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EDITORIAL COMMENTARY

Antipseudomonal Antibiotics in Diabetic Foot Infections: A Practical Perspective From a Community Hospital

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In a recent issue of *Open Forum Infectious Diseases*, Veve and colleagues published a multicenter retrospective study from 2013 to 2020 evaluating the prescribing practices of diabetic foot infections (DFIs) in the United States. The authors identified discordant use of antipseudomonal therapy (88%) as compared with the confirmed culture prevalence of *Pseudomonas aeruginosa* (PsA; 9%) among 292 patients. Immunocompromised status and previous outpatient treatment failure of DFI were risk factors associated with isolation of PsA in culture [1]. Notably, they excluded individuals with osteomyelitis. The authors concluded that antimicrobial stewardship programs should focus on avoiding antipseudomonal antibiotics when their use is not warranted according to patient-specific risk factors. Despite these robust data, experiences from other institutions, and national guidance discouraging this practice for over a decade, the use of broad-spectrum antimicrobial therapy including antipseudomonal coverage has endured, in part related to the morbidity associated with DFI [2–11].

The antimicrobial stewardship program at Valley Medical Center, a 321-bed community hospital in the metropolitan Seattle region, has worked to address overuse of antipseudomonal antibiotic prescribing among patients admitted with DFIs. Our institution-specific guidelines were recently adjusted to recommend a nonantipseudomonal β-lactam, ceftriaxone, and an anti–methicillin-resistant *Staphylococcus aureus* agent, vancomycin, as initial empiric therapy, regardless of the presence or suspicion of bone involvement. Empiric antipseudomonal coverage, such as piperacillin-tazobactam, may still be considered in patients presenting with sepsis and DFI. To evaluate clinician prescribing practices at our institution, we retrospectively reviewed a convenience sample of 100 patients admitted with DFI between 1 January 2019 and 1 January 2021. Cases were identified according to their admitting *ICD-10* codes for DFIs. Individuals were excluded if they had noninfected diabetic foot ulcers or the following conditions: cancer, hardware involvement, psoriasis, and septic arthritis. The data were evaluated descriptively, and the study was approved by the University of Washington Medicine Valley Medical Center's Research Oversight Committee.

During a 2-year period, 149 patients with DFI were identified; the 100 patients reviewed and summarized herein represent 67% of the total number admitted with DFI. Eighty-one patients (81%) had cultures collected: 54 of 81 (66.7%) were surgical samples and 31 of 54 (57.4%) were bone cultures. Among all patients, 67% were considered to have a recurrent DFI, defined as a prior DFI diagnosis within 1 year of their index admission. Like Veve et al, we found discordant rates of antipseudomonal coverage (91%) when compared with isolation of PsA in culture (5%). The most common antipseudomonal agents used were piperacillin/tazobactam (82%), fluoroquinolones (30%), and cefepime (12%), followed by meropenem (1%). Among the 5 patients with PsA, 4 had osteomyelitis, 4 had recurrent DFI, 2 had documented PsA in wound cultures isolated within 1 year prior to admission, and none were immunosuppressed. Additional baseline characteristics are presented in Table 1 and isolated pathogens in Table 2.

Out of all 100 patients, nearly two-thirds (64%) were admitted with osteomyelitis related to their DFI. Of 64 patients with osteomyelitis, 58 (90.6%) underwent surgical intervention, with 23 debridements, 5 resections, 35 minor amputations, and 11 major amputations, as opposed to 19 of 36 (52.8%) patients without osteomyelitis, who underwent 13 debridements, 0 resections, 7 minor amputations, and 3 major amputations. In addition, utilization of antipseudomonal antibiotics was higher in patients with osteomyelitis (62/64, 96.9%) at a median duration of 21 days (IQR, 14.8–31) when compared with those without osteomyelitis (29/36, 80.6%) at a median duration of 13.5 days (IQR, 10–18). Prior larger

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Table 1. Patient Characteristics

	DFI, No. (%) or Median (IQR)	
	PsA (n = 5)	Non-PsA (n = 95)
Demographics		
Age, y	56 (50–60)	61 (51–67)
Gender		
Male	4 (80)	74 (78)
Female	1 (20)	21 (22)
Race/ethnicity		
African American	2 (40)	18 (19)
Caucasian	2 (40)	46 (48)
Hispanic/Latino	0	15 (16)
Other	1 (20)	16 (17)
Comorbidities		
A1c, %	8.1 (7.2–8.6)	8.8 (7.2–11.1)
>7%	4 (80)	72 (76)
>10%	0	32 (34)
Cardiovascular disease	4 (80)	35 (37)
Body mass index, kg/m^2	33.6 (24.7–39.5)	30.6 (25.6–35.7)
Tobacco use		
Active	1 (20)	25 (26)
Former	1 (20)	15 (16)
Admission		
Intensive care unit	1 (20)	10 (11)
Diagnosis		
Severe DFI[a]	4 (80)	84 (88)
Osteomyelitis	4 (80)	60 (63)
Sepsis	2 (40)	26 (27)
DKA	0	4 (4)
Infection		
Antibiotics within 30 d[b]	2 (40)	25 (26)
Recurrence within 1 y	4 (80)	63 (65)
Cultures drawn	5 (100)	76 (80)
Superficial swabs	3 (60)	55 (58)
Surgical	3 (60)	51 (54)
Both	1 (20)	30 (32)
Infectious disease consult	3 (60)	68 (72)

Abbreviations: A1c, hemoglobin A1c; DFI, diabetic foot infection; DKA, diabetic ketoacidosis; PsA, *Pseudomonas aeruginosa*.

[a]Severe DFI defined per Infectious Diseases Society of America guidelines: local infection with erythema >2 cm from ulceration, with signs of systemic inflammatory response and/or involvement of deeper tissues including the bone.

[b]Any oral and/or intravenous antibiotics.

studies have noted higher readmission rates for patients with osteomyelitis [12], which may be influenced by longer antibiotic courses to avoid the need for amputation [13]. However, the need for major amputations in our cohort was low. Additionally, all-cause readmission within 30 days after discharge from index admission was numerically lower among cases with osteomyelitis (11/64, 17.2%) as compared with those without osteomyelitis (11/36, 30.6%). Although these data captured only system-wide readmissions and those from hospitals whose data were accessible by a Care Everywhere feature in the electronic medical record, our experience found that readmission rates were lower among individuals with osteomyelitis, which may be in part due to the surgical management that patients received. Altogether, our data demonstrate that the complexity of DFI management and the substantial morbidity may not be solely related to a lack of sufficient empiric coverage. Greater advocacy for surgical interventions, when appropriate, and improving preventative care via diabetes management and other social factors should be emphasized in addition to empiric initiation of broad-spectrum antibiotics for this patient population.

DFIs vary widely in clinical presentation and are often polymicrobial [2]. The Infectious Diseases Society of America guidelines discourage the use of empiric treatment of PsA except for cases with septic clinical presentations or specific risk factors (eg, geographic location or prior isolation of PsA) [3, 4]. The study by Veve et al contributed additional information about PsA risk

Table 2. Microbes Isolated out of Microbiological Cultures Drawn (n = 112)

	Isolates	
	No.	%
Streptococcus spp	38	33.9
Enterococcus spp	19	17.0
Methicillin-susceptible *Staphylococcus aureus*	19	17.0
Coagulase-negative *Staphylococcus*	17	15.2
Methicillin-resistant *Staphylococcus aureus*	17	15.2
Bacteroides spp	11	9.8
Escherichia coli	8	7.1
Finegoldia spp	8	7.1
Proteus mirabilis	7	6.3
Pseudomonas aeruginosa	5	4.5
Enterobacter spp	5	4.5
Morganella morganii	5	4.5
Proteus spp	5	4.5
Citrobacter spp	3	2.7
Serratia spp	3	2.7
Klebsiella spp	2	1.8
Stenotrophomonas spp	2	1.8

factors, including failure of outpatient therapy and immunocompromised status. Unfortunately, these risk factors may be challenging to apply to all patients. For example, in our single center, 4 of 5 patients with PsA isolated in culture had recurrent infection, but among all 67 patients with recurrent infection, only 4 (6%) had PsA. Similarly, 4 of 5 patients with PsA isolated had osteomyelitis, but most cases with osteomyelitis did not have PsA isolated (60/64, 93.8%). Initiating antipseudomonal therapy based on risk factors alone might still lead to unnecessarily broad antimicrobial coverage. Of note, fluoroquinolones, beyond their antipseudomonal activity, are a useful oral anti-infective strategy, especially in infections with bone involvement [14].

With perceived commonality of PsA in DFI and limitations in predicting what organisms will be cultured, many institutions still pursue empiric antipseudomonal choices for patients admitted with DFI [5]. Therefore, the goal of antimicrobial stewardship programs in the management of DFIs may not be to affect initial empiric therapy for all patients presenting with DFIs. Instead, the role of antimicrobial stewardship should be a 2-pronged approach: focus on rapid de-escalation based on national guidance and empower providers with institutional microbiological data. In a randomized multicenter trial including 576 patients with moderate to severe DFI, clinical response rates were similar for patients receiving either ertapenem or piperacillin/tazobactam despite growing enterococci in 64 isolates and PsA in 28 isolates. This further suggests that US clinicians should feel confident to exclude or de-escalate from antipseudomonal antibiotic coverage in clinically stable cases even when lacking microbiological data or dealing with a polymicrobial DFI that has been surgically managed [15]. Although utilizing newer diagnostic technology to assist with early identification of potential pathogens should be used when possible, using this as a singular strategy may introduce excess antipseudomonal antibiotic exposure due to variable turnaround time when utilizing off-site microbiology laboratories [16].

Due to the heterogeneity of literature and morbidity associated with DFI, the message to use broad-spectrum antimicrobial therapy including antipseudomonal coverage has been an enduring one despite national guidance discouraging this practice for over a decade. Recognizing the clinical concern and treatment heuristic that trigger initial antipseudomonal coverage of DFI, antimicrobial stewardship programs can take a nuanced approach. Considering the important gains from harm reduction in days of antipseudomonal antibiotic exposure, rapid de-escalation may be more successful initially before changing entrenched beliefs upfront about the risk of PsA in DFI [17, 18].

Notes

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