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Mortality Associated With *Stenotrophomonas maltophilia* Bloodstream Infection in Patients With Leukemia

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BACKGROUND

- *Stenotrophomonas maltophilia* is an important opportunistic infection in patients with hematologic malignancy
- Mortality associated with *S. maltophilia* is elevated in patients with hematologic malignancy and approaches 100% in patients who develop hemorrhagic pneumonia
- Trimethoprim-sulfamethoxazole is the historic drug of choice for treatment of serious *S. maltophilia* but use may be precluded by allergy, toxicity, and/or resistance
- Data on optimal treatment of *S. maltophilia* infection in patients with hematologic malignancy are limited

OBJECTIVES

The purpose of this study was to investigate the clinical characteristics and outcomes associated with *S. maltophilia* bloodstream infection in patients with leukemia and, secondarily, to compare alternative treatment options to trimethoprim-sulfamethoxazole

METHODS

Clinical Cohort

- Retrospective cohort study of adults with leukemia and *S. maltophilia* bloodstream infection (BSI) at MD Anderson between 1/1/11 and 11/30/2015
- Clinical and outcomes data were extracted from the electronic medical record

Statistical Analysis

- Descriptive statistics used for assessment of clinical cohort
- Drug treatment comparisons performed with multivariable, time-varying Cox proportional hazards modeling to account for immortal time bias
- Primary analysis excluded patients who died within 24 hours of BSI onset to limit to patients with potential for 24 hours of active therapy

RESULTS

Table 1. Patient characteristics (n = 85)

Characteristic	
Age (years)[a]	55 (20 – 89)
Pitt bacteremia score[a]	1 (0 – 9)
Male gender	37 (44)
Primary diagnosis	
ALL	19 (22)
AML	51 (60)
Other leukemia	15 (18)
Prior HCT	26 (31)
Neutropenic at time of index culture	64 (75)
Primary source of infection	
GI	3 (4)
Respiratory	26 (31)
GU	2 (2)
SSTI	4 (5)
CVC	22 (26)
Disseminated / unknown	28 (33)
Polymicrobial index culture	24 (28)

Excludes 11 patients who died with 24 hours. All values reported as n (%) unless otherwise specified.
Neutropenic defines as absolute neutrophil count (ANC) < 500 cells/mm^3
[a]Median (interquartile range)

Table 2. Microbiologic characteristics

Drug	MIC50	MIC90	Susceptible
Ceftazidime	16	>=256	46
Levofloxacin	2	>=16	66
Minocycline	0.5	2	100
Moxifloxacin (n = 45)	0.38	3	N/A
Ticarcillin-clavulanate (n = 80)	32	>=256	46
Tigecycline (n = 66)	1	>=4	N/A
Trimethoprim-sulfamethoxazole	N/A	N/A	96

Susceptibility determined by MD Anderson clinical microbiology laboratory according to CLSI M-100 (Jan 2022) criteria as applicable

MIC: minimum inhibitory concentration (mcg/mL)

Table 3 Treatment characteristics

Drug (any use; n = 85)	
Ceftazidime	34 (40)
Levofloxacin	19 (22)
Moxifloxacin	18 (21)
Ticarcillin-clavulanate	4 (5)
Trimethoprim-sulfamethoxazole	61 (72)
Minocycline	22 (26)
Ceftazidime-avibactam	1 (1)
Tigecycline	34 (40)
Any combination/sequential therapy	60 (70)
Trimethoprim-sulfamethoxazole-based combination/sequential therapy	49 (58)

Percentages add to more than 100% when accounting for combination and/or sequential therapy
All values reported as n (%)

Table 4. Patient outcomes

Outcome	% with outcome
Death in 14 days	20 (24)
Death in 30 days	32 (38)
Time to defervesce (n = 37)[a,b]	3 (2 – 6)
Time to blood culture clearance (n = 66) [a,b]	4 (2 – 7)

Values reported as n (%) unless otherwise specified
[a]Median (interquartile range)
[B]n refers to total with characteristic at baseline

Table 5. Multivariable Cox proportional hazards regression for death in 14 days

Variable	Hazard ratio	95% CI	p-value
Minocycline use	0.64	0.20 – 2.06	0.45
Trimethoprim-sulfamethoxazole use	0.15	0.05 – 0.44	<0.01
Tigecycline use	3.13	1.00 – 9.73	0.05
Ceftazidime use	0.60	0.18 – 2.00	0.40
Levofloxacin use	1.01	0.29 – 3.59	0.99
Moxifloxacin use	0.65	0.16 – 2.60	0.55
HCT	0.31	0.05 – 1.82	0.20
Pitt bacteremia score	1.37	1.12 – 1.65	<0.01

DISCUSSION

- All deaths occurred in patients without neutrophil recovery and with non central-line related infections
- Majority of patients treated with trimethoprim-sulfamethoxazole which appeared to have a protective effect relative to other antimicrobials
- Tigecycline use associated with worse outcomes compared to other antimicrobials
- Despite multivariable model, selection bias likely contributes significantly to observed outcomes
- Isolates were nearly universally susceptible to trimethoprim-sulfamethoxazole and minocycline according to current CLSI standards

CONCLUSIONS

- Trimethoprim-sulfamethoxazole remains the drug of choice for patients with leukemia and *S. maltophilia* BSI
- All patients with catheter-related bloodstream infection and neutrophil recovery survived
- Future randomized, controlled trials of treatment should ensure that sufficiently high-risk patients are enrolled to ensure meaningful data are obtained

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