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Stenotrophomonas maltophilia infections and approaches to treatment

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ABSTRACT

Background: Current knowledge of the epidemiology of *Stenotrophomonas maltophilia* is limited to studies from several small international medical centers. Additionally, real-world approaches to treatment are not well described.

Methods: We included admissions to any Veterans Affairs (VA) medical center nationally, with positive *S. maltophilia* cultures collected from any culture site between January 2010 and April 2019. We reviewed epidemiologic factors of clinical characteristics and treatment. Treatment was assessed by mapping out all antibiotic exposures each day, and identifying differences (heterogeneity) in the antibiotics used and duration of their use.

Results: Over the study period, we identified 7,814 hospital admissions with positive *S. maltophilia* cultures. Patients were older (mean age 68.1 year) and male (97.6%), with 26.4% in the intensive care and 56.5% admitted from other healthcare settings. Respiratory cultures were most common (48.5%), followed by urine (19.8%), skin and soft tissue (17.5%), and blood (5.3%). Admissions were mostly 12 days long (median), with an inpatient mortality rate of 14.3%.

The median time to culture collection from admission was day 2 of the hospitalization, and the median time to culture completion was 4 days. Changes in therapy occurred before culture completion for 87.6% of admissions. Most admissions utilized different treatment approaches (antibiotic drug and duration treatment heterogeneity 90.3%), with a median of 4 changes in therapy. Fluroquinolones were utilized in 45.6% of admissions (initiated median 4 days from admission) and sulfamethoxazole/trimethoprim in 29.5% (initiated median 7 days from admission). Inpatient mortality was significantly higher among those with changes in therapy versus those without changes (15.7% vs 5.5%, p<0.0001), and among those without changes, mortality was significantly higher with combination therapy versus monotherapy (12.1% vs 3.1%, p<0.0001).

Conclusion: Among more than 8,000 admissions with positive *S. maltophilia* cultures in the VA nationally, identification of the organism and targeted therapy did not occur until 4-7 days from admission. Differences in clinical outcomes were observed among the different treatment approaches.

***Updated to exclude *S. maltophilia* admissions without records of antibiotics (n=411).**

BACKGROUND

While *S. maltophilia* resistance to sulfamethoxazole / trimethoprim remain generally low, hypersensitivity, drug toxicity, and other adverse drug events often preclude use of sulfamethoxazole / trimethoprim. However, it unknown how often sulfamethoxazole / trimethoprim is used in the treatment of *S. maltophilia* infections.

OBJECTIVES

To describe patients hospitalized with *S. maltophilia* positive cultures, and antibiotic treatments received over the course of the hospitalization.

METHODS

- Hospitalizations with *S. maltophilia* positive cultures, Jan 2010-April 2019. Included subsequent admissions more than 30 days from the previous discharge date.
- Exposure mapping identified all antibiotics from 7 days prior to culture until discharge, or 30 from culture for longer hospital stays.
- Assessed combination therapy, duration of therapy, and changes in therapy.

RESULTS

Demographics and clinical characteristics	N=7,814
Age (years), mean (SD)	68.1 (11.2)
Male, n (%)	7,625 (97.6%)
White, n (%)	5,786 (74.1%)
Admitted from home/community, n (%)	3,401 (43.5%)
Treating specialty intensive care, n (%)	2,065 (26.4%)
Hospitalization 30 days prior to admission, n (%)	1,951 (25.0%)
Time to culture from admission (days), median (IQR)	2 (0-10)
Co-infections, n (%)	4,711 (60.3%)
Clinical Outcomes	
Inpatient mortality, n (%)	1,119 (14.3%)
30-day mortality (from culture), n (%)	1,350 (17.3%)
Reinfection within 30 days of discharge, n (%)	268/6,695 (4.0%)
Length of hospital stay, from admission (days), median (IQR)	12 (5-29)
Length of hospital stay, from culture (days), median (IQR)	7 (3-17)
S. maltophilia readmission, n (%)	331 (4.5%)

SD = standard deviation, IQR = interquartile range.

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RESULTS

Treatment	Overall N=7,814	Inpatient mortality N=1,119 (14.3%)	Inpatient survival N = 6,695 (85.7%)
Sulfamethoxazole/trimethoprim	2,308 (29.5%)	**393 (35.1%)**	**1,915 (28.6%)**
Aminoglycoside[1]	590 (7.6%)	**175 (15.6%)**	**415 (6.2%)**
Carbapenems[2]	1,489 (19.1%)	**455 (40.7%)**	**1,034 (15.4%)**
Extended-spectrum cephalosporins[3]	3,093 (39.6%)	**523 (46.7%)**	**2,570 (38.4%)**
Fluoroquinolones[4]	3,565 (45.6%)	540 (48.3%)	3,025 (45.2%)
Antipseudomonal penicillins + β-lactamase inhibitors[5]	3,916 (50.1%)	**714 (63.8%)**	**3,202 (47.8%)**
Polymyxins[6]	83 (1.1%)	**44 (3.9%)**	**39 (0.6%)**
Tetracyclines[7]	735 (9.4%)	**87 (7.8%)**	**648 (9.7%)**

Data are n (%). Bolded indicates p-value <0.05 for comparison of inpatient mortality and inpatient survival (chi-square test).
[1] Aminoglycosides (amikacin, gentamicin, tobramycin). [2] Carbapenems (imipenem, meropenem, doripenem). [3] Extended-spectrum cephalosporins (cefepime, ceftazidime, cefotaxime, ceftriaxone). [4] Fluoroquinolones (ciprofloxacin, levofloxacin). [5] Antipseudomonal penicillins + β-lactamase inhibitors (piperacillin/tazobactam, clavulanate/ticarcillin). [6] Polymyxins (colistin, polymyxin B). [7] Tetracyclines (tetracycline, minocycline, doxyclycline).

Treatment patterns		N=7,814
Change in therapy	Number with change, n (%)	6,766 (86.6%)
	Day of change from culture, median (IQR)	0 (-3 to 2)
	Number of changes, median (IQR)	4 (2-6)
	Unique change patterns with length of therapy, n (%)	6,654 (98.3%)
	Unique change patterns without length of therapy, n (%)	6,098 (90.1%)
No change in therapy	Number without change, n (%)	1,048 (13.4%)
	Unique non-change patterns with length of therapy, n (%)	405 (38.6%)
	Unique non-change patterns without length of therapy, n (%)	134 (12.8%)

IQR = interquartile range.

CONCLUSIONS

Among hospitalized patients with *S. maltophilia* infections, about ¼ required intensive care and most were admitted from other healthcare settings. Mortality within 30 days of culture occurred among 17.3% of patients, with reinfection rates of <5%. There was substantial variation in treatment approaches (treatment heterogeneity 90.3%), which may be due, in part, to the high rate of co-infection (60.3%). Time to culture report completion and initiation of targeted therapy did not occur until 4 and 4-7 days from admission, respectively. Both resistance rates and treatment heterogeneity were significantly lower among those who survived.