Outpatient parenteral antimicrobial therapy in Brazil

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Introduction

The use of outpatient parenteral antimicrobial therapy (OPAT) as a treatment strategy with the aim of dehospitalizing patients has been growing since its advent during the 1970s.[1] OPAT has become a safe and standardized practice for patients presenting with various infections who require long-term parenteral antimicrobial therapy. International consensus guidelines have determined that OPAT can be performed in ambulatory care clinics, specialized infusion centers, or at home.[1–3] In Brazil, initiatives to implement OPAT regimens began in the 2010s, with the publication of national guidelines by the Brazilian Society of Infectious Diseases in 2017.[4]

Healthcare structure in Brazil and OPAT

Brazil has a robust public health system, *Sistema Único de Saúde* (SUS), that provides universal health coverage for every person living in the country, with the Brazilian population estimated at 217 million people in 2023.[5] It is funded by the federal administration but has administrative responsibilities at all levels of government: federal, state, and municipal. The delivery of care is handled at the state and municipal level. Brazilian Constitution defines the universal right to comprehensive care at all levels such as primary, secondary, and tertiary. SUS offers many services free of charge such as prevention services, primary care, outpatient care, inpatient care, maternity care, mental health services, pharmaceuticals, dental care, vision care, and physical therapy for residents and visitors, including undocumented individuals.[6] Home care is also contemplated by SUS through a specific policy called 'Melhor em Casa' (Better at Home) that, although it is quite comprehensive, has not yet been implemented in all 5560 municipalities in the country.[7] Despite the scope of the SUS's activities allowing the performance of OPAT, a specific health policy for its practice has not yet been established.

Private sector is also present at the financing and provision levels of healthcare. Private health insurance (PHI) is voluntary and can be classified as duplicate coverage as it covers medically necessary curative services that are also covered under SUS. In 2019, 24.2% of Brazilians had PHI, while in 2008, this proportion was around 22%, about 50 million people by the current projection of country's population.[8]

In Brazil, OPAT is a treatment option available in both public and private health systems. For services linked to SUS, there is a predominance of use of ambulatory care units and day hospitals for the infusion of antimicrobials. Usually, the patient or their caregivers are responsible for organizing transport to the healthcare unit for the infusion. In the private system, however, there is a predominance of home care as model of choice for OPAT.[9–12]

Organization of OPAT in Brazil and guidelines

In 2017, the Brazilian Society of Infectious Diseases published the recommendations for performing OPAT in Brazil. This document was prepared by a group of specialists and covers the guidelines for carrying out this treatment modality in the country, including the categories of health professionals necessary for its operation. Multidisciplinary team trained to make evaluations regarding patients' eligibility for OPAT and to conduct follow-up on this type of therapy. These team should be led by a physician, preferably an infectious diseases specialist with experience in using long-term parenteral antimicrobials. In addition, each team needs to include a nurse

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with experience in manipulating central venous access and a social worker. A clinical pharmacist may also be included in the team, although this is still an uncommon professional in most Brazilian healthcare services (Table 1).

These recommendations also provide information on venous access (with preference for using peripherally inserted central catheter) and care orientations (Table 2), as well as recommendations for appropriate dosages, dilution, reconstitution, and infusion of antimicrobials (Table 3), in addition to laboratory monitoring routines (Table 4). The elaboration of these guidelines considered the particularities of both healthcare services and patients in the country; therefore, only antimicrobials that can be administered once or twice a day were considered. Patients' social conditions and vulnerability factors were also taken into account among the factors determining eligibility for OPAT.[4] Considering aspects of patient safety for the Brazilian reality, self/carer administered OPAT is not allowed in Brazil and only healthcare professionals trained in handling venous accesses can infuse antimicrobials.

Experiences with OPAT with Brazil

The first experience of a structured OPAT program in Brazil was published in 2016 and reports the results of a 1-year partnership between a reference orthopedic hospital and the public (linked to SUS) municipal healthcare network in the city of São Paulo which started in 2013. This initiative made it possible to dehospitalize 116 patients, making 11,698 bed-days available for patients requiring hospitalization and few adverse events related to OPAT. This study motivated the development of national guidelines later published in 2017.[9] After the publication of the national guidelines, other studies were published reporting experiences with OPAT.

Two other studies that report the treatment of patients in SUS showed favorable results regarding clinical outcomes but were conflicting regarding the cost-effectiveness analysis. While a study carried out with 291 trauma patients in the south of Brazil showed that OPAT was effective in reducing costs, another study carried out with 23 kidney and liver transplant patients using carbapenems in the northeast region showed higher costs related to OPAT. In this case, the result was related to the higher cost of ertapenem, a carbapenem used on an outpatient basis as compared with meropenem, used for hospitalized patients.[10,13] Another study with 39 patients designed specifically to evaluate the cost-utility of OPAT for SUS, however, showed that this treatment modality was effective in this regard by allowing overall savings of 31.86% from the hospital perspective and 26.53% from the SUS perspective, with favorable clinical outcomes and perception of quality of life.[14]

Regarding OPAT in PHI, two other studies were published. Both studies analyzed a considerable number of patients (441 in one study and 278 in another) also reported favorable clinical outcomes, although they did not assess cost-effectiveness aspects. These two publications also report on the positive impact of antimicrobial stewardship programs in the context of OPAT.[11,12] Table 5 provides a summary of studies on OPAT in Brazil.

General considerations and future prospects

Although OPAT was adopted late in Brazil, with the first large-scale experience initiated in 2013 and reported in 2016, published reports show that the country's experiences with this type of treatment are favorable.[9–14] Publication of national guidelines, which considered the particularities of the country, allowed the dissemination of OPAT services and the advancement of dehospitalization in Brazil.[4] It is still necessary, however, to make progress with these strategies, especially regarding financing of antimicrobials. While there is no specific public policy for OPAT in SUS, this treatment modality may be unfavorable from a financial point of view in some situations, such as shown in one of the reported studies.[12] Creation of this policy and strengthening of existing programs such as 'Melhor em Casa' would certainly contribute to an even greater expansion of OPAT in Brazil and the consequent optimization of beds and hospital resources.

Within the scope of PHI, OPAT also shows strong expansion in Brazil and proves to be effective from a clinical point of view, lacking specific studies that corroborate the cost-effectiveness of this treatment modality in this model of healthcare system.

Table 1. Professionals required for an OPAT program and their attributes according to the Brazilian guidelines.

Professional	Main attributes
Physician (preferably an infectious diseases specialist)	Team leadership
	Clinical evaluation of patient's infectious conditions and their comorbidities
	Determination of whether clinical stability allowing OPAT exists
	Prescription of the antimicrobial to be used
	Participation in the decision of what type of catheter should be used by patients
	Participation in assessments on patient's and caregiver's capacity for comprehension
	Initial evaluation on patients who are recommended for OPAT
	Clinical and laboratory monitoring of patients undergoing OPAT
	Clinical evaluation of possible events presented during treatment
Nurse (with experience in manipulation of central lines)	Prescription of drug infusion procedures for OPAT (reconstitution and dilution of antimicrobials and duration of infusion) in accordance with the protocol
	Participation in the decision regarding what type of catheter should be used by patients
	Participation in assessments of patient's and caregiver's capacity for comprehension
	Supervision of antimicrobial infusion
	Daily inspection of the catheter insertion site and communication with the doctor in the event of abnormalities
	Minimum of once-weekly changing of dressings at catheter insertion site
	Patient guidance regarding catheter care
	Patient guidance regarding drug storage precautions
	Obtaining samples for carrying out laboratory tests
Social worker	Evaluation of patient's home sanitary conditions, in the event of referral for home care OPAT
	Participation in assessments of patient's and caregiver's capacity for OPAT understanding
	Documentation of patient's and their caregiver's consent to OPAT
	Evaluation of patient's social conditions for OPAT (especially transportation)
	Establishment of contact between hospital service and the reference center for OPAT
Clinical pharmacist	Participation in assessments of patient's and caregiver's capacity for OPAT understanding
	Participation in prescription of drug infusion procedures for OPAT (antimicrobial reconstitution and dilution, and duration of infusion), in accordance with the protocol
	Patient guidance about drug storage precautions
	Participation in clinical and laboratory monitoring of patients undergoing OPAT

OPAT, outpatient parenteral antimicrobial therapy.

Table 2. Types of central lines indicated for OPAT in Brazil according to the Brazilian guidelines.

Type of central line	Indication	Duration	Considerations
Valved peripherally inserted central catheter (valved PICC)	Antimicrobial treatment with estimated duration longer than 14 days	Up to 6 months	• Cost-effective • Easy insertion • Lower incidence of infection • Lower risk of air embolism and reflux • Higher safety for home care therapy
Tunneled semi-implanted central catheter	Antimicrobial treatment with estimated duration longer than 14 days	Up to 6 months	• Surgical implantation • Open extremity • Blockage using heparin solution is needed • Low risk of infection • Second choice for treatment, when insertion of PICC is not possible
Totally implanted central catheter	Antimicrobial treatment with estimated duration longer than 14 days	Up to 5 years	• High cost • Surgical implantation • Blockage using heparin solution is needed • Access through Huber needle, replaced every 7 days • High risk of infection with daily manipulation (generally indicated for chemotherapy against cancer, which requires less manipulation) • Indication only for OPAT should be avoided

OPAT, outpatient parenteral antimicrobial therapy; PICC, peripherally inserted central catheter.

Table 3. Recommendations and instructions for reconstitution, dilution, and infusion for the antimicrobials to be used within the OPAT regimen in Brazil according to the Brazilian guidelines.

Antimicrobial	Dosage and posology for normal renal and hepatic functions	Reconstitution	Dilution	Duration of infusion
Amikacin	15 mg/kg once a day	Not required	100–200 ml of 0.9% SS, 5% GS, or Ringer's lactate solution	30–60 min
Gentamicin	5 mg/kg once a day	Not required	50–200 ml of 5% GS	30–120 min
Cefepime	2 g twice a day	10 ml of sterile distilled water	50–100 ml of 0.9% SS, 5% GS, or Ringer's lactate solution	30 min
Ceftaroline	600 mg twice a day	20 ml of sterile distilled water	50–250 ml of 0.9% SS, 5% GS, or Ringer's lactate solution	30 min
Ceftazidime	2 g twice a day	5–10 ml of sterile distilled water	50–100 ml of 0.9% SS, 5% GS or Ringer's lactate solution	30–60 min
Ceftriaxone	2 g once a day	10 ml of sterile distilled water	50–100 ml of 0.9% SS, 5% GS, or Ringer's lactate solution	15–30 min
Ertapenem	1 g once a day	10 ml of sterile distilled water	50 ml of 0.9% SS	30 min
Meropenem	2 g twice a day	20 ml of sterile distilled water	250 ml of 0.9% SS or 5% GS	60 min
Vancomycin	15 mg/kg twice a day	10 ml of sterile distilled water	200 ml of 0.9% SS or 5% GS	60 min
Teicoplanin	6 mg/kg once a day	10 ml of sterile distilled water	50–100 ml of 0.9% SS, 5% GS, or Ringer's lactate solution	60 min

(Continued)

Table 3. (Continued)

Antimicrobial	Dosage and posology for normal renal and hepatic functions	Reconstitution	Dilution	Duration of infusion
Daptomycin	4–6 mg/kg once a day	10 ml of 0.9% SS	50 ml of 0.9% SS	30 min
Linezolid	600 mg twice a day	Not required	50–100 ml of 0.9% SS, 5% GS, or Ringer's lactate solution	30–120 min
Tigecycline	50 mg twice a day	Not required	50 ml of 5% GS	30–60 min
Anidulafungin	100 mg once a day	30 ml of its own diluent	100 ml of 0.9% SS or 5% GS	90 min
Caspofungin	50 mg once a day	10 ml of sterile distilled water	100 ml of 0.9% SS	60 min
Micafungin	100 mg once a day	5 ml of 0.9% SS	50 ml of 0.9% SS or 5% GS	60 min
Voriconazole	3–4 mg/kg twice a day	19 ml of sterile distilled water	200–250 ml of 0.9% SS, 5% GS, or Ringer's lactate solution	60–120 min
Amphotericin B (lipid complex)	5 mg/kg once a day	20 ml of sterile distilled water	200–500 ml of 5% GS	120 min
Amphotericin B (liposomal)	3–5 mg/kg once a day	10 ml of sterile distilled water	200–500 ml of 5% GS	120 min

GS, glucose solution; OPAT, outpatient parenteral antimicrobial therapy SS, saline solution.

Table 4. Recommendations on routine laboratory tests and monitoring of adverse events for OPAT in Brazil according to the Brazilian guidelines.

Antimicrobial	Laboratory tests to be performed and periodicity					Considerations
	Complete blood cell analysis	Renal evaluation (urea and creatinine)	Hepatic evaluation (AST, ALT, alkaline phosphatase, and gamma GT)	Potassium	CPK	
Amikacin	14 days	7 days	14 days	7 days	–	Ototoxicity may occur: monitor hearing and vestibular functions
Gentamicin	14 days	7 days	14 days	7 days	–	Ototoxicity may occur: monitor hearing and vestibular functions
Cefepime	14 days	14 days	14 days	–	–	
Ceftaroline	14 days	14 days	14 days	–	–	
Ceftazidime	14 days	14 days	14 days	–	–	
Ceftriaxone	14 days	14 days	7 days	–	–	
Ertapenem	14 days	14 days	14 days	–	–	A decrease in the convulsive threshold may occur
Meropenem	14 days	14 days	14 days	–	–	A decrease in the convulsive threshold may occur
Vancomycin	7 days	7 days	7 days	7 days	–	Serum level control (vancomycin) can be performed every 7 days
Teicoplanin	14 days	14 days	14 days	–	–	

(Continued)

Table 4. (Continued)

Antimicrobial	Laboratory tests to be performed and periodicity					Considerations
	Complete blood cell analysis	Renal evaluation (urea and creatinine)	Hepatic evaluation (AST, ALT, alkaline phosphatase, and gamma GT)	Potassium	CPK	
Daptomycin	14 days	14 days	14 days	–	7 days	
Linezolid	7 days	14 days	14 days	–	–	Optical neuropathy may occur: monitor visual acuity
Tigecycline	14 days	14 days	7 days	–	–	Nausea may occur even in the absence of hepatic enzyme alterations: consider concomitant administration of antiemetics
Anidulafungin	14 days	14 days	14 days	–	–	
Caspofungin	14 days	14 days	14 days	–	–	
Micafungin	14 days	14 days	14 days	–	–	
Voriconazole	14 days	14 days	14 days	–	–	
Amphotericin B (lipid complex)	7 days	3 days	7 days	3 days	–	Weekly test of magnesium may be necessary
Amphotericin B (liposomal)	7 days	3 days	7 days	3 days	–	Weekly test of magnesium may be necessary

ALT, alanine transaminase; AST, aspartate transaminase; CPK, creatine phosphokinase; GT, glutamyl transferase; OPAT, outpatient parenteral antimicrobial therapy.

Table 5. Summary of published studies on OPAT in Brazil.

Author	City	Healthcare system	Number of patients	OPAT venue	Main infections diagnoses	Main drugs used in OPAT	Conclusions of the study
Oliveira *et al.*[9]	São Paulo	SUS	116	Primary care facilities, day hospital	Chronic osteomyelitis, acute osteomyelitis, soft tissue infection	Teicoplanin, ertapenem, tigecycline	450 primary care health professionals were trained to manipulate catheters and monitor patients. Positive clinical outcomes, with only 3 OPAT-related adverse events. In 1 year, it was possible to redirect 11,698 bed-days to patients in need of orthopedic hospitalization
Psaltikidis *et al.*[14]	Campinas	SUS	39	Day hospital	Central nervous system syphilis, urinary tract infection, osteomyelitis	Ceftriaxone, amikacin, meropenem	Favorable clinical outcomes, with improved perception of quality of life by patients. OPAT allowed 1112 days less hospitalization and proved to be cost-effective compared with inpatient treatment

(Continued)

Table 5. (Continued)

Author	City	Healthcare system	Number of patients	OPAT venue	Main infections diagnoses	Main drugs used in OPAT	Conclusions of the study
Cassettari *et al.*[11]	São Paulo	PHI	441	Home care	Urinary tract infection, pulmonary infection, surgical site infection	Teicoplanin, ceftriaxone, meropenem	Low rate of treatment failure (0.4%). Outpatient stewardship program was effective and safe
Salles *et al.*[12]	Santo André	PHI	276	Home care, outpatient clinics	Pneumonia, urinary tract infection	Ceftriaxone	Palliative care and not having had a postdischarge physician office visit within the first 30 days after inclusion in the OPAT program were risk factors for hospital readmission and mortality
Loesch *et al.*[10]	Curitiba	SUS	291	Day hospital, home care	Urinary tract infection, pneumonia, osteomyelitis	Not mentioned	OPAT allowed for significant cost savings and reduction in length of stay. OPAT also reduced risk. OPAT also reduced the risk of contamination of patients with multidrug-resistant bacteria
Freitas *et al.*[13]	Fortaleza	SUS	23	Day hospital	Urinary tract infection, bloodstream infection	Ertapenem (only)	95.65% clinical cure among patients with liver and kidney transplants and infections with Gram-negative bacilli susceptible only to carbapenems. Cost of treatment in OPAT was higher than that of hospitalization due to the high price of ertapenem (reference drug) compared with meropenem (generic drug)

OPAT, outpatient parenteral antimicrobial therapy; PHI, private health insurance; SUS, Sistema Único de Saúde (Brazilian public health system).

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Author contributions

Priscila R Oliveira: Data curation; Methodology; Writing – original draft; Writing – review & editing.

Vladimir Cordeiro Carval ho: Conceptualization; Writing – review & editing.

David Everson Uip: Writing – review & editing.

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