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Serratia marcescens Bacteremia and Endocarditis: A Treatment Assessment from an Academic Medical Center

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ABSTRACT

Background: Introduction: *Serratia marcescens* (SM) is often an opportunist that has been associated as a cause of healthcare-associated infection and in some people who inject drugs (PWID). Decisions about the treatment of SM infections are difficult given the small clinical studies available and concerns for multidrug resistance. SM has the ability to produce inducible AmpC β-lactamase and may acquire extended-spectrum β-lactamase (ESBL). Evidence-based guidance is lacking in terms of identifying preferred antimicrobial therapy of SM bacteremia and endocarditis. Compared to other reports, our hospital has one of the largest SM data sets to compare.
Methods: This observation study included adult patients admitted to our hospital (2016-2019) with SM bloodstream infections, including endocarditis. Patients were excluded from the analysis, if they had a concomitant infection with another gram-negative organism. Our evaluation was designed to: compare outcomes associated with different antibiotic regimens, evaluate how care differed in PWID patients versus others, and identify factors associated with obtaining infectious diseases expert consultations (ID Consult).
Results: Forty-three patients met study inclusion/exclusion. Twenty-eight patients (65.1%) had an ID Consult. Twenty-four (55.8%) were PWID. Endocarditis was diagnosed in 30.2% of patients. The most common regimen was cefepime +/- aminoglycoside, followed by a carbapenem +/- aminoglycoside. Combination therapy was only recommended during ID Consult. Piperacillin-tazobactam was used in 11.6% of patients. No regimen displayed an efficacy or safety advantage over another. Most patients (90.7%) cleared their blood stream within 48 hours of antibiotic start. Phenotypic susceptibility testing did not identify either ESBL or AmpC production in any of the isolates, including recurrences. Multi-drug resistance was not appreciated. Significant factors associated with obtaining ID Consult were: PWID (p=0.004), endocarditis (p=0.0002), sepsis (p=0.022), surgical intervention (p=0.003).
Conclusions: We could not identify an advantage with any particular antibiotic treatment regimen in this study. Induction of AmpC or selection of ESBL organisms was not displayed by any of the organisms.

INTRODUCTION:

Serratia marcescens is often an opportunist gram-negative bacilli that has been associated as a cause of healthcare-associated infection and in some people who inject drugs (PWID). Decisions about the treatment of *S. marcescens* infections are difficult given the small clinical studies available and concerns for multidrug resistance. *S. marcescens* has the ability to produce inducible AmpC β-lactamase and may acquire extended-spectrum β-lactamase (ESBL). Evidence-based guidance is lacking in terms of identifying preferred antimicrobial therapy of *S. marcescens* bacteremia and endocarditis. Some experts advocate the use of carbapenems, while others try to use carbapenem-sparing regimens when possible.[1] This study was designed to assess the treatment approach for *S. marcescens* bacteremia/ endocarditis at our hospital.

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METHODS AND ANALYSIS:

- This observation study included adult patients admitted to the WVU Medicine Ruby Memorial Hospital between 2016 and 2019 with *S. marcescens* bloodstream infections, including endocarditis.
- Patients were excluded from the analysis if they had a concomitant infection with another gram-negative organism.
- Our evaluation was designed to: compare outcomes associated with different antibiotic regimens, evaluate how care differed in PWID patients versus others, and identify factors associated with obtaining infectious diseases expert consultations (ID Consult).
- Susceptibility testing was performed using Vitek 2 automated susceptibility testing and Kirby-Bauer testing.
- Biostatistical analysis was performed using JMP Software (SAS Institute).
- This study was granted exempt Status by the WVU Institutional Review Board.

Table 1: Patient Characteristics (n=43)

Characteristic	Number (%) unless specified
Age (years) mean ± Standard deviation	48.7 ± 15.0
Gender (female /male)	19 / 24
BMI (kg/m^2) ± Standard deviation	29.4 ± 8.95
Intravenous drug abuse	24 (55.8)
Endocarditis	13 (30.23)
Prosthetic heart valve	6 (13.95)
β-lactam allergy reported	9 (20.93)
Serum creatinine (mg/dL) mean [range]	0.92 [0.4 – 6.78]
Abnormal hepatic enzymes	7 (16.28)
Septic at diagnosis	17 (39.53)
Gram-positive cocci or Candida isolated in blood	10 (23.26)
Had Infectious Diseases consult	28 (65.12)
Valve surgery as part of treatment	9 (20.93)

RESULTS:

- Forty-three patients met study inclusion/exclusion for this study and their characteristics are summarized in table 1.
- Endocarditis was diagnosed in 13 (30.2%) of patients.
- Twenty-eight patients (65.1%) had ID Consults.
- No regimen displayed an efficacy or safety advantage over another.
- The most common regimen was cefepime +/- aminoglycoside, followed by a carbapenem +/- aminoglycoside. Some patients had “mixed” regimens that included limited days of particular antibiotic(s) with switches or additions to other therapies
- Combination therapy was only recommended for endocarditis and with an ID Consult.
- Most patients (90.7%) cleared their blood stream within 48 hours of antibiotic start.
- Phenotypic susceptibility testing did not identify either ESBL or AmpC production in any of the isolates, including recurrences.
- When all characteristics were compared by multi-logistic regression, only PWID (p=0.004), endocarditis (p=0.0002), sepsis (p=0.022), and surgical intervention (p=0.003), were independently associated with obtaining an ID Consult.

Figure 1. Antimicrobial Susceptibility Report*

	Amox-Clav	Cefazolin	Pip-Tazo	Tetracycline	Tobramycin	Ceftriaxone	Cefepime	Carbapenem	Levofloxacin
Patient 1	R	R	S	R	S	S	S	S	S
Patient 2	R			S	S	S	S	S	S
Patient 3	R	R		R	S	S	S	S	
Patient 4	S		S	S	S	S	S	S	
Patient 5	R	R	S	R	S	S	S	S	S
Patient 6	R	R	S	R	INT	S	S	S	S
Patient 7	R	R	S	R	S	S	S	S	S
Patient 8	R	R	S	S	S	S	S	S	S
Patient 9	R	R		R	S	S	S	S	S
Patient 10	R	R	S	R	S	S	S	S	S
Patient 11	R	R	S	R	S	S	S	S	S
Patient 12	R	R	S	S	S	S	S	S	S
Patient 13	R	R	S	R	S	S	S	S	S
Patient 14	R	R	S	R	S	S	S	S	S
Patient 15	R	R	S	R	S	S	S	S	S
Patient 16	R	R	S	R	S	S	S	S	S
Patient 17	R	R	S	R	S	S	S	S	S
Patient 18	R	R	S	S	S	S	S	S	S
Patient 19	R	R	S	S	S	S	S		
Patient 20	R	R	S	R	S	S	S	S	S
Patient 21	R	R	S	R	S	S	S		
Patient 22	R	R	S	R	S	S	S	S	S
Patient 23	R	R	S	R	S	S	S	S	S
Patient 24	R	R	INT	R	S	S	S	S	INT
Patient 25	INT				INT	S	S	S	S
Patient 26	R	R	S	R	S	S	S	S	S
Patient 27	R	R	S	R	S	S	S	S	
Patient 28	R	R	S	S	S	S	S	S	S
Patient 29	R	R	S	S	S	S	S	S	S
Patient 30	R	R	S	R	S	S	S	S	S
Patient 31	R	R	S	R	S	S	S	S	S
Patient 32	R	R	S	R	S	S	S	S	S
Patient 33	R	R	S	R	S	S	S	S	S
Patient 34	R	R	S	R	S	S	S	S	S
Patient 35	R	R	S	R	S	S	S	S	S
Patient 36	R	R		R	S	S	S	S	
Patient 37	R	R	S	R	INT	S	S	S	S
Patient 38	R	R	S	S	S	S	S	S	S
Patient 39	R	R	S	R	S	S	S	S	
Patient 40	R	R	S	S	S	S	S	S	
Patient 41	R	R	S	S	S	S	S	S	

*Two patients did not have complete susceptibility reports, and are not included here

Table 2: Antibacterial Regimens Used

Gram-negative treatment	Number (%)	Clinical Response		
		Resolved/Cured	Recurrence	Died of underlying condition
Cefepime	19 (44.2%)	13	3	3
Carbapenem (Meropenem)	6 (13.9%)	3	0	3
Piperacillin-tazobactam	5 (11.6%)	3	2	0
Cefepime + aminoglycoside or fluoroquinolone	6 (13.9%)	5	0	1
Meropenem + aminoglycoside or fluoroquinolone	2 (4.6%)	1	1	0
Mixed therapies	5 (11.6%)	5	0	0

DISCUSSION:

Compared to other published reports, our study has one of the largest single center *S. marcescens* bacteremia/endocarditis data sets. The majority of antibiotic courses provided carbapenem-sparing treatment with an overall recurrence rate <14%. Cefepime alone or in combination made up the majority of courses. Piperacillin-tazobactam was the main therapy in five patients, despite the concern for inducible AmpC expression. Piperacillin-tazobactam has been used with success in bacteremic infections with AmpC producing organisms.[1,2] We did see two recurrences in the five patients treated with piperacillin-tazobactam. Combination therapy was only used for endocarditis and with an ID Consult. This approach was deemed reasonable for non-HACEK gram-negative (not specific to *S. marcescens*) endocarditis in the American Heart Association endocarditis guidelines.[3] The quick bacteremia clearance rate (<48 hours) experienced by most patients may reflect the oft-reported low pathogenicity of *S. marcescens*, and may promote the use of short courses of IV antibiotics.[4-6]

CONCLUSION:

We could not identify an advantage with any particular antibiotic treatment regimen in this study. Induction of AmpC or selection of ESBL organisms was not displayed by any of the organisms. This data suggests that carbapenem-sparing regimens may be a good first choice. Prospective randomized studies should be performed to better evaluate antimicrobial treatment options and duration for *S. marcescens* bacteremia/endocarditis.

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