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Outpatient Parenteral Antibiotic Therapy in an Academic Practice in Rhode Island

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Abstract

Outpatient parenteral antimicrobial therapy (OPAT) is an increasingly utilized treatment modality that has been proven to be safe and cost-effective for treating infections that require prolonged antimicrobial treatment. Adequate patient selection, a structured OPAT team with an effective communication system, and routine clinical monitoring are key elements to establish a successful OPAT program. The Infectious Diseases and Immunology Center at The Miriam Hospital offers a multidisciplinary OPAT model coordinated by infectious diseases specialists and serves as a major referral center in Rhode Island.

Keywords

OPAT; antibiotics; infection; Rhode Island

Introduction

Outpatient parenteral antimicrobial therapy (OPAT) refers to the administration of intravenous antimicrobials to patients who suffer from chronic infections that warrant parenteral therapy but these patients are otherwise stable enough to receive this therapy in an outpatient setting. Since its introduction in the 1970's, OPAT has been shown to be a safe, practical and cost-effective treatment modality.[1] In the United States, it is estimated that more than 250,000 Americans receive OPAT services every year.[2] OPAT helps to reduce healthcare costs by reducing the length of inpatient hospitalizations and the uptake of OPAT has been facilitated by the development of antimicrobials with convenient dosing schedules and the development and utilization of convenient and safe long-term IV catheters.[3]

Structure of the OPAT Program

The Infectious Diseases and Immunology Center at The Miriam Hospital, located at 1125 North Main Street in Providence, is the largest provider of outpatient infectious diseases treatment in Rhode Island. The clinic provides longitudinal OPAT for persons who have been discharged from the hospital and serves as a specialty referral resource to community health care providers in New England. Every month, the clinic sees approximately 100 new patients, of whom 75% are patients who have been discharged from either Rhode Island Hospital or The Miriam Hospital on at least one IV antimicrobial medication.

According to guidelines released by the Infectious Diseases Society of America, key elements of a successful OPAT program include: 1) A health care team comprised of infectious diseases specialists that work in collaboration with the primary care or referring physicians, a nurse and pharmacist knowledgeable in antibiotic infusion therapy, and a case manager who can help coordinate care and manage reimbursements; 2) An accessible and rapid communication system between the patient and OPAT team members; and 3) Established policies that outline the responsibilities of each team member, offer patient education materials, and help measure outcomes. [4]

As outlined in Figure 1, the Miriam Hospital OPAT program starts with the patient being seen by the Infectious Diseases consultation team inside the hospital, or the patient is referred to the clinic by a community provider for infectious diseases evaluation. The OPAT physicians are responsible for ensuring the patient's suitability for OPAT, prescribing the intravenous antimicrobial regimen, formulating a treatment plan, and monitoring for adverse events or medical complications that may arise during the course of therapy. Once OPAT is considered appropriate, insertion of a long-term intravenous catheter for intravenous antimicrobial administration is arranged with interventional radiology or at an ambulatory infusion suite. A peripherally inserted central catheter (PICC) is the most common type of catheter used for OPAT administration. PICC lines are inserted into the basilic or brachial veins and extend into the superior vena cava; the positioning is confirmed with a chest x-ray. PICC lines can remain in place for over 90 days and seldom need to be exchanged.[5] Midline peripheral intravenous catheters, tunneled venous catheters or ports inserted for other purposes (i.e. parenteral nutrition, hemodialysis or chemotherapy) can also be used for OPAT.

Depending on the location of the patient, antimicrobials are infused either at a skilled nursing facility or at the patient's home. For home administration, the OPAT program partners with a community-based infusion company which provides dedicated pharmacists, arranges for home delivery of the antimicrobial medication, and provides nursing and educational support. OPAT delivered at the patient's home often involves visiting nurses and the patient's own family members who can assist with infusions. Patient's can even be taught to self-administer the antimicrobial safely, thus increasing the patient's independence and involvement with their own healthcare. Patients are typically seen by a visiting nurse at least once weekly to assess the IV catheter and to collect blood for routine laboratory testing as ordered by the prescribing physician. Constant communication and coordination between the patient and the OPAT team comprised of the pharmacist, visiting nurse, OPAT physician, and the referring physician has allowed us to successfully implement OPAT services to our patients. This process is greatly facilitated by a dedicated physician's assistant based within the Infectious Diseases and Immunology Center at The Miriam Hospital who acts a liaison between patients and physicians, evaluates patients at routine follow-up visits, and who is responsible for monitoring safety labs and adverse reactions to treatment in conjunction with the physicians. Patients discharged from the hospital are seen within 2–3 weeks, and then biweekly throughout the course of treatment.

Patient Selection and Clinical Indications

Candidates for OPAT include clinically stable patients who can understand the risks and benefits of therapy, have a safe environment to support care, and can assume the costs of therapy through their health insurance provider or self-pay. OPAT should be avoided in patients for whom oral antibiotic therapy is equally effective, continued hospitalization is warranted, or if a safe environment for OPAT cannot be established. Patients with active injection drug use often require intravenous antimicrobial administration in a monitored setting and are not appropriate for OPAT.

OPAT is typically used to treat bacterial infections, however certain severe fungal, viral or even protozoal infections might require prolonged intravenous antimicrobials. The most common conditions treated with OPAT include skin and soft tissue infections, bone and joint infections, endocarditis, bloodstream infections, complicated urinary tract infections, meningitis, and respiratory infections. In 2013, the Infectious Diseases and Immunology Center at The Miriam Hospital treated a total of 712 patients with OPAT. As displayed in Figure 2, bone and joint infections including osteomyelitis, discitis, septic arthritis, and prosthetic joint infections were the most common indication followed by bacteremia/ endovascular infections and skin/soft tissue infections. The majority of these infections require a prolonged course of intravenous treatment (at least 4–6 weeks). Some infections including those that involve retained foreign bodies such as orthopedic hardware may require a longer course of therapy (months) sometimes followed by suppressive oral antibiotic therapy.

Antimicrobial selection and administration

The antimicrobial agent for OPAT should be selected based on the susceptibility testing of the infecting organism, pharmacokinetic and pharmacodynamics properties, safety profiles of the possible antimicrobials to be used, and the patient’s drug allergy history. Ideally, the selected antimicrobial should be bactericidal, should reliably penetrate into the site of infection (including biofilms in the case of infections that involve retained foreign bodies), and can be administered at a convenient dosing schedule. The half-life of the drug determines the dosing frequency, where as its temperature and pH stability defines the preparation of the drug and optimal storage. Antibiotics with time dependent-killing activity such as beta-lactams require frequent dosing and may be best given through a continuous infusion, if preparation remains stable. Long-half life drugs that allow once daily dosing are preferred, such as ceftriaxone and ertapenem. Table 1 includes parenteral antibiotics commonly used in our practice, dosing schedules for adults with normal renal function, common pathogens and types of infections treated with OPAT.

Laboratory monitoring and possible complications of therapy

Adverse events and response to therapy are monitored at scheduled intervals through routine lab work and clinic visits according to the Infectious Diseases Society of America (IDSA) OPAT guidelines. Most antimicrobials require monitoring with weekly complete blood count and renal function tests; some antimicrobials also require weekly liver function tests. Serum drug concentrations help monitor the potential for toxicity as well as predicted

efficacy for certain antimicrobials including the aminoglycosides and vancomycin. C-reactive protein (CRP) and erythrosedimentation rate (ESR) can be useful surrogate markers of inflammation that can be helpful in monitoring response to therapy, particularly with osteomyelitis. [6, 7]

Adverse events encountered during OPAT can be classified as either catheter-related or antimicrobial-related. Complications associated with indwelling intravascular devices include bloodstream infections, thrombosis, mechanical obstruction and chemical phlebitis.[8] Regular flushing of the catheter to ensure patency, use of local anticoagulants, and sutureless vascular devices can reduce the rate of these complications. [9] Most of our patients have routine catheter dressing changes by skilled nurses that help identify early catheter related complications and allow for the placement of new vascular access when warranted. Possible complications associated with the antimicrobials themselves include: drug-related hypersensitivity reactions such as rash or more severe cutaneous or systemic reactions (anaphylaxis); antibiotic-associated diarrhea; bone marrow suppression that may include leukopenia or thrombocytopenia; and secondary infections such as mucosal candidiasis. [10] Clostridium difficile infection (CDI) occurs in 15–25% of antibiotic associated diarrhea cases and although fluorquinolones, clindamycin, and broad-spectrum B-lactams are most frequently implicated, CDI can potentially occur with any antibiotic exposure. [11, 12] Co-administration of probiotics might reduce the risk of CDI, although evidence is inconclusive. [13] Certain antimicrobials are associated with higher risk of nephrotoxicity (i.e. aminoglycosides, vancomycin and amphotericin B). Patients who receive aminoglycosides are at risk of developing vestibular and oto-toxicity and routine clinical monitoring is recommended. The rate of hospital admissions due to OPAT related complications is approximately 9% in other academic institutions. [14] Clinicians prescribing OPAT are responsible for educating their patients regarding the possible side effects related to their therapy and to provide education regarding monitoring for adverse events.

In an effort to reduce complications of OPAT and to continuously improve the delivery of OPAT to our patients, the Infectious Diseases and Immunology Center at The Miriam Hospital has implemented an ongoing quality review of OPAT patients. Once per month, we have a multidisciplinary conference to review patient outcomes and to identify areas for improvement. For example, we have identified cases where there have been barriers to effective communication between our Center and patients, or between our Center and care providers at skilled nursing facilities. This review process enables us to improve policies and procedures and create an ongoing educational opportunity for our staff and trainees.

Conclusions

OPAT has become increasingly utilized for the treatment of infections that require a prolonged course of parenteral treatment. OPAT enables patients to return home and regain their independence and also helps to decrease healthcare costs. The Infectious Diseases and Immunology Center at The Miriam Hospital has successfully implemented a multidisciplinary OPAT program. Our goal is to continue to safely deliver OPAT services, optimize the delivery of these services, and improve patient outcomes in RI.

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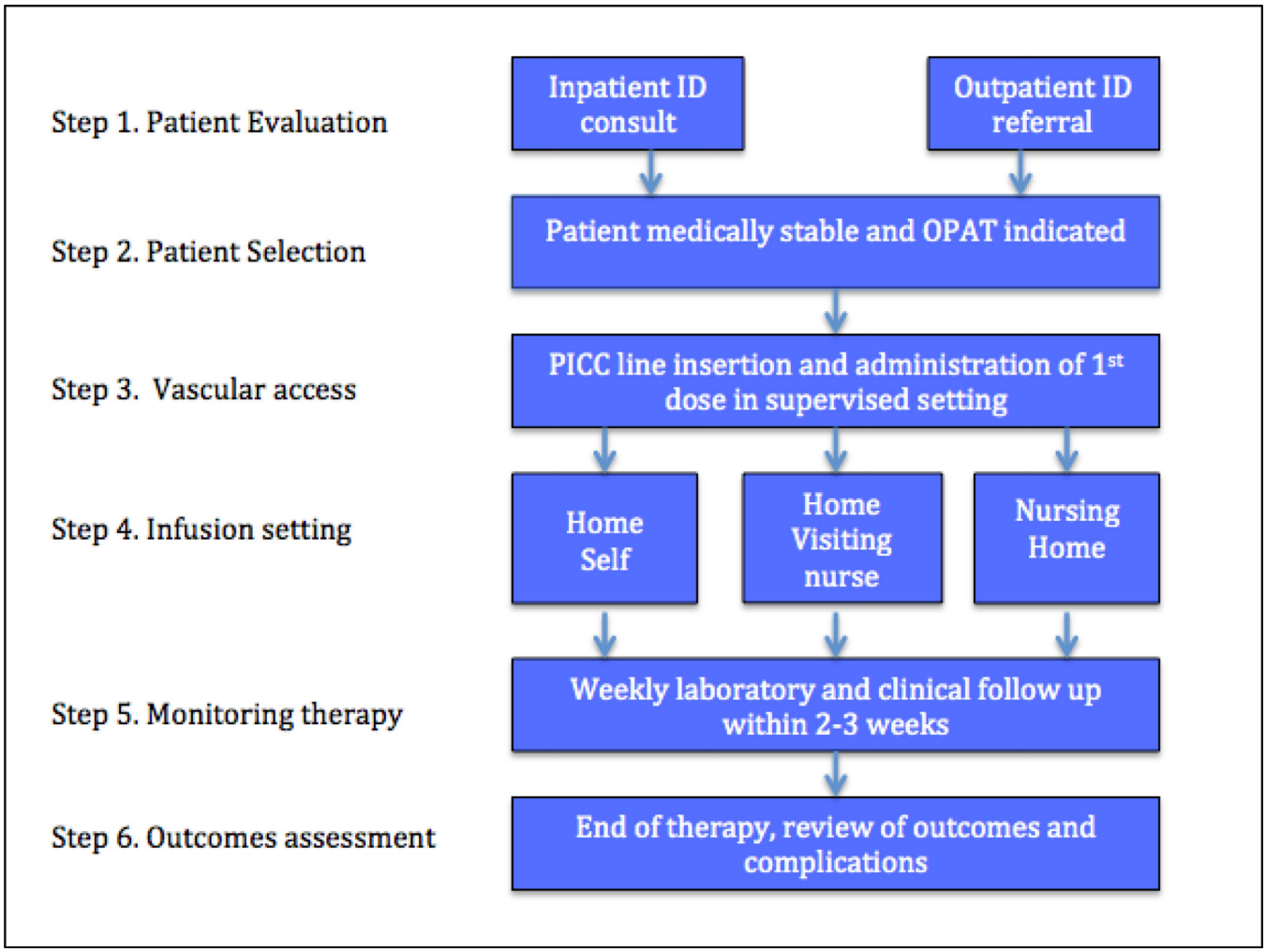

Figure 1.
Structure of the OPAT Program.

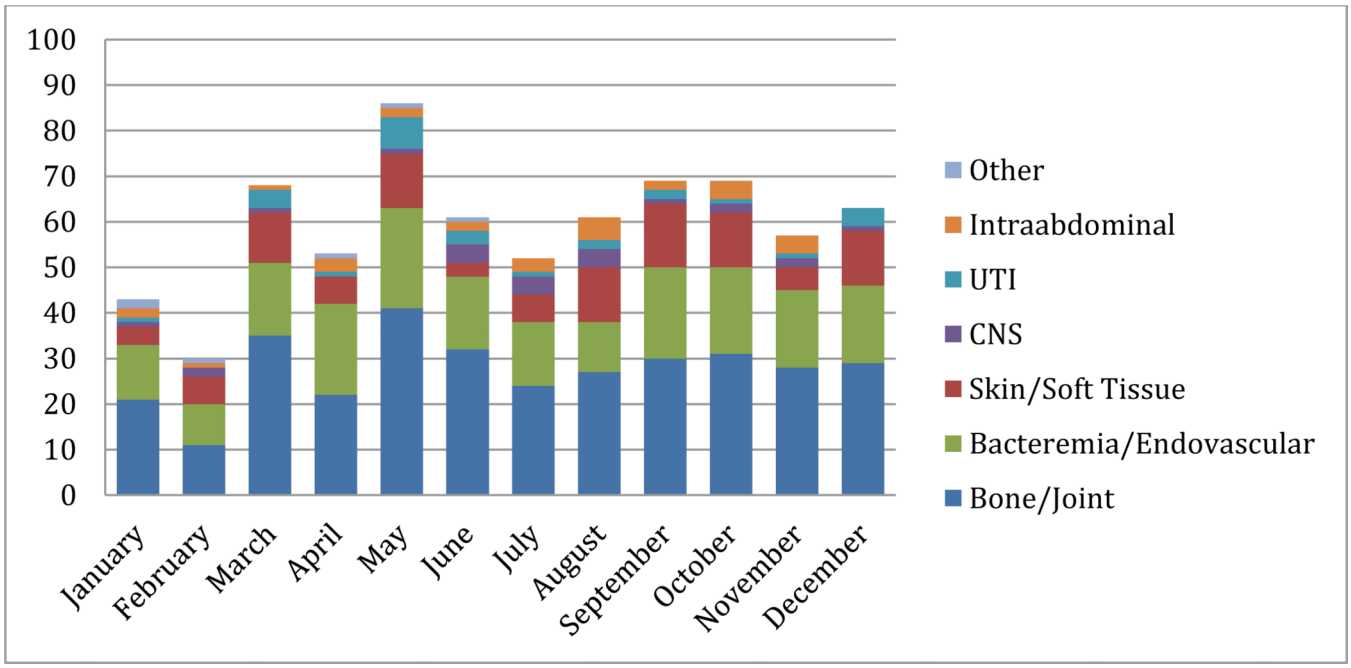

Figure 2.
Infections treated with OPAT at the Infectious Diseases and Immunology Center at The Miriam Hospital in 2013.

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Table 1

Commonly Prescribed Antimicrobials, Dosing Schedules, Pathogens, and Types of Infections in the Adult OPAT Program
(Individual treatment decisions should be based on the antimicrobial susceptibility of pathogens and appropriate use of guidelines from the Infectious Diseases Society of America, www.idsociety.org)

Antimicrobial Class	Antimicrobial drug	Adult Dosing Schedule Assumes normal creatinine clearance (glomerular filtration rate > 50ml/min)	Pathogens	Common diagnoses treated
Penicillins	Penicillin G	3–4 MU every 4 hours or 18–24 MU via continuous infusion over 24 hours	Streptococci	Endocarditis
	Ampicillin	2 gm every 4–6 hours	Enterococcus Listeria monocytogenes	Endocarditis/bacteremia Meningitis
	Nafcillin	2 gm every 4 hours or 12 gm via continuous infusion over 24 hours	MSSA	Endocarditis/bacteremia Septic arthritis Osteomyelitis Skin/soft tissue infections CNS infections
	Ampicillin-Sulbactam	1.5–3 gm every 6 hours	Streptococci MSSA Gram-negatives* Anaerobes	Diabetic foot infections Aspiration pneumonia Intra-abdominal infections
	Piperacillin-Tazobactam	3.375–4.5 gm every 6 hours	Streptococci MSSA Gram-negatives $^{\beta}$ Anaerobes	Intra-abdominal infections Pleuro-pulmonary infections
Cephalosporins	Cefazolin	1–2 gm every 8 hours	MSSA	Septic arthritis Osteomyelitis Skin/soft tissue infections
	Ceftriaxone	1–2 gm every 24 hours (2gm every 12 hours for CNS dosing)	Streptococci MSSA Gram-negatives*	Endocarditis/bacteremia Septic arthritis Osteomyelitis Skin/soft tissue infections CNS infections
	Cefepime	1–2 gm every 8 hours	Streptococci MSSA Gram-negatives $^{\beta}$	Intra-abdominal infections Pleuro-pulmonary infections Osteomyelitis CNS infections
Monobactam	Aztreonam	1–2 gm every 8 hours	Gram-negatives $^{\beta}$	Intra-abdominal infections Pleuro-pulmonary infections Genitourinary tract infections
Glycopeptides	Vacnomycin	15mg/kg every 12 hours	Streptococci Enterococcus MSSA MRSA	Endocarditis/bacteremia Septic arthritis Osteomyelitis Skin/soft tissue infections

Antimicrobial Class	Antimicrobial drug	Adult Dosing Schedule Assumes normal creatinine clearance (glomerular filtration rate > 50ml/min)	Pathogens	Common diagnoses treated
				CNS infections Pleuro-pulmonary infections
Aminoglycosides	Gentamicin	1mg/kg every 8 hours for synergy in combination with a beta-lactam antibiotic	Enterococcus MSSA MRSA	Endocarditis
Lipopeptide	Daptomycin	6mg/kg every 24 hours	MSSA MRSA Enterococcus	Endocarditis/bacteremia Septic arthritis Osteomyelitis Skin/soft tissue infections
Carbapenems	Meropenem	1–2gm every 8 hours	Streptococci MSSA Gram-negatives [β] Anaerobes	Intra-abdominal infections Skin/soft tissue infections CNS infections
	Ertapenem	1 gm every 24 hours	Streptococci MSSA Gram-negatives* Anaerobes	Intra-abdominal infections Skin/soft tissue infections Osteomyelitis
Antivirals	Acyclovir	10 mg/kg every 8 hours	Herpes simplex virus Varicella zoster virus	CNS infections Disseminated infections
Antifungals	Amphoterocin B (liposomal preparations)	5mg/kg every 24 hours	Aspergillosis Zygomycetes Candidiasis Cryptococcosis	Invasive fungal infections CNS infections