

A Review of Outpatient Parenteral Antimicrobial Therapy Practices and Experience at The Ottawa Hospital

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ABSTRACT

Background: Outpatient parenteral antimicrobial therapy (OPAT) allows patients who require IV antimicrobials but whose condition is otherwise stable to receive therapy in the home.

Objective: To describe the current practices and clinical outcomes of adult patients who received parenteral antimicrobial therapy after discharge from The Ottawa Hospital.

Methods: The charts of 75 patients who received OPAT between November 1, 2003, and October 31, 2004, were reviewed to determine the indication for parenteral antibiotic therapy, the antimicrobial regimen selected, the extent of monitoring, the occurrence of complications, and the outcome of therapy.

Results: Of the 75 patients whose charts were selected for review, 66 were included in the study. The most common infections treated were cellulitis (28 patients [42%]), osteomyelitis (8 patients [12%]), postsurgical wound infection (7 patients [11%]), and abscess and endocarditis (5 patients [8%] each). Cefazolin was the most commonly prescribed antimicrobial. Complications occurred in 19 (29%) of the 66 patients, and most of these related to the IV access. Overall, the majority of patients (56 or 85%) had a successful outcome.

Conclusion: The majority of patients who received OPAT after discharge were treated successfully. However, the development of a formal multidisciplinary OPAT program could enhance quality of care through improvements in patient education, documentation, and monitoring.

Key words: outpatient, antimicrobial, intravenous, home therapy, outpatient parenteral antimicrobial therapy

RÉSUMÉ

Historique : L'antibiothérapie parentérale externe (APE) permet au patient nécessitant une antibiothérapie et dont l'état de santé est par ailleurs stable, de recevoir le traitement à domicile.

Objectif : Décrire les pratiques actuelles et les résultats cliniques de l'APE chez des patients adultes ayant reçu leur congé de l'Hôpital d'Ottawa.

Méthodes : Les dossiers de 75 patients qui ont reçu une APE entre le 1er novembre 2003 et le 31 octobre 2004 ont été examinés afin de déterminer l'indication sous-tendant l'antibiothérapie parentérale, le régime antibiotique choisi, la durée du suivi, la fréquence des complications, et le résultat du traitement.

Résultats : Parmi les 75 patients dont les dossiers ont été sélectionnés pour examen, 66 ont été admis à l'étude. Les infections les plus courantes faisant l'objet d'une antibiothérapie étaient les suivantes : cellulite (28 patients [42 %]), ostéomyélite (8 patients [12 %]), infection postchirurgicale d'une plaie (7 patients [11 %]), abcès et endocardite (5 patients [8 %] chaque). La céfazoline était l'antibiotique le plus prescrit. Des complications sont survenues chez 19 patients (29 %), la plupart liées à l'accès intraveineux. Dans l'ensemble, le traitement a réussi chez la majorité des patients (56 ou 85 %).

Conclusions : Le traitement a réussi chez la majorité des patients qui ont reçu une APE après leur congé de l'hôpital. Cependant, la mise au point d'un programme d'APE multidisciplinaire officiel pourrait accroître la qualité des soins, grâce à des améliorations au chapitre de l'éducation des patients, de la documentation et du suivi.

Mots clés : patient externe, antibiotique, intraveineux, traitement à domicile, antibiothérapie parentérale externe

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INTRODUCTION

Outpatient parenteral antimicrobial therapy (OPAT) was first introduced in 1974, and its use has been increasing steadily, particularly in the past 20 years. The development of new antibiotics that can be administered daily, improvements in vascular access and drug administration devices, and the emphasis on cost containment have played important roles in the evolution of OPAT.¹⁻⁴ The guidelines of the Infectious Diseases Society of America (IDSA) define OPAT as the intravenous, intramuscular, or subcutaneous administration of at least 2 doses of an antimicrobial agent, on 2 different days, without admission to hospital.¹ OPAT is usually administered to expedite hospital discharge of patients who need continued parenteral antimicrobial therapy, although it may also be used to avoid hospital admission altogether.⁵ A variety of infections, including skin and soft-tissue infections, endocarditis, pneumonia, and osteomyelitis, have been treated successfully with OPAT.^{1,3}

Although device-related and antimicrobial-related adverse events have been recognized, OPAT has many advantages. This type of therapy is as effective and safe as therapy provided in hospital and has the advantage of lower costs; patients also prefer outpatient therapy.^{1,6-8} The use of OPAT has led to shorter hospital stays and lower hospital-associated costs and should also reduce the potential for nosocomial infections.^{1,2,9}

The literature describing OPAT programs in Canada is limited. Experience with OPAT has been described for hospitals in Vancouver,¹⁰ Calgary,⁴ Manitoba,⁹ the province of Quebec,^{11,12} and Hamilton¹³; the institutions differed in the structure of their programs and in selection of antimicrobials.¹² The Ottawa Hospital is an 1100-bed, multicampus, university-affiliated teaching hospital; the hospital has 2 acute care campuses (Civic and General) and encompasses the University of Ottawa Heart Institute. Although OPAT is frequently prescribed at this institution, its use has not been reviewed, and no formal OPAT program exists. Rather, OPAT is organized on an individual basis, and follow-up is structured at the discretion of each treating physician. Therefore, the health records of patients who were treated at The Ottawa Hospital and the University of Ottawa Heart Institute and who received OPAT were reviewed, with the goal of describing the patient population, indications, antimicrobial selection, complications, and patient outcomes for this type of therapy.

METHODS

The study protocol was approved by the Research and Ethics Boards of The Ottawa Hospital and the University of Ottawa Heart Institute. Patients who were treated at either of these institutions between November 1, 2003, and October 31, 2004, and who received OPAT were identified for this review by the Community Care Access Centre (CCAC), which coordinates OPAT in the Ottawa region. Of these, a convenience sample of 75 patient charts (i.e., every third patient) was chosen. In the context of this study, "outpatient" was defined as a patient receiving therapy at home or in a clinic; parenteral therapy was limited to IV administration. Patients could be included more than once if they had received multiple, nonconcurrent OPAT courses for multiple infections; however, no patients in the identified sample had nonconcurrent courses of therapy. The CCAC obtained verbal consent from the selected patients before the chart review.

The charts were reviewed to determine the indication, admitting service, antimicrobial regimen selected, concurrent use of warfarin or oral contraceptives (to assess potential drug interactions), monitoring plan, complications, and outcome of therapy. Requests and results for laboratory investigations, culture and susceptibility testing, and serum levels of antibiotic were recorded as part of the monitoring assessment, when available.

Outcomes were categorized as "successful", "successful with complications", or "failed". The outcome was considered "successful" if the initial antimicrobial course was completed as prescribed and "successful with complications" if the patient completed OPAT for the original infection but experienced an adverse event or complication, whether or not a change in therapy was required. The outcome was considered "failed" if OPAT was discontinued prematurely because of an adverse event or complication. Worsening of the infection or readmission to hospital for reasons attributable to the infection being treated were also classified as "failed".

RESULTS

A total of 236 adult patients were identified by CCAC as having been treated at The Ottawa Hospital or the University of Ottawa Heart Institute with a prescription for IV antimicrobial therapy between November 1, 2003, and October 31, 2004. Consent was obtained from the 75 patients in the selected convenience sample, and their charts were reviewed.



Nine of these were subsequently excluded: 2 had not received any IV therapy, 6 had not received IV antimicrobial therapy, and for 1 there was insufficient documentation. Therefore, a total of 66 patients were included in the study. Thirty patients had been treated at the Civic Campus, 26 at the General Campus, and 10 at the University of Ottawa Heart Institute.

Demographic Characteristics

Of the 66 patients, 33 were men, and the mean patient age was 57.2 years (range 19 to 88 years). None of the study patients were taking oral contraceptive agents. Of the 8 patients who were taking warfarin, none received an antimicrobial agent known to have a clinically important interaction with warfarin. Table 1 describes the incidence of allergies, type of IV access, and type of infection treated.

Antimicrobial agents were initiated in hospital in 35 cases (53%), in the emergency department in 29 cases (44%), and in the Infectious Disease Clinic in 2 cases (3%). Among the patients who were hospitalized at the time of initiation of therapy, there was an even distribution between the medical and surgical wards (19 [54%] and 16 [46%], respectively). Before discharge, the length of hospital stay (for those who were formally admitted) ranged from 2 to 72 days (mean 16.6 days).

Venous Access

Three types of venous access were used to administer antimicrobial agents: peripherally inserted central venous catheters (PICC lines), peripheral lines, and subcutaneously implanted venous access devices (Table 1). Most of the peripheral lines (28/30) were inserted in the emergency department. PICC lines were inserted for 33 of the 35 patients who had been admitted to hospital. Cefazolin and clindamycin were the most common antibiotics administered through a peripheral line.

Type of Infection

The most common indication for OPAT was cellulitis, but a wide variety of infections were treated (Table 1). Infectious disease specialists were involved in the care of 40 (61%) of the patients, of whom 30 (75%) were initially treated in hospital and 10 (25%) were initially treated in the emergency department or the Infectious Diseases Clinic. Cellulitis, abscess, endocarditis, osteomyelitis, and postsurgical wound infections were the most common infections for which an infectious disease specialist was consulted. The majority of

Table 1. Characteristics of 66 Patients Who Received Outpatient Parenteral Antimicrobial Therapy

Characteristic	No. (%) of Patients*
Drug allergy status†	
No known drug allergies	32 (48)
Any antibiotic allergy	21 (32)
Penicillin	10
Sulfa	7
Cephalosporin	1
Other	6
Allergy to a non-antibiotic drug	13 (20)
Unknown	5 (8)
Intravenous access	
Peripherally inserted central venous catheter	35 (53)
Peripheral catheter	30 (45)
Subcutaneously implanted venous access device	1 (2)
Type of infection	
Cellulitis	28 (42)
Osteomyelitis	8 (12)
Postoperative wound infection	7 (11)
Abscess	5 (8)
Endocarditis	5 (8)
Intra-abdominal infection	2 (3)
Urinary tract infection	2 (3)
Other‡	6 (9)
Combination of urinary tract and wound infections	1 (2)
Combination of urinary tract infection and diverticulitis	1 (2)
Combination of cellulitis and herpes zoster	1 (2)

*Within each characteristic, percentages may not sum to 100 because of rounding.

†Some patients had more than one allergy.

‡One case each of cholelithiasis, fungal sinusitis, lymphadenitis, neurosyphilis, prostatitis, and septic joint.

patients who were not seen by an infectious disease specialist (20/26 or 77%) had cellulitis.

Antimicrobial Regimen

Most of the patients in this study (54 or 82%) were treated with a single antimicrobial agent (Table 2). Cefazolin was the most frequently prescribed agent, and in 22 of the 31 courses of therapy with this drug, it was used to treat cellulitis. A combination of 2 parenteral antimicrobial agents was used in treating 11 patients, and 1 patient received 3 antibiotics concurrently. Endocarditis was the most common infection requiring combination IV therapy.

Treatment Duration

The total duration of combined inpatient and outpatient IV antimicrobial therapy ranged from 3 to

Table 2. Antimicrobial Agents Prescribed as Outpatient Parenteral Antibacterial Therapy (OPAT)

Agent	No (%) of Patients (n = 66)*
Cefazolin†	31 (47)
Gentamicin	6 (9)
Ceftriaxone	5 (8)
Clindamycin	5 (8)
Vancomycin	5 (8)
Cloxacillin	4 (6)
Piperacillin/tazobactam	4 (6)
Ampicillin	3 (5)
Ciprofloxacin	3 (5)
Metronidazole	3 (5)
Meropenem	2 (3)
Penicillin G	2 (3)
Amphotericin B	1 (2)
Acyclovir	1 (2)
Cefotaxime	1 (2)
Ceftazidime	1 (2)
Cefuroxime	1 (2)
Linezolid	1 (2)

*The number of prescriptions for parenteral antimicrobial therapy (79) was greater than the number of patients because some patients were treated parenterally with more than one agent for the original infection (11 patients had a combination of 2 parenteral antimicrobial agents, and 1 patient received 3 parenteral antibiotics concurrently). †Includes 9 patients who were treated with concomitant oral probenecid and 3 patients who received concomitant oral rifampin.

169 days (mean 32.8 days, median 23.5 days). The duration of OPAT varied between 2 and 169 days (mean 27.3 days; median 20.5 days).

Complications

Nineteen (29%) of the 66 patients in this study experienced a total of 25 complications (Table 3). Most of the complications (15 or 60%) were attributed to IV access as opposed to the antimicrobial agent (10 or 40%). The most common access-related complications were interstitial IV line, occlusion of the IV line, and phlebitis. Eight of the 14 patients with an access-related complication had a PICC line.

Nausea was the most common antimicrobial-related complication, and amphotericin B was associated with the greatest number of adverse effects. One patient experienced neutropenia associated with piperacillin/tazobactam, which was recognized only upon readmission to hospital.

Outcomes

For most patients (56 or 85%), OPAT was successful. A large proportion of patients (40 or 61%) had a

Table 3. Types of Complications Experienced by 66 Patients Receiving Outpatient Parenteral Antimicrobial Therapy

Complication	No. (%) of Patients (n = 66)*
Access related	
Interstitial of IV line	6 (9)
Occlusion of IV line	3 (5)
Phlebitis	3 (5)
Bleeding	1 (2)
Leakage of peripherally inserted central venous catheter	1 (2)
Thrombosis	1 (2)
Drug related	
Nausea	3 (5)
Acute renal failure	1 (2)
Allergic reaction	1 (2)
Hypokalemia	1 (2)
Nephrotoxicity	1 (2)
Neutropenia	1 (2)
Vomiting	1 (2)
Yeast infection	1 (2)

*One (2%) of the patients had more than one access-related complication, and 2 (3%) had complications of both types. No patients had more than one drug-related complication.

successful outcome with no complications related to OPAT, and 16 (24%) had a successful outcome but experienced a complication during their course of therapy. Of the latter group, 3 patients required a change in therapy because of an adverse event or complication. One of these patients, who was being treated with cefotaxime, experienced thrombophlebitis, and another patient, who was receiving concurrent cloxacillin and gentamicin, required a change in therapy after development of phlebitis and interstitial positioning of the IV line. The third patient experienced an allergic reaction, which resolved following a change in therapy.

Of the 10 patients (15%) for whom OPAT failed, 5 were readmitted to hospital for reasons attributable to the infection and 5 experienced a worsening of the infection that required a change in the antimicrobial regimen. Of note, these patients all continued to receive the new antimicrobial regimen on an outpatient basis. None of the patients in this study had OPAT failure because of premature discontinuation of OPAT related to an adverse event or complication.

Of the 5 patients who were readmitted to hospital, 1 patient required amputation as a consequence of poor healing of a diabetic ulcer with osteomyelitis, and another patient, who had a wound infection after heart surgery, was readmitted for treatment of newly



diagnosed osteomyelitis. Two patients were readmitted for worsening infection (of a wound in 1 patient and cellulitis in 1 patient). The fifth patient with failed OPAT had an intra-abdominal abscess and was readmitted because of emergence of fever, chills, and abdominal pain.

Monitoring

Only 12 patients (18%) had a monitoring plan identified in the health record. The monitoring plans included monitoring of serum electrolyte concentrations, complete blood cell count, and determination of serum concentrations of creatinine, blood urea nitrogen, gentamicin, or vancomycin. The results of these laboratory tests and the names of the physicians to whom these results were sent were not recorded in any of the charts reviewed.

DISCUSSION

The objective of this study was to review current practices related to OPAT for adult patients treated at The Ottawa Hospital and the University of Ottawa Heart Institute. This review allowed description of the patients who received OPAT, the extent of involvement of infectious disease specialists in the care of these patients, the most common diagnoses and antimicrobial regimens used, and the complications and outcomes that occurred. During the 1-year study period, 236 patients received OPAT.

There were similarities and differences between the experience reported here and that described for other OPAT programs. Of the patients who received OPAT in this study, there were slightly more patients who had been admitted to hospital (53%) than were discharged from the emergency department (44%). The majority of patients discharged from the Vancouver Hospital and Health Sciences Center were also inpatients,² whereas in Calgary⁴ and at the Hôpital Charles LeMoine in Greenfield Park, Quebec,¹¹ most of the patients enrolled in the OPAT program originated from the emergency department. A variety of infections, including wound infections, osteomyelitis, endocarditis, and abscesses, were treated at The Ottawa Hospital and the University of Ottawa Heart Institute; cellulitis was the most common diagnosis (42% of patients). The American OPAT Outcomes Registry has reported skin and soft-tissue infections (23%), osteomyelitis (15%), septic arthritis or bursitis (5%), bacteremia (5%), wound infection (4%), pneumonia (4%), and pyelonephritis (3%) as the most common infections treated with OPAT.¹

The differences between the US registry data and the findings from the study reported here may be due to the small sample size of this study and/or differences in patient populations. Other Canadian hospitals have reported skin and soft-tissue infections, bone and joint infections, and endocarditis as the infections most frequently treated with OPAT,^{2,4,9,12,13} consistent with the findings reported here.

In this review, the majority (82%) of OPAT patients were treated with a single antimicrobial agent. The most common agent used as monotherapy was either a penicillin or cephalosporin. This finding is unsurprising, given that beta-lactams can be used to treat a variety of infections and are generally safe and well tolerated. Monotherapy was also more common in Quebec^{11,12} and Manitoba,⁹ whereas combination therapy was reported more often in Vancouver.¹⁰ The OPAT Outcomes Registry in the United States listed ceftriaxone and vancomycin as the top 2 antibiotics used for OPAT.¹ The most commonly prescribed antimicrobial at The Ottawa Hospital and the University of Ottawa Heart Institute was cefazolin.

The average duration of OPAT (27.3 days) observed in this review was comparable to the duration of therapy in the Vancouver program (22.5 days).² In Calgary, however, most patients were treated for less than 7 days.⁴ This discrepancy may be explained by the high incidence of soft-tissue infections (64%) in the Calgary program.⁴

Guidelines often recommend that when outpatient therapy is prescribed, a physician with OPAT experience, such as an infectious disease specialist, should be involved.^{1,14} In this study, the infectious disease service was involved in the care of 61% of the patients, including all patients with endocarditis and two-thirds of those with osteomyelitis. Neither the report from the Manitoba program⁹ nor that from the Hôpital Enfant-Jésus (Quebec City, Quebec)¹² mention involvement of infectious disease specialists in the delivery of OPAT. Although the report from the Hôpital Charles LeMoine (Greenfield Park, Quebec) mentioned involvement of infectious disease specialists in the initial organization of the program, the extent of such involvement in direct patient care was not reported.¹¹ However, specialist involvement was an integral part of the programs in Calgary,⁴ Vancouver¹⁰ and Hamilton.¹³ Complex and/or less common infections and infections requiring long-term treatment are examples of situations in which involvement of infectious disease specialists would be particularly valuable. In the study reported here, 2 patients with



osteomyelitis were not seen by an infectious disease specialist, and in both cases, OPAT failed. Although involvement of infectious disease specialists does not guarantee a successful outcome, these physicians may have more experience recognizing the early signs and symptoms of toxic effects, treatment failure, and complications and can make adjustments as needed. In addition, the possibility of replacing OPAT with oral therapy could perhaps be more readily recognized by someone with more experience in treating infectious diseases.²

Complications were reported for 29% of the patients in this sample, the majority attributed to the IV access. We documented adverse effects attributable to the antimicrobial agent in 7 (11%) of the patients, a proportion similar to that observed in the Hamilton¹³ and Vancouver² programs (close to 14% in both studies). Although complications were reported for the studies from Manitoba⁹ and Calgary,⁴ the overall incidence of adverse events was not provided. In contrast to the Jefferson Hospital Home Infusion Program in Pennsylvania¹⁵ but similar to the situation in Vancouver,² a higher proportion of adverse events in the current study were related to IV access than to the antimicrobial agent. Slightly more than half of the access-related complications involved PICC lines. Unlike the Jefferson Hospital,¹⁵ where infection was the most common complication associated with venous access, no line-related infections were documented in the current study. However, the patients in the Jefferson program¹⁵ had a longer median duration of OPAT than the Ottawa patients (40 and 20.5 days, respectively). Three of the patients in the current study (5%) required a change in the originally prescribed antimicrobial regimen because of an adverse reaction, which coincides with the premature discontinuation rate reported by the OPAT Outcomes Registry (3% to 10%).¹ In the Ottawa patients, however, outpatient management was continued.

We observed a tendency toward less extensive monitoring of therapy for patients receiving OPAT than is usually the case for the inpatient population at The Ottawa Hospital and the University of Ottawa Heart Institute. Given this apparent lack of monitoring and documentation, some adverse events might have been missed. We are particularly concerned about the possibility of less common and more severe adverse events, such as aminoglycoside-related nephrotoxicity or ototoxicity. Clinical and laboratory monitoring by a health care professional experienced in antimicrobial therapy (e.g., an infectious disease specialist or pharmacist) is especially important for antimicrobials

such as aminoglycosides and amphotericin B, because of the greater potential for serious adverse events. Four of the 6 patients discharged on gentamicin had requisitions for hematological and/or biochemical laboratory tests, whereas only 2 had requisitions for determination of serum gentamicin concentration. However, the extent and adequacy of patient monitoring, including laboratory testing, after hospital discharge was difficult to accurately assess. Of the 12 patients with monitoring plans explicitly stated in the health record, the results were either not available or not documented in the charts. Furthermore, it was not evident which physician (family physician, infectious disease specialist, or admitting physician) was responsible for outpatient care and monitoring. The IDSA guidelines include suggestions for the monitoring of laboratory parameters for specific antimicrobials, and the frequency at which these tests should be performed.¹ We could not determine if these recommendations were followed.

Overall, 85% of the patients in this study completed their course of antimicrobial therapy, although 16 of these patients experienced a complication during therapy. The success rate of the Vancouver OPAT program was similar (86%).¹⁰ In Manitoba, the overall failure rate was 8%⁹ (15% in the current study); however, the definitions of failure differed, so these results cannot be directly compared.

Two limitations of the current study were its small sample size and retrospective nature. The charts of about one-third of the patients discharged on OPAT from The Ottawa Hospital and the University of Ottawa Heart Institute were reviewed. Although these patients should constitute a representative sample, the distribution of infections, the choice of antimicrobial regimen, and the identification of complications might have been different if more patients had been reviewed. Also, if the study had been performed prospectively, more detailed information about reasons for changes to the antimicrobial regimen, laboratory results, adverse effects, and complications might have been available.

This study provided the opportunity to describe our experience with OPAT in patients treated at The Ottawa Hospital and the University of Ottawa Heart Institute and thus to understand and appraise current practices at these institutions. This review indicates that, as in other programs, the majority of patients were successfully managed with OPAT, and the rate of complications was similar to those reported elsewhere. Nevertheless, a formalized OPAT program with defined policies and procedures and good systems for recording patient information may result in improvements in documentation,



coordination of patient care, communication among health care professionals, and identification and management of adverse events and complications. We believe that such a program would reduce costs of care and reduce risk to patients. By providing timely, comprehensive care through an organized multidisciplinary program, the quality of care for patients receiving OPAT would be continuously assessed and promoted.

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