

# PHARMACEUTICAL INTERVENTIONS AND THEIR CLINICAL OUTCOMES IN AN INPATIENT POST-TRANSPLANT UNIT

## INTERVENÇÕES FARMACÊUTICAS E SEUS RESULTADOS CLÍNICOS EM UMA UNIDADE DE INTERNAÇÃO PÓS-TRANSPLANTE

### INTERVENCIONES FARMACÉUTICAS Y LOS RESULTADOS CLÍNICOS EN UNA UNIDAD DE HOSPITALIZACIÓN POST-TRASPLANTE

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#### ABSTRACT

To contribute to the formation of knowledge in Brazil about the impact of the clinical pharmacist's role in the care of inpatient post-transplant by analyzing the results of the pharmaceutical interventions performed. A descriptive study was conducted from January to July/2014. Data were collected from the records of the Clinical Pharmacy Service (medication reconciliation, prescription analysis and pharmacotherapeutic follow-up), including all patients with drug-related problems and documented pharmaceutical interventions. Epidemiological variables and related to the clinical activities of the pharmacist were described. A total of 131 patients had drug-related problems, especially, during "Pharmacotherapeutic follow-up". The most frequent categories were: "not prescribed required medicine" (125; 21.7%), "overdosing" (97; 16.8%) and "underdosing" (93; 16.1%). The main drugs involved were "ganciclovir" (81; 13.4%) and "tacrolimus" (33; 5.5%). The pharmaceutical interventions included "dose/adequacy" (193; 33.4%), "inclusion" (122; 21.1%) or "suspension" (122; 21.1%) of medication. The main clinical outcomes were "prevention" (481; 83.4%) or "improvement" (59; 10.2%) of health problems, such as "adverse effects" (170; 29.5%), "infection" (133; 23%) and "rejection" (41; 7.1%), being identified a significant relationship ( $p < 0.05$ ) between the acceptance of interventions and these outcomes, as well as between the non-acceptance and the occurrence of negative outcomes associated with medication. Our findings demonstrated that the pharmaceutical interventions, carried at all stages of care to inpatient post-transplant, integrated with the multidisciplinary team, were able to provide clinical outcomes in the prevention and improvement in health problems related to medication, such as adverse events, infection and rejection.

**keywords:** Clinical Pharmacy Service; Kidney transplantation; Liver transplantation; Patient safety.

#### RESUMO

Contribuir para a formação do conhecimento, no Brasil, sobre o impacto do papel do farmacêutico clínico no cuidado ao paciente pós-transplante internado, analisando os resultados das intervenções farmacêuticas realizadas. Foi realizado um estudo descritivo de janeiro a julho/2014. Os dados foram coletados dos registros do Serviço de Farmácia Clínica (conciliação medicamentosa, análise de prescrição e acompanhamento farmacoterapêutico), incluindo todos os pacientes com problemas relacionados a medicamentos e intervenções farmacêuticas documentadas. Variáveis epidemiológicas e relacionadas às atividades clínicas do farmacêutico foram descritas. Um total de 131 pacientes apresentaram problemas relacionados a medicamentos, especialmente durante o "Acompanhamento Farmacoterapêutico". As categorias mais frequentes foram: "medicamento não prescrito" (125; 21.7%), "sobredose" (97; 16.8%) e "subdose" (93; 16.1%). Os principais fármacos envolvidos foram "ganciclovir" (81; 13.4%) e "tacrolimus" (33; 5.5%). A intervenção farmacêutica incluiu "dose (adequação)" (193; 33.4%), "inclusão" (122; 21.1%) ou "suspensão" (122; 21.1%) do medicamento. Os principais resultados clínicos foram "prevenção" (481; 83.4%) ou "melhora" (59; 10.2%) de problemas de saúde, como "efeitos adversos" (170; 29.5%), "infecção" (133; 23%) e "rejeição" (41; 7.1%), sendo verificada uma relação significativa ( $p < 0,05$ ) entre a aceitação da intervenção e esses resultados, bem como entre a não aceitação e a ocorrência dos resultados negativos associados à medicação. Nossos achados demonstraram que as intervenções farmacêuticas, realizadas em todos os estágios de atendimento ao paciente pós-transplante internado, integrada à equipe multidisciplinar, foram capazes de fornecer resultados clínicos na prevenção e melhora de problemas de saúde relacionados à medicação, tais como efeitos adversos, infecção e rejeição.

**Palavras-chave:** Serviço de Farmácia Clínica; Transplante de rim; Transplante de fígado; Segurança do paciente.

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## RESUMEN

Contribuir a la formación del conocimiento, en Brasil, sobre el impacto del papel del farmacéutico clínico en el cuidado al paciente post-trasplante hospitalizado, analizando los resultados de las intervenciones farmacéuticas realizadas. Se hizo un estudio descriptivo de Enero a Julio/2014. Los datos fueron colectados a partir de los registros del servicio de farmacia clínica (reconciliación medicamentosa, análisis de la prescripción y seguimiento farmacoterapéutico), incluyendo todos los pacientes con problemas relacionados con medicamentos e intervenciones farmacéuticas documentadas. Se han descrito variables epidemiológicas y relacionadas con las actividades clínicas del farmacéutico. Un total de 131 pacientes tenían problemas relacionados con los medicamentos, especialmente durante el "seguimiento farmacoterapéutico". Las categorías más frecuentes fueron: "medicamentos sin receta" (125; 21,7%), "sobredosis" (97; 16,8%) y "dosis insuficiente" (93; 16,1%). Los principales agentes implicados fueron "ganciclovir" (81; 13,4%) y "tacrolimus" (33; 5,5%). La intervención farmacéutica incluyó "ajuste de la dosis" (193; 33,4%), "inclusión" (122; 21,1%) o "suspensión" (122; 21,1%) del medicamento. Los principales resultados clínicos fueron "prevención" (481; 83,4%) o "mejora" (59; 10,2%) de los problemas de salud, como "efectos adversos" (170; 29,5%), "infección" (133; 23%) y "rechazo" (41; 7,1%), se observó una relación significativa ( $p < 0,05$ ) entre la aceptación de intervenciones y estos resultados, así como entre la no aceptación y la aparición de resultados adversos asociados con la medicación. Nuestros resultados demostraron que las intervenciones farmacéuticas, realizadas en todas las etapas de atención post-trasplante de internación, integrada con el equipo multidisciplinar, fueron capaces de proporcionar resultados clínicos en la prevención y mejora en los problemas de salud relacionados a la medicación, tales como: los efectos adversos, la infección y el rechazo.

**Palabras clave:** Servicio de Farmacia Clínica; Trasplante de riñón; Trasplante de hígado; Seguridad del paciente.

## INTRODUCTION

Transplantation is the treatment of choice for most cases of organ failures in the final stage, but the success of the procedure depends not only on a proper surgical technique, requiring also the understanding of the immunological processes, appropriate conservation of organs and use of effective immunosuppressive therapies<sup>1</sup>.

Besides using multiple drugs to maintain immunosuppression, transplant patients are also treated for associated chronic diseases such as hypertension, hyperglycemia, and hyperlipidemia, which increases the risk of medication errors, drug interactions, adverse reactions and repeated use of drugs, factors associated with an increased risk of rejection<sup>2</sup>.

The occurrence of medication errors in health care facilities is considered a matter of concern by the World Health Organization (WHO), which establishes the need to ensure the quality of care and patient safety in health care facilities<sup>3</sup>. In this regard, collaborative role of the pharmacist in preventing prescription and medication errors, by performing clinical activities aimed at optimization of pharmacotherapy, is emphasized<sup>4</sup>.

These clinical activities are particularly relevant in highly complex treatments as with transplant patients. The participation of the pharmacist, together with the multidisciplinary team, performing the necessary pharmaceutical interventions (PI) and monitoring the clinical outcomes achieved, shows benefits in the management of drug-related problems (DRP), in achieving therapeutic results<sup>5-8</sup> and also reducing costs and decreasing length of hospital stay<sup>9</sup>.

In the ambulatory care environment of the post-transplant patient, the contribution of the clinical pharmacist to reducing DRP by performing PI has been assessed<sup>12,5-6,10</sup>. However, there is still little information on the impact of clinical pharmacy practice on the care of transplant patients during hospitalization<sup>11</sup>.

The objective of this study was to contribute to the formation of knowledge in Brazil about the impact of the clinical pharmacist's role in the care of transplant patients admitted to a post-transplantation unit by analyzing the results of the pharmaceutical interventions performed.

## METHODS

This was a descriptive and retrospective study, with analytical approach, based on primary data, conducted in the period of January to July 2014, in an inpatient post-transplant unit at a university hospital with tertiary level care and transplant referral. The ward had 12 beds for kidney transplant patients and 8 beds for liver transplant patients.

Data were collected from the records of the Clinical Pharmacy Service, including all patients with DRP and documented PI, during the course of medication reconciliation, prescription analysis and pharmacotherapeutic follow-up, which were carried out by a team composed of pharmacy residents

and a pharmacist from the service with experience in the care of transplant patients, integrated cooperation with a multidisciplinary team composed of doctor, nurse, nutritionist, psychologist, social worker and physiotherapist.

The medication reconciliation is the first evaluation moment of the pharmacist towards the transplanted patient, identifying the discrepancies and reconciling the medicines necessary to the pharmacotherapy continuation, as recommended by Almanasreh et al.<sup>12</sup>. Through the identification of the recently transplanted patients the pharmacotherapeutic follow-up is initiated<sup>13</sup>. Daily the prescriptions are validated according to criteria of necessity, effectiveness and safety by the clinic pharmacist<sup>12</sup>, that is, are analyzed in relation to pharmaceutical form, dosage, dosing, administration via and symptoms presented by the patient.

The pharmaceutical practice was based on the protocols of the hospital's liver and kidney transplant service and the Ministry of Health of Brazil guidelines<sup>14-17</sup>. As reference information related to the medicines used by transplant patients (uses, dosing, dose adjustments, administration, drug interactions and compatibility, adverse effects) the databases Medscape<sup>18</sup> and Micromedex<sup>19</sup> were consulted, as well as scientific papers, as needed.

The role of the pharmacy team was to identify, prevent and resolve drug-related problems that account for the risk or occurrence of negative outcomes associated with medication (rNOM/NOM), thereby carrying out the PI necessary. This study focused on the monitoring and evaluation of clinical outcomes achieved by checking laboratory and clinical parameters of the patient to see if the pharmacist's performance had influence on therapeutic results.

Pharmaceutical interventions were carried with multidisciplinary team, patient or caregiver and consisted of a change or suggestion for change in therapy, drug information, patient counseling or lab tests order, being performed face-to-face and in multiple contacts an admission of the patient or at the time of prescription.

We analyzed the information recorded on a standard form and entered in a database. The epidemiological variables of the study were: gender, age and type of transplant ('kidney' or 'liver'). The variables related to clinical activities of the pharmacist were: Drug-related problem (DRP); negative result associated with medication (NOM) / risk of NOM (rNOM), Drug involved in DRP; Category of NOM / rNOM; Health problem; Pharmaceutical intervention (PI); Time of PI; Contact for PI; Significance of PI; Clinical outcome, which were classified according to terms used in the institution, standardized by consensus by Clinical Pharmacy Service of the hospital and based on a theoretical framework<sup>13,20</sup> (Table 1).

Categorical variables were expressed as frequencies and percentages and continuous variables as means and standard deviations. Statistical analysis was performed using Fisher's exact test<sup>21</sup> in the Statistical Package for Social Sciences (SPSS), version 17.0, where  $p < 0.05$  was considered significant.

The study was conducted in accordance with the guidelines and regulatory norms of research involving human subjects and was approved by the Research Ethics Committee (CAAE: 36975414.9.0000.5045).

**TABLE 1.** Definition and classification of variables related to clinical pharmacist activities

Variable	Definition/Classification
Drug-related problem (DRP)	Situation where drug use causes or may cause a negative result associated with medication (NOM) <sup>22</sup> .
Drug involved in DRP	Medication associated with problem that causes or can cause an NOM, classified according to ATC (Anatomical Therapeutic and Chemical Classification) <sup>23</sup> .
NOM/risk of NOM (rNOM)	The patient shows at least risk of developing a health problem associated with medication 'rNOM' or the patient has a health problem associated with medication 'NOM' <sup>24</sup> .
Category of NOM/rNOM	Classified according to the Third Consensus of Granada as: Necessity (untreated health problem or effect of unnecessary medicine) Effectiveness (non-quantitative ineffectiveness or quantitative ineffectiveness) and Safety (non-quantitative safety problem or quantitative safety problem) <sup>25</sup> .
Health problem	Any complaint, observation or fact viewed as a deviation from normal and that affected, affects or can affect functional capacity of patient <sup>25</sup> .
Pharmaceutical intervention (PI)	Measure planned, documented and performed together with health care professionals or with patient, with the objective of resolving or preventing problems that interfere or can interfere with drug therapy <sup>26</sup> .
Time of PI	Time at which the intervention is performed, categorized as: Admission (done after medication reconciliation at admission), Hospitalization (done after evaluation of the prescription of the hospitalized patient), Pharmacotherapeutic follow-up (done during pharmacotherapeutic follow-up of hospitalized patient) and Discharge (done after medication reconciliation at discharge from the hospital or during orientation of the patient).
Contact for PI	Professional, patient or caregiver through whom intervention is carried out: Patient, caregiver, doctor, nurse, pharmacist or others.
Significance of PI	Measure of importance PI in drug therapy and its contribution to improving the care of the patient, classified as: Appropriate (enhances the quality of care, quality of life of the patient or quality of therapy), Indifferent (did not produce significant changes in care of the patient) and Inappropriate (decreased the quality of care or quality of therapy) <sup>27</sup> .
Clinical outcome	Categorized according to Cipolle, Strand and Morley, with adaptation, as: Improved (less health problem after PI), Stable (health problem with positive or negative development after PI), Worsened (worse health problem after PI), Not evaluated (outcome of health problem was not evaluated) and Prevented (PI prevented DRP from being a health problem) <sup>28</sup> .

## RESULTS

The present study analyzed the records of 577 DRP, occurring at a mean rate of  $82.4 \pm 35.5$  DRP/month. A total of 131 patients were involved in the DRP identified, with a mean of  $4.5 \pm 3.06$  DRP/patient. They had a mean age of  $49.7 \pm 10.9$  years (minimum 15 and maximum 78 years), 63.4% (n=83) were male. Kidney transplant patients accounted for 58% (n=76) and 42% (n=55) were liver transplant patients.

Among the DRP identified, the most common were 'Necessary drug not prescribed' (21.7%, n=125), 'Overdosing' (16.8%, n=97) and 'Underdosing' (16.1%, n=93) (Table 2).

The drug-related problems involved 605 medications, where in 28 cases, two drugs associated with the problem. The main drugs were 'ganciclovir' (13.4%, n=81) 'tacrolimus' (5.5%, n=33) and 'pyridoxine' (5.0%, n=30). The most common categories, according to the ATC, were Anti-infectives for systemic use (38.3%, n=232), Digestive tract and metabolism (16.5%, n=100), Blood and hematopoietic organs (13.7%, n=83) and Antineoplastic and immunomodulatory agents (10.4%, n=63).

Among the drug-related problems identified, the main pharmaceutical interventions performed were 'Dose (adequacy)' (33.4%, n=193), 'Inclusion of medication' (21.1%, n=122) and 'Suspension of medication' (21.1%, n=122). The PI were performed to resolve or prevent the occurrence of health problems associated with the medication, where the main ones were 'Adverse effects' (29.5%, n=170), 'Infection' (23.0%, n=133) and 'Rejection' (7.1%, n=41) (Table 3).

After the completion of the pharmaceutical interventions, in 97.1% (n=560) of cases, the patient showed risk (rNOM) of developing a health problem associated with the medication or worsening, associated with the drug, of an existing health problem; and in 2.9% (n=17) of cases, the patient had, in fact, a health problem associated with the medicine (NOM).

The risk or the occurrence of NOM was mainly of type 'untreated health problem' (37.8%, n=218), 'quantitative safety problem' (25.8%, n=149) and 'quantitative ineffectiveness' (17.9%, n=103). Clinical outcomes 'prevented' (83.4%, n=481) and 'improved' (10.2%, n=59) were found most often, and in 95.5% (n=551) of cases, the PI was 'accepted' (Table 4).

Statistical analysis was performed to determine the relationship between the occurrence of negative outcomes associated with medication

or risk of negative outcomes associated with medication with the acceptance of PI and the relationship between clinical outcome and acceptance of PI. For statistical analysis, the clinical outcomes 'prevented' and 'improved' were grouped in the same category, represented by the outcome 'desirable' and the outcomes 'stable', 'worsened' and 'not evaluated' were grouped in the category 'undesirable.' After analysis, it was observed that in 30.8% (n=8) of cases of PI not accepted (n=26), the patient showed an NOM, demonstrating a significant relationship between the non-acceptance of the PI and the occurrence of an NOM. It was also observed that in 97.6% (n=538) of cases where there was acceptance of PI (n=551), the clinical outcome was desirable, thereby demonstrating a significant relationship between acceptance of the PI and the outcome clinical 'prevented' or 'improved' regarding health problem (Table 5).

Pharmaceutical interventions were performed at all stages of care of the transplant patients during hospitalization, where the majority of PI (54.7%, n=331) involved drug-related problems identified during 'Pharmacotherapeutic follow-up', which was performed with newly transplant patients, with emphasis on the monitoring of potentially dangerous drugs, immunosuppressant, prophylactic antibiotics, prevention and management of drug interactions and incompatibilities, dose adjustment for renal function, and monitoring of serum levels of immunosuppressant and ADR. The PI done during 'hospitalization' (32.1%, n=185), started with the daily pharmaceutical analysis of prescription medications.

The medication reconciliation process was responsible for 2.8% (n=16) of PI performed in 'admission' of the patient, at which point the regular drugs used before admission were reviewed and compared with the prescription, with the aim of identifying possible discrepancies. At the time of discharge from the hospital, 7.8% (n=45) of PI aimed to ensure that the necessary medications were appropriately prescribed allowing the continuous proper use by the patient at home.

The contact for the pharmaceutical interventions was mainly with the 'doctor' (96%, n=554) and 99.5% (n=574) of PI cases were considered 'appropriate,' because their objective was to increase the quality of care, the quality of life or quality of therapy (Table 6).

**TABLE 2.** Category Drug-related problems (DRP, n=577) identified

Drug-related problem	n	%
Necessary drug not prescribed	125	21.7
Overdosing	97	16.8
Underdosing	93	16.1
Prescribed unnecessary drug	39	6.8
Unavailability (lack)	35	6.1
Inadequate treatment time	34	5.9
Unavailability (not standard)	27	4.7
Inadequate dilution/reconstitution	18	3.1
Inadequate scheduling	15	2.6
Therapy duplication	15	2.6
Test not requested/done	15	2.6
Inadequate administration route	14	2.4
Inadequate selection	13	2.3
Incorrect writing	9	1.6
Lacking/inadequate documentation	8	1.4
Interaction (drug-drug or drug-food)	6	1.0
Adverse drug reaction	6	1.0
Others	8	1.4
Total	577	100.0

**TABLE 3.** Category Pharmaceutical interventions (n=577) and Health problems (n=577)

Pharmaceutical intervention	n	%	Health problem	n	%
Dose (adequacy)	193	33.4	Adverse effects	170	29.5
Inclusion of medication	122	21.1	Infection	133	23.0
Suspension of medication	60	10.4	Rejection	41	7.1
Adequacy of dispensation process	40	6.9	Peripheral neuropathy	28	4.9
Treatment time (adequacy)	31	5.4	Anemia	27	4.7
Substitution of medication	22	3.8	Toxicity	21	3.6
Scheduling (adequacy)	20	3.5	Hypokalemia	19	3.3
Dilution/reconstitution (adequacy)	19	3.3	Hyperkalemia	15	2.6
Requisition of necessary tests	16	2.8	Gastric discomfort	13	2.3
Pharmaceutical form (adequacy)	15	2.6	Hypomagnesemia	12	2.1
Administration route (adequacy)	12	2.1	Hypertension	10	1.7
Correction of written mistake	10	1.7	Others	88	15.2
Dosage (adequacy)	5	0.9			
Others	12	2.0			
Total	577	100.0	Total	577	100.0

**TABLE 4.** Category Result Negative Associated with Medication (NOM) or risk NOM (rNOM) (n=577), Clinical outcome (n=577) and Acceptance of Pharmaceutical Intervention (PI) (n=577)

NOM/rNOM	n	%	Clinical outcome	n	%	Acceptance of PI	n	%
Untreated health problem	218	37.8	Prevented	481	83.4	Yes	551	95.5
Effect of unnecessary medication	42	7.3	Improved	59	10.2	No	26	4.5
Non-quantitative ineffectiveness	23	4.0	Stable	17	2.9			
Quantitative Ineffectiveness	103	17.9	Worsened	9	1.6			
Non-quantitative safety problem	42	7.3	Not evaluated	11	1.9			
Quantitative safety Problem	149	25.8						
Total	577	100.0	Total	577	100.0	Total	577	100.0

**TABLE 5.** Correlation of pharmaceutical intervention (PI) acceptance with negative result associated with medication (NOM) or risk of NOM (rNOM) and clinical outcome

		Acceptance of PI						
		Yes		No		Total		
		n	%	n	%	n	%	
NOM	NOM	9	1.6	8	30.8	17	2.9	*p<0.001
	rNOM	542	98.4	18	69.2	560	97.1	
Total		551	100.0	26	100.0	577	100.0	
Clinical outcome	Desirable	538	97.6	2	7.7	540	93.6	*p<0.001
	Not desirable	13	2.4	24	92.3	37	6.4	
Total		551	100.0	26	100.0	577	100.0	

Legend: \*p<0.05, Fisher's exact test (SPSS version 17.0). 'Desirable': situation in which clinical outcome was 'Prevented' or 'Improved'; 'Not desirable': situation in which clinical outcome was: 'Stable', 'Worsened' or 'Not evaluated'.

**TABLE 6.** Classification of time of pharmaceutical intervention (PI) (n=577), contact for PI (n=577) and clinical significance of PI (n=577)

Time of PI	n	%	Contact for PI	n	%	Significance of PI	n	%
Pharmacotherapeutic follow-up	331	57.4	Doctor	554	96.0	Appropriate	574	99.5
Hospitalization	185	32.1	Nurse	20	3.5	Indifferent	2	0.3
Discharge	45	7.8	Patient	2	0.3	Inappropriate	1	0.2
Admission	16	2.8	Pharmacist	1	0.2			
Total	577	100.0	Total	577	100.0	Total	577	100.0

## DISCUSSION

Our study evaluated the clinical pharmacy activities in a post-transplant inpatient unit, and we identified DRP, which were addressed by the clinical pharmacist specialized in transplantation and the pharmacy residents in transplant, together with the multidisciplinary team or the patient, to be resolved. In fact, the literature shows the relevance of including the pharmacist in the team caring for the transplant patient<sup>5,6,10,29</sup> and the benefits arising from the participation of the pharmacist specialist, positively influencing the achievement of desired clinical outcomes<sup>30</sup>. Also, the resident in the care team of the transplant patient cooperates for the safety of the care process and is useful in preventing the occurrence

of DRP<sup>11</sup>. Nunes et al. reported that the presence of pharmacy residents in the hospital environment allows them to make interventions in the environment of the wards at times close to those when the problems occur, often preventing such problems from resulting in damage to the patients, which was also observed in our service<sup>31</sup>.

The most frequently identified problems were related to necessary medication not prescribed, overdosing and underdosing, and therefore, the main NOM or rNOM found were untreated health problem, quantitative safety problem and quantitative ineffectiveness, similar to that found by Chisholm et al. in a study that identified 844 problems with drugs in transplant patients, and most of them involved an untreated indication, overdosing and underdosing<sup>32</sup>. Stemer and Lemmens-Gruber also showed that in most studies, the most common problems identified

by the pharmacist in the transplant service were those related to incorrect dose<sup>6</sup>. In our center, we found that the pharmacist, in monitoring the serum levels of immunosuppressant (tacrolimus, cyclosporine and everolimus) and providing dose adjustment for renal function of the patient, identified problems of inadequate dose and intervened with physicians to avoid ineffectiveness or safety of treatment. The pharmaceutical intervention in patients with kidney disease may be associated with definite benefit in the evolution of renal function<sup>33</sup>.

After identifying the drug-related problems, the main recommendations suggested by the pharmacist were adjustment of the dose, inclusion of a drug and suspension of a drug, to resolve or prevent the occurrence or worsening of health problems: adverse effects, infection and rejection, among others. It is clear, therefore, the active participation of the pharmacist in the management of the most worrisome problems related to post-transplant drug therapy. One of the greatest challenges is maintaining a balance of immunosuppression, given that an overdosing can lead to toxicity, especially nephrotoxicity in the case of calcineurin inhibitor, adverse effects such as hypercalcemia, diabetes, hyperlipidemia, hypertension and gastrointestinal complications, and increase risk of infections, such as cytomegalovirus, herpes and candidiasis; on the other hand, underdosing can lead to rejection and graft loss<sup>6</sup>.

We found that the categories of drugs involved most frequently in DRP were anti-infectives for systemic use, digestive tract and metabolism, blood and hematopoietic organs and antineoplastic and immunomodulatory agents, which is consistent with the prescription profile for hospitalized transplant patients, who generally use immunosuppressant, prophylactic drugs recommended in the protocol, antibiotics in the case of infection, and medications for the treatment of comorbidities. This result was similar to that found by Stermer and Lemmens-Gruber, who showed that the classes of drugs most involved in the intervention of clinical pharmacist in transplantation are immunosuppressive, cardiovascular and antibiotic drugs<sup>6,34</sup>. In our study, the class of blood and hematopoietic organs had a frequency higher than that found in the literature, involving mainly studies performed on an outpatient basis, while our study was conducted in an inpatient unit, where one sees a different prescription profile<sup>6,10</sup>.

In total, there was a clinical outcome of prevention or improvement in health problems in 93.5% of cases, and the problem remained stable in 2.9% of cases. There have been no other studies assessing clinical outcome after PI in hospitalized kidney transplant patients, making this study different.

Our acceptance rate of interventions was close to that reported by other authors<sup>5,10,11</sup>. An important finding of this study, not addressed in other studies, was the statistically significant relationship between the acceptance of the pharmaceutical interventions and the clinical outcome of prevention or improvement in health problem as well as between the non-acceptance of the PI and the occurrence of negative outcomes associated with medication, demonstrating that the participation of the clinical pharmacist in the therapeutic decision, at the time of prescription, in fact, produces a favorable clinical impact on treatment.

The main time to identify drug-related problems was during pharmacotherapeutic follow-up, which showed the need to perform this process in an inpatient post-transplant unit, as a tool for promoting the safety of transplant patients, so as to identify, prevent and resolve more problems due to drugs, compared with the analysis of prescription focused only on drug therapy. The process of medication reconciliation accounted for interventions at admission and discharge of the patient. Viktil and Blix demonstrated that the participation of the clinical pharmacist in the medication reconciliation, pharmacotherapeutic follow-up and guidance in the hospital, performing pharmaceutical interventions in an integrated manner with the health care team, results in improved clinical outcomes for the patient, as also observed in our work<sup>35</sup>.

We estimate that our data are able to represent the possible findings of the clinical pharmacist activities in other transplant centers with similar systematized activities because, although the study has been conducted in a single center in Brazil, the institution studied is considered as referral in this issue. Internationally, Brazil has currently a well-established structure for conducting transplant, being positioned as the second country in the world in absolute number of transplants, meeting the demand of

approximately 45% of the annual need for kidney transplants and 37% of liver transplantation<sup>36</sup>.

This work presents some limitations properly related to descriptive studies. To show results with greater accuracy, it would be important to compare with another institution. Also, our work helps disseminate the process including the documentation and nomenclature used in order to make possible the reproduction of this service in more hospitals, thus, other institutions may adopt this methodology to achieve desirable clinical outcomes, performing systematized processes in clinical pharmacy practice integrated with the multidisciplinary team.

## CONCLUSION

Our findings demonstrated that the clinical pharmacy activities conducted on post-transplant inpatients can identify, prevent and resolve drug-related problems and pharmaceutical interventions, carried at all stages of care of the inpatient post-transplant, in an integrated manner with the multidisciplinary team, were able to provide clinical outcomes in the prevention or improvement in health problems related to medication, such as adverse events, infection and rejection, contributing for the safety of the transplant patient during hospitalization.

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Authors have no conflict of interest to declare.

## Contributors

LSA, BSM, LFL, RMAC, FRO and VPM contributed to data collection. MMF and EDRN collaborated to the study planning and coordination. PYF collaborated to the study planning. All authors contribute to study conception, analysis and interpretation of results, writing and approval of the final version.

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