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Perspectives of Patients on Outpatient Parenteral Antimicrobial Therapy: Experiences and Adherence

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Background. Nonadherence to medication is a burden to the US health care system and is associated with poor clinical outcomes. Data on outpatient parenteral antimicrobial therapy (OPAT) treatment plan adherence are lacking. The purpose of this study is to determine the rate of nonadherence and factors associated with it.

Methods. We surveyed patients discharged from a tertiary hospital on OPAT between February and August 2019 about their baseline characteristics, OPAT regimen, adherence, and experience with OPAT.

Results. Sixty-five patients responded to the survey. The median age was 62 years, and 56% were male. The rate of reported nonadherence to intravenous (IV) antibiotics was 10%. Factors associated with nonadherence to IV antibiotics included younger age, household income of <\$20 000, and lack of time for administering IV antibiotics (30 vs 64 years, $P < .01$; 83% vs 20%, $P < .01$, and 33% vs 4%, $P = .04$, in the nonadherent vs adherent groups, respectively), while less frequent administration (once or twice daily) and having friend or family support during IV antibiotic administration were associated with better adherence (17% vs 76%, $P < .01$, and 17% vs 66%, $P = .03$, in the nonadherent vs adherent groups, respectively). Most patients attended their infectious diseases clinic visits ($n = 44$, 71%), and the most commonly cited reasons for missing an appointment were lacking transportation ($n = 12$, 60%), not feeling well ($n = 8$, 40%), and being unaware of the appointment ($n = 6$, 30%).

Conclusions. Less frequent antibiotic dosing and better social support were associated with improved adherence to OPAT. In contrast, younger age, lower income, and lack of time were associated with nonadherence.

Keywords. OPAT; adherence; no-show; compliance; social support.

Outpatient parenteral antimicrobial therapy (OPAT) is an effective modality for treating patients with serious infectious diseases (ID) outside of a hospital setting [1, 2]. By allowing patients to receive treatment at home, OPAT avoids expenses associated with prolonged hospital stays, reduces exposure to nosocomial pathogens, and allows patients to maintain a normal lifestyle [3]. OPAT is generally considered safe but requires close monitoring for therapy-related complications and treatment failure [4]. Past studies have shown that readmission rates for OPAT patients range from 6% to 26% [5–7]. These readmissions can result from worsening infection, line complications, or comorbidities [5–7].

Medication nonadherence is a burden to the US health care system, leading to higher health care costs and worse patient outcomes. The annual cost of medication nonadherence in the United States is estimated to be \$300 billion [8, 9]. Nonadherence to oral antibiotics has been linked to poor clinical outcomes such as infection relapses, need for new antibiotics, and additional medical procedures [10]. Factors that are associated with nonadherence to oral antibiotics include prescription of multiple antibiotics and changing health care providers for outpatient care [10]. In another study, increased dosing frequency negatively impacted oral antibiotic adherence rates [11]. Antibiotics taken once, twice, or 3 times daily had adherence rates of 80%, 69%, and 38%, respectively [11]. Reasons for missing scheduled oral doses include being away from home, asleep, or simply forgetting [10]. However, there is a lack of literature on the rates and predictors of nonadherence in OPAT.

The Infectious Diseases Society of America recommends close clinical follow-up for OPAT patients [12]. Thus, patients' adherence to office visits is a vital component of OPAT care. A recent study showed that attendance at follow-up OPAT clinic visits was associated with a lower readmission rate compared with those who had no follow-up visit [13]. Adherence to OPAT follow-up appointments has been reported to be high,

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but factors such as transportation, illness, and work commitments impede some patients from attending their scheduled appointments [14].

This study aims to quantify the rate of nonadherence among OPAT users and understand the reasons leading to “no-show” appointments. We conducted a survey to gather detailed information about patient-identified factors related to nonadherence.

METHODS

Instrument

The survey was developed in collaboration with an ID physician and an ID pharmacist. This survey contained 21 multiple choice or Likert-style items and 2 free-text items allowing respondents to provide additional comments. The survey was piloted with a group of content experts, and questions were modified based on their feedback. The survey recorded the respondents’ demographics, experience with and adherence to OPAT, communication with health care providers, and barriers to receiving optimal OPAT care (Appendix).

Study Population and Distribution

The Infectious Diseases Clinic at Washington University in St. Louis School of Medicine monitors patients who are discharged from Barnes-Jewish Hospital on OPAT following inpatient care. The OPAT program follows 1500 patients annually. About one-third of the patients are discharged to post-acute care facilities, while the rest are discharged home with home health and outpatient infusion centers. The majority of the patients (50%) discharged home on OPAT are cared for by BJC Home Care Services, while the rest are covered by multiple different home health care agencies such as Coram and Option Care Health. Only patients who were discharged home were asked to participate in the survey. Patients discharged on OPAT were scheduled to follow-up with an ID provider in 2 weeks. The appointment is usually scheduled before hospital discharge, and the instructions are printed and handed to the patient upon hospital discharge. For the small number of patients who are discharged before appointment scheduling, the clinic staff contact the patient to make the appointment for the visit. Patients receive an automated call from the clinic to remind them about the appointment 3 days before the visit and a text message 2 days before the visit. The most common infection category in our OPAT program is bone and joint infections (40%), followed by bloodstream infections (21%), intra-abdominal infections (11%), and skin and soft tissue infections (8%). The clinic distributed our surveys to patients returning for their follow-up appointments between February and August 2019. Patients then placed the confidential, anonymous surveys in a locked survey box. The survey was also sent via mail to patients’ home addresses on April 29, 2019, and July 22, 2019, to patients who

had completed their course within the last 30 days. Patients were asked to mail the completed survey back to the investigators in an anonymous, prestamped return envelope. The study was approved by the Washington University School of Medicine Human Research Protection Office and St. Louis College of Pharmacy’s Institutional Review Board.

Data Analysis

Categorical data were presented using frequencies. To analyze risk factors associated with nonadherence, we used the Fisher’s exact test for categorical variables and the Mann-Whitney *U* test for continuous variables. For multiple choice questions, we analyzed the responses based on the percentage of patients who answered “agree” or “strongly agree” as opposed to other answers. Differences were considered statistically significant if $P < .05$. All quantitative analyses were performed using SAS 9.4 software (Cary, NC, USA).

We also analyzed qualitative data. Participants were asked to answer the free-text questions “Explain the barriers you encounter to taking your IV antibiotics as prescribed” and “Please use the space below to share any additional information about your experience taking IV antibiotics or to elaborate on a question listed above.” Three authors (S.D., C.S., and Y.H.) systematically read responses and independently categorized them. Disagreements were resolved by discussion between the team members. Percentages of respondents who answered each item and illustrative quotes are presented.

RESULTS

A total of 174 surveys were mailed to adult OPAT patients. Twenty-seven (16%) participants responded and completed the survey. Additionally, 38 participants completed surveys in the clinic during the study period, resulting in a total of 65 survey responses. Respondents’ median age (interquartile range [IQR]) was 62 (53–69) years, and 55% were male. Sixteen respondents (27%) had an annual income below \$20 000, and 19 (33%) were unemployed. Almost half of the respondents had to pay a copayment or coinsurance in order to receive IV antibiotics ($n = 30$, 49%). Thirty-five (55%) respondents received only 1 IV antibiotic, 17 (27%) received 2, and 12 (19%) received at least 3. Most respondents received intravenous antibiotics either once or twice a day (24, 38%, or 19, 30%, respectively). Thirty-four respondents (55%) spent at least an hour administering their antibiotics, including 14 (23%) who spent 2 hours per day (Table 1).

Most respondents (90%) reported strict adherence to IV antibiotics, while 6 (10%) reported missing 1–2 doses per week. Thirty-seven respondents (60%) reported having no reminder system in place, while 28 (45%) reported using an alarm, “chart,” or reminder from someone. Thirty-nine respondents (62%) had a family member or friend help them administer IV

Table 1. Characteristics and Responses of 65 Patients who Responded to the Survey

Characteristics	No. (%) or Median (IQR)
Age, y	62 (53–69)
Sex (female; 58 responses)	26 (44.8)
Annual household income (59 responses)	
<\$20 000	16 (27.1)
\$20 000–\$50 000	21 (35.6)
\$50 000–\$100 000	17 (28.8)
\$100 000+	5 (8.5)
Employment (57 responses)	
Employed	20 (35.1)
Unemployed	19 (33.3)
On disability	18 (31.6)
Does insurance cover cost of antibiotics (61 responses)	
All of the cost	30 (49.2)
Part of the cost	30 (49.2)
None	1 (1.6)
How many IV antibiotics prescribed (64 responses)	
1	35 (54.7)
2	17 (26.6)
3	2 (3.1)
4 or more	10 (15.9)
How often do you take IV antibiotics (63 responses)	
Once daily	24 (38.1)
Twice daily	19 (30.2)
Three times daily	16 (25.4)
Other	4 (6.3)
How much time do you spend per day taking IV antibiotics (62 responses)	
<30 min	12 (19.4)
30–60 min	16 (25.8)
1–2 h	20 (32.3)
2+ h	14 (22.6)
How many other medications do you take (63 responses)	6 (3–10)
Whom do you ask if you have questions about IV antibiotics (63 responses) ^a	
Home health service	47 (74.6)
Pharmacy	22 (34.9)
Primary doctor	21 (33.3)
Nurse	3 (4.8)
I wait until next doctor visit	2 (3.2)
If I miss my doctor's appointment, it is because... (62 responses) ^a	
I have never missed an appointment	44 (71)
Reasons for missed clinic appointment (20 of 61 responses) ^a	
I don't have a ride	12 (60)
I don't feel well	8 (40)
I was unaware of the appointment	6 (30)
I don't have time off work	2 (10)
I was hospitalized	1 (5)
How do you remember to take your IV antibiotics (62 responses) ^a	
I just remember	37 (59.7)
I have an alarm set up	14 (22.6)
Someone reminds me	14 (22.6)

Table 1. Continued

Characteristics	No. (%) or Median (IQR)
How many doses of IV antibiotics have you missed per week (62 responses)	
1–2	6 (9.7)
3–4	0
>4	0
None	56 (90.3)
Who administers your IV antibiotics (63 responses) ^a	
A family member/friend	39 (61.9)
Self only	18 (28.6)
A nurse	6 (9.5)

Abbreviations: IQR, interquartile range; IV, intravenous.

^aRespondents were able to select all responses that applied; numbers may add up to more than 100%.

antibiotics, and 18 (29%) reported administering IV antibiotics independently (Table 1). Respondents contacted a variety of health care resources when they had questions about their IV antibiotic therapy including home health service ($n = 47$, 75%), pharmacist ($n = 22$, 35%), or primary physician ($n = 21$, 33%). Most respondents ($n = 44$, 71%) were compliant with ID doctor appointments. Reasons for missed clinic appointments were mostly due to lack of transportation in 12 (60%), not feeling well in 8 (40%), and being unaware of the appointment in 6 (30%) responses. In the subset of respondents who answered the survey by mail, 18 (62%) reported adherence to clinic visits. Among the 11 mail-in respondents who reported missing a clinic visit, the most common reasons were not feeling well in 7 (63%) and lack of transportation in 4 (36%) responses.

Seventeen respondents (27%) felt they spent too much time administering antibiotics. Only 4 (6%) said they did not have enough time to administer the prescribed antibiotics. Twenty-one respondents (34%) reported not knowing the side effects of their medication, while 6 respondents (10%) reported having a serious side effect from the antibiotics (Tables 1–2).

Factors that were associated with medication nonadherence included younger age, household income of <\$20 000, and not having enough time for IV antibiotic administration (30 vs 64 years, $P < .01$; 83% vs 20%, $P < .01$, and 33% vs 4%, $P = .04$, in the nonadherent vs adherent groups, respectively), while less frequent administration and having friend or family support during IV antibiotic administration were associated with lower risk of nonadherence (17% vs 76%, $P < .01$, and 17% vs 66%, $P = .03$, in the nonadherent vs adherent groups, respectively). Lack of knowledge about side effects and medication reminders were not found to be associated with nonadherence (Table 3).

A total of 24 patients provided free-text responses about barriers to receipt of IV antibiotics (Table 4). Common barriers included difficulties with the administration of antibiotics by the

Table 2. Responses of Survey Participants to the Multiple Choice Questions

Likert Scale Question Responses	Agree/Strongly Agree, No. (%)	Neutral, No. (%)	Disagree/Strongly Disagree, No. (%)
I don't have enough time to administer my antibiotics	4 (6.3)	5 (7.8)	55 (85.9)
I don't know the side effects of my medications	21 (33.9)	10 (16.1)	31 (50)
I spend too much time administering antibiotics	17 (27.4)	13 (21)	32 (51.6)
I do NOT have a consistent way to get my IV antibiotics	0	4 (6.5)	58 (93.5)
I would like to be able to take my IV antibiotics outside the home	6 (9.8)	13 (21.3)	42 (68.9)
I would be interested in a device that makes it easier to move around during IV antibiotic administration	20 (31.7)	23 (36.5)	20 (31.7)
I would be interested in a device that monitors how I take my IV antibiotics and shares this information with my doctor	27 (42.9)	25 (39.7)	11 (17.5)
I experience serious side effects from my IV antibiotics	6 (9.7)	9 (14.5)	47 (75.8)

Abbreviation: IV, intravenous.

patient (n = 5, 21%), central line–related issues (n = 5, 21%), extensive time needed to administer IV antibiotics (n = 4, 17%), challenges with going to doctor appointments while on IV antibiotics (n = 3, 13%), medication side effects (n = 2, 8%), and limitations in social activities (n = 1, 4%).

Furthermore, 24 respondents provided additional free-text responses about their overall experience on OPAT. The most common themes included were about experiencing side effects (n = 7, 29%) and having a great experience with OPAT (n = 5, 21%), whereas 2 patients (8%) commented about the financial cost of OPAT. As one respondent explained, “Out of pocket costs [were] too high. Still paying on the \$4,000 bill.” One respondent discussed being frustrated about not receiving the results of the weekly lab draws. Despite the reported challenges with OPAT, 21% of participants providing free-text responses felt that the use of OPAT was easy and satisfying. As one respondent stated, “Very easy. Anyone can do it” (Table 5).

DISCUSSION

This study examined patient-reported rates of nonadherence with OPAT and identified factors associated with nonadherence. Overall, patients self-reported relatively high rates of adherence

to therapy, with 90% of respondents reporting no missed doses in an average week. OPAT medication nonadherence was found to be disproportionately associated with being young, low-income, self-reportedly busy, and without social support. Nonadherence to clinical follow-up was more common, as 29% reported missing an ID appointment. The most common reason leading to “no-show” appointments at the ID clinic was lack of transportation.

This study supports a strong positive correlation between medication adherence and age. The median ages of the nonadherent and adherent groups were 30 and 64, respectively. This may be surprising, as the geriatric population is more prone to chronic and recurrent illness, which may require chronic medication with multiple drugs. However, others have also found that younger adults are more likely to be nonadherent to therapy in various other populations [15–18]. Therefore, other risk factors such as knowledge of the drug's purpose, complexity of the drug regimen, and type of prescriber should be considered when planning OPAT treatment regimens [19].

Multiple socioeconomic factors have been found to affect adherence. Higher rates of medication nonadherence have been

Table 3. Factors Associated With Nonadherence With IV Antibiotics

Variable	Adherent Patients (n = 56), No. (%) or Median (IQR)	Nonadherent Patients (n = 6), No. (%) or Median (IQR)	P Value
Age, y	64 (57–69)	30 (19–39)	<.01
Sex (female)	23 (46)	1 (20)	.37
Low income (<\$20 000)	10 (19.6)	5 (83.3)	<.01
Less frequent administration (daily or twice daily) for IV antibiotics	41 (75.9)	1 (16.7)	<.01
Family support in administration of IV antibiotics	37 (66.1)	1 (16.7)	.03
I spend too much time administering antibiotics	15 (27.3)	2 (33.3)	>.99
I don't have enough time to administer my antibiotics	2 (3.6)	2 (33.3)	.04
I would like to be able to take my IV antibiotics outside the home	5 (9.4)	1 (16.7)	.49
I don't know the side effects of my medications	20 (37)	1 (16.7)	.41
Patient having a reminder set up	21 (38.2)	3 (50)	.67
I missed an infectious diseases clinic appointment	16 (29.1)	4 (66.7)	.08

Abbreviations: IQR, interquartile range; IV, intravenous.

Table 4. Concerns Raised About Barriers in OPAT

Complaint	Frequency (% of 24 who Responded to Item)	Illustrative Quote
Difficulty in administering IV antibiotics by the patient	5 (20.8)	<p>"[I had difficulty in] making sure everything stays sterile while using the medicine"</p> <p>"Cannot push plunger slow enough—too difficult to push in all the ml's over such a long time doing it manually"</p> <p>"[I had difficulty] learning how to switch bags. making sure every 8 hours to take the oral antibiotic"</p> <p>"My girlfriend had to go in the hospital for 2 days and it was hard to do but I did them. She called to remind me"</p>
Peripherally inserted central catheter issues	5 (20.8)	<p>"PICC line isn't waterproof"</p> <p>"[I had a] clog in my IV port"</p> <p>"[Had difficulty] changing clothing [while having PICC line in place]"</p>
Time needed to administer IV antibiotics	4 (16.7)	<p>"That it was three times a day and 1.5 hrs each time. Very easily snagged"</p> <p>"It takes too long"</p>
Challenges with doctor appointments	3 (12.5)	<p>"Making appointments around the IV meds"</p> <p>"The only time I may have an issue is the time of day. I normally take antibiotic around lunch time everyday unless I'm at Dr Appointment which may delay the time of day its administered"</p>
Medication side effects	2 (8.3)	"I had severe side effects to all the medications I was prescribed"
Limitation in social activities	1 (4.2)	"Not being able to go and socialize while taking them"

Abbreviations: IV, intravenous; OPAT, outpatient parenteral antimicrobial therapy; PICC, peripherally inserted central catheter.

reported in a study assessing low-income, uninsured patients [20]. Individuals with lower income tend to be younger, which is a known risk factor for nonadherence [21]. Social support networks also have an impact on adherence to OPAT. This study showed that having a friend or family member assist with IV antibiotic administration was associated with better rates of OPAT adherence. This is consistent with prior studies that have shown the association between medication adherence and practical social support, which can be defined as having a family member who helps with medications or transportation [22].

Previous studies have found mixed results for using reminders as an aid to assist with medication adherence [23, 24]. In our study, we did not find an association between reminders and adherence. This adds up to a mixed collection of results in the literature on the efficacy of reminders across multiple modalities to improve medication adherence. Vervloet et al. found

that text message reminders improve medication adherence to oral medication in type 2 diabetes patients who are electronically monitored in real time [23]. Liu et al. showed that reminders from medication monitors improved adherence in tuberculosis patients, but text message reminders did not. In general, many types of interventions have attempted to improve adherence in diverse treatment regimens, but most have failed [24].

Our study showed that simpler regimens with once- or twice-daily dosing were associated with improved adherence to IV antibiotics. This is consistent with literature that reports lower rates of adherence with multiple administrations per day [11]. Unlike oral antibiotics, IV antibiotics require significantly more time to administer. In this survey, 55% of patients reported spending more than an hour per day to administer the antibiotics, with nearly a quarter of all patients spending at least 2

Table 5. Summary of Additional Comments Provided by Patients About Their Experience

Comment	Frequency (% of 24 who Responded to Item)	Illustrative Quote
Experienced side effects	7 (29.2)	<p>"Had allergic reaction and had to stop treatment"</p> <p>"The antibiotic I was taking caused constipation and lowered my white blood cell count"</p> <p>"The side effects were terrible! Especially after 2 weeks! I was happy when it was over. Thanks."</p>
Did have a good experience	5 (20.8)	<p>"I was happy with the ability to use the device provided and I didn't need an IV pole like in the hospital"</p> <p>"I like taking at home instead of an outpatient location. Especially since its daily. Very convenient"</p> <p>"Very easy. Anyone can do it"</p>
Financial cost	2 (8.3)	<p>"Out of pocket costs [were] too high. Still paying on the \$4,000 bill"</p> <p>"I called billing 3x with no return call. I have supplies left that I did not need. Would like to get credit for those supplies! I did not"</p>

Abbreviation: IV, intravenous.

hours per day. Clinicians should keep this in mind when recommending an OPAT regimen and use simpler regimens when feasible.

The strengths of this study include novelty in examining adherence in the OPAT population, of which data are scarce. The participants spanned different ages and socioeconomic backgrounds, allowing us to examine the effects of these factors on adherence. This study identified OPAT-specific factors that are associated with nonadherence so that clinicians can identify those at high risk and address preventable factors to improve adherence.

Despite a small sample size, this is the largest study addressing nonadherence in OPAT. The response rate to the mail survey was low; however, this could in part be due to the lack of reminders. As the responses were anonymized, we were not able to compare the respondents with the nonrespondents to see if the 2 groups were different. However, the fact that responses came from patients across different age groups and socioeconomic backgrounds improves the generalizability of the survey results. Additionally, like other studies, the main limitation of the results presented here is a dependency on subjective self-reporting. These descriptions may be unreliable for 3 different reasons: (1) subjects may have forgotten when and how they took their medication, (2) they may not have been truthful out of the perceived fear that their answers would affect their continued treatment, or (3) patients who were unconcerned with their care may not have answered survey questions, whereas patients concerned about their health did respond (nonresponder bias). We addressed each of these concerns as follows. First, to decrease the likelihood of forgetfulness, surveys were administered to current patients in the clinic or mailed to patients who recently completed their OPAT treatment. Second, patients were notified that surveys were anonymous, and identifying information was removed. Third, while the nonresponder bias might have resulted in a lower response rate from nonadherent patients, we collected enough responses from patients who reported nonadherence and were able to identify some risk factors associated with medication adherence. The outcomes of this study can lead to a more efficient workflow that improves patient care, medication adherence, and clinic attendance.

CONCLUSIONS

Although younger age, lower income, and lack of time for IV antibiotic administration were factors associated with nonadherence, less frequent dosing regimens and having friend or family support during IV antibiotic administration were protective. Lack of transportation was also the main risk factor for missing follow-up ID clinic visits. With the information collected in this survey, we garnered a better understanding of this patient population, which will lead to targeted efforts to improve care for OPAT patients.

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