Mandatory infectious diseases approval of outpatient parenteral antimicrobial therapy (OPAT): clinical and economic outcomes of averted cases

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Objectives: The use of outpatient parenteral antimicrobial therapy (OPAT) has been increasing worldwide due to its evident clinical utility; however, there is also concern about overuse and increased risk to patients in terms of antibiotic toxicity and intravenous line-associated complications. At our university-affiliated county teaching hospital with mandatory Infectious Diseases (ID) approval for all OPAT courses, we looked at clinical outcomes and cost savings of patients denied OPAT.

Methods: Electronic medical records of patients denied OPAT were retrospectively reviewed. Demographic, medical, infection-specific and drug-specific data were collected for each patient, including the regimen ultimately recommended by ID in lieu of OPAT. Patients were determined to have clinical cure, probable cure or treatment failure based on resolution or recurrence of infection for up to 1 year after OPAT denial. The amount of money saved in direct OPAT costs in these patients was calculated.

Results: Fifty-six patients were denied OPAT during the study period and were discharged with either oral or no additional antibiotics. Clinical cure was documented in 42 patients (75%), probable cure in 7 patients (12.5%) and treatment failure in 7 patients (12.5%). Of the seven treatment failures, only one patient (1.8%) was deemed to be a true failure after thorough chart review. Overall, the estimated OPAT-specific cost saving was $215,424 or $3,847 per patient.

Conclusions: Mandatory ID approval of all OPAT courses can decrease healthcare costs while maintaining good clinical outcomes.

Keywords: antimicrobial stewardship, mandatory approval, healthcare costs, OPAT

Introduction

The use of outpatient parenteral antimicrobial therapy (OPAT) has been increasing in recent years probably due, in part, to the demand for lowering healthcare costs. The use of OPAT provides significant cost savings and improvement in patient quality of life when compared with hospitalization.1,2 However, despite its obvious clinical utility, there is potential for both inappropriate use and overuse of OPAT, as well as the potential for other unforeseen complications, such as adverse events, line complications (occlusion, thrombosis, infection), contributions to bacterial resistance, impact on daily life and death.

In 2004, the Infectious Diseases Society of America (IDSA) published updated guidelines addressing many aspects of OPAT, including appropriate patient selection.2 Prior studies have demonstrated that Infectious Diseases (ID) consultation for patients being considered for OPAT decreases the number of inappropriate courses of OPAT, optimizes safety of antibiotic therapy and decreases overall cost.3,4 The primary objective of this study was to evaluate the clinical outcomes of patients in whom OPAT was averted by ID consultation at an inner city, academic, county teaching hospital. The secondary objectives of this study were to affirm the benefit of ID Consult Service involvement in patient selection for OPAT, including OPAT cost savings, and to
heighen the awareness of the use of oral antibiotic alternatives, when appropriate.

**Methods**

This study was a retrospective case series performed at Wishard Health Services/Eskanazi Health (WHS), a 339 bed, university-affiliated, safety net, county teaching hospital in Indianapolis, Indiana. In 2011, the payer mix of patients admitted to WHS was Medicaid 31%, Health Advantage 25%, self-pay 16%, commercial insurance 11%, Medicare 10% and other 6%. Health Advantage is a hospital-managed charity care programme offered to residents of Marion County, Indiana who fall at or below the 200% federal poverty level and do not qualify for other assistance or insurance programmes. Patients approved for Health Advantage are required to seek medical care within the WHS system. A formal OPAT programme has been in existence at WHS since July 2008, whereby, according to a hospital quality mandate, the inpatient ID Consult Service must review and approve the use of OPAT and peripherally inserted central catheter (PICC) placement for OPAT (through formal consultation or informal chart review) before the patient is discharged from the hospital. If OPAT is not approved by the ID Consult Service, an alternative outpatient regimen, such as oral antibiotic therapy or no additional antibiotic therapy, is recommended by the ID attending physician, taking into account relevant microbiological and clinical data. These denials for OPAT were recorded by the project team whenever possible.

WHS participates in the Indiana Network for Patient Care (INPC), a state-wide informatics network that links registration records, laboratory and radiographic tests, hospital admissions and clinic and emergency room visits from 5 local hospital systems (90 hospitals throughout the state) and over 100 hospital-based clinics/day surgery facilities in one electronic medical record (EMR). The EMRs of patients for whom OPAT was not approved by the inpatient ID Consult Service at WHS between 1 July 2008 and 31 December 2010 were retrospectively reviewed. Children, pregnant women and prisoners were excluded from the analysis. Demographic (age, gender, race, body mass index, allergies, payer source, social history), medical (comorbidities, primary service), infection-specific (type of infection, microbiology, medical/surgical management of infection) and drug-specific (previous/current antibiotic therapy, OPAT regimen requested by primary service, treatment recommended by the inpatient ID Consult Service) information was collected for each patient, when available. In addition, the clinical outcome data for each patient were collected for 1 year following OPAT denial, and the outcome was classified as definitive cure, probable cure or treatment failure according to the following definitions applied during data analysis: definitive cure, no documented persistence or recurrence of infection during at least one subsequent clinic or hospital visit for medical care within 1 year after OPAT denial; probable cure, presumed eradication of infection due to lack of evidence of patient return for medical care in the state-wide INPC EMR (outpatient, inpatient or emergency room) within 1 year of OPAT denial; and treatment failure, worsening or recurrence of the same infection requiring hospitalization or initiation of OPAT, or the patient died as a direct result of the specific infection within 1 year of OPAT denial.

The overall rates of definitive cure, probable cure and treatment failure were defined by the ratio of the number of patients who experienced each of these clinical outcomes divided by the total number of patients in whom OPAT was denied during the study period.

Table 1. Baseline characteristics of patients in whom OPAT was denied; n = 56

<table>
<thead>
<tr>
<th>Age (years), mean ± SD</th>
<th>54 ± 17</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%)</td>
<td>19 (34)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>37 (66)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td>37 (66) white, 16 (29) black, 2 (4) Hispanic, 1 (2) Asian</td>
</tr>
<tr>
<td>Smoker, n (%)</td>
<td>22 (39)</td>
</tr>
<tr>
<td>Obese (body mass index ≥ 30 kg/m²), n (%)</td>
<td>22 (39)</td>
</tr>
<tr>
<td>Diabetic, n (%)</td>
<td>22 (39)</td>
</tr>
</tbody>
</table>

The averted OPAT cost savings were calculated as the difference between what would have been spent on the requested course of OPAT and what was actually spent on the treatment regimen recommended by the inpatient ID Consult Service. The overall cost of the requested course of OPAT was calculated as the sum of the costs associated with line placement, antibiotic therapy costs, laboratory monitoring costs, nurse visit costs and home care company per diem costs for home infusion therapy, which incorporate fees from compounding, delivery and monitoring of therapy. The type of line that would have been utilized, and subsequent cost, was dependent upon the length of requested OPAT. For requested OPAT courses of 100% daily peripheral line was utilized in the calculation at a cost of $490. For requested OPAT courses of 4–13 days, a midline catheter was utilized in the calculation at a cost of $490 (sum of line insertion fee from contracted vendor, introducer and midline catheter). For requested OPAT courses of ≥ 14 days, a PICC line was utilized in the calculation at a cost of $760 (sum of insertion fee from contracted vendor, introducer, PICC, chest X-ray confirming placement). The average wholesale price (AWP, First Data Bank) of the antibiotic(s) in the requested OPAT regimen was utilized to calculate the drug costs. The recommendations for laboratory monitoring during OPAT were derived from the IDSA OPAT guidelines and utilized to calculate the type and frequency of laboratory monitoring that would have occurred during the requested course of OPAT. The cost of each of these laboratory tests was obtained from the hospital billing department and included a creatinine determination or basic metabolic panel ($58), comprehensive metabolic panel ($167), complete blood count with differential ($76), creatine kinase ($43) and vancomycin serum concentration determination ($54). The costs of nursing visits and per diem antibiotic charges were obtained from the home infusion company utilized by the WHS OPAT programme. The number of nursing visits per requested OPAT course was calculated based on the duration of OPAT and included an initial (training) visit, a completion (line removal) visit and weekly nursing visits for line dressing changes and blood draws for laboratory monitoring during OPAT. Each nursing visit costs $125 for a 2 h visit. The home care per diem charge was calculated as $75 per day for the first antibiotic and $37.50 per day for each additional antibiotic for the duration of home infusion therapy. Lastly, the drug cost of the treatment regimen recommended by the inpatient ID Consult Service (in lieu of OPAT) was calculated using the AWP of the oral antibiotic(s) recommended, if applicable.

This study was reviewed and approved by the Indiana University Institutional Review Board.

**Results**

During the study period, 577 requests for OPAT were received by the inpatient ID Consult Service and 60 were not approved (10.4% denial rate). Of the 60 patients denied OPAT during the study period, 56 met the inclusion criteria. Four patients were incarcerated and thus excluded from the analysis. The demographic characteristics of the 56 patients in whom OPAT was not approved are described in Table 1. Sixty-six percent of the patients were male. The mean age of the patients was 54 years (range 20–87 years). OPAT was requested for the treatment of skin and soft tissue infection (n = 15, 27%), diabetic foot infection with
that grew coagulase-negative Staphylococcus in the absence of foreign material or evidence of infection and was felt to be a contaminant. The other patient sustained a gunshot wound causing injury to the rectum and the surgical team requested prophylactic antibiotics needed to prevent infection. The reasons for denial of OPAT are summarized in Table 2. Overall, 89% (50/56) of patients were denied OPAT either because they had an infection that could be treated with an oral antibiotic based on available culture data (61%, 34/56) or because the patient did not have culture data but had an infection that could be treated with oral antibiotics based on likely infecting organisms (29%, 16/56). No further antibiotic therapy was recommended for six patients (11%).

The most common OPAT regimens requested by the primary medical/surgical teams included vancomycin plus piperacillin/tazobactam (21/56, 38%), vancomycin monotherapy (11/56, 20%), piperacillin/tazobactam monotherapy (6/56, 11%) and vancomycin plus meropenem (3/56, 5%). Of the 21 patients receiving vancomycin and piperacillin/tazobactam at the time of OPAT request, 10 were switched to two oral antibiotic agents, 7 were switched to one oral antibiotic and 4 had their antibiotics discontinued altogether by the inpatient ID Consult Service. For the 50 patients in whom OPAT was converted to oral therapy, the most common oral antibiotics recommended by the ID Consult Service included levofloxacin (n = 23/50, 46%), trimethoprim/sulfamethoxazole (n = 11/50, 22%), amoxicillin/clavulanate (n = 8/50, 16%), metronidazole (n = 5/50, 10%), ciprofloxacin (n = 5/50, 10%) and linezolid (n = 4/50, 8%).

Of the 56 evaluable patients in whom OPAT was denied, 42 (75%) were categorized as definitive cures, 7 (12.5%) as probable cures and 7 (12.5%) as treatment failures. Six of the seven treatment failures (Table 3) occurred in patients who were either non-compliant with the prescribed oral antibiotic regimen (n = 1) or had infections that were deemed to be incurable by the ID Consult Service based on the underlying disease processes (n = 5), regardless of the route of antibiotic administration. Only one patient who was denied OPAT (1.8%) was a true treatment failure based on our predetermined study definition.

OPAT cost savings

Cost data for the original requested OPAT regimen and the regimen recommended by the ID Consult Service were calculated for all 56 patients included in the study. The overall cost of the OPAT regimens that were requested by the primary teams was estimated at $246 324, while the overall cost of the alternative treatment recommended by the inpatient ID Consult Service was $309 000. Therefore, the overall cost avoidance of averted OPAT in these 56 patients was $215 424 or $3 847 per patient. The most costly requested OPAT regimen included 6 weeks of intravenous vancomycin and piperacillin/tazobactam for the treatment of Enterobacter cloacae osteomyelitis of the right distal tibia, with an estimated cost of $13 727. The inpatient ID Consult Service recommended 6 weeks of oral levofloxacin, which provided a cost saving of $12 183 for this patient alone.

Discussion

In this study, we aimed to confirm the hypothesis that requiring ID approval for OPAT is an effective way to limit the inappropriate use of parenteral antibiotics without sacrificing clinical outcomes. During the study period, 10% (60/577) of patients for whom OPAT was requested by the primary medical/surgical teams were not approved by ID. Of the 56 evaluable patients for whom OPAT was not approved, the overall cure rate was 87.5% (49/56), which is quite favourable considering the primary healthcare providers thought intravenous antibiotics were necessary to eradicate the infection, and the patients were largely indigent with high rates of smoking, obesity and diabetes mellitus (Table 1).

When examining the details of the seven patients categorized as probable cures due to a lack of documented follow-up information in the EMR, three of these patients received oral antibiotics for the treatment of a urinary tract infection, three received oral antibiotics for the treatment of skin and soft tissue infections and one patient received oral antibiotics for the treatment of healthcare-associated pneumonia. The culture data for four of these seven patients

![Pie chart showing types of infections for which OPAT was requested: Intra-abdominal (9%), BJI (9%), SSTI (27%), UTI (14%), PNA (12.5%), CRBSI (5%), DFJ/OM (16%), DFI (4%).](image-url)
<table>
<thead>
<tr>
<th>Age (years), gender</th>
<th>Comorbidities</th>
<th>Infection type</th>
<th>ID recommended treatment</th>
<th>Duration of time to failure</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>57, male</td>
<td>DM, PVD, obesity, CAD, HTN, HLD, CVA</td>
<td>possible AKA wound infection and/or OM</td>
<td>no additional antibiotics</td>
<td>4 months</td>
<td>patient had recently completed 4 weeks of intravenous antibiotic therapy for <em>E. coli</em> AKA wound infection with no radiographic or clinical evidence of ongoing infection; readmitted with <em>E. coli</em> sepsis and died</td>
</tr>
<tr>
<td>54, male</td>
<td>lung CA, COPD, CAD, HTN</td>
<td>post-obstructive PNA</td>
<td>oral SXT + amoxicillin/clavulanate</td>
<td>1 month</td>
<td>oral antibiotic recommended as suppression (not cure) until pneumonectomy; surgery was delayed and patient ran out of oral antibiotics</td>
</tr>
<tr>
<td>49, female</td>
<td>CHF, OSA, obesity, HTN</td>
<td>cellulitis</td>
<td>oral levofloxacin + clindamycin</td>
<td>3 weeks</td>
<td>patient with recurrent LE cellulitis felt to be related to morbid obesity</td>
</tr>
<tr>
<td>51, male</td>
<td>PVD, HTN, CAD, SZ</td>
<td>cellulitis with LE ulcer</td>
<td>oral levofloxacin + dicloxacillin</td>
<td>4 months</td>
<td>progression of PVD, planned revascularization not performed</td>
</tr>
<tr>
<td>45, male</td>
<td>Crohn’s</td>
<td>intra-abdominal</td>
<td>oral levofloxacin + metronidazole</td>
<td>1 month</td>
<td>abscess resolved with oral antibiotics, but recurred once oral antibiotics were completed and drain was removed; recurrence probably due to uncontrolled Crohn’s disease</td>
</tr>
<tr>
<td>46, female</td>
<td>DM, obesity, CAD, CKD, HTN, HLD, venous stasis</td>
<td>cellulitis of LE</td>
<td>oral ciprofloxacin + clindamycin</td>
<td>6 weeks</td>
<td>recurrent cellulitis due to severe venous stasis with chronic LE oedema</td>
</tr>
<tr>
<td>27, male</td>
<td>none</td>
<td>trauma with rectal injury</td>
<td>oral ciprofloxacin + metronidazole</td>
<td>1 week</td>
<td>GSW with rectal injury; developed gluteal abscess</td>
</tr>
</tbody>
</table>

DM, diabetes mellitus; CA, cancer; CAD, coronary artery disease; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVA, cerebral vascular accident; GSW, gunshot wound; HTN, hypertension; HLD, hyperlipidaemia; LE, lower extremity; OM, osteomyelitis; OSA, obstructive sleep apnoea; PNA, pneumonia; PVD, peripheral vascular disease; SZ, seizure; SXT, trimethoprim/sulfamethoxazole.

*a* True treatment failure.
demonstrated an organism susceptible to the chosen oral antibiotic regimen, so there is little reason to suspect that these patients would have failed therapy. Culture data were not available for the three remaining patients, but, based on their clinical syndrome and response in the hospital, ID felt that oral antibiotics were appropriate. One may argue that probable cure patients could have sought medical attention at a medical centre outside the INPC EMR catchment area if they worsened. While we think this to be unlikely given the reach of the INPC, the overall cure rate would decrease to 75% (42/56) if these three patients were combined with the patients in the treatment failure category (n = 7), which is still acceptable.

Overall, 7 of 56 (12.5%) patients who were denied OPAT experienced a treatment failure according to our study definition. The medical records of these seven patients were further reviewed by one of the ID physician study investigators (D. O.). During this review, it was determined that six of the seven treatment failure patients were non-compliant with the prescribed oral antibiotic regimen or were thought by the ID Consult Service to have an incurable infection with a high likelihood of recurrence at the time of OPAT request due to an underlying chronic disease process, regardless of the route of antibiotic administration (Table 3). Several of these patients were given oral antibiotics as a bridge to a surgical or debridement procedure planned in the future. If these six patients are excluded from the treatment failure group, the true failure rate is only 1.8%, where denial of OPAT may have truly contributed to the treatment failure. This one failure was in a 57-year-old male in whom OPAT was requested for a suspected above-the-knee amputation (AKA) wound infection and/or osteomyelitis. The patient had already received 4 weeks of broad-spectrum intravenous antibiotics in the hospital, had no clinical signs of infection and had a nuclear medicine bone scan of the femur demonstrating no osteomyelitis. The inpatient ID Consult Service did not recommend further antibiotic therapy and the patient was discharged without antibiotics. Four months later, the patient was readmitted to the hospital with purulent drainage from his AKA site and Escherichia coli bacteraemia, and he died. Susceptibility testing indicated that the bloodstream isolate of E. coli was probably the same organism that had grown from an AKA wound culture months earlier. It is possible that the denial of OPAT therapy contributed to this treatment failure. However, the patient had a known history of severe peripheral vascular disease and diabetes mellitus, which were also likely contributing factors.

As demonstrated in our small, single-hospital study, denial of OPAT led to a direct OPAT cost saving of $215 424 or $3847 per patient. This cost saving does not take into account the suspected decrease in the number of hospital days or the potential costly OPAT-associated complications that may have been encountered if OPAT had not been denied. Therefore, we feel that the overall cost saving is probably underestimated in our study.

As seen in our study, the knowledge required to use OPAT appropriately is largely restricted to practitioners and pharmacists experienced in the care of serious infections. Many general healthcare providers are uncomfortable with de-escalating broad-spectrum antimicrobials or switching to oral antibiotics, as evidenced by the information derived from this study. At the time of OPAT request, 38% of the patients were on vancomycin and piperacillin/tazobactam, which is rarely an appropriate outpatient regimen. And, in some cases, OPAT was requested for anti-infectives with extremely high oral bioavailability that almost never need to be given intravenously, such as fluconazole, metronidazole and levofloxacin. Some infections historically treated with prolonged parenteral antibiotics may be safely treated using oral antibiotics, including community-acquired pneumonia, intra-abdominal infections, osteomyelitis, complicated urinary tract infections, pyelonephritis and skin/soft tissue infections. The appropriate use of oral antibiotics in lieu of OPAT for the treatment of these infections has the potential to produce significant cost savings while avoiding OPAT-associated complications. Without ID approval of OPAT, healthcare systems and third party payers will unnecessarily spend healthcare dollars for patients who are probably not candidates for OPAT, while exposing them to avoidable risks. By implementing a formal OPAT programme at our hospital that delays PICC line insertion and initiation of OPAT until ID approval has been obtained, the inpatient ID Consult Service has been able to prevent unnecessary catheter placement and inappropriate OPAT, leading to substantial cost savings. Other potential non-monetary benefits of assuring appropriate OPAT usage include appropriate antimicrobial stewardship, avoidance of line-related complications, Clostridium difficile colitis, antibiotic adverse events and bacterial resistance.

There are a number of limitations to this study. This was a retrospective case review, which may have limited our ability to accurately collect all pertinent medical information for each individual patient denied OPAT. Our sample size was relatively small, which precluded comparative statistical analysis between groups. If the EMR did not contain specific information on the desired OPAT regimen requested by the primary team, an assumption was made that the antibiotic regimen the patient was receiving at the time of request for OPAT was the intended outpatient regimen. It is possible that this may not have always been the case. However, prior to the initiation of the formal OPAT programme, patients were discharged on vancomycin and piperacillin/tazobactam inappropriately without ID involvement on several occasions. Also, this was not a comprehensive cost avoidance study and a detailed analysis of all the possible variables affecting cost was not addressed. We simply calculated the direct savings of averted OPAT courses while demonstrating a high cure rate. This study has probably underestimated the overall benefit of the programme since there is a chance that additional OPAT denials were not captured as informal conversations that may have occurred between the inpatient ID Consult Service and the primary medical teams might not have been recorded. The actual OPAT denial rate was probably higher.

Conclusions
The mandatory approval of OPAT by an inpatient ID Consult Service prevents inappropriate antibiotic usage, line complications and unnecessary costs while still leading to successful clinical outcomes in most patients. Other hospitals should consider such a programme.

Funding
This study was conducted as part of our routine work.

Transparency declarations
None to declare.
References


