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Infection Trends, Susceptibility Pattern, and Treatment Options for *Stenotrophomonas maltophilia* Infections in Trauma Patients: A Retrospective Study

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Abstract

Introduction *Stenotrophomonas maltophilia* is an emerging environmental, gram-negative, multidrug-resistant organism, associated with risk factors such as prolonged hospitalization, invasive procedures, admission to the intensive care unit, mechanical ventilation, use of indwelling catheters, administration of immunosuppressants or corticosteroids, human immunodeficiency virus infection, underlying malignancy, and organ transplantation. The organism, despite being of low invasiveness in immune-competent individuals, is difficult to treat because of intrinsic resistance to several antimicrobial agents.

Materials and Methods This study focuses on commonly encountered resistance from among the isolates over a duration of 7 years from 2012 to 2018, analyzed retrospectively. Identification and susceptibility testing were performed using Vitek 2 (BioMérieux, Marcy-l'Etoile, France).

Results Bloodstream infections were found to be most common (52.02%), followed by respiratory infections (35.83%). The median age of the patients was 36 years, and male to female ratio was 143:27. The median duration of hospital stay was 18 days, and mortality was seen in 18.82% of patients. Susceptibility to cotrimoxazole and levofloxacin was seen in 97.1% of isolates (168 out of 173) and 90.1% of isolates (156 out of 173), respectively.

Conclusion Despite being effective in a majority of *S. maltophilia* isolates, both cotrimoxazole and levofloxacin have their shortcomings. Cotrimoxazole is bacteriostatic and can cause bone marrow suppression and resistance to levofloxacin sometimes develops during therapy. Thus, the therapy should be decided considering the characteristics of both of these drugs.

Keywords
- *Stenotrophomonas maltophilia*
- trauma
- bloodstream infections

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Introduction

Stenotrophomonas maltophilia is a gram-negative nonfermentative organism. It is widely distributed in nature but is an uncommon pathogen in the community setting. In the hospital setting, *S. maltophilia* is notable for causing catheter-related bacteremia, pneumonia, soft tissue infection, meningitis, prosthetic valve endocarditis, and ocular infections, particularly among critical care and oncology patients.[1] *S. maltophilia* is not a highly virulent pathogen, but it has emerged as an important nosocomial pathogen owing to risk factors like underlying malignancy, the presence of indwelling devices, chronic respiratory disease, immunocompromised host, prior use of antibiotics, and long-term hospitalization or intensive care unit (ICU) stay.[2] *S. maltophilia* of either environmental or clinical origin is also capable of adhering to abiotic as well as living surfaces, thereby producing biofilms, which eventually hamper immune cells, impede the diffusion of antimicrobial drugs, and allow for persistence in central venous lines.[3,4]

It is usually resistant to multiple antimicrobials, including expanded-spectrum penicillins, third-generation cephalosporins, carbapenems, aminoglycosides, and quinolones. Trimethoprim–sulfamethoxazole is the antimicrobial agent of choice for this pathogen but is bacteriostatic. Further, resistance to this agent is increasing. Certain combinations of antibiotics have been found to be synergistic and may be appropriate for patients harboring resistant organisms or with severe infections.[1,2]

Materials and Methods

Study Design

The study was conducted at the Department of Microbiology, at an apex 248 bedded trauma hospital having 12 polytrauma ICU beds and 20 neurotrauma ICU beds. The duration of the study was from 2012 to 2018. A total of 170 patients admitted to wards and ICU with positive cultures for *S. maltophilia* were included. One hundred seventy-three nonrepetitive isolates of *S. maltophilia* were analyzed. The samples included blood, tracheal aspirate, bronchoalveolar lavage (BAL), pleural fluid, cerebrospinal fluid (CSF), urine, pus, and tissue. Samples were processed according to standard protocol. Identification and antimicrobial susceptibility testing were determined via Vitek-2 (BioMérieux, Marcy-l'Etoile, France) GN ID Card N-280 and disk diffusion using Kirby-Bauer's method. Blood culture was performed using the Bact T/ALERT system (BioMérieux, Marcy-l'Etoile, France). Isolates were considered separate if they occurred with different antibiotic susceptibilities or 14 or more days apart. The isolates that developed resistance to fluoroquinolone subsequently were taken to be resistant.

The patients' demographic and clinical outcome was obtained from the hospital information system.

Statistical Analysis

Descriptive statistical analysis was performed using Microsoft Excel 2013 (Microsoft Corp., Redmond, Washington, United States). Additional statistical analyses were performed with SPSS software version 24.0 and *p*-values less than 0.05 were considered statistically significant.

Results

A total of 173 episodes of *S. maltophilia* infections occurred from 2012 to 2018, ranging from a high of 46 infections in 2013 to a low of 15 in 2015, 2016, and 2017, and a median of 19.

The samples positive for growth of *S. maltophilia* included predominantly blood ($n = 90$, 52.02%), BAL ($n = 29$, 165.76%), tracheal aspirate ($n = 33$, 19.07%), and overall respiratory samples were 62/173 (35.83%). The remaining samples included, pus/wound ($n = 10$), body fluid four ($n = 4$), CSF ($n = 3$), urine ($n = 2$) and one each of central venous catheter tip and tissue. A major proportion of bloodstream infections (BSIs; 52 out of 90) occurred in the years 2013 to 2014, which also have a strikingly higher rate of *S. maltophilia* episodes (►**Fig. 1**).

Patient Profile

The age of patients ranged from 2 to 90 years; the median age was 36 years. Males outnumbered females, that is 143 out of 170 (84.1%). The median duration of stay was 18 days. Mortality for the duration of hospital stay was found to be 32 out of 170 (18.82%), respectively.

Susceptibility Profile and Coisolation Inclination

Antimicrobial susceptibility testing by Vitek-2 (BioMérieux, Marcy-l'Etoile, France) reports only cotrimoxazole and levofloxacin for *S. maltophilia*. Disc diffusion for minocycline was performed in a limited number of isolates and was excluded from the data.

About 90.1% of isolates (156 out of 173) were found to be susceptible to levofloxacin, and 97.1% of isolates (168 out of 173) were found to be susceptible to cotrimoxazole. Resistance to levofloxacin during therapy emerged in two isolates. One of the *S. maltophilia* isolates was found to be resistant to both levofloxacin and cotrimoxazole. No correlation was found between drug-resistant *S. maltophilia* and mortality; the patients who succumbed did not harbor more resistant isolate than those who survived.

The susceptibility trends over the years are shown in ►**Fig. 2**. Few samples yielded another pathogen apart from *S. maltophilia*, five of which were lower respiratory samples. This included tracheal aspirates ($n = 3$) having growth of *Acinetobacter baumannii* in two and *Pseudomonas aeruginosa* in one sample; BAL ($n = 2$), one of which grew *Pseudomonas aeruginosa* while the other grew *A. baumannii* alongside. In one urine sample, *S. maltophilia* was coisolated with *Escherichia coli.* All other samples were monomicrobial. Interestingly, three out of these *S. maltophilia* (tracheal aspirate = 1, BAL = 2) were cotrimoxazole resistant.

Discussion

The occurrence of *S. maltophilia* infection shows an exceptionally higher number of cases in 2013 and 2014 (46 [27%] and 41 [24.1%] cases, respectively), well above the median of

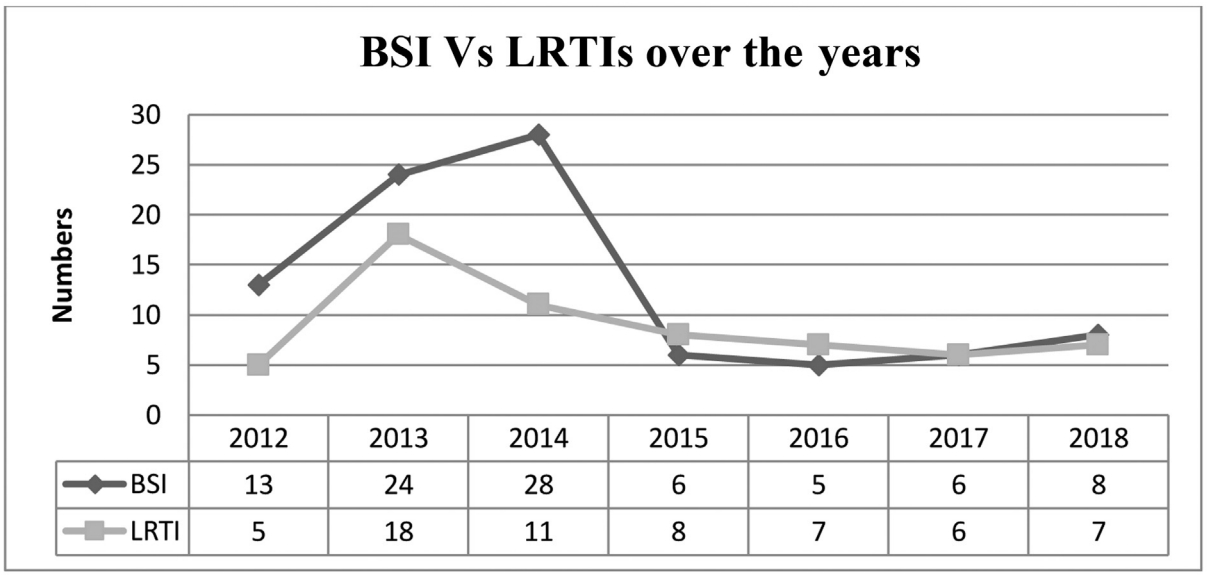

Fig. 1 Bloodstream infection (BSI) and lower respiratory tract infection (LRTI) by *Stenotrophomonas maltophilia*.

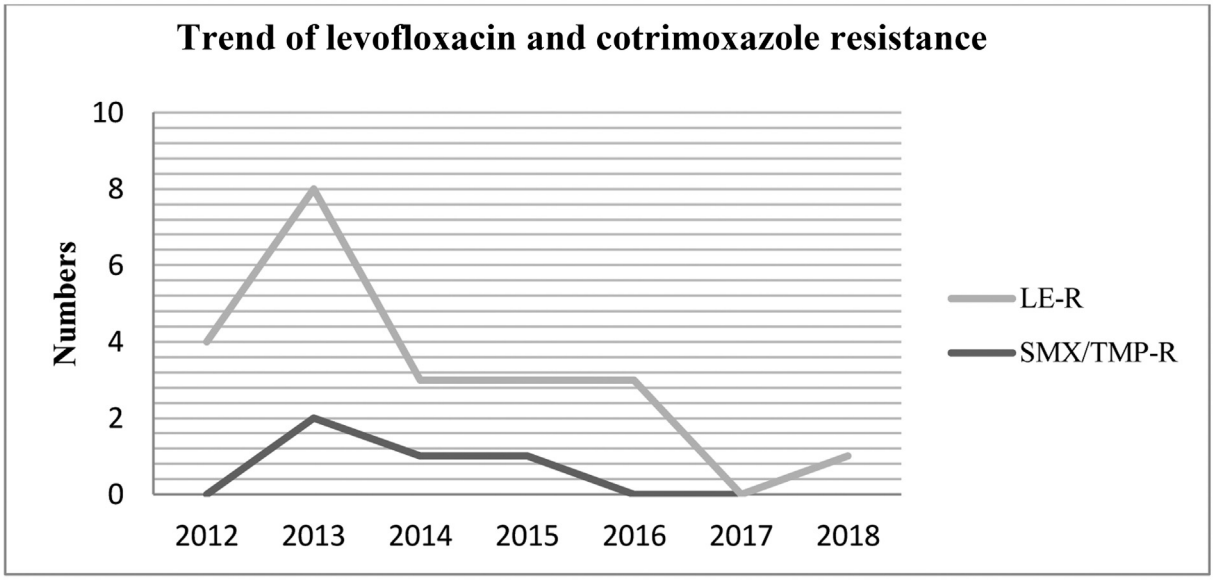

Fig. 2 Resistance to levofloxacin and cotrimoxazole over the years. Note: LE-R and SMX/TMP-R represent resistance to levofloxacin and cotrimoxazole, respectively.

19, which coincides with very high numbers of BSIs. Statistically, the spike in the number of BSIs in 2013 to 2014 is for only two data points that would be an outbreak or an incidental finding, but not a trend (►**Fig. 1**). Overall if we compare the average number of BSIs and lower respiratory tract infections (LRTIs) over the years, independent sample *t*-test shows no statistically significant difference between BSIs and LRTIs (*t*-statistic value = 1.015, *p*-value = 0.330). The possible explanation is high central line usage and associated BSIs over this period. From 2015 and onward, BSIs tended to decline so that there were almost equal numbers of BSIs and LRTIs. The source of *S. maltophilia* bacteremia is usually either the colonized/infected lungs, a central line, or the gastrointestinal tract.[5] Trauma patients frequently have interventions that include placement of central lines, indwelling catheters, external drains, and mechanical ventilation among others, as such a predilection to a specific infection type is not expected.

The mortality in our study was 18.8%. A previous retrospective analysis of 5 years from the same center showed 13% mortality.[6] The increase in mortality compared with previous data indicates that the infection prevention and control (IPC) team should emphasize environmental surveillance and infection control measures should be routinely monitored. Other centers have documented mortality in the range of 14 to 69%.[7,8] Singhal et al have noted the specific mortality ranging from 23.0 to 77.0% and 21.0 to 62.0% for pneumonia and bacteremia, respectively.[9] The relatively lower mortality in

trauma patients could be related to them being predominantly young, the median age of 36 years (ranging from 02 to 90 years), and without underlying conditions such as malignancy or chronic respiratory ailments.

In the current study, 97.1% of isolates were found to be susceptible to cotrimoxazole and 90.1% of isolates were found to be susceptible to levofloxacin. Cotrimoxazole sensitivity documented in other studies ranged from 78 to 100%, and levofloxacin ranged from 70 to 91%.[10–14] Susceptibility to cotrimoxazole was found to be 86.7% by Chawla et al, 72.7% by Chawla et al, 100% by Malini et al, 91.3% by Nayyar et al, and 87.9% by Gajdács and Urbán.[14] Susceptibility to levofloxacin was found to be 78.8% by Chawla et al, 2014, 80% by Nayyar et al, and 91% by Gajdács and Urbán.[10–14]

Resistance to both cotrimoxazole and levofloxacin was detected in only one isolate. Concurrent levofloxacin and cotrimoxazole resistance have been documented elsewhere too, being 5.8% by Gajdács and Urbán and 10.6% by Wu et al.[14,15] There was no significant difference for levofloxacin or cotrimoxazole resistance between BSIs and LRTIs. (Fisher's exact test, *p*-value of 0.422 for levofloxacin and 0.500 for cotrimoxazole).

In our study, polymicrobial infections were observed in six cases among which five (05) were from lower respiratory samples, and one from the urine sample. We also noted coisolation in these infections of *A. baumannii* ($n = 3$) and *Pseudomonas aeruginosa* ($n = 2$) that are also nonfermenters, suggesting similar causality or source of acquisition. In a rare case of UTI, *S. maltophilia* was isolated alongside *Escherichia coli.* It is important to remember that the treatment of these organisms is entirely different from *S. maltophilia,* and one must not miss the possibility of isolating two nonfermenters from tracheal aspirate or BAL. According to our findings, the antibiogram profile shows more susceptibility to cotrimoxazole suggesting it is a better treatment modality in our settings. Cotrimoxazole monotherapy is appropriate for the treatment of nonimmunocompromised patients and nonlife-threatening infections. For bacteremia, pneumonia, and infections in neutropenic or immunocompromised patients' combination, antimicrobial therapy is suggested. The other effective drugs are minocycline, ceftazidime, ticarcillin–clavulanic acid, chloramphenicol, and recently U.S. Food and Drug Administration-approved drug cefiderocol.[1]

Conclusion

Cotrimoxazole and levofloxacin are effective in a large percentage of *S. maltophilia* isolates. Cotrimoxazole is bacteriostatic and is not without adverse effects such as bone marrow suppression, especially when used for a longer duration. Levofloxacin is an effective alternative but resistance during therapy may be a problem. Within these limited options, appropriate therapy has to be decided considering the characteristics of each of these drugs. In conclusion, cotrimoxazole should be considered as the optimum treatment modality unless a contraindication exists.

Conflict of Interest
None declared.

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