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BRIEF REPORT

Put the Vanc Down, Flip It and Reverse It: Comparison of Vancomycin and Daptomycin Health Care Utilization and Cost in Outpatient Parenteral Antimicrobial Therapy

Amber C. Streifel,[1] Katie Luis,[2] Monark Nakrani,[1] Diana Yu,[1] Monica K. Sikka,[2] Cara D. Varley,[2,3] Alyse Douglass,[2] Heather Mayer,[2] Kathleen Young,[2] and James S. Lewis II[1]

[1]Department of Pharmacy, Oregon Health & Science University, Portland, Oregon, USA, [2]Division of Infectious Diseases, Department of Medicine, Oregon Health & Science University, Portland, Oregon, USA, and [3]Epidemiology Programs, School of Public Health, Oregon Health & Science University–Portland State University, Portland, Oregon, USA

Vancomycin and daptomycin are frequently used in outpatient parenteral antimicrobial therapy (OPAT). We analyze health care utilization and cost to the health care system for vancomycin vs daptomycin in the outpatient setting and find that vancomycin results in significantly higher health care utilization and similar cost per course compared with daptomycin in OPAT.

Keywords. antimicrobial stewardship; cost analysis; daptomycin; OPAT; vancomycin.

Vancomycin and daptomycin are commonly used in the outpatient setting to treat infections caused by gram-positive pathogens. The benefits of outpatient parenteral antimicrobial therapy (OPAT) have been established [1, 2], but providers and patients must consider potential complications associated with long-term parenteral antimicrobial therapy in the outpatient setting, such as adverse drug events (ADEs), vascular access complications, and subsequent hospital readmission [3–5]. Vancomycin has historically been the drug of choice for treating serious infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA) [6]. However, vancomycin requires therapeutic drug monitoring to optimize therapy, which is challenging in the outpatient setting. Younger patients may require frequent administration or continuous infusion, which adds further complexity [7]. Alternatively, daptomycin does not require serum drug concentrations and is dosed once daily, making it easier to accommodate in the outpatient setting. However, daptomycin has a higher acquisition cost and requires weekly creatinine phosphokinase (CK) monitoring to minimize risks of muscle toxicity.

Given the current challenges of balancing the convenience and cost-savings of OPAT with the potential for ADEs and interventions, we sought to compare the rates of complications, as well as antimicrobial interventions, for adult patients who receive vancomycin vs daptomycin across multiple outpatient settings.

METHODS

This single-center, retrospective cohort study included adult patients who received at least 72 hours of vancomycin or daptomycin via home infusion or at an infusion center or skilled nursing facility (SNF) from January 1, 2017, to May 30, 2022, through the OPAT program at Oregon Health & Science University (OHSU). Patients who received concurrent antimicrobials (except for rifampin), who received OPAT via alternative settings such as dialysis centers, or who were transferred to the care of an outside provider during their OPAT treatment course were excluded from the study.

The protocol was approved by the OHSU institutional review board. Patients were identified through an OPAT patient repository, which was supplemented with chart review of electronic health records.

The primary outcome was a composite of events requiring intervention, including adverse drug reactions, elevated laboratory markers, line complications, emergency department (ED) visits, and hospital readmissions during the OPAT course. Secondary outcomes included the rates of interventions, additional phone calls, changes to alternative antimicrobial therapy, and cost for medication and management.

ADE included acute kidney injury (serum creatinine >1.5 mg/dL or a 1.5-fold increase from baseline), tinnitus, neutropenia (absolute neutrophil count <1500 units/L), rash or itching, gastrointestinal adverse effects, eosinophilia (eosinophil count >0.5 K/cu mm or 3% of the differential), myalgias, or other specific reactions noted by the infectious disease (ID) physician in the patient chart. Elevated laboratory markers requiring OPAT team intervention, but not intended to represent clinical equivalency, were defined as serum vancomycin concentration ≥20 mg/L or serum CK level ≥500 units/L.

Descriptive and inferential statistics were used for baseline characteristics and outcomes. Continuous variables were evaluated using the *t* test or Wilcoxon rank-sum test and chi-square test for categorical variables. Poisson regression

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Correspondence: Amber C. Streifel, PharmD, Department of Pharmacy, Oregon Health & Science University, 3181 SW Sam Jackson Park Road, Portland, OR 97239 (streifel@ohsu.edu).

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Table 1. Demographics and Infection Characteristics

Characteristic	Vancomycin (n = 290)	Daptomycin (n = 119)	*P* Value
Age, mean (SD), y	60	54	<.0001
Female, No. (%)	148 (51)	55 (46)	NS
Benefit group, No. (%)			
Private/commercial	49 (17)	27 (23)	.0122
Medicare	144 (50)	38 (32)	
Medicaid	85 (29)	46 (39)	
Other	12 (4)	8 (6.7)	
Comorbid condition, No. (%)			
Diabetes mellitus	86 (30)	27 (23)	NS
Coronary artery disease	51 (18)	6 (5)	.0009
Congestive heart failure	50 (17)	14 (12)	NS
Stroke	20 (7)	2 (2)	NS
Chronic obstructive pulmonary disease	31 (11)	14 (12)	NS
Cirrhosis	14 (5)	7 (6)	NS
Chronic kidney disease	37 (13)	16 (13)	NS
Surgery during admission	237 (82)	92 (77)	NS
Infection, No. (%)			
Bone & joint	187 (64)	74 (62)	NS
Uncomplicated bacteremia	19 (7)	10 (9)	NS
Pulmonary	7 (2)	0 (0)	NS
Endocarditis	20 (7)	11 (9)	NS
CNS infection	9 (3)	4 (3)	NS
Intra-abdominal	4 (1)	1 (0.8)	NS
Skin and soft tissue infection	25 (9)	8 (7)	NS
Complicated bacteremia	19 (7)	11 (9)	NS
Pathogen, No. (%)			
MRSA	103 (36)	47 (40)	<.0001
MSSA	4 (1)	13 (11)	
Coagulase-negative *Staphylococcus* spp.	57 (20)	22 (18)	
Enterococcus spp.	2 (0.7)	5 (4)	
Other gram-positive organism	22 (8)	5 (4)	
No cultures	4 (1.4)	2 (1.7)	
Cultures negative	31 (11)	5 (4)	
Polymicrobial	66 (23)	19 (16)	
Additional characteristics			
Positive blood culture, No. (%)	92 (32)	53 (45)	.014
Hospital length of stay, median (IQR), d	22 (6–14)	13 (6–15)	NS
ICU length of stay, median (IQR), d	1 (0–0)	1 (0–0)	NS
Vascular access, No. (%)			
Tunneled catheter	16 (5.5)	7 (5.9)	NS
Single-lumen peripherally inserted central catheter	251 (87)	99 (83)	NS
Double-lumen peripherally inserted central catheter	16 (5.5)	7 (5.9)	NS
Port	5 (1.7)	6 (5)	NS
OPAT setting, No. (%)			
Home infusion	136 (47)	74 (62)	<.0001
Infusion center	26 (9)	30 (25)	
Skilled nursing facility	128 (44)	15 (13)	
Course duration, median (IQR), d			
Anticipated OPAT course	29 (21–36)	32 (24–38)	NS
Actual OPAT course	27 (15–37)	31 (19–38)	NS

Abbreviations: CNS, central nervous system; ICU, intensive care unit; IQR, interquartile range; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*; NS, not significant; OPAT, outpatient parenteral antimicrobial therapy.

was used to estimate the relative risk (RR) for outcomes. All statistical tests were 2-sided with an assumed statistical significance level of .05. SAS software (version 9.4; SAS Institute, Cary, NC, USA) was used for all statistical analyses.

For the health care system cost analysis, institutional finance data and national estimates in the published literature at the time of publication were used to estimate cost. Wholesale acquisition cost (WAC) was used for medications. Cost to the

Table 2. OPAT Outcomes

	Vancomycin (7893 d)	Daptomycin (3643 d)	Rate Ratio	95% CI
Total events requiring intervention (composite)	503	192	0.86	(0.72–1.01)
Total adverse drug events	110	66	1.30	(0.96–1.76)
Intervention lab markers (vancomycin trough >20 mg/dL, creatine kinase >500 units/L)	77	12	0.34	(0.18–0.62)
Line complications	137	32	0.51	(0.34–0.74)
Emergency department visits	60	48	1.73	(1.19–2.53)
Hospital readmissions	36	25	1.50	(0.9–2.50)
Total additional Interventions	406	72	0.38	(0.3–0.49)
Total additional phone calls	1330	440	0.72	(0.72–0.79)

Adverse Drug Events	Vancomycin, No. (%)	Daptomycin, No. (%)
Acute kidney injury	25 (8.6)	11 (9.2)
Tinnitus	2 (0.69)	1 (0.8)
Neutropenia	4 (1.4)	0 (0)
Rash/itch	21 (7.2)	8 (6.7)
Gastrointestinal ADR	24 (8.3)	13 (11)
Eosinophilia	20 (7)	11 (9.2)
Muscle ache	5 (1.7)	9 (7.6)
Other ADE	9 (3)	12 (10)

Abbreviations: ADE, adverse drug event; ADR, adverse drug reaction; OPAT, outpatient parenteral antimicrobial therapy.

hospital for readmission days was estimated based on our average institutional spend for a patient on a medical or surgical floor. Estimates for registered nurse (RN) and pharmacist time were calculated using national average hourly wages [8, 9], recently published lab costs [10], and time estimates from OHSU OPAT team members. The total costs were summed and reported as the mean cost per course of vancomycin or daptomycin in OPAT. The cost of each setting (SNF, home infusion, infusion center) was not factored in as some of these costs are variable and a national average is difficult to estimate.

RESULTS

Patients

Four hundred nine OPAT patients met inclusion criteria; 290 received vancomycin and 119 daptomycin. Baseline characteristics were generally similar between the groups (Table 1). The mean age of the vancomycin group was 60 years vs 54 years in the daptomycin group ($P < .0001$). Patients in the vancomycin group had a significantly higher proportion of comorbid coronary artery disease. The most common indication in both groups was bone and joint infection (64% vancomycin vs 62% daptomycin), and the most common pathogen was MRSA (36% vancomycin vs 40% daptomycin).

More patients in the vancomycin group had Medicare as their primary insurance benefit than daptomycin (50% vs 32%, respectively). Daptomycin was more likely to be utilized in home infusion (62% vs 47% in the vancomycin group). In the SNF setting, vancomycin was used more often than daptomycin (44%, and 13%, respectively).

Outcomes

There were no statistically significant differences between groups in total events requiring intervention. However, we identified differences in line complications (vancomycin vs daptomycin: RR, 0.51; 95% CI, 0.34–0.74) and ED visits (RR, 1.73; 95% CI, 1.19–2.53). Patients receiving daptomycin experienced fewer laboratory events requiring intervention than those receiving vancomycin (RR, 0.34; 95% CI, 0.18–0.62). Rates of additional interventions and phone calls were lower for patients receiving daptomycin compared with vancomycin (interventions: RR, 0.38; 95% CI, 0.3–0.49; phone calls: RR, 0.72; 95% CI, 0.72–0.79). Sixty (20.1%) patients receiving vancomycin switched to an alternative antibiotic during their OPAT course, vs 23 (19%) daptomycin patients.

Although not statistically significant, patients in the daptomycin group experienced a higher incidence of ADEs (Table 2). The ADEs were primarily gastrointestinal effects and rash or itching (10 patients); only 1 patient required a change in antimicrobial therapy. Other adverse events in the daptomycin group consisted of dizzy spells, slight burning sensation after administration, and eosinophilic pneumonia—a serious ADE that occurred in 1 (2%) daptomycin patient.

Cost Analysis

The medication acquisition cost for daptomycin was higher than for vancomycin (mean cost per course, $744.24 vs $289.29); however, once time spent on interventions and dose adjustments, additional laboratory monitoring, and line complications were totaled, the cost of a course of daptomycin ($996.76) was lower than the cost of an outpatient course of vancomycin ($1351.98) (Table 3).

Table 3. Cost Analysis

	Vancomycin Cohort	Daptomycin Cohort
Cost of RN time on additional phone calls and interventions	$91.80	$65.12
Medication cost (per course mean)	$289.29	$744.24
Lab cost (includes standard weekly plus additional; mean per course)	$93.75	$77.67
Cost of PharmD time lab review and dose adjustment (mean per course)	$51.86	$0.82
Line complications (per course mean)	$87.92	$67.76
Total estimated per course (without hospital readmission)	$1351.34	$996.76
Readmission (cost per mean duration)	$25 280.3	$23 528.20
Total estimated cost per course (with hospital readmission)	$27 982.98	$25 521.72

Abbreviation: RN, registered nurse.

DISCUSSION

Rates of intervention required by the OPAT team and overall health care utilization were lower for patients receiving daptomycin than those receiving vancomycin. There were no statistically significant differences in the rates of total events requiring intervention.

These findings build upon those of prior studies. A 2014 retrospective cohort study reported that adult patients receiving daptomycin as home infusion therapy experienced 60% fewer antimicrobial adverse events and required 80% fewer antimicrobial interventions than similar patients receiving vancomycin [11]. In 2018, another retrospective cohort study similarly found that patients receiving vancomycin experienced more ADEs compared with daptomycin-treated patients [12]. Additionally, a recent cost-minimization study conducted in the inpatient setting reported both time and cost-savings with the use of daptomycin compared with vancomycin [10].

Our study expands the scope of prior work to include cost estimates in multiple outpatient settings. Increasingly in the United States, treatment setting is a driver for antimicrobial selection, which is often influenced by a patient's insurance coverage. Although now available generically, the medication cost of daptomycin continues to limit its use across all treatment settings. As represented in our data, patients with Medicare coverage are more likely to receive OPAT in an SNF, given that home infusion services are not covered by Medicare parts A & B, thereby increasing the likelihood of receiving vancomycin, as SNFs have historically rejected daptomycin on the basis of cost. Although daptomycin carries a higher medication cost, it requires less health care utilization in terms of additional labs and required care management by the OPAT team, as demonstrated by our cost analysis. These findings suggest that there are significant direct and indirect cost considerations beyond drug acquisition cost for OPAT patients. Additional factors to consider include patient satisfaction with a once-daily intravenous daptomycin push (infused over 2 to 5 minutes) compared with longer infusion times (often at least 1 to 2 hours) and more frequent daily doses for vancomycin, as well as coordination of trough concentrations. Another layer of complexity is added in the outpatient setting with the recommendation of vancomycin area under the curve monitoring rather than trough concentrations, which often involves additional cost in terms of software purchase [7].

This study has limitations. As a retrospective study, data were limited to the information available in the electronic health record. This may have led to an underestimation of the actual rate of adverse drug reactions, complications, interventions, and additional phone calls. In addition, variability in age and comorbidity burden at baseline limits the comparability of outcomes. Cost analysis only estimates the cost to the health care system and does not factor in cost to the patient or time spent by other team members or antibiotic vendors.

CONCLUSIONS

Daptomycin is a suitable alternative to vancomycin for the treatment of gram-positive infections in the OPAT setting in terms of reduced health care utilization. Despite higher medication cost, the cost to the health care system for OPAT vancomycin vs daptomycin is similar, with less time spent on management by OPAT teams.

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