Characterization of Bacterial Infections in Allogeneic Hematopoietic Stem Cell Transplant Recipients Who Received Prophylactic Levofloxacin With Either Penicillin or Doxycycline

Bridgette L. Therriault, PharmD; John W. Wilson, MD; Jason N. Barreto, PharmD; and Lynn L. Estes, PharmD

OBJECTIVE: **To describe the effect of a combination prophylactic regimen of levofloxacin, a synthetic chemotherapeutic antibiotic of the fluoroquinolone drug class, with either penicillin or doxycycline on the changing epidemiology of bacterial infections and antimicrobial resistance patterns of isolated organisms in the allogeneic hematopoietic stem cell transplant (HSCT) patient population.**

PATIENTS AND METHODS: **We conducted a single-center, retrospective cohort study of all allogeneic HSCT recipients from January 1, 2003, through August 31, 2008, who received prophylactic levofloxacin in combination with penicillin (or with doxycycline in penicillin-allergic patients) from allogeneic stem cell infusion until neutrophil engraftment.**

RESULTS: **Of the 258 patients who underwent allogeneic HSCT during the study period, 231 received levofloxacin prophylaxis, 76 (33%) of whom developed an infection within 3 months after transplant. Over time, the ratio of gram-positive to gram-negative (GN) infections decreased from 2.11 in 2004, the first year that GN organisms were isolated, to 1.11 in 2008 (*P*=.20). Emergence of fluoroquinolone-resistant GN bacteria was observed (*P*=.02), whereas resistance to extended-spectrum β-lactams did not change over time. Combined vancomycin-resistant enterococci colonization and infection rates increased during the study period (*P*=.04). *Clostridium difficile* colitis was uncommon.**

CONCLUSION: **Levofloxacin with penicillin or doxycycline prophylaxis may contribute to the emergence of resistant GN infections in allogeneic HSCT recipients over time. Our findings provide additional support for the current standard of practice of administering empiric monotherapy with an antipseudomonal β-lactam if these patients develop fever or are suspected to have an infection.**

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BAL = bronchoalveolar lavage; CoNS = coagulase-negative staphylococci; GN = gram-negative; GP = gram-positive; HSCT = hematopoietic stem cell transplant; MDR = multidrug-resistant; VRE = vancomycin-resistant enterococci

The utility of prophylactic antibiotics during the period of chemotherapy-induced neutropenia has been a source of controversy for decades. Reductions in gram-negative (GN) bacteremia, febrile episodes, and hospitalizations have been documented with the use of a prophylactic regimen.[1-6] Newer fluoroquinolones, particularly levofloxacin, have emerged as preferred agents because of their potent activity against GN bacteria, enhanced gram-positive (GP) coverage, excellent oral bioavailability, and favorable patient tolerance. Historically, the National Comprehensive Cancer Network, the Centers for Disease Control and Prevention, and the Infectious Diseases Society of America have offered conflicting recommendations regarding the use of a prophylactic antibiotic regimen after allogeneic hematopoietic stem cell transplant (HSCT).[7-9] Although this patient population is at high risk of fever and subsequent infection during the neutropenic period, a reduction in infection-related mortality rates has not been clearly demonstrated, and emergence of multidrug-resistant (MDR) organisms has remained a concern. Recently, the American Society for Blood and Marrow Transplantation endorsed fluoroquinolone prophylaxis if neutropenia is anticipated for 7 days or more, again emphasizing the risk of perpetuating fluoroquinolone-resistant bacteria.[10]

Infections caused by MDR organisms are associated with increased mortality, hospital length of stay, and health care costs.[11] Given these concerns, the Infectious Diseases Society of America suggests that, if a prophylactic regimen is used in asymptomatic, afebrile, neutropenic patients, hospital and HSCT center antibiotic-susceptibility profiles should be reviewed routinely.[8] In allogeneic HSCT recipients, the patient population at highest risk of developing infection during the period of neutropenia, the effect of fluoroquinolone prophylaxis on infections over time has not been adequately described, nor is there adequate information identifying the evolution of resistance patterns of those organisms isolated.

Since 1998, levofloxacin has been used with penicillin (or doxycycline for penicillin-allergic patients) at Mayo Clinic in Rochester, MN, as prophylaxis during the neutropenic period after HSCT. This study aimed to evaluate the impact of this prophylactic regimen on the etiology and resistance profiles of organisms implicated in infection during the first 3 months after allogeneic HSCT. Also of interest was the incidence of *Clostridium difficile* colitis and vancomycin-resistant enterococci (VRE) colonization and infection in this patient population.

From the Department of Pharmacy (B.L.T., J.N.B., L.L.E.) and Division of Infectious Diseases (J.W.W.), Mayo Clinic, Rochester, MN.

Individual reprints of this article are not available. Address correspondence to Bridgette L. Therriault, PharmD, at her current affiliation: Wesley Medical Center, 550 N Hillside, Wichita, KS 67214 (bridgettet8@yahoo.com).

PATIENTS AND METHODS

Study Design

We studied a retrospective cohort of patients who underwent allogeneic HSCT from January 1, 2003, through August 31, 2008. Patients were identified through a database maintained by the Blood and Marrow Transplant Center at our institution. Patients were included in the analysis if they were aged at least 18 years and were taking 500 mg of levofloxacin orally once daily or 750 mg orally once daily before or on the day of transplant as a part of a prophylactic antibiotic regimen. Duplicate isolates, potential colonizing organisms, and organisms isolated without available susceptibility data were excluded. Swabs positive for VRE were limited to 1 occurrence per patient. Similarly, a positive *C difficile* assay result was considered to be a duplicate if more than 1 result was positive during the first 3 months after transplant.

Institutional Protocols

For allogeneic HSCT recipients, levofloxacin prophylaxis usually begins on day 1 of transplant and is continued for the duration of neutropenia (specifically, until the absolute neutrophil count is $>0.5 \times 10^9$/L). On day one, 500 mg of penicillin V potassium orally twice daily (or doxycycline 100 mg orally twice daily in penicillin-allergic patients) is initiated and is continued for at least a year after transplant. Active surveillance for VRE colonization occurs on inpatient admission and twice weekly thereafter while the patient remains hospitalized. A rapid polymerase chain reaction assay is used to establish VRE colonization and the presence of *C difficile* toxin; however, the former was detected with stool cultures before July 2004 and the latter with Enzyme ImmunoAssay before July 2007.

Definitions

Infection was defined as a test culture positive for an organism isolated from blood, urine, or cerebrospinal, bronchoalveolar lavage (BAL), pleural, or peritoneal fluid. Given that BAL samples come from a nonsterile source, we included isolated bacteria from lavage cultures that were clinically correlated with respiratory infection in the medical record. Duplicate isolates were defined as a positive culture result within a 7-day period with the same organism maintaining an identical susceptibility profile. Any change in susceptibility profile, reappearance of the same organism after a previously negative culture result from the same site, or appearance of the organism in a separate site was determined to be a new infection and counted as a separate occurrence. Suspected colonizers were defined as coagulase-negative staphylococci (CoNS), *Corynebacterium* spp., *Propionibacterium* spp., *Micrococcus* spp., or *Stomatococcus* spp. isolated from a single culture. If any of these organisms were isolated from 2 consecutive cultures, they were included as an infection. Organisms with intermediate susceptibility were considered nonsusceptible, and a GN MDR pathogen conferred resistance to 2 or more of the following: third- or fourth-generation cephalosporin, fluoroquinolone, carbapenems (eg, imipenem, meropenem), piperacillin-tazobactam, or aminoglycoside.

Statistical Analyses

The GP:GN ratio for bacterial infections was calculated for each year of the study, and the distribution between GP and GN bacterial infections was compared across calendar years using an exact Wilcoxon signed rank test for the ordered contingency table to look for a time trend. Time trends in antibiotic susceptibility were assessed for each drug or drug class using the same method. All tests were 2-sided, and P values $<.05$ were considered statistically significant.

Ethical Considerations

All study patients gave consent to have their records reviewed for medical studies, pursuant to Minnesota law. This retrospective cohort study was approved by the Mayo Clinic Institutional Review Board.

RESULTS

Patient Demographics

During the study period, 258 adults underwent allogeneic HCST at our institution. Of the 231 who met criteria for inclusion into this study, 76 (33%) developed a qualifying infection within 3 months after transplant (Figure 1). Baseline characteristics of these patients are listed in Table 1. Of the 76 patients, 13 (17%) received 500 mg of levofloxacin orally once daily, and 63 (83%) received 750 mg of levofloxacin orally once daily. Additional antibiotic prophylaxis included penicillin (n=55; 72%) and doxycycline (n=13; 17%). Six patients received levofloxacin monotherapy only, and 2 patients received concomitant vancomycin for GP bacteremia. These patients were pooled for analysis.

The most common indications for allogeneic HSCT were acute myelogenous leukemia (n=27; 36%) and myelodysplastic syndrome (n=15; 20%). Most patients who developed an infection received a myeloablative conditioning regimen (n=50; 66%). The median duration of levofloxacin-based combination antimicrobial prophylaxis was 14 days (range, 3-39 days).

Epidemiology of Infections

The median time from initiation of combination levofloxacin-penicillin or levofloxacin-doxycycline prophylaxis

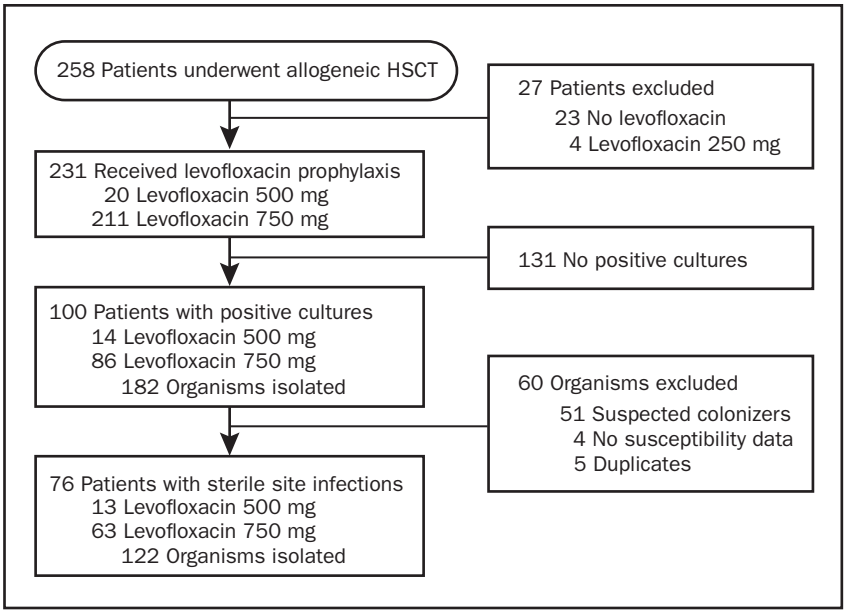

FIGURE 1. Study design. Flow diagram of patient screening and eligibility. HSCT = hematopoietic stem cell transplant.

to positive culture result was 27 days (range, 2-99 days). Among 108 positive culture results, 89 (82%) were isolated from blood, 14 (13%) from urine, 4 (4%) from BAL fluid, and 1 (1%) from the eye. A single organism was isolated in most positive cultures (n=95; 88%). Thirteen polymicrobial infections with 27 isolated organisms were identified: 16 GP and 11 GN.

Of the 122 bacterial pathogens isolated, 78 (64%) were GP bacteria and 44 (36%) were GN bacteria. The most common GP organisms recovered were CoNS (n=37; 47%) and *Enterococcus* spp. (n=24; 31%), whereas the most common GN organisms were *Pseudomonas aeruginosa* (n=8; 18%), *Klebsiella* spp. (n=8; 18%), *Enterobacter* spp. (n=7; 16%), and *Escherichia coli* (n=6; 14%). A description of the organisms implicated in bacterial infections for each calendar year of the study is provided in Table 2. The ratio of GP:GN organisms decreased over time, from 2.11 in 2004 to 1.11 in 2008, but this decrease did not reach statistical significance (Figure 2; *P*=.20).

ANTIBIOTIC RESISTANCE

The only *Staphylococcus aureus* isolate was resistant to oxacillin and all tested fluoroquinolones (ie, moxifloxacin, ciprofloxacin, and levofloxacin). Among the 37 isolates of CoNS, 34 (92%) were resistant to oxacillin, and 29 (78%) were resistant to the 3 fluoroquinolones. Of the 5 viridans group streptococci isolates, 3 (60%) were resistant to penicillin; fluoroquinolone susceptibility was performed on only

TABLE 1. **Patient Characteristics**[a]

Patients, No.	76
Female, No. (%)	36 (47)
Age (y), mean (range)	47 (18-67)
Race, No. (%)	
White	71 (93)
Hispanic	3 (4)
African American	1 (1)
Asian	1 (1)
Primary diagnosis, No. (%)	
Acute myelogenous leukemia	27 (36)
Myelodysplastic/myeloproliferative disorder	15 (20)
Multiple myeloma and other plasma cell disorders	9 (12)
Acute lymphoblastic leukemia	7 (9)
Non-Hodgkin lymphoma	5 (7)
Chronic myelogenous leukemia	4 (5)
Hodgkin lymphoma	1 (1)
Other[b]	8 (11)
Conditioning regimen, No. (%)	
Myeloablative	
Cyclophosphamide + total body irradiation	31 (41)
Cyclophosphamide + busulfan	11 (14)
Melphalan + total body irradiation	3 (4)
BEAM	1 (1)
Cyclophosphamide + total body irradiation + ATG	1 (1)
Nelarabine	1 (1)
Melphalan	1 (1)
Melphalan + thioTEPA + fludarabine + ATG	1 (1)
Reduced intensity	
Melphalan + fludarabine	20 (26)
Fludarabine + total body irradiation	4 (5)
Fludarabine + busulfan + ATG	1 (1)
Melphalan + fludarabine + alemtuzumab	1 (1)

[a] ATG = antithymocyte globulin (equine); BEAM = carmustine, etoposide, cytarabine, and melphalan; thioTEPA = *N*,*N*´,*N*´´-triethylenethiophosphoramide.

[b] Chronic lymphoblastic leukemia, treatment-related myelodysplastic syndrome, and amyloidosis.

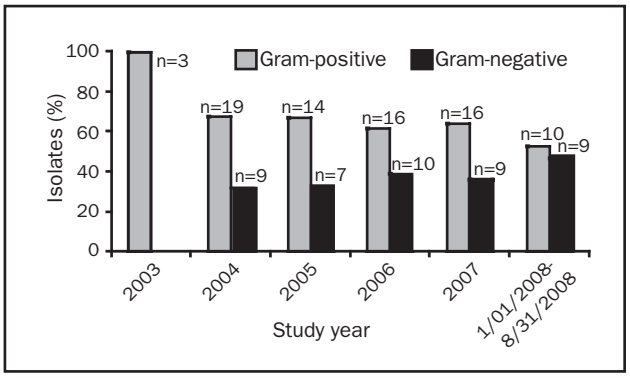

FIGURE 2. Epidemiology of infection. Percentage of isolates caused by gram-positive and gram-negative organisms per year (*P*=.20; exact Wilcoxon signed rank test).

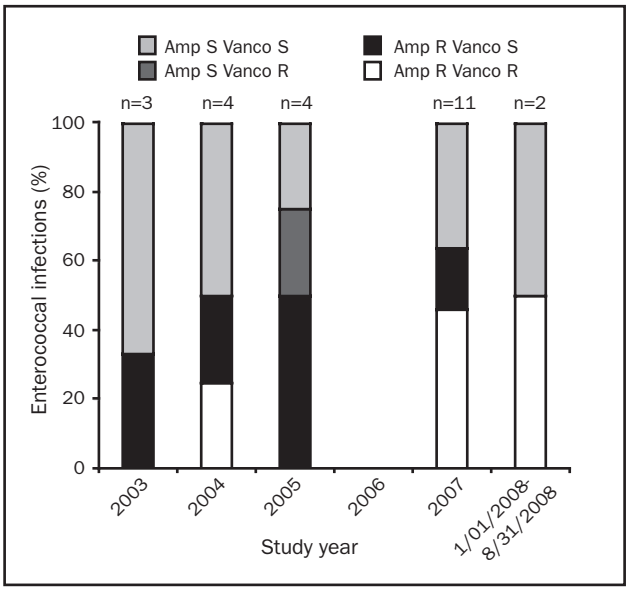

FIGURE 3. Epidemiology of infection-causing *Enterococcus* spp. There were no *Enterococcus* spp. isolates in 2006. Amp = ampicillin; R = resistant; S = susceptible; Vanco = vancomycin.

1 isolate, which was resistant to levofloxacin. Our laboratory does not routinely perform fluoroquinolone susceptibility testing to the viridans group streptococci. A total of 12 (50%) ampicillin-resistant and 8 (33%) vancomycin-resistant isolates of *Enterococcus* spp. were identified. The changing epidemiology of infections with *Enterococcus* spp. is depicted in Figure 3. With the exception of 2007, when 5 VRE infections occurred, the incidence of VRE infection remained relatively low and consistent during the study period. Overall, for GP organisms with available susceptibility data, 43 (78%) of 55 isolates were resistant to levofloxacin, 31 (69%) of 45 isolates were resistant to moxifloxacin, and 42 (78%) of 54 isolates were resistant to ciprofloxacin.

Isolates that were resistant to GN are summarized in Table 3. Of 8 *P aeruginosa* isolates, 5 (63%) were resistant

TABLE 2. **Epidemiology of Infection**[a]

Organisms	2003	2004	2005	2006	2007	2008[b]	Total
Gram-positive, No. (%)	3 (100)	19 (68)	14 (67)	16 (62)	16 (64)	10 (53)	78 (64)
Staphylococcus spp.	0	12	5	10	4	7	38
CoNS	0	12	5	10	4	6	37
S aureus	0	0	0	0	0	1	1
Viridans group streptococci	0	1	2	2	0	0	5
Enterococcus spp.	3	4	4	0	11	2	24
E faecalis	2	1	1	0	4	1	9
E faecium	1	1	2	0	4	1	9
Unspeciated	0	2	1	0	3	0	6
Corynebacterium spp.	0	0	1	1	0	1	3
Micrococcus spp.	0	1	1	2	0	0	4
Other[c]	0	1	1	1	1	0	4
Gram-negative, No. (%)	0 (0)	9 (32)	7 (33)	10 (38)	9 (36)	9 (47)	44 (36)
Pseudomonas spp.	0	3	1	0	3	1	8
Klebsiella pneumoniae	0	3	1	1	3	0	8
Enterobacter spp.	0	1	0	2	1	3	7
Escherichia coli	0	0	1	1	2	2	6
Stenotrophomonas spp.	0	1	1	3	0	1	6
Acinetobacter spp.	0	0	1	0	0	1	2
Other[d]	0	1	2	3	0	1	7

[a] CoNS = coagulase-negative staphylococci.
[b] January 01, 2008, through August 31, 2008.
[c] *Aerococcus viridans*, *Staphylococcus lugdunensis*, *Stomatococcus*, acid-fast bacilli resembling mycobacteria (n=1 of each).
[d] *Chryseobacterium*, *Sphingomonas*, *Neisseria*, *Moraxella*, *Leuconostoc*, *Leptotrichia*, unspeciated gram-negative rod (n=1 of each).

TABLE 3. **Resistance Among Most Commonly Isolated Gram-Negative Organisms**

Organism	No.	FQ	3rd C	Cef	P-T	CBPs	AG	MDR
Pseudomonas spp.	8	4 (50)	4 (50)	4 (50)	4 (50)	5 (63)	5 (63)	5 (63)
Klebsiella spp.	8	2 (25)	0	0	0	0	0	0
Enterobacter spp.	7	2 (29)	3 (43)	0	2 (29)	0	0	2 (29)
Escherichia coli	6	5 (83)	1 (17)	1 (17)	0	0	3 (50)	4 (67)
Stenotrophomonas spp.	6	3 (50)	5 (83)	5 (83)	5 (83)	6 (100)	6 (100)	6 (100)
Acinetobacter spp.	2	1 (50)	1 (50)	1 (50)	1 (50)	1 (50)	1 (50)	1 (50)

AG = aminoglycoside; CBP = carbapenem (eg, imipenem, meropenem); Cef = cefepime; FQ = fluoroquinolone; MDR = multidrug resistant (resistance to 2 classes of antibiotics); P-T = piperacillin-tazobactam; 3rd C = ceftriaxone, cefotaxime.

to 2 or more antibiotic classes, and 4 (50%) were resistant to 3 or more. The 4 *P aeruginosa* isolates identified before 2006 retained susceptibility to fluoroquinolones; however, the latter 4 isolates were resistant to fluoroquinolones. Most of the 6 *E coli* isolates were resistant to fluoroquinolone (n=5; 83%). In contrast, most of the 8 *Klebsiella* spp. isolates retained susceptibility to this antibiotic class, with only 2 (25%) of the isolates conferring resistance. Overall, for GN organisms with reported fluoroquinolone susceptibility, 13 (31%) of 42 isolates were resistant to levofloxacin, and 18 (43%) of 42 were resistant to ciprofloxacin. Discordant fluoroquinolone susceptibility was noted in 3 (50%) of the *Stenotrophomonas* spp. isolates, 1 (50%) of the *Acinetobacter* spp. isolates, and 1 (13%) of the *Klebsiella* spp. isolates. One extended-spectrum β-lactamase–producing organism, *E coli*, was identified during the study period.

Trends of GN antimicrobial resistance over time are noted in Figures 4 and 5. Increasing resistance to fluoroquinolones is observed when all GN isolates are combined (*P*=.02). No change in resistance to cefepime, piperacillin-tazobactam, or the carbapenems was seen (*P*=.68, *P*=.62, and *P*=.82, respectively). If resistance among the 4 most common GN isolates is examined independently, the same trends are observed. There was, however, a statistically significant increase in resistance to both fluoroquinolones and aminoglycosides in these organisms over time (Figure 5, *P*=.05). Again, no change in resistance to cefepime, piperacillin-tazobactam, or the carbapenems was noted (*P*=.94, *P*=.82, and *P*=.50, respectively).

C difficile and VRE

The incidence of *C difficile* and VRE during the study period was minimal in patients who received levofloxacin and penicillin prophylaxis (n=231). Eight patients (3.5%) developed *C difficile*–associated disease. Colonization or infection by VRE was present in 33 patients (14%), and a statistically significant increase in combined VRE infection and colonization was discovered over time (*P*=.04). The 20 patients with newly discovered VRE had a documented negative VRE swab result before receipt of levofloxacin and a positive VRE swab result or VRE infection within 3 months after transplant. Notably, 5 VRE infections oc-

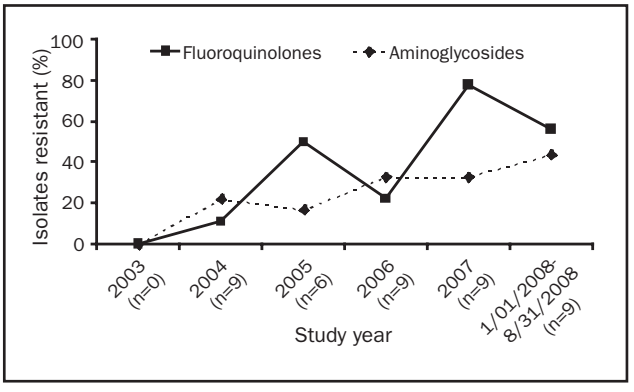

FIGURE 4. Gram-negative resistance to fluoroquinolones (*P*=.02; exact Wilcoxon signed rank test) and aminoglycosides (*P*=.26; exact Wilcoxon signed rank test).

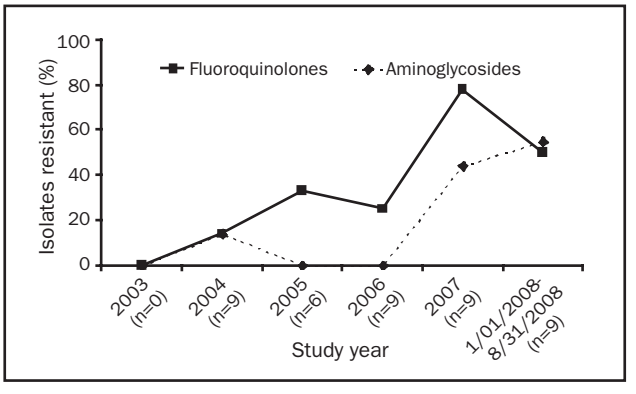

FIGURE 5. Resistance of *Pseudomonas*, *Klebsiella*, and *Enterobacter* spp. and *Escherichia coli* to fluoroquinolones and aminoglycosides (*P*=.05 for both classes of drugs; exact Wilcoxon signed rank test).

curred in 2007, whereas only one or none occurred in the other study years.

DISCUSSION

During the course of this study, approximately one-third of patients developed infection within 3 months of undergoing allogeneic HSCT. The incidence of GP and GN bacterial infections did not significantly change over time at our institution. Rates of fluoroquinolone-resistant GN organisms (particularly *P aeruginosa*) increased, whereas resistance to extended-spectrum β-lactams remained stable. The incidence of VRE colonization and *C difficile* infection was negligible during the study period.

During 2003, only 19 allogeneic HSCTs were performed, compared with 45 to 55 transplants per year in all other study years. The low number of infections detected in 2003 (3 GP bacterial infections vs >20 infections observed in the other years of the study) is reflected by this observation. Not surprisingly, CoNS was the most commonly isolated organism overall. These isolates likely represented true infection in a neutropenic host given our strict inclusion criteria. Consistent with other investigations, potential colonizing organisms had to be isolated from 2 consecutive cultures to be considered an infection.[12,13] A steady decrease in the ratio of GP:GN organisms has been observed in multiple studies in patients undergoing HSCT who received fluoroquinolone prophylaxis.[12,14,15] The percentage of GN bacterial infections increased slightly during the study period; however, that increase did not reach statistical significance, likely because of the small sample size. We anticipate that eventually more GN bacterial infections will emerge with continued use of fluoroquinolone-based combination antimicrobial prophylaxis and subsequent selective pressure.

Our study contributes to the growing body of evidence that using prophylactic antibiotics in neutropenic patients selects for resistant organisms implicated in infections.[16-19] Fluoroquinolone-resistant and MDR *P aeruginosa* and *E coli* were frequently identified in our allogeneic HSCT patients who received fluoroquinolone-based combination antimicrobial prophylaxis. These findings are consistent with a recent study describing prophylactic fluoroquinolone use as a risk factor for the isolation of MDR *E coli* in a broad neutropenic population.[20] Other factors that play a role in the acquisition of resistance in this patient population, including previous antibiotic use, previous hospitalizations, and potential nonadherence, were not assessed in this study. Despite these limitations, our study suggests that the use of levofloxacin for prophylaxis, our current standard of practice, may be contributing to the resistance patterns observed in GN organisms. Fluoroquinolone resistance rates have increased, whereas resistance to broader-spectrum antibiotics has not changed appreciably over time. We did not measure rates of infection reduction for patients receiving prophylaxis compared with those who were not. However, given our observations, we encourage transplant centers that routinely use fluoroquinolone prophylaxis in allogeneic HSCT recipients to empirically use antipseudomonal β-lactams in the event of a febrile episode and subsequent infection.

Although our institution is a large, academic, tertiary care center, rates of bacterial resistance have remained historically low. Only 1 extended-spectrum β-lactamase–producing organism was identified in our study, whereas rates as high as 25% to 44% have been observed in allogeneic HSCT recipients at other centers.[12,21] In comparing our study data with our institutional antibiogram, we note that the rate of fluoroquinolone-resistant organisms is considerably higher in our allogeneic HSCT recipients than in our general patient population, reflecting not only their higher antimicrobial exposures but perhaps also their more extensive exposure to the inpatient hospital setting. Therefore, institutional antibiograms that are compiled from all pooled patient groups may not be as useful in guiding empiric antibiotic selection in those who undergo allogeneic HSCT and other patient groups with heavy antibiotic exposures. Aminoglycosides are infrequently used at our institution. The appearance of aminoglycoside-resistant organisms over time, particularly in the most commonly isolated GN organisms, is both statistically and clinically significant. We hypothesize that a possible cross-resistance exists between fluoroquinolones and aminoglycosides, as has been described in vitro with *P aeruginosa*.[22,23]

Rates of VRE colonization are increasingly reported in those who undergo HSCT, ranging from 10% to as high as 40% at some centers[24,25]; however, numerous epidemiologic studies have noted a marginal (<5%) incidence of VRE infection in the HSCT patient population.[12,15,19] Although the earlier time period of our study is consistent with these trends, a few concerning features were identified. First, 5 VRE infections occurred in 2007, which could represent either a contained outbreak or a more generalized trend of increased VRE prevalence in our allogeneic HSCT patient population. The latter is plausible, given the overall statistically significant increase in the occurrence of VRE (if colonization and infection are combined) during the study period. Additionally, most of the documented VRE cases in the 3 months after transplant were newly discovered cases. This increase in VRE detection may reflect an increased surveillance, our laboratory transition in 2004 from stool culture to the more

sensitive polymerase chain reaction assay for identification of VRE, propagation of VRE through antimicrobial selective pressure, or an increase in imported VRE in patients referred to our institution from other medical centers. Given these confounders, we cannot confirm whether a levofloxacin-based antimicrobial prophylaxis program is contributing to the increased occurrence of VRE at our center. Newer literature suggests a 30% risk of developing VRE infection in a colonized allogeneic HSCT patient.[24] Because VRE colonization is also a risk factor for 100-day mortality after allogeneic HSCT,[25] we encourage transplant centers to continue to closely monitor VRE colonization.

Fluoroquinolone usage has been associated with the development of hypertoxin-producing *C difficile*–associated disease.[26] In our study, the incidence of *C difficile* was surprisingly minimal in the 3 months after allogeneic HSCT; however, transplant centers should continue to monitor for *C difficile* infection in symptomatic patients.

This study has several limitations. Because we studied a retrospective cohort with a small sample size, we are unable to accurately identify a causal relationship between the use of levofloxacin and the changing epidemiology of infections in our patient population. A risk factor analysis would help determine whether a relationship exists. With the exception of reviewing the patients' prophylactic antibiotics, we did not assess other factors that could contribute to changing epidemiology and resistance profiles of the organisms isolated, such as previous antibiotic use and nonadherence to the prophylactic regimen. Additionally, we recognize that the use of penicillin and doxycycline with levofloxacin can affect the selection of GP bacterial infections; however, we think the use of doxycycline is unlikely to contribute significantly to the GN resistance trends observed.

Although many factors contribute to the acquisition of resistance, administration of fluoroquinolone prophylaxis during the period of chemotherapy-induced neutropenia may be a driving factor in the allogeneic HSCT patient population. As the rates of drug-resistant *P aeruginosa, E coli,* and other GN bacteria climb, the utility of fluoroquinolones to treat infections in these patients is likely to decline in the near future. In time, perhaps, the benefits of antimicrobial prophylaxis for infection rate reduction may need to be weighed against the risks of promoting resistance to select drugs. Rates of VRE colonization and infection are also increasing in HSCT recipients, making rigorous surveillance critical. Fortunately, the incidence of *C difficile* colitis was low in our study. We encourage HSCT centers to conduct similar studies and routinely monitor antimicrobial resistance patterns in this patient population.

CONCLUSION

A fluoroquinolone-based prophylactic regimen is a potential contributor to the emergence over time of resistant GN infections in those who undergo allogeneic HSCT. Our findings provide additional support for the current standard of practice, which is to administer empiric monotherapy with an antipseudomonal β-lactam if these patients develop fever and are thought to have an infection.

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