2%; n= 672), sendo predominantes adequações de dose (18,2%; n= 122) e de diluição/reconstituição (9,8%; n= 66). No transplante renal, as recomendações de educação sobre o uso de medicamentos (17,6%; n=100) e de elaboração de estratégias de adesão ao tratamento (17,6%; n=100) apresentaram predominância. As classes terapêuticas mais frequentes foram os antibacterianos de uso sistêmico (31,2%; n= 458) e os imunossupressores (25,1%; n= 368). As taxas de aceitação das recomendações realizadas no transplante renal e hepático foram de 95,1% (n= 541) e 95,4% (n= 641), respectivamente. **Conclusões:** O presente estudo obteve alta frequência de recomendações farmacêuticas e esse resultado demonstra que a detecção de problemas relacionados aos medicamentos gera recomendações farmacêuticas que podem contribuir para a redução de resultados negativos associados aos medicamentos e aumentar a segurança do paciente.

Palavras-chave: Assistência Farmacêutica, Segurança do Paciente, Transplante de rim, Transplante de fígado.

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Introduction

Over the years, transplants have been increasingly successful, increasing patient life expectancy[1,2]. Brazil is currently the second country in the world in number of transplants. Looking back over the past ten years, a 71% increase in kidney transplant and an 85% increase in liver[3,4] were observed. In Ceará, the absolute number of kidney and liver transplants, which occurred from January to September 2018, were 164 and 162, respectively[5,6].

Transplanted patients require lifelong immunosuppression and, in addition to immunosuppressive therapy, use antimicrobial drugs to prevent and often treat secondary infections[7,8]. Additional medications to treat concomitant chronic illnesses such as hypertension, diabetes, osteoporosis, and hyperlipidemia are often needed, making the drug regimen larger in number and complexity[2]. Thus, polypharmacy is frequent in the population of transplanted patients, increasing the possibility of drug-related problems (DRPs).

DRPs, whose identification follows the principles of need, effectiveness and safety, may be related to adverse drug reactions (unavoidable, patient-related and always harmful) or medication errors (avoidable and which may or may not cause patient harm)[9,10]. These errors can increase length of stay, morbidity, mortality and institutional costs. However, they can be prevented by making Pharmaceutical Recommendations (PRs), which should be planned, documented and performed by the pharmaceutical professional[11,12,13].

The literature reports that performing PRs, with the purpose of optimizing pharmacotherapy, promoting, protecting and recovering health, in transplanted patients enables the reduction of negative results associated with medications and improves patient safety[9,13,14]. As a consequence, most solid organ transplant centers incorporate the pharmacist in today's multidisciplinary approach as they play an important role in the care of transplanted patients[6,7].

However, PR studies conducted with special patient groups, such as transplanted patients, are still scarce in the literature[9]. In this sense, this study was conducted to analyze the pharmaceutical recommendations made during the hospitalization period of patients in a liver and kidney transplant unit of a public teaching hospital.

Methods

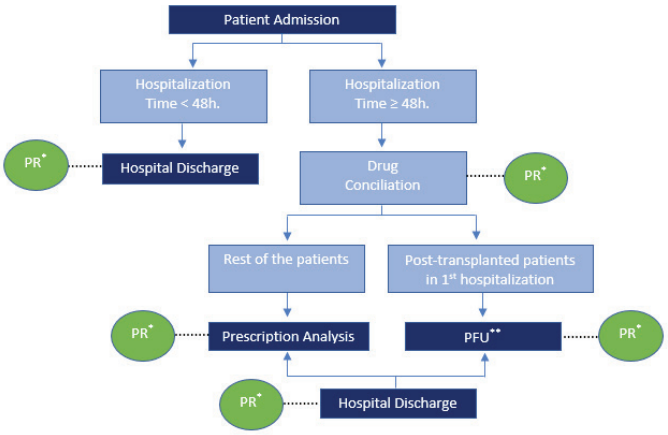
This is a cross-sectional study in which the records of pharmaceutical recommendations contained in the database of the Clinical Pharmacy Unit of a Federal University Hospital in Fortaleza, Brazil, were analyzed and analyzed. These recommendations were made during the development of the daily activities of clinical pharmacists in kidney and liver transplant wards from May 2017 to April 2018. The study was conducted in accordance with the guidelines and regulatory standards for research involving human subjects, and was submitted to the Research Ethics Committee of the institution and approved under opinion No. 2,699,465 and CAAE 74283417.4.0000.5045.

The University Hospital under study is integrated to the SUS and offers high complexity health care routinely performing kidney and liver transplants, among other tasks. The hospital has more than 200 hospitalization beds and outpatient clinics. The transplant inpatient unit has 5 wards and consists of a total of 20 beds, 12 for kidney transplant and 08 reserved for liver transplants. In this unit, both newly transplanted patients and late transplanted patients hospitalized for any complications are hospitalized[15].

The pharmaceutical recommendations made at the institution are recorded in a standardized form by the service and then stored in a database of the Clinical Pharmacy Unit, from which data were collected for the period determined for the study and another database was created using *Microsoft Office Excel* 2013, which contained the PRs performed at the Kidney and Liver Transplant Unit from May 2017 to April 2018.

The PRs were directed to the multidisciplinary team, patients and caregivers and were performed at four different times: admission, hospitalization, pharmacotherapeutic follow-up (PFU) and discharge. The pharmaceutical recommendations made upon admission refer to those that occurred after drug conciliation, when the drugs used before hospitalization were reviewed and compared with the prescription, in order to identify possible discrepancies. The PRs performed at the time of PFU refer to those that were made after offering this clinical service through the analysis of its form, and it was performed only for recent post-transplant patients in their first hospitalization. On the other hand, inpatient PRs are those performed after analysis of the prescription of hospitalized patients who were not under pharmacotherapeutic follow-up. And finally, the PRs performed at discharge are those that occurred after drug conciliation at hospital discharge, with the aim of ensuring that the necessary medications were properly prescribed, and/or during pharmaceutical orientation to the patient and caregivers (Figure 1).

Figure 1. Methodological flowchart of the pharmaceutical recommendations from May 2017 to April 2018 in a transplant unit of a university hospital.



*PR: Pharmaceutical Recommendation (possible time of)
**PFU: Pharmacotherapeutic Follow-Up

The clinical pharmaceutical practice was based on the institutional protocols of the kidney and liver transplant service and on the Clinical Protocols and Therapeutic Guidelines established by the Ministry of Health[16-19]. For the consultation of information related to medications such as indication, dosage, dose adjustments, administration, interactions, compatibility, among others, the Micromedex[20], Medscape[21] and UpToDate[22] databases were used, as well as scientific works when needed.

The study included pharmaceutical recommendations made in kidney and liver transplant wards that occurred from admission to hospital discharge. Pharmaceutical recommendations that were repeatedly recorded, those that were incomplete and/or poorly described precluding their proper classification and those directed to outpatients were excluded from the study.

The variables analyzed in the present study were the following: gender, age, type of transplant, drug-related problem, pharmaceutical recommendation, time of the PR, acceptability, reason for not accepting the recommendation, and drugs involved.

The classification of the DRPs and of the PRs was performed according to the definition systematized by the hospital's Clinical Pharmacy Unit, which is based on the Second Granada Consensus[10]. Already the drugs involved were categorized according to the second level of the Anatomical Therapeutic Chemical (ATC) classification, adopted by the World Health Organization (WHO) to frame all types of drugs according to the organ or system of action and their chemical, pharmacological and therapeutic properties[23].

Acceptability was measured from the visualization of the change suggested in the prescription, and the PRs of education and elaboration of adherence strategies directed to patients and caregivers were all considered accepted.

The categorical variables of this study were expressed as absolute and relative frequencies and the numerical variables as arithmetic mean and standard deviation, using Microsoft Office Excel® 2013. The characterization data of the population were analyzed by means of the *Student*'s t-test and of the *Fisher*'s exact test in the *Graph Pad Prism*, version 7.0d (USA) statistical program, considering a significant P value < 0.05.

Results

During the period analyzed, 1,097 drug-related problems were detected and 1,241 pharmaceutical recommendations were made involving 325 patients. Of the PRs registered in the database, 24 were not accounted for in this study, since 8 of them had incomplete and/or poorly described information and 16 were noted repeatedly. Most were renal transplant patients (55.4%), male (64.3%) and with a mean age of 50.8 ± 14.5 years old. There was no significant difference in the parameters described between liver and kidney transplant patients, except for a slight increase in the proportion of males in liver patients (Table 1).

Table 1. Demographic characteristics of the patients involved in the pharmaceutical recommendations from May 2017 to April 2018 in a transplant unit of a university hospital.

Variables	Hepatic transplant	Renal transplant	Total	p
Number of patients	145 (44.6%)	180 (55.4%)	325	-
Mean age ± SD[a]	52.4 ± 14.7	49.5 ± 14.3	50.8 ± 14.5	0.0736[b]
Age group	**n (%)**	**n (%)**	**n (%)**	-
≤ 24 years old	10(6.9)	12(6.7)	22(6.8)	> 0.9999[c]
25 – 59 years old	91(62.8)	121(67.2)	212(65.2)	0.4143[c]
≥ 60 years old (elderly)	44(30.3)	47(26.1)	91(28.0)	0.4561[c]
Gender	**n (%)**	**n (%)**	**n (%)**	-
Male	110(75.9)	99(55.0)	209(64.3)	0.0001[c*]
Female	35(24.1)	81(45.0)	116(35.7)	

[a] SD: Standard Deviation; [b]: Student's t test; [c]:Fisher's exact test
*: Relative Risk: 1.744; 95% Confidence Interval: 1.302-2.391

The DRPs detected in the period determined for the study corresponded to a mean of 91.4 ± 25.6 DRPs/month, with 57.3% identified in liver transplant. The most frequent DRPs, considering renal and liver transplant were the following: missing information (13.4%), non-adherence/need for guidance (13.1%) and overdose (9.5%) (Table 2).

With regard to liver transplant, the other drug related problems were the following: inadequate scheduling, use of non-prescription drug, illegibility, insufficient amount for treatment, therapeutic duplication, inadequate selection, low convenience, drug-drug interaction, contraindication and incompatibility. In renal transplant, the other DRPs detected were adverse drug reaction, inadequate schedule, drug-nutrient interaction, insufficient amount for treatment, use of non-prescription drug, therapeutic duplication, inadequate selection, low convenience, drug-drug interaction, contraindication. and incompatibility.

The pharmaceutical recommendations made corresponded to a mean of 103.4 ± 26.2 PRs/month. Most of them were performed in liver transplant (54.2%), with a mean of 4.6 PRs/patient in this specialty and of 3.2 PRs/patient in kidney transplant.

Considering the two types of transplant, the most frequent PRs were the following: dose adequacy (17.1%), educating about medication use (11.6%) and elaborating a treatment adherence strategy (11.6%) (Table 3).

The other PRs that occurred in liver transplant were scheduling (adequacy), procurement of drug/health product, drug/health product availability, and technical information on the drug and dosage (adequacy). In renal transplant, the other PRs performed were suspension of unnecessary examinations, scheduling (adequacy), procurement of drug/health product, drug/health product availability, technical information on the drug and dosage (suitability).

The PRs performed involved a total of 1,466 medications, with 174 different drugs. In 362 cases one recommendation involved two drugs and, in 26 cases, three drugs were related to one recommendation. The most common were the following: tacrolimus (12.3%; n = 180), sodium mycophenolate (9.5%; n = 139), piperacillin + tazobactam (7.6%; n = 11) and meropenem (5.9%; n = 86).

Evaluating the drugs based on the second level of the ATC classification, the most prevalent therapeutic classes were systemic antibacterials (31.2%), immunosuppressors (25.1%) and blood substitutes and infusion solutions (7.8 %). Table 4 addresses the ten most prevalent therapeutic classes and the most frequent PRs.

Table 2. Classification of the identified drug-related problems (n = 1097) from May 2017 to April 2018 in a transplant unit of a university hospital.

Drug-related problems	Total N= 1,097 n (%)	Hepatic transplant N= 628 n (%)	Renal transplant N= 469 n (%)
Missing information*	147(13.4)	110(17.5)	37(7.9)
Non-adherence/need for guidance	144(13.1)	44(7.0)	100(21.3)
Overdose	104(9.5)	68(10.8)	36(7.7)
Necessary medication not prescribed	86(7.8)	54(8.6)	32(6.8)
Unnecessary medication prescribed	69(6.3)	35(5.6)	34(7.3)
Missing/Inadequate documentation	64(5.8)	30(4.8)	34(7.3)
Underdose	58(5.3)	36(5.7)	22(4.7)
Unavailability (lack)	52(4.7)	19(3.0)	33(7.0)
Incorrect wording of the prescription	49(4.5)	33(5.3)	16(3.4)
Inadequate treatment time	43(3.9)	26(4.1)	17(3.6)
Inadequate route of administration	38(3.5)	27(4.3)	11(2.4)
Inadequate pharmaceutical form/presentation	31(2.8)	23(3.7)	8(1.7)
Inadequate dilution/reconstitution	27(2.5)	18(2.9)	9(1.9)
Unavailability (non-standard)	25(2.3)	9(1.4)	16(3.4)
Exam not requested/performed	24(2.2)	17(2.7)	7(1.5)
Inadequate infusion time	23(2.1)	16(2.6)	7(1.5)
Others	113(10.3)	63(10.0)	50(10.7)

* No information on dilution, infusion time, route of administration, dose, prescriber and/or patient data, among others.

Table 3 . Classification of the pharmaceutical recommendations made (n = 1241) from May 2017 to April 2018 in a transplant unit of a university hospital.

Pharmaceutical recommendations	Total N= 1241 n (%)	Hepatic transplant N= 672 n (%)	Renal transplant N= 569 n (%)
Dose (adequacy)	212(17.1)	122(18.2)	90(15.8)
Education on medication use	144(11.6)	44(6.6)	100(17.6)
Development of a treatment adherence strategy	144(11.6)	44(6.6)	100(17.6)
Suspension of medication	91(7.3)	48(7.1)	43(7.6)
Inclusion of medication	87(7.0)	55(8.2)	32(5.6)
Dilution/Reconstitution (adequacy)	85(6.9)	66(9.8)	19(3.3)
Infusion time (adequacy)	85(6.9)	65(9.7)	20(3.5)
Adequacy for the dispensing process	62(5.0)	29(4.3)	33(5.8)
Drug substitution	60(4.9)	25(3.7)	35(6.2)
Correction in the wording	51(4.1)	35(5.2)	16(2.8)
Treatment time (adequacy)	49(4.0)	32(4.8)	17(3.0)
Pharmaceutical form/presentation (adequacy)	43(3.5)	27(4.0)	16(2.8)
Route of administration (adequacy)	42(3.4)	32(4.8)	10(1.8)
Request for necessary exams	31(2.5)	22(3.3)	9(1.6)
Others	55(4.4)	26(3.9)	29(5.1)

Table 4. Main therapeutic classes involved in the pharmaceutical recommendations made from May 2017 to April 2018 in a transplant unit of a university hospital.

ATC classification	Total n (%)	Pharmaceutical recommendations	Prevalence n (%)
		Dose (adequacy)	116(25.3)
Antibacterials for systemic use (J01)	458(31.2)	Infusion time (adequacy)	86(18.9)
		Dilution/Reconstitution (adequacy)	74(16.2)
		Educating on medication use	267(42.1)
Immunosuppressors (L04)	368(25.1)	Developing strategies for treatment adherence	267(42.1)
		Drug substitution	32(5.0)
		Dilution/Reconstitution (adequacy)	74(64.4)
Blood substitutes and infusion solutions (B05)	115(7.8)	Inclusion of medication	19(16.5)
		Suspension of medication	9(7.8)
		Dose (adequacy)	17(33.3)
Medications for acidity disorders (A02)	51(3.5)	Route of administration (adequacy)	10(19.6)
		Pharmaceutical form/presentation (adequacy)	8(15.7)
		Dose (adequacy)	20(48.8)
Antivirals for systemic use (J05)	41(2.8)	Treatment time (adequacy)	5(12.2)
		Adequacy for the dispensing process	3(7.3)
		Drug substitution	12(32.4)
Corticosteroids for systemic use (H02)	37(2.5)	Dose (adequacy)	8(21.6)
		Dilution/Reconstitution (adequacy)	4(10.8)
		Drug substitution	22(78.6)
Antihistamines for systemic use (R06)	28(1.9)	Pharmaceutical form/presentation (adequacy)	2(7.1)
		Acquisition of medication/health product	1(3.6)
		Infusion time (adequacy)	7(25.9)
Antimycotics for systemic use (J02)	27(1.8)	Appreciation (adequacy)	4(14.8)
		Adequacy for the dispensing process	3(11.1)
		Appreciation (adequacy)	6(23.1)
Antianemic preparations (B03)	26(1.8)	Dose (adequacy)	5(19.2)
		Adequacy for the dispensing process	3(11.5)
		Suspension of medication	10(40.0)
Painkillers (NO2)	25(1.7)	Drug substitution	6(24.0)
		Dose (adequacy)	4(16.0)

The PRs were performed during all the stages of hospitalization and, considering both specialties, most of them occurred during hospitalization (50.6%; n = 628). The PRs performed at discharge represented 26.8% (n = 333), whereas the ones performed during pharmacotherapy follow-up corresponded to 21.4% (n = 266) and those performed after the admission conciliation of patients represented 1,1% (n = 14). Table 5 shows the main PRs performed according to the moment of hospitalization.

Regarding acceptability, 95.3% (n = 1182) of the PRs were accepted. Of the recommendations made in kidney transplant, 95.1% (n = 541) were accepted and in liver transplant the acceptance rate was 95.4% (n = 641).

The reason for not accepting the PRs has a standardized classification by the institution's Clinical Pharmacy Unit and, considering the two specialties, the most predominant was "judged the previous option better", with 64.4% (n = 38). The other reasons for not accepting were "not accepted, but changed the pharmacotherapeutic conduct", "without justification" and "accepted verbally and did not change". which represented 11.9% (n = 7) each.

Discussion

In the present study, it was possible to identify a high frequency of pharmaceutical recommendations made in wards of kidney and liver transplant patients. This result demonstrates that the detection of drug-related problem generates PRs that can contribute to reducing drug-related negative outcomes and to increasing patient safety[9,14].

When analyzing the epidemiological profile, it is observed that the study population was predominantly male and non-elderly, with a mean age of 50.8 years old, corroborating another study conducted in 2014 in Fortaleza, in this same transplant center, which had a higher frequency of the male gender and a mean age of 49.7 years old[14]. These data may suggest homogeneity among populations, allowing for the comparison of their results.

The most frequently identified DRPs in the present study, considering both specialties, were missing information, non-adherence/need for guidance, overdose and not prescribing the necessary medication. Similar results were also found in work by Adriano et al., where the most common DRPs were not prescribing the necessary medication, overdose, underdose and prescription of unnecessary medication[14]. In a literature review, Stemer and Lemmens-Gruber report that the problems most commonly identified by the pharmacist in the transplant service were overdose and underdose[8]. It can be observed that the DRP related to the dose was common to all three studies, although methodological differences in the classification of the DRPs and in the profile of each institution may generate different DRPs.

In this study, the most prevalent DRP was related to missing information, corroborating a paper on prescribing errors in a hospital in southern Brazil, where a high frequency of missing information was observed in the prescriptions analyzed[24]. Neri et al. also noted a significant increase in the percentage of lack of information relevant to the safety of drug dispensing and administration[25]. The omission of information is considered a serious flaw in the prescription process, which negatively influences communication between professionals[23,25]. The absence of electronic prescribing at the unit during the study period, a feature that would improve the feasibility of prescribing analysis by the pharmacist and other professionals and reduce the harm to patients related to prescribing errors, may have favored the occurrence of such problem.

Table 5. Main pharmaceutical recommendations made by time of hospitalization from May 2017 to April 2018 in a transplant unit of a university hospital.

Time	Type of pharmaceutical recommendation	TXR* n (%)	TXH** n (%)	Total n (%)
Admission	Inclusion of medication	5(45.5)	6(54.5)	11(100)
	Dose (adequacy)	1(33.3)	2(66.7)	3(100)
Hospitalization	Dose (adequacy)	51(38.1)	83(61.9)	134(100)
	Dilution/Reconstitution (adequacy)	15(22.1)	53(77.9)	68(100)
	Suspension of medication	29(46.8)	33(53.2)	62(100)
	Infusion time (adequacy)	15(24.2)	47(75.8)	62(100)
	Drug substitution	20(50)	20(50)	40(100)
	Inclusion of medication	0(0)	32(100)	32(100)
	Dose (adequacy)	35(49.3)	36(50.7)	71(100)
	Suspension of medication	14(48.3)	15(51.7)	29(100)
	Infusion time (adequacy)	5(21.7)	18(78.3)	23(100)
Pharmacotherapeutical Follow-up	Inclusion of medication	6(30)	14(70)	20(100)
	Drug substitution	14(73.7)	5(26.3)	19(100)
	Dilution/Reconstitution(adequacy)	4(23.5)	13(76.5)	17(100)
	Treatment time (adequacy)	9(43.5)	7(56.5)	16(100)
	Adequacy for the dispensing process	8(57.1)	6(42.9)	14(100)
	Educating on medication use	100(69.4)	44(30.6)	144(100)
	Developing strategies for treatment adherence	100(69.4)	44(30.6)	144(100)
Discharge	Adequacy for the dispensing process	15(71.4)	6(28.6)	21(100)
	Inclusion of medication	9(75)	3(25)	12(100)
	Dose (adequacy)	3(75)	1(25)	4(100)
	Request for necessary exams	1(33.3)	2(66.7)	3(100)

*TxR: Renal transplant.
**TxH: Hepatic transplant

After identifying the drug-related problems, the main suggested recommendations, considering kidney and liver transplant, were regarding dose adequacy, drug use education, and strategies for adherence to treatment. A higher frequency of the PR related to dose adequacy was also identified in a study of transplanted patients in which PRs were performed and dose adjustment was among the most prevalent[6]. Another analysis also reported that the transplant team pharmacists are closely involved with drug selection recommendations and dose adjustments[26]. Monitoring of serum immunosuppressor levels (tacrolimus, cyclosporine, everolimus and sirolimus) and other drugs, together with continuous assessment of patients' renal function, allows clinical pharmacists to identify inadequate dose problems and to intervene with the medical professional to prevent the occurrence of adverse events, infections, and rejection, among other health problems.

The pharmaceutical recommendations related to drug use guidelines and treatment adherence strategies for transplant patients are reported in the literature[9,27]. In many centers, the transplant team pharmacists are involved in educating patients about their medication regimen to make them aware that adherence to treatment is essential for post-transplant success and prevention of hospital readmissions[6]. In this institution, a larger number of kidney transplants are performed if compared to liver transplant as most liver transplants are performed in partnership with another hospital[3]. Thus, it reflects in a greater number of educational recommendations and strategies for adherence to treatment in kidney transplant, as they are performed mainly at the time of pharmaceutical orientation at hospital discharge of newly transplanted patients.

The PRs differed in quantity and type between the two specialties, suggesting that the profiles of patients and health professionals may interfere with the recommendations. Despite the lower number of liver transplant patients, there were more pharmaceutical recommendations, per patient in this unit, most of them focused on solving process problems such as dose adequacy, dilution/reconstitution and infusion time. The lower number of medical professionals during the daily routine in the wards, associated with the presence of medical students who undergo a biweekly internship in this specialty, may be related to the larger number and types of recommendations made. According to literature data, people in training constantly make mistakes[28]. Given this, it is evident that the pharmacists' previous analysis of the prescriptions may enable the detection of errors and minimize possible damage to the patients, thus contributing to the patient safety process[24].

The two therapeutic classes most involved in the pharmaceutical recommendations were systemic antibacterials and immunosuppresors. This prescription profile is consistent with hospitalized transplant patients, since the use of immunosuppressive drugs to prevent graft rejection makes them more susceptible to infection[14]. This result was similar to a study conducted in Austria which found that the most involved PR therapeutic classes were immunosuppressors, cardiovascular agents and antimicrobials[8].

In the present study, most of the recommendations that occurred involving immunosuppressors were focused on patient education at discharge in order to advise on the importance of proper use of immunosuppressor, increase adherence and contribute to the success of transplant. These results are consistent with the study by Ravichandran et al., where most of the drug guidance was on the use of immunosuppressive drugs[6]. Already the most frequent recommendations involving antibacterials were focused on dose adequacy, dilution/reconstitution and infusion time, in order to avoid medication errors, as well as to promote the optimization of pharmacotherapy and the appropriate use of these drugs which are controlled by an Antimicrobial Use Management Program established in the institution.

The pharmaceutical recommendations of this study were more frequent at the time of hospitalization with patients without pharmacotherapeutic follow-up. Although PFU is very effective in preventing and resolving pharmacotherapy problems[13], the higher number of PRs involving not followed-up patients may be related to the existence of criteria to offer this clinical service to the patients. Thus, the number of patients under follow-up during the study period may have been lower than the number of patients admitted without PFU or may be related to a possible failure to record the time of the recommendation. This result differs from the previous study conducted in this institution, since most PRs were performed during the pharmacotherapeutic follow-up[14]. However, very similar data were obtained with regard to the PRs performed after conciliation on admission, which resulted in a smaller number in both studies.

The acceptance of the pharmaceutical recommendations was similar to that identified in previous studies conducted at the same institution involving the same population[7,14]. Similar acceptance rates were also reported in a literature review of the role of clinical pharmacists in the care of patients undergoing solid organ transplant in which seven studies reported an acceptance level above 95%[8]. When comparing the acceptability of the PRs in kidney and liver transplant, very similar results are observed, demonstrating that the active presence of the clinical pharmacist in the unit made it possible to gain confidence and a good relation with the other members of the multidisciplinary team of both specialties.

Among the limitations of the study are the probable failure to record the time of the recommendation and the possible underestimation of the PRs, so their number is probably higher than presented. In addition, the non-assessment of the economic impact of the PRs and the non-determination of the clinical outcomes limit the conclusions of the study. However, this study evaluated the pharmaceutical recommendations in transplanted patients hospitalized longer than those already performed in the institution under study and originally stratified the results between the renal and liver transplant specialties.

The information from this study reinforces the importance of monitoring the drug therapy in transplanted patients who are mostly polymedicated in view of the high frequency of identified DRPs. In addition, it is clear that the pharmaceutical recommendations may differ according to the type of patient, to the professional profile involved, and to the presence of students. Further studies are needed to assess the impact of these recommendations on the clinical outcomes of the patients and on the hospital costs.

Conclusion

In the present study, it was possible to identify a high frequency of pharmaceutical recommendations made in wards of kidney and liver transplanted patients. The detection of drug-related problems by the pharmacist generates pharmaceutical recommendations that can promote the optimization of drug therapies, increase patient compliance and safety, and contribute to the reduction of institutional costs, length of stay and negative outcomes of the pharmacotherapy, although these impacts have not been measured in this study.

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Authors' contribution

MKCP, MMG: participated in the project design. MKCP, EFC: data analysis and interpretation. MKCP: article writing and responsibility for all the paper's information, ensuring accuracy and integrity of any part of the work. MMG, EFC, CCA, KXB and ABO: relevant critical review of the intellectual content and final approval of the version to be published.

Conflict of interest

The authors declare no conflicts of interest.

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