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Dehospitalization: pharmacoeconomic aspects and the impacts of days saved from hospitalization in renal transplant patients using carbapenems

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Abstract

Objective: To carry out a cost-minimization analysis and of the outcomes in patients subjected to OPAT with carbapenems at a teaching hospital in the state of Ceará. **Methods**: This is a descriptive and retrospective observational study with a quantitative approach, characterized as a cost-minimization pharmacoeconomic analysis of the treatment performed with meropenem in patients hospitalized at the renal transplant units of a teaching hospital from the state of Ceará and in dehospitalized subjects that migrated to OPAT with ertapenem in outpatient services. The clinical outcome was assessed by measuring the readmission rate up to 30 days after finishing the treatment. **Results**: Eight patients were selected for the study. The microbiological profile verified predominance of infections caused by Enterobacteriaceae (*Klebsiella pneumoniae* and *Escherichia coli*), representing 75% of the microbiological isolates. The cost analysis showed a daily cost of US$ 60.04 in the treatment conducted with meropenem in hospitalized patients. In contrast, the daily cost for OPAT performed with ertapenem was US$ 78.79. The total cost of the treatments was US$ 7,515.89 for the institution, and, in an unprecedented way, we evidenced a cost reduced by US$ 1,029.45 if the treatment were entirely conducted during the hospitalization (US$ 6,484.44). **Conclusion**: An incremental cost was observed during dehospitalization when compared to the treatment performed during hospitalization; on the other hand, higher bed turnover can be observed, which makes it possible to perform more transplants.

Keywords: Antimicrobials, OPAT, Dehospitalization, Carbapenems.

Desospitalização: aspectos farmacoeconômicos e os impactos dos dias salvos de internação em pacientes transplantados renais em uso de carbapenêmicos

Resumo

Objetivo: Realizar uma análise de custo minimização e o desfecho dos pacientes submetidos a OPAT de carbapenêmicos em um hospital de ensino do estado do Ceará. **Métodos**: Trata-se de um estudo observacional descritivo e retrospectivo com abordagem quantitativa, caracterizado como uma análise farmacoeconômica de custo minimização do tratamento realizado com meropenem de pacientes internados nas unidades de transplante renal de um hospital de ensino do estado do Ceará e pacientes desospitalizados que migraram para a OPAT com ertapenem nos serviços ambulatoriais. O desfecho clínico foi avaliado a partir da mensuração da taxa de reinternação até 30 dias após a finalização do tratamento. **Resultados**: Foram selecionados oito pacientes para o estudo. O perfil microbiológico constatou o predomínio de infecções causadas por Enterobacteriaceaes (*Klebsiella pneumoniae* e *Escherichia coli*), representando 75% dos isolados microbiológicos. A análise de custo, constatou um custo diário de U$ 60,04 no tratamento conduzido com o meropenem em pacientes internados, em contraste, o custo diário na OPAT realizada com ertapenem foi de U$ 78,79. Os tratamentos realizados totalizaram um custo de U$ 7.515,89 para a instituição, e de forma inédita evidenciamos um custo reduzido de U$ 1029,45 se o tratamento fosse integralmente realizado durante a internação hospitalar (U$ 6.484,44). **Conclusão**: Observou-se um custo incremental durante a desospitalização em relação ao tratamento realizado durante internação hospitalar, em contrapartida pode-se observar uma maior rotatividade de leito, o que possibilita a realização de mais transplantes.

Palavras-chave: Antimicrobianos, OPAT, Desospitalização, Carbapenêmicos.

Introduction

Outpatient Parenteral Antibiotic Therapy (OPAT) consists in the intravenous administration of antimicrobial therapy on at least two separate occasions and on different days, either on an outpatient or home care basis. It is designed for individuals with infectious conditions (skin and soft tissue infections, pulmonary system infections, Central Nervous System infections, intra-abdominal infections, cardiovascular/bloodstream infections and urogenital tract infections, among others) requiring parenteral treatment but who are stable enough not to require hospitalization[1].

This strategy has been growing over the years, becoming a service provision model in various countries, widely incorporated into the United States of America's and the United Kingdom's health care strategies[2,3], as it has shown positive aspects in terms of hospitalization costs and bed occupancy, in addition to beneficial impacts on quality of life for the patients and their family members. In Brazil there are guidelines established by health authorities[4] aiming at regulating and implementing this strategy; however, studies assessing its implementation feasibility are scarce.

Carbapenems (meropenem, imipenem and ertapenem) constitute a special group of broad-spectrum antimicrobials with essential use in the treatment of infections caused by Extended-Spectrum Beta-Lactamases (ESBLs)[5]. Strategically, this medication class is among the most commonly employed by antimicrobial stewardship programs during OPAT in the dehospitalization process. In this scenario, ertapenem has essential characteristics that make it an excellent therapeutic option during OPAT, given its optimal therapeutic convenience (once a day dosage) and broad action spectrum[6,7].

Numerous international studies emphasize the benefits of OPAT with carbapenems, specifically the migration to outpatient treatment with ertapenem, given the greater convenience for the patients, avoiding prolonged stays in hospital institutions and reducing the risks associated with hospital-acquired infections, especially in immunocompromised patients (transplant recipients), in addition to the pharmacoeconomic aspects[6,8,9], where transitioning to an outpatient regime with ertapenem would lead to cost reductions for health services.

In Brazil there are no studies evidencing the effectiveness, safety and, especially, the economic viability of OPAT with antimicrobials when compared to in-hospital treatments with this class of medications. In this context, the objective of this study was to evaluate the pharmacoeconomic outcome of implementing OPAT with ertapenem after using meropenem during hospitalization.

The study specifically aims at assessing the hospitalization-free days and at assessing cost minimization of the treatment during the strategy through the implementation of Outpatient Parenteral Antimicrobial Therapy (OPAT).

Methods

A descriptive, observational and retrospective study was conducted, characterized as a pharmacoeconomic cost-minimization analysis (calculating the cost difference between alternative interventions that produce equivalent results) of the antimicrobial treatment of patients admitted to the renal transplant unit at the Walter Cantídio University Hospital (*Hospital Universitário Walter Cantídio*, HUWC) who initiated their therapeutic path during hospitalization with meropenem and who, after positive culture results with a sensitive microorganism, completed their treatments in the OPAT regime using ertapenem at the institution's day-hospital service. HUWC has 198 beds and is characterized for providing high-complexity services, ranging from organ and tissue transplants to outpatient care, distributed across its various specialties.

Data collection took place from February to March 2023, by tracking the dispensing of in-hospital meropenem and outpatient ertapenem between January 2021 and December 2022, in the following institutional systems: Master® and the University Hospital Management App (*Aplicativo de Gestão para Hospitais Universitários*, AGHU®).

Initially, the information collected referred to demographic (gender, age, mean hospitalization time) and epidemiological (prior use of antimicrobials and previous hospitalizations in health institutions) characteristics of the patients hospitalized in the renal transplant service that were using meropenem and completed their treatment with outpatient ertapenem after hospital discharge. In relation to the clinical outcome, the hospital readmission rate was calculated within 30 days after treatment completion and clinical cure. All the cultures were screened using the Master® institutional system, individually analyzed, and classified based on the microorganism isolated and its sensitivity profile.

After tracking the medications dispensed, a review of medical records was conducted to assess treatment duration and doses administered. The following values were used for the pharmacoeconomic calculation: bed-day (as recommended in the Management System of the SUS Table of Procedures, Medications and Orthoses and Prostheses (*Sistema de Gerenciamento da Tabela de Procedimentos, Medicamentos e Órteses e Próteses*, SIGTAP); inputs necessary for drug administration; hospitality; and medication acquisition cost. In terms of the inputs, the values of the Infusion Pump Set (IPS), extension set, intravenous infusion device (*Scalp*) and syringe were considered. The prices were obtained from the Master® system.

In the dehospitalization setting, the treatment cost was calculated based on the hospital-day value, equivalent to the bed-day value, plus the purchase price of ertapenem and of the supplies used for the Infusion Pump Set (IPS), extension set, intravenous infusion device (*Scalp*) and syringe.

The cost minimization calculation was based on the difference between the treatment carried out with meropenem during hospitalization, based on a complete therapeutic course of 10 to 14 days with meropenem (unit price US$ 3.95), and the treatment initiated in-hospital with meropenem and completed on an outpatient basis with ertapenem (unit price US$ 48.42), using the exchange rate provided by the Central Bank of Brazil in April 2023.

The research was conducted after due approval by the Research Ethics Committee, under protocol number 3,697,674.

Results

The results obtained identified 8 patients who underwent OPAT with ertapenem during the period analyzed. In relation to gender, there was predominance of female subjects, accounting for 75%

of the patients, when compared to 25% males (2 patients). The mean age of the patients selected in the study was 49 years old (SD: ±14.36). The mean hospitalization time for the patients undergoing hybrid treatments (hospitalization + day hospital) was 15 days (SD: ±10.14) (**Table 1**).

The mean treatment duration for these patients, combining hospitalization and day hospital, was 14 days (SD: ±1.41). In relation to antimicrobial use, there was a mean of 6 days for meropenem (SD: ±2.55) and 8 days for ertapenem (SD: ±2.79) (**Table 1**).

Table 1. Demographic data corresponding to the renal transplant patients in the institution

Variables		Renal transplant		
		N	**DP**	**%**
Gender	Male	2		25
	Female	6		75
Age	Mean (years old)	49	± 14,36	-
Previous antimicrobial use	-	5		62,5
Hospitalization time	Mean (days)	15	±1,41	-
Outcome	Cure	8		100%
	Readmission	0		0%

Source: PGTA/HUWC database.

In the analysis of the microbiological aspects, two cultures did not present microbiological growth. However, due to the patient's clinical aspects, it was decided to continue the treatment on an outpatient basis (day hospital). In total, 06 cultures were positive, with growth of *Klebsiella pneumoniae* in 03 isolates (50% of the positive samples) and *Escherichia coli* also in 03 isolates (50% of the positive samples). We note that all cultures showed a sensitivity profile to carbapenems, enabling dehospitalization (**Table 2**).

Table 2. Prevalence of microorganisms isolated in the cultures from the renal transplant patients

Microorganism	N	%
Klebsiella pneumoniae	3	37,5
Escherichia coli	3	37,5
Negative	2	25

Source: PGTA/HUWC database.

The pharmacoeconomic analysis evidenced a daily cost of US$ 60.04 for the meropenem treatment in hospitalized patients. In contrast, the daily cost for OPAT with ertapenem was US$ 78.79. In total, 53 treatment days were conducted during hospitalization, and 55 days in the outpatient regime (day hospital), resulting in a total cost of US$ 7,515.89 for the institution. Considering that the treatments were entirely performed during hospitalization, the cost would be US$ 6,484.44, representing a reduction of US$ 1,029.45 when compared to the hybrid treatment (patients subjected to OPAT) (**Table 3**).

Table 3. Minimization cost analysis between in-hospital treatment and OPAT

	Daily treatment cost	Total of the treatment conducted
OPAT (ertapenem)	US$ 78,79	-
Hospitalization (meropenem)	US$ 60,04	US$ 6.484,44
OPAT + Hospitalization (ertapenem and meropenem)	-	US$ 7.515,89
Cost difference	US$ 18,75	US$ 1.031,44

Source: PGTA/HUWC database.

With the dehospitalization process, it was possible to achieve a total of 55 hospitalization-free days for the 8 patients that had the opportunity to undergo outpatient antimicrobial therapy.

Discussion

In terms of pharmacoeconomic data, this study allowed revealing conflicting results with the literature when comparing patients who underwent treatment in the in-hospital setting and those who migrated to OPAT, thus verifying in a novel way relatively higher costs in the group subjected to the outpatient regime. Additionally, we presented an infection profile of the post-renal transplant patients entirely caused by *Enterobacteriaceae* (*Klebsiella pneumoniae* and *Escherichia coli*), thus contributing to the development of the institution's epidemiological profile.

Nearly 62% of the infections by *Klebsiella pneumoniae* in renal transplant recipients have a urinary topography[10]. It is important to note that Urinary Tract Infections (UTIs), especially in immunosuppressed patients, can progress to sepsis, representing a significant cause of morbidity and mortality, including loss of the transplanted organ. In this scenario, bacterial resistance becomes a significant challenge in the clinical practice with this population segment, given the production of resistance mechanisms such as ESBLs[11]. Consequently, a similar profile to the one found in the literature was found, assuming that 50% of the infections were caused by *K. pneumoniae* and 50% by *E. coli*, a prevalent microorganism in infections among transplant patients[12].

The antimicrobials included for OPAT in this study were meropenem and ertapenem. According to the literature, ertapenem is a broad-spectrum carbapenem and the ideal choice for OPAT due to its parenteral single dose a day and good *in vitro* activity against ESBL bacteria, which represented nearly 75% of the microorganisms isolated in our study, taking into account that 2 of the collected cultures were negative[12]. Such being the case, the OPAT strategy with the listed medications would ensure safe therapy for patients in ambulatory regimes.

Pharmacoeconomic analyses in the field of antimicrobials play a crucial role in developing strategies that seek to minimize costs in health services, such as OPAT, so that investments can be redirected to other areas in need[13]. Our analysis evidenced that

implementing OPAT with carbapenems in post-renal transplant patients had an atypical behavior, resulting in incremental costs when compared to in-hospital treatment.

In a study conducted in Chile between 2009 and 2011 with 192 pediatric patients, the OPAT treatment efficacy, safety and cost were compared to in-hospital treatments for patients affected by urinary tract infections. The OPAT treatment proved to be equivalent to in-hospital care, also showing that the prevalence of adverse events was higher in the inpatient regime group. The treatment mean direct cost was four times higher among the hospitalized patients, mainly due to the bed daily cost, indicating that home therapy would be an economically viable alternative for treatment[14].

One of the reasons that may explain the incremental cost observed in this study, diverging from most literature reports directed to dehospitalization pharmacoeconomic analyses, is based on the discrepancy between the unit price of meropenem and ertapenem, generic and similar, respectively.

In addition to the cost aspects already explained, there was also an impact of early dehospitalization on the patients who migrated to OPAT, with a period of approximately 2 months (55 days) with none of the aspects affecting the patients' quality of life due to their return home and partial resumption of their daily activities, in addition to lowering their exposure to the complication risks resulting from hospitalization, such as new opportunistic infections.

In a study conducted with a population of older adults in a tertiary-level hospital, Izaias et al. (2014) pointed out that the mean hospitalization time for the patients with hospital-acquired infections resulted in a 15-day increase when compared to those who were not affected by infections during their hospitalization, thus reflecting in increased costs due to antibiotic treatments, tests and other procedures[15]. Therefore, in addition to all the potential benefits already mentioned, the dehospitalization process would also lead to greater bed turnover in the institution, allowing for the possibility of new admissions and, consequently, the performance of new transplants.

Among other aspects, studies show cost minimization when the OPAT strategy is implemented[16]. In this analysis, a 100% cure rate was observed for the patients undergoing outpatient antimicrobial therapy, indicating positive aspects in the patients' quality of life and no compromise in the effectiveness of their therapeutic regime.

Estimates highlight that the achieved savings reach over US$ 44,000.00 per Quality-Adjusted Life Year (QALY) if OPAT is adopted instead of hospitalization. Studies like these show how beneficial OPAT services can be for the patients and how economical it can be for the institutions, when considering other variables such as the patients' quality of life and the reduction of their exposure to the hospital environment[16].

The following stand out among the limitations of the current study: the higher cost of acquiring ertapenem when compared to meropenem for the institution, which was one of the main reasons for conflicting results with other pharmacoeconomic analyses; as well as the small number of patients selected for the study. In addition, there was no screening for possible adverse reactions during antimicrobial therapy; therefore, new prospective studies are required so that this aspect can be monitored.

Conclusion

An incremental cost was observed during dehospitalization when compared to treatments performed during hospitalization. On the other hand, increased bed turnover can be observed, consequently leading to more renal transplants due to potential bed availability and contributing benefits to hospitalized patients, who will be able to return to their normal activities with less exposure to healthcare-associated infections.

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Collaborators

TCF contributed to writing and developing the project.

JAS contributed to writing and reviewing the project.

MGL contributed to writing and reviewing the project.

ABO contributed to preparing, developing and reviewing the project.

CCA contributed to preparing, developing and reviewing the project.

ESG contributed to preparing, developing and reviewing the project.

HPR contributed to preparing, developing and reviewing the project.

Declaration of conflict of interests

The authors declare that there is no conflict of interest in relation to this article.

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