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ORIGINAL ARTICLE

Comparisons between patients with trimethoprim–sulfamethoxazole-susceptible and trimethoprim–sulfamethoxazole-resistant *Stenotrophomonas maltophilia* monomicrobial bacteremia: A 10-year retrospective study

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Background/purpose: The impact of bacteremia due to the resistance of *Stenotrophomonas maltophilia* to trimethoprim–sulfamethoxazole (TMP–SXT) is uncertain. This study compared the clinical characteristics and outcomes of patients with TMP–SXT-susceptible (TSSSM) and TMP–SXT-resistant *S. maltophilia* (TSRSM) monomicrobial bacteremia.
Methods: The medical records of adult patients with TSSSM and TSRSM monomicrobial bacteremia from January 2004 to December 2013 were reviewed and classified into two groups, namely, TSSSM and TSRSM.
Results: There were 184 patients with monomicrobial *S. maltophilia* bacteremia. The mean age was 68.3 years. Most patients were males (72.8%), had high Charlson Comorbidity Index

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scores, previously prescribed antimicrobial agents, and indwelling medical devices. The 14-day and in-hospital mortality rates were 23.9% and 47.2%, respectively. There were 128 patients (69.6%) with TSSSM and 56 (30.4%) with TSRSM. The incidence of TSSSM bacteremia increased during the study period. The TSSSM and TSRSM groups had similar demographic and clinical characteristics and no significant differences in 14-day and in-hospital mortality (24.2% vs. 23.2%, $p = 0.833$; 50.0% vs. 41.1%, $p = 0.264$, respectively). Patients with TSSSM bacteremia had an increased risk of septic shock ($p = 0.044$) and neutropenia ($p = 0.028$) at bacteremia onset. Logistic regression analysis indicated that acquisition of TMP—SXT resistance was an independent risk factor for prolonged hospitalization ($p = 0.018$) and catheter-related *S. maltophilia* bacteremia was inversely associated with prolonged hospitalization after bacteremia ($p = 0.032$).

Conclusion: There were no significant differences in mortality for patients with TSSSM and TSRSM bacteremia, but patients with TSRSM bacteremia were associated with prolonged hospitalization after bacteremia onset.

Introduction

Stenotrophomonas maltophilia is a nonfermenting Gram-negative bacillus that has emerged as an important nosocomial pathogen primarily affecting immunocompromised patients.[1] Infection with this pathogen can manifest as pneumonia, bloodstream infection, wound infection, or urinary tract infection.[1] Treatment of these infections is difficult because *S. maltophilia* is intrinsically resistant to a variety of structurally unrelated antimicrobial agents, including β-lactams, cephalosporins, carbapenems, quinolones, and aminoglycosides although ticarcillin—clavulanic acid combination, some cephalosporins (ceftazidime, cefoperazone, and cefepime), and new fluoroquinolones seem to show effective *in vitro* activity against *S. maltophilia*.[2] Antibiotic resistance is mainly due to the presence of β-lactamases, efflux pump systems, enzymatic modification, outer membrane changes, and target site modification.[3]

Trimethoprim—sulfamethoxazole (TMP—SXT) is the drug of choice for susceptible *S. maltophilia* infections based on *in vitro* activity and anecdotal reports of favorable clinical outcomes.[2,4,5] However, recent antimicrobial susceptibility studies have reported the emergence of TMP—SXT-resistant *S. maltophilia* (TSRSM), in which resistance is mediated by acquisition of class 1 integrons and insertion element common region linked to the *sul*2 genes.[6—8] TSRSM species have been reported in Taiwan since 2000.[9] Infection by TSRSM species poses a major dilemma for the clinician because of the limited treatment options available, none of which have been validated clinically.[2,10,11]

Patients with *S. maltophilia* bacteremia often have polymicrobial infections and 20—40% of such infections are catheter related.[1] The bacteria most commonly recovered concomitantly with *S. maltophilia* are coagulase-negative staphylococci and enterococci.[12,13] Few studies on *S. maltophilia* bacteremia have excluded cases with polymicrobial bacteremia in order to eliminate confounding effects from other bacteria.[14,15] There have been no comparisons of patients with *S. maltophilia* bacteremia due to TSRSM and TMP—SXT-susceptible *S. maltophilia* (TSSSM).

We conducted a 10-year retrospective cohort study on the clinical characteristics and outcomes of patients with TSSSM and TSRSM monomicrobial bacteremia in our institute.

Methods

Study design and data collection

This study was conducted at the Tri-Service General Hospital, National Defense Medical Center, a 1700-bed a tertiary referral center in northern Taiwan. This 10-year retrospective cohort study examined patients who were hospitalized from January 1, 2004, to December 31, 2013. Medical charts were reviewed after obtaining the approval of the Institutional Review Board of the hospital (TSGHIRB approval number: 2-101-05-074). All patients with monomicrobial *S. maltophilia* bacteremia and with clinical symptoms or signs of infection were included for further analysis. Patients who had polymicrobial bacteremia or who were aged <18 years were excluded. If a patient had multiple episodes of bacteremia, only data from the first episode were included.

Definitions

S. maltophilia bacteremia was defined by the presence of a blood culture that yielded *S. maltophilia* from one or more collected blood samples. Hospital-acquired bacteremia was defined by a positive blood culture obtained from patients hospitalized for >48 hours after admission. Healthcare-associated bacteremia was defined by a positive blood culture obtained from patients within 48 hours of admission and fulfilled any of the standard criteria (e.g., residence in a nursing home).[16] Community-acquired bacteremia was defined by a positive blood culture obtained within the 48