Open Forum Infectious Diseases

BRIEF REPORT

Vancomycin or Daptomycin for Outpatient Parenteral Antibiotic Therapy: Does It Make a Difference in Patient Satisfaction?

Katherine H. Wu,[1] George Sakoulas,[2,3] and Matthew Geriak[3]

[1]Skaggs School of Pharmacy, University of California, San Diego, La Jolla, California, USA, [2]Division of Host-Microbe Systems and Therapeutics, Department of Pediatrics, University of California, San Diego School of Medicine, La Jolla, California, USA, and [3]Sharp Memorial Hospital, San Diego, California, USA

A 5-question telephone survey was administered to compare satisfaction between patients receiving vancomycin vs daptomycin outpatient parenteral antimicrobial therapy (OPAT). Twenty-seven patients completed the survey (40%). Vancomycin had higher daily interference score than daptomycin (P = .03). All patients receiving daptomycin reported a satisfaction score ≥8/10, as compared to 67% of patients who received vancomycin (P < .03). OPAT antibiotics with less cumbersome administration regimens may translate into higher patient satisfaction and quicker return to life normalcy.

Keywords. daptomycin; MRSA; outpatient infusion therapy; vancomycin.

With the development of new antimicrobials agents, outpatient parenteral antimicrobial therapy (OPAT) has increasingly been used to manage patients with serious bacterial infections [1]. OPAT allows for a more rapid and efficient transition from inpatient to outpatient settings, thus shortening costly lengths of hospital stay, allowing a quicker return to work, improving patient satisfaction, and reducing the likelihood of hospital-acquired infection [2–6].

Numerous antibiotic options are available to clinicians in selecting OPAT [7], centered initially on spectrum of activity, but also involving characteristics specific to the antibiotics, including tolerability, infusion time, number of daily doses, drug concentration monitoring, and the possibility of self-administration. While these latter characteristics are less relevant in the inpatient setting, their importance looms larger in the OPAT setting. How important is it to the patient to have an antibiotic with decreased infusion time, reduced number of daily doses, and decreased blood draws? In this study, our main goal was to get patient feedback about whether or not the choice of antibiotic played a role in how satisfied they were with their treatment.

The treatment of resistant gram-positive infections has evolved considerably in the last 2 decades through the approval of several antibiotics [8]. While vancomycin has been the treatment standard for decades due to its low drug acquisition cost, it has cumbersome dosing characteristics of 2–3 doses per day in patients with normal renal function. With each vancomycin infusion being 60–90 minutes, it is extremely onerous for OPAT [9]. The need for therapeutic drug monitoring not only places an increased burden on providers, due to drug serum level concentration–predicated dose adjustment, but creates opportunity for dosing errors to occur. These factors create a medical need for less cumbersome antibiotics in OPAT that may improve productivity of both patients and providers, and reduce provider liability, the value of which cannot be quantified financially.

Vancomycin and daptomycin are commonly utilized antibiotics in OPAT [10–13]. At our OPAT treatment center, both groups require weekly renal monitoring. Daptomycin-treated patients require weekly creatine phosphokinase levels to be drawn, and vancomycin drug levels are also drawn weekly. The difference is that repeated vancomycin drug level monitoring often results in dose changes over the duration of treatment based on the pharmacokinetics. From a drug administration standpoint, vancomycin is usually infused twice per day, infused over 60–120 minutes. Daptomycin is a less cumbersome option [14, 15] requiring 1 dose every 24–48 hours (depending on renal function) that can be administered in 2 minutes. Surprisingly, there is a paucity of data in the literature examining the role of antibiotic therapy in impacting patient experience with OPAT.

METHODS

The treating physician conducted a brief 5-question survey with his patients post–OPAT treatment by phone as part of an internal quality assurance measure. The study team was given the surveys to analyze the results, retrospectively. The surveys were screened to meet the following criteria: Subjects were required to be ≥18 years of age and to have completed a course of either vancomycin or daptomycin OPAT at home. All those receiving care at the infusion center, nursing facility, or clinics were excluded. Subjects were excluded if complete data were unavailable.

Received 10 June 2021; editorial decision 28 July 2021; accepted 16 August 2021.

Correspondence: Matthew Geriak, PharmD, Research Pharmacy, Sharp Memorial Hospital, 7901 Frost St, San Diego, CA 92123, USA (matthew.geriak@sharp.com).

Open Forum Infectious Diseases®2021

https://doi.org/10.1093/ofid/ofab418

The survey scores were summarized and analyzed using Stata version 16 software. The quantitative questions (1 and 2) were analyzed using Wilcoxon rank-sum test. The qualitative questions (3 and 4) were analyzed using Fisher exact test. For question number 5, patients who had an overall score ≥8 were said to have high satisfaction of the given antibiotic. Data were then analyzed by 2-tailed Fisher exact test. The comparison of the duration of treatment between the 2 arms was analyzed by the Mann-Whitney *U* test.

RESULTS

Sixty-eight patients received the follow-up calls and 41 patients were excluded (60%). Reasons for exclusion were as follows: could not contact patient (n = 36), patient declined to participate (n = 3), and language barrier (n = 2). Twenty-seven patients completed the survey (40%). The daptomycin treatment group was 87% male and 63% white ethnicity and the vancomycin treatment group was 67% male and 67% white ethnicity. Infection types for the daptomycin treatment group included complicated soft tissue infection (n = 8 [53%]), bone/joint infection (n = 4 [27%]), and bacteremia/endocarditis (n = 3 [20%]). For the vancomycin group, infection types were bone/joint (n = 7 [58%]), complicated soft tissue infection (n = 3 [25%]), and bacteremia/endocarditis (n = 2 [17%]). The most common bacterial pathogens in the daptomycin arm were methicillin-resistant *Staphylococcus aureus* (MRSA) in 5 patients (33%), *Enterococcus faecalis* in 3 patients (20%), and methicillin-susceptible *S aureus* in 2 patients (13%). The most common bacterial pathogens in vancomycin OPAT patients were MRSA in 5 patients (41%), and *Staphylococcus epidermidis* in 4 patients (34%). The remaining 3 vancomycin patients (25%) did not have a specified pathogen.

All daptomycin-treated patients received once-daily dosing. Among the vancomycin treatment group, 5 patients received a dose every 24–48 hours, 5 patients received a dose every 12 hours, and 2 patients received a dose every 8 hours. The median time period between completion of OPAT and survey administration was 85 weeks (range, 4–127 weeks) and 56 weeks (range, 9–127 weeks) for the daptomycin and vancomycin treatment groups, respectively. The median duration of OPAT was 31 days (range, 14–71 days) and 16 days (range, 6–64 days) for the daptomycin and vancomycin treatment groups, respectively ($P = .09$, Mann-Whitney *U* test).

The survey questions and results are shown in Table 1. The median daily interference scores indicate a difference between treatment groups ($P = .03$). Patients reported having more daily interference while receiving vancomycin. Question 4 was excluded from analysis since all patients reported that the infection itself, not the antibiotic therapy, made them take time off work. All patients who received daptomycin reported high satisfaction, compared with 67% of patients who received vancomycin (Table 1, $P = .03$). The remaining scores did not indicate a difference between treatment groups.

DISCUSSION

Vancomycin and daptomycin are commonly utilized in OPAT of infections caused by gram-positive organisms. While vancomycin has been the treatment standard for decades due to its low drug acquisition cost, its onerous dosing characteristics of 2–3 infusions every 60–90 minutes in patients with normal renal function renders it potentially very disruptive and inconvenient for patients when used in OPAT [9]. While all OPAT generally calls for weekly bloodwork to monitor for adverse drug effects (eg, creatinine phosphokinase for daptomycin, hematological studies for β-lactam myelotoxicity), the need for vancomycin therapeutic drug monitoring places an increased burden on physicians, pharmacists, and laboratory personnel to consider dose adjustment, opening up opportunities for medical errors and nephrotoxic overdosing to occur. These factors create a medical need for less cumbersome antibiotics in OPAT

Table 1. Questionnaire Scores of Daptomycin and Vancomycin Outpatient Parenteral Antimicrobial Therapy

Question	Daptomycin (n = 15)	Vancomycin (n = 12)	P Value	Z Statistic
Age, y, mean (SD)	55 (16)	58 (11)	NA	NA
Question 1: How much did OPAT interfere with your daily routine? None = 0, mild = 2, moderate = 5, severe = 8; very severe = 10 Score: Median (75th percentile)	0 (2)	5 (8)	.03	–2.14
Question 2: How bad were the OPAT side effects? (0 to 10) None = 0, very severe = 10 Score: Median (75th percentile)	0 (0)	0 (5)	.12	–1.55
Question 3: Did you need to go back to the hospital to treat the same infection (yes or no) Score: % readmitted (yes)	13.3%	8.33%	1.00	NA
Question 4: Did the OPAT require you to take time off from work? (yes or no) Score: % yes	100%	100%	NA	NA
Question 5: How would you score your overall satisfaction with OPAT? (0 to 10) Unsatisfied = 0; extremely satisfied = 10 Score: % patient score ≥8	100%	67%	.03	NA

Abbreviations: NA, not applicable; OPAT, outpatient parenteral antimicrobial therapy; SD, standard deviation.

that may improve productivity for both patients and providers and reduce provider liability, the value of which cannot be quantified financially. While our study was too small to capture differences in adverse drug effects, prior studies show consistency in demonstrating that vancomycin is associated with significantly higher adverse drug events than daptomycin in OPAT [16, 17]. This would be anticipated to weigh on patient satisfaction differences in a larger study.

While high acquisition cost of daptomycin has often been restrictive in its utilization, the expiration of patent, rendering daptomycin generic in the United States, has resulted in a significant drug acquisition price drop and convergence in price of vancomycin and daptomycin. Daptomycin is commonly utilized in OPAT as a much less cumbersome option, requiring only 1 dose every 24 hours (or every 48 hours for creatinine clearance <30 mL/minutes) that can be administered in as little as 2 minutes [10–15]. Such different properties in administration would suggest an impact on the patient OPAT experience, depending on which of the 2 agents is utilized. Such studies have never been performed, which is surprising, especially given that patient satisfaction is a metric of increasing relevance in clinical decision making.

Despite the survey being extremely brief (generally administered over the phone in 2 minutes or less), only a 40% survey response was obtained. Patients receiving daptomycin had better satisfaction scores in this brief survey and had less life disruption and return to normal living. Adverse side effects and readmission rates were not significantly different between the 2 antibiotic treatment groups.

The results of this study confirm what has generally been assumed in that patient satisfaction in OPAT ties significantly into the ease of administration of therapy. Several years ago before daptomycin became generic in the United States, the acquisition cost of daily doses of daptomycin was several hundred dollars. In May 2021, the daptomycin cost was $31 per 500 mg [18] compared to vancomycin at $9/g. When adding up the vancomycin multiple doses per day, the therapeutic drug monitoring, laboratory blood draws, and ancillary supplies [19], the cost differential between daptomycin and vancomycin is becoming negligible. Therefore, selection of OPAT in daptomycin that is very close to vancomycin in price, yet much easier to administer, led to more satisfied patients in our sample population. Nevertheless, given great heterogeneity in insurance reimbursement, best practices still require confirmation with the patient's third-party payor (frequently by a hospital case manager or discharge planner) to determine payments for OPAT that the patient is responsible for. In some instances, daptomycin may be accompanied by "copays" that are higher than those of vancomycin, which patients are unable, or unwilling, to cover for the sake of OPAT convenience.

Our study has some very important limitations. First, the population sample was small, the fraction of captured patients was low, and data were collected in 1 geographical area. Second, recall bias needs to be considered given that some patients received and completed their treatment roughly 2 years prior to the survey. Third, overall satisfaction score may be artificially high because the treating physician verbally administered the survey over the phone and not anonymously. Finally, we deployed a survey that semi-quantitatively assessed patient experiences, but it has not been previously validated.

In summary, this study showed that antibiotics such as daptomycin with fewer doses per day and shorter infusion times led to higher patient satisfaction and less life disruption on OPAT. Larger studies are needed to further examine this issue to better evaluate the balance between higher drug acquisition costs, perceived patient satisfaction, and patient productivity.

Notes

Author contributions. K. H. W.: execution, data gathering and organization, data analysis, manuscript preparation. G. S.: study design, data analysis, statistics, data gathering, manuscript preparation. M. G.: research team oversight, IRB submission, study design, organization, data analysis, statistics, manuscript preparation and submission. All authors gave their approval for the final version of the manuscript to be published.

Acknowledgments. We thank all of the patients who responded to the questions in our survey; Francisco Aldrete for his assistance in the data mining of patients treated with antibiotics in the outpatient setting; and the Sharp Institutional Review Board (IRB) for waiving the review fees.

Patient consent statement. The design of the work has received approval by the local ethical committee (Sharp Healthcare IRB study number 1906805). The IRB of record determined that this research is not subject to regulation under 45 Code of Federal Regulations (CFR) part 46. Determination applies to the following documents: University of California, San Diego Summer Research Training Program Application, dated 19 February 2019; a HIPAA waiver was allowed per 45 CFR 164.512(i)(2)(ii). This study conformed to the Helsinki Declaration of 1964, as revised in 2013, concerning human and animal rights.

Financial support. This research was supported by the Sharp Healthcare Foundation (San Diego, California); the funding was only for the labor of the local IRB review and the Sharp Center of Research support staff.

Potential conflicts of interest. G. S. has consulted for AbbVie, Ferring, and Paratek Pharmaceuticals and on the speaker's bureaus for AbbVie and Paratek Pharmaceuticals. All other authors report no potential conflicts of interest.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Bowling J, Lewis J, Owens A. Outpatient parenteral antimicrobial therapy. Hospital Medicine Clinics **2013**; 2:e45–56.
2. Williams DN, Baker CA, Kind AC, Sannes MR. The history and evolution of outpatient parenteral antibiotic therapy (OPAT). Int J Antimicrob Agents **2015**; 46:307–12.
3. Mitchell ED, Czoski Murray C, Meads D, et al. Clinical and cost-effectiveness, safety and acceptability of community intravenous antibiotic service models: CIVAS systematic review. BMJ Open **2017**; 7:e013560.
4. McCarthy MW, Keyloun KR, Gillard P, et al. Dalbavancin reduces hospital stay and improves productivity for patients with acute bacterial skin and skin structure infections: the ENHANCE trial. Infect Dis Ther **2020**; 9:53–67.
5. Buke C, Armand-Lefevre L, Lolom I, et al. Epidemiology of multidrug-resistant bacteria in patients with long hospital stays. Infect Control Hosp Epidemiol **2007**; 28:1255–60.
6. Wyllie DH, Walker AS, Peto TE, Crook DW. Hospital exposure in a UK population, and its association with bacteraemia. J Hosp Infect **2007**; 67:301–7.

7. Tice AD, Rehm SJ, Dalovisio JR, et al; Infectious Diseases Society of America. Practice guidelines for outpatient parenteral antimicrobial therapy. IDSA guidelines. Clin Infect Dis **2004**; 38:1651–72.
8. Tabaee A, Anand VK, Yoon C. Outpatient intravenous antibiotics for methicillin-resistant *Staphylococcus aureus* sinusitis. Am J Rhinol **2007**; 21:154–8.
9. Polk RE, Healy DP, Schwartz LB, et al. Vancomycin and the red-man syndrome: pharmacodynamics of histamine release. J Infect Dis **1988**; 157:502–7.
10. Crompton JA, North DS, Yoon M, et al. Outcomes with daptomycin in the treatment of *Staphylococcus aureus* infections with a range of vancomycin MICs. J Antimicrob Chemother **2010**; 65:1784–91.
11. Kullar R, Davis SL, Kaye KS, et al. Implementation of an antimicrobial stewardship pathway with daptomycin for optimal treatment of methicillin-resistant *Staphylococcus aureus* bacteremia. Pharmacotherapy **2013**; 33:3–10.
12. Fowler VG Jr, Boucher HW, Corey GR, et al; *S aureus* Endocarditis and Bacteremia Study Group. Daptomycin versus standard therapy for bacteremia and endocarditis caused by *Staphylococcus aureus*. N Engl J Med **2006**; 355:653–65.
13. Moise PA, Culshaw DL, Wong-Beringer A, et al. Comparative effectiveness of vancomycin versus daptomycin for MRSA bacteremia with vancomycin MIC >1 mg/L: a multicenter evaluation. Clin Ther **2016**; 38:16–30.
14. Oleson FB Jr, Berman CL, Kirkpatrick JB, et al. Once-daily dosing in dogs optimizes daptomycin safety. Antimicrob Agents Chemother **2000**; 44:2948–53.
15. Caulder CR, Sloan A, Yasir A, Bookstaver PB. Infusion-related reaction following daptomycin two-minute rapid intravenous administration. Hosp Pharm **2014**; 49:644–6.
16. Schrank GM, Wright SB, Branch-Elliman W, LaSalvia MT. A retrospective analysis of adverse events among patients receiving daptomycin versus vancomycin during outpatient parenteral antimicrobial therapy. Infect Control Hosp Epidemiol **2018**; 39:947–54.
17. Shrestha NK, Mason P, Gordon SM, et al. Adverse events, healthcare interventions and healthcare utilization during home infusion therapy with daptomycin and vancomycin: a propensity score-matched cohort study. J Antimicrob Chemother **2014**; 69:1407–15.
18. Drugs.com. Daptomycin prices, coupons and patient assistance programs. https://www.drugs.com/price-guide/daptomycin#:~:text=The%20cost%20for%20daptomycin%20intravenous,on%20the%20pharmacy%20you%20visit. Accessed 10 May 2021.
19. Shah NP, Reddy P, Paladino JA, et al. Direct medical costs associated with using vancomycin in methicillin-resistant *Staphylococcus aureus* infections: an economic model. Curr Med Res Opin **2004**; 20:779–90.