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COMPARISON OF PATIENT OUTCOMES IN A PHARMACIST-LED PARENTERAL ANTIMICROBIAL THERAPY PROGRAM

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Background

Outpatient parenteral antimicrobial therapy (OPAT) is defined as the administration of parenteral antimicrobials in at least two doses given on different days and without a hospitalization between.[1] Rather than a patient being required to remain in a hospital solely to receive antimicrobial therapy after medical discharge, he or she can complete a portion of the therapy as an outpatient. The ability to discharge a patient on intravenous (IV) antimicrobial therapy has been shown to potentially reduce the high costs associated with chronic administration of antibiotics,[2] increase the patient's quality of life by granting improved flexibility and convenience, and reduce the likelihood that the patient will acquire a nosocomial infection.[2] As a result, OPAT has grown at a breakneck pace since its inception in the 1970s, and projections of its market share predict that it will soon reach the multibillion-dollar-a-year threshold.[1]

Interprofessional collaboration and careful selection of patients designated to receive OPAT are critical to ensuring successful therapy. Beyond the clinical expertise offered by infectious diseases (ID) physicians, coordination of social support and third-party authorizations between case management and pharmacy contribute significantly to a patient's ability to receive appropriate therapy. In some cases, the provision of home-based OPAT services can prevent an otherwise medically unnecessary stay at a subacute rehabilitation facility to receive IV antimicrobials for patients without reliable transportation to an infusion center. Additionally, in patients for whom adequate monitoring and follow-up cannot be guaranteed, complications related to vascular access devices and adverse drug reactions can lead to significant harm.[3] Both social and medical evaluations should therefore be integral in the process of identifying patients appropriate to receive OPAT.

Furthermore, input from pharmacists to assist in the appropriate selection of antimicrobials and of durations of therapies has the potential to stem the rising tide of resistant microorganisms. The interventions related to spectrum and duration can lead to vastly reduced rates of adverse effects due to unnecessary antimicrobial use and can also reduce the likelihood that the patient may encounter an infection caused by a resistant organism later in life.[4] Additionally, it may reduce the rate of multidrug-resistant organisms, which is especially critical for patients who must be admitted but are also most at risk. Through appropriate recommendations related to the spectrum and duration of therapy, selection of resistant microorganisms can be minimized, which partially mitigates these risks.

In November 2016 at a community hospital, a dedicated pharmacist was hired to continue to build a formal OPAT program for all patients discharged on IV antimicrobials under the care of the ID physician group. Through a collaborative-practice agreement, the pharmacist's responsibilities upon consultation were to evaluate and create a plan with recommendations related to antimicrobial selection (including drug, dose, route, frequency, and duration) as well as monitoring parameters. The pharmacist also provided patient education and assistance to case managers involved with disposition planning. Upon patients' discharge from the hospital, the pharmacist continued weekly monitoring throughout the duration of therapy of all patients who received such consultative services during their inpatient stay. Because of the relatively new nature of this OPAT program and the number of "good catch" events—in which a potential medical error related to the therapy or monitoring was prevented—observed since the program's formal inception, this study sought to examine the impact of an OPAT program for those patients receiving OPAT at hospital discharge.

Methods

This was a retrospective observational cohort study examining patients with an order for an IV antibiotic following discharge from a community hospital within the period of December 1, 2016, to May 31, 2017. Patients who received OPAT consults during their index hospital stay were compared to those patients who did not receive consults in the same period. Only adult patients were included in this study. Patients residing in a nursing home or long-term care facility prior to admission and those also receiving oral antimicrobials were excluded from the analysis. The primary objective was the proportion of patients in each group readmitted within 30 days of discharge and OPAT initiation, which was stratified by the reason for readmission (ID process, adverse drug event, or unrelated reason).

Baseline demographic information collected included age, sex, weight, and length of stay prior to discharge. Type of infection, antimicrobial selection (including agents with antipseudomonal activity or requiring therapeutic drug monitoring), duration of treatment, and disposition at hospital discharge were also collected from the electronic medical record. As avoiding unnecessary short-term acute rehabilitation (SAR) stays in cases where therapy can be altered and coordinated with home healthcare is one potential benefit of OPAT, change in disposition from admission to discharge was also collected.

Statistical Analysis

The Fisher's exact test and chi-square analyses were utilized as appropriate for nominal endpoints including the 30-day readmission rate, use of each antimicrobial class, and use of agents with a high risk for a *Clostridioides difficile* infection, such as ceftriaxone, or requiring therapeutic drug monitoring. The Wilcoxon rank-sum test was utilized to determine the significance of differences in length of stay and duration of therapy. Statistical Package for the Social Sciences (SPSS) software was utilized for these analyses. All other variables and baseline demographic information were described utilizing descriptive statistics.

Results

No statistically significant differences between groups were seen in terms of demographic information (Table 1).

	OPAT Consult (*n* = 95)	**No OPAT Consult (*n* = 22)**	***p* Value**
Median Age (IQR)	61 (21)	63 (26)	0.503
Sex (%)			
M	42 (44)	6 (27)	0.146
F	53 (56)	16 (73)	
Median Weight (IQR)	91 kg (35 kg)	79 kg (41 kg)	0.085
Median Index LOS (IQR)	6 (5)	7 (8)	0.313

Table 1. Patient Demographics

No statistically significant difference between the readmission rates of the OPAT consult group and the non-consult group was observed; however, the rate for the former was less than half of the latter, numerically (14.73% vs. 31.82%, p = 0.07). Additionally, the proportion of patients requiring a change in disposition did not vary significantly between groups (Table 2), with 39 (41%) patients with a consult and 12 (55%) patients without a consult being discharged to a SAR center or extended-care facility (ECF; p = 0.252). Bacteremia associated with various sources of infection was the most common type of infection requiring IV therapy in both groups, constituting 35% of patients in the OPAT consult group and 59% of the patients without a consult. Differences in provider type and indication for therapy between groups were statistically significant ($p < 0.0001$; 3×10^{-12}). The median total days of therapy for patients with a consult was 24, in comparison to 25 in the non-consult group (p = 0.095).

	OPAT Consult (n = 95)	**No OPAT Consult (n = 22)**	***p* Value**
Disposition Change	39 (41%)	12 (55%)	0.252
Indication for Therapy			3×10^{-12}
Empyema	7	2	
Osteomyelitis	11	2	
Bacteremia	33	13	
Intra-Abdominal Infection	10	3	
Skin and Soft Tissue Infection (SSTI)	25	0	
Other	9	2	
Primary Provider Type			0.000095
Pulmonary	5	7	
Cardiology	10	1	
Surgery	25	4	
Internal Medicine	52	8	
Oncology	3	2	
Median Days of Therapy (IQR)	24 (19)	25 (17)	0.095

Table 2. Disposition Change, Therapy Indication, and Provider Type, All Patients

The most significantly differing trends between groups were evident in prescribing practices. The usage of antipseudomonal coverage was significantly lower in the OPAT consult group (39.58% vs. 86.36%, $p = 0.00006$). Additionally, utilization of ceftriaxone, known for its potential to predispose patients to *C. difficile* infections, was also significantly lower in the OPAT consult group (9.47% vs. 45.45%, $p = 0.00004$). Differences in other key antibiotics that serve as stewardship targets were also seen with piperacillin-tazobactam, cefepime, and vancomycin (Table 3). Also of interest, patients without an OPAT consult who were discharged to a SAR center or ECF were significantly more likely to have been prescribed agents requiring therapeutic drug monitoring (100% vs. 59.56%, $p = 0.038$) and to have later required readmission (54.55% vs. 16.22%, $p = 0.001$).

Drug Choice	**OPAT Consult (*n* = 95)**	**No OPAT Consult (*n* = 22)**	***p* Value**
Ampicillin	5	2	0.495
Ampicillin-Sulbactam	12	2	0.645
Piperacillin-Tazobactam	13	11	0.0001
Cefazolin	15	3	0.801
Ceftazidime	1	0	0.203
Ceftriaxone	9	10	0.00004
Cefuroxime	1	1	0.255
Cefepime	10	7	0.011
Meropenem	8	5	0.054
Ertapenem	4	1	0.944
Gentamicin	6	5	0.017
Tobramycin	0	4	0.0002
Vancomycin	39	19	0.0001
Linezolid	0	2	0.023
Daptomycin	1	0	0.213
Metronidazole	2	5	0.0002
Clindamycin	2	2	0.104
Fluconazole	2	2	0.104
Antipseudomonal Agents	37	19	0.00006

Table 3. Therapeutic Drug Choice, All Patients

Readmitted Subgroup

When examining readmitted patients as a subgroup, several differences between those receiving a consult and those without were seen (Table 4). Significant differences in the indications for therapy ($p = 0.009$) were seen in this population, with bacteremia and SSTIs as the most common infection types in the OPAT consult (71%) and non-consult (43%) groups, respectively. Additionally, a trend was seen showing that patients in this subgroup without a consult were more likely to have experienced a change in disposition (85.71% vs. 42.86%, $p = 0.061$).

	OPAT Consult (n = 14)	**No OPAT Consult (n = 7)**	***p* Value**
Median Age (IQR)	61 (16)	64 (26)	0.711
Sex			
Male	8	5	0.525
Female	6	2	
Indication for Therapy			0.009
Osteomyelitis	2	1	
Bacteremia	3	5	
Intra-Abdominal Infection	2	1	
Skin and Soft Tissue Infection (SSTI)	6	0	
Other	1	0	
Median Index Length of Stay in Days (IQR)	6 (2)	7 (3)	0.352
Median Days to Readmission (IQR)	12 (14)	9 (6)	0.368
Disposition at Discharge			
Home	8	1	0.061
ECF or SAR	6	6	
Disposition Change	6 (43%)	6 (86%)	0.061
Median Total Days of	28 (24)	28 (27)	0.190

Therapy (IQR)			
Reason for Readmission			
ID Process			0.216
Adverse Drug Event	2	3	
Unrelated Process	3	1	
	9	3	

Table 4. Readmitted Patients

Discussion

No statistical significance in terms of the primary objective (30-day readmission rate) was seen in the study; however, the more than twofold difference in readmission rate can certainly be seen as clinically significant. The readmission rate of 14.74% was also similar to the 21.5% readmission rate reported by another study, which somewhat adds to the confidence with which the results from this study can be interpreted.[5]

Considerable improvements in antimicrobial stewardship were seen when comparing the group of patients receiving a consult to those who did not. This enhancement in stewardship was primarily via reduced utilization of antipseudomonal coverage, vancomycin, and ceftriaxone, which demonstrated the key role that such programs can have on selecting therapy with an appropriately narrow spectrum. One way by which OPAT can reduce costs and improve patient outcomes comes via the involvement of ID specialists to improve the selection of appropriately narrow-spectrum antimicrobials. By avoiding the use of overly broad coverage, the risk of off-target eradication of the gut microbiome and subsequent development of a *C. difficile* infection can be significantly reduced. Beyond the clinical impact of this variety of infectious diarrhea, *C. difficile*'s propensity for toxin production leads to 4.8 billion dollars in additional costs to hospitals in the United States annually.[6] For example, unnecessary use of ceftriaxone, a cephalosporin utilized for a variety of infections, has become one of many potential targets for antimicrobial stewardship programs because of its common use and propensity for causing this type of infection.[6,7] It is imperative that therapies be selected appropriately to cover only the types of microorganisms likely to be causing the patient's infection and that therapies be narrowed when culture and susceptibility data are available. This is a major point of potential impact for pharmacist-led OPAT services.

The difference in readmissions seen for patients without a consult sent to a SAR center or ECF may hint at a potential positive influence seen with the inclusion of a dedicated ID clinical pharmacy specialist to coordinate careful monitoring during the course of OPAT. Especially when utilizing agents requiring therapeutic drug monitoring, such as vancomycin or aminoglycosides, the potential for significant adverse effects is considerable. Additionally, poor availability of lab data during the course of OPAT has been noted to be a significant risk factor for readmission, which may partially explain the difference seen here.[8] The potentially increased debility or acuity of patients more likely to be sent to a SAR center or ECF, in comparison to a patient able to be sent home, could have also contributed to this observation; however, an increase in readmission for patients discharged to these facilities after receiving a consult was not observed.

The need for appropriate monitoring and communication between healthcare systems should be given careful consideration prior to the implementation of OPAT. One report noted that 26% of sites surveyed had a team specifically designated to handle OPAT cases.[5] A survey of practitioners involved in an OPAT service indicated that up to 70% had seen such therapy implemented without a consult from an ID specialist, and another study showed that the addition of a pharmacist or ID physician or pharmacist to an OPAT team raised adherence to monitoring by 32% and 64%, respectively.[9,10] One study showed that cases reviewed by an ID physician led to changes in therapy from parenteral to oral agents in 27%–40% of cases.[9] This shows the value of a dedicated OPAT team's ability to improve patient care via appropriate selection of antimicrobial therapy from a therapeutic perspective, which often reduces costs.

Although poor communication can be a barrier to the success of OPAT, adverse effects have been cited as the primary reason for OPAT discontinuation or therapy modification in 3%–5% of cases.[9] The rate of readmission, potentially requiring a change in therapy, in this study for adverse events in the OPAT and non-OPAT groups was similar to this cited figure, at 3.2% and 4.5%, respectively. A survey of ID physicians conducted in 2012 showed that only 22% of the OPAT programs in which they worked had a way to track medication errors, "near misses," or adverse events.[5] Additionally, it is of utmost importance that patients who are to receive OPAT be carefully selected to ensure that they have appropriate social and financial support to receive therapy at home, at an infusion center, or at another location. The potential ramifications for patients inappropriately selected for outpatient therapy include both clinical decompensation as well as the potential for enhanced resistance by the responsible pathogen due to incomplete eradication.

Several limitations should be considered when interpreting the results of this study. The small sample size and timing of the study period at the advent of the program could have affected the results. This trend could possibly have been due to the novelty of the new program or to increased provider confidence in the utilization of a formalized OPAT program able to more consistently offer improved monitoring and follow-up after discharge. The lack of assessments related to appropriateness of therapy, comorbidities, severity of infection, and causative pathogen limits the generalizability of these findings.

As OPAT services continue to expand in the United States, further investigations utilizing larger sample sizes and examining shifting trends in patient outcomes should be conducted in order to further assess the value of the program and monitor for potential quality-improvement opportunities. Furthermore, patient and provider satisfaction data could be included to better assess the improvements in quality of life and perception of value associated with the program. This study suggests a potential indication for the potential patient-care improvements related to improved patient outcomes that OPAT services can offer to patients.

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