Antibiotic Resistance Surveillance of Clinical Isolates of \textit{Stenotrophomonas maltophilia} Strains in the Central South of China from 2016 to 2019

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Abstract

\textbf{Background}: Due to the difficulty of treatment caused by its numerous mechanisms of resistance, only four kinds of antibiotics are recommended for the therapy of \textit{Stenotrophomonas maltophilia} infections associated with significant morbidity and mortality.

\textbf{Objectives}: In this four-year study, we aimed to determine the evolution of drug resistance to \textit{S. maltophilia} base on drug classification guidelines recommended by the Institute of Clinical and Laboratory Standards.

\textbf{Methods}: A total of 1876 strains of \textit{S. maltophilia} was separated from multifarious clinical specimens among January 2016 and December 2019. VITEK 2 Compact microbial system was used for speciation level identification and antibiotic sensitivity test.

\textbf{Results}: A total of 1876 strains of \textit{S. maltophilia} strains were separated from sputum specimen type (70.63%), followed by bronchial (6.18%), blood (4.16%), and bronchoalveolar lavage samples (4.32%). Moreover, 695 strains of \textit{S. maltophilia} strains were separated from intensive care unit (ICU) department (37.05%), and then neurosurgery ward (10.66%), integrative Chinese and western medicine ward (7.25%), general surgery ward (6.66%). The results of minocycline antibiotic of \textit{S. maltophilia} with a drug resistance rate of 0.3%. From 2016 to 2019, the resistance rate of cefoperazone/sulbactam decreased from 20.8% to 15.2%, the resistance rate of trimethoprim-sulfamethoxasole decreased from 7.9% to 4.5%. The resistance rate of minocycline fluctuate in 0.0% between 0.7%. However, the resistance rate of levofloxacin increased from 7.7% to 8.0%.

\textbf{Conclusions}: In this study, \textit{S. maltophilia} was detected in a variety of specimen types of different clinical departments, with the most detected in ICU patients and sputum specimen. \textit{S. maltophilia} was sensitive to minocycline and levofloxacin, but the situation of cefoperazone/sulbactam resistance was not optimistic. The results of this study indicate that minocycline is considered to be the most effective antibiotic for the treatment of \textit{S. maltophilia}. Therefore, we still need to strengthen the drug resistance monitoring, timely acquisition of \textit{S. maltophilia} drug resistance changes, and actively take effective measures to deal with the drug resistance of \textit{S. maltophilia}.

\textbf{Keywords}: \textit{Stenotrophomonas maltophilia}, Distribution, Antibiotic, Resistance

1. Background

\textit{Stenotrophomonas maltophilia} is an arising opportunistic pathogenic microorganism, systematic classified by the WHO as one of the governing multidrug-resistant pathogen in a hospital ward (1). \textit{Stenotrophomonas maltophilia} is a Gram-negative environmental bacterium that can cause respiratory tract infections with cystic fibrosis, associated with bloodstream and urinary tract infections. More seriously, it can break blood-brain barrier following the emergence of risk factors such as whole blood cell reduction or tumor, long-term use of immunosuppressive agents or broad-spectrum antibacterial agents such as fifth generation cephalosporins in hospital (2). \textit{Stenotrophomonas maltophilia} is a well-traveled and universal bacterium originated from an extent of environmental surroundings, including severe habitats, even if in nature it is principally affiliated with plants. \textit{Stenotrophomonas maltophilia} can also conquer acute unnatural slots in common rooms, space capsules, and hospitals (3).

\textit{Stenotrophomonas maltophilia} has developed into an international cosmopolitan hominid microorganism, which does not occasionally affect healthful entertainer but occurs with tremendous morbidity and mortality in immunocompromised and weakened human beings (4). \textit{Stenotrophomonas maltophilia} maintain virulence com-
ponents inclusive of DNase, RNase, hyaluronidase, fibrinolysin, protease, lipases, and elastase (5-7). These pathogens can live in medical sections and hold to the par
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Incorrect application of broad-spectrum antibiotics such as trimethoprim-sulfamethoxazole suggests hazard factor for S. maltophilia infections (10). Stenotrophomonas maltophilia strains are naturally resistant to various antibiotics by reason of presence of the sul and dfrA gene and genes encoding efflux pumps (ll). Furthermore, 6'-N-amino
glycoside acetyltransferase-encoding gene, aac(6')-
lak exhibited decreased susceptibility to aminoglycoside
antibiotic and enzymes that appease erythromycin (12). As
a result of constant and unreasonable use of the broad-
spectrum antibiotics, multi-drug resistance microorgan-
isms have been periodically emerged inside and outside
the hospital (13).

2. Objectives

Therefore, the purpose of this study is to clarify the dis-
tribution of clinical departments and specimens of S. mal-
tophilia in our hospital from 2016 to 2019, and the changes
in the resistance rate of antibiotics recommended by CLSI
for the treatment of this bacteria.

3. Methods

3.1. Research Center Overview

The current study was conducted in the microbiology
laboratory of Central South University Xiangya Hospital,
Changsha, China. The hospital is a 3500-bed medical in-
stitution that has a commitment to provide the best pos-
sible medical care to the provincial capital of Hunan and
adjacent area. Therefore, our hospital is a regional medical
center with strong technical strength. All in all, it provides
health care services to nearly 3.3 million people every year.

3.2. Strain Information Collection and Antibiotic Susceptibility Testing Appraisal

There are 1876 S. maltophilia strains separated from
different clinical specimens between January 2016 and De-
cember 2019 were brought into the research. This study
summarized the specimen distribution, department dis-
tribution, and drug resistance of S. maltophilia by retro-
spective analysis. Qualified specimen type was inoculated
on 5% sheep blood plate (Guangzhou Detgerm, China),
vancocycin chocolate plate (Guangzhou Detgerm, China)
or McConkey plate (Guangzhou Detgerm, China) for 24
hours at 37°C. Blood culture specimens were analyzed by
BD BACTEC™FX40 automated blood culture system (Bec-
ton Dickinson, USA) or Mérieire BacT-ALERT 3D120 au-
tomated blood culture system (Bio Mérieux, France).

The total resistance rates of isolated S. maltophilia
strains to cefoperazone/sulbactam, levofloxacin, trimethoprim-
sulfamethoxazole, minocycline was 18.6%, 8.6%, 5.1%,
0.4%, respectively. The difference between cefoper-
zone/sulbactam and levofloxacin is statistically significant
(\( \chi^2 = 80.20, P < 0.0001 \)). The difference between cefopera-
zone/sulbactam and trimethoprim-sulfamethoxazole is
statistically significant (\( \chi^2 = 163.2, P < 0.0001 \)). The
difference between cefoperazone/sulbactam and minocycline
is statistically significant (\( \chi^2 = 360.0, P < 0.0001 \)). There
is no statistically significant difference between levofloxacin
Table 1. The Distribution of Clinical Departments of *Stenotrophomonas maltophilia* in Xiangya Hospital from 2016 to 2019

| Department          | 2016 | 2017 | 2018 | 2019 | Total | CR (%) |
|---------------------|------|------|------|------|-------|--------|
| ICU                 | 182  | 205  | 166  | 142  | 695   | 37.05  |
| Neurosurgery        | 65   | 40   | 64   | 31   | 200   | 10.66  |
| ICWM                | 46   | 46   | 24   | 20   | 136   | 7.25   |
| General surgery     | 16   | 30   | 52   | 27   | 125   | 6.66   |
| Cadre ward          | 48   | 16   | 15   | 15   | 94    | 5.01   |
| Burn surgery        | 32   | 23   | 21   | 8    | 84    | 4.48   |
| Pediatrics          | 28   | 21   | 17   | 16   | 82    | 4.37   |
| Neurology           | 18   | 15   | 26   | 19   | 78    | 4.16   |
| Neonatology         | 20   | 11   | 5    | 6    | 42    | 2.24   |
| Outpatient          | 17   | 12   | 6    | 23   | 58    | 3.09   |
| Dermatology         | 14   | 8    | 11   | 8    | 41    | 2.19   |
| Cardiology          | 12   | 15   | 3    | 12   | 42    | 2.24   |
| Respiratory medicine| 6    | 10   | 9    | 13   | 38    | 2.03   |
| Hematology          | 8    | 5    | 9    | 16   | 38    | 2.03   |
| Cardiac surgery     | 11   | 6    | 2    | 12   | 31    | 1.65   |
| Orthopedics         | 4    | 7    | 1    | 2    | 14    | 0.75   |
| Infectious diseases | 4    | 0    | 6    | 1    | 11    | 0.59   |
| Rheumatology        | 3    | 2    | 4    | 3    | 12    | 0.64   |
| Endocrinology       | 0    | 5    | 3    | 0    | 8     | 0.43   |
| Gastroenterology    | 0    | 5    | 2    | 1    | 8     | 0.43   |
| Stomatology         | 2    | 2    | 1    | 2    | 7     | 0.37   |
| Plastic surgery     | 2    | 1    | 1    | 0    | 4     | 0.21   |
| IMD                 | 1    | 0    | 3    | 0    | 4     | 0.21   |
| Otolaryngology      | 1    | 2    | 1    | 1    | 5     | 0.27   |
| Rehabilitation medicine | 3  | 0    | 0    | 0    | 3     | 0.16   |
| Special needs ward  | 0    | 2    | 1    | 0    | 3     | 0.16   |
| Transplant center   | 2    | 0    | 0    | 1    | 3     | 0.16   |
| Nephrology          | 1    | 0    | 1    | 0    | 2     | 0.11   |
| Urology             | 0    | 2    | 0    | 1    | 3     | 0.16   |
| Ophthalmology       | 0    | 1    | 1    | 0    | 2     | 0.11   |
| Gynecology          | 1    | 0    | 0    | 0    | 1     | 0.05   |
| Tumor radiotherapy  | 0    | 1    | 0    | 1    | 2     | 0.11   |
| Total               | 547  | 493  | 455  | 381  | 1876  | 100.00 |

Abbreviations: CR, composition ratio; ICWM, integrative Chinese and western medicine; IMD, International Medical Department.

and trimethoprim/sulfamethoxasole ($\chi^2 = 17.65, P = 0.0233$). The difference between levofloxacin and minocycline is statistically significant ($\chi^2 = 76.58, P < 0.0001$). The difference between trimethoprim/sulfamethoxasole and minocycline is statistically significant ($\chi^2 = 51.1, P < 0.0001$). The resistance rates of *S. maltophilia* strains of antibiotics are displayed in Table 3 and Figure 5.

5. Discussion

Not long ago, non-fermentative bacteria (*P. aeruginosa, Acinetobacter, S. maltophilia* and *Alcaligenes*) have been progressively identified as a decisive reason for hospital infection (14). Various dilemmas are confronted with the therapy of these infections by virtue of multiplex antibi-
Table 2. The Distribution of Specimen Types of Stenotrophomonas maltophilia in Xiangya Hospital from 2016 to 2019

| Specimen Type       | 2016 | 2017 | 2018 | 2019 | Total | CR (%) |
|---------------------|------|------|------|------|-------|--------|
| Sputum              | 411  | 351  | 292  | 271  | 1325  | 70.63  |
| Bronchial           | 30   | 38   | 32   | 16   | 116   | 6.38   |
| Bl                  | 16   | 13   | 25   | 27   | 81    | 4.32   |
| Blood               | 24   | 19   | 23   | 12   | 78    | 4.16   |
| Wound               | 21   | 15   | 9    | 10   | 55    | 2.93   |
| Drain               | 5    | 12   | 20   | 11   | 48    | 2.56   |
| Abdominal fluid     | 2    | 7    | 13   | 8    | 30    | 1.60   |
| Bile                | 2    | 5    | 14   | -    | 21    | 1.12   |
| Catheter site       | 8    | 5    | 3    | -    | 16    | 0.85   |
| Tracheal aspirate   | 7    | 4    | 5    | 5    | 21    | 1.12   |
| Blood vessel        | 3    | 4    | 3    | 4    | 14    | 0.75   |
| Tissue              | 5    | 2    | 3    | -    | 10    | 0.53   |
| Cerebrospinal fluid | -    | 5    | 3    | 2    | 10    | 0.53   |
| Secretion           | 5    | 2    | -    | -    | 7     | 0.37   |
| Urine               | 2    | 3    | 2    | 2    | 9     | 0.48   |
| Throat              | 2    | 1    | 1    | -    | 4     | 0.21   |
| Urine, clean-voided | -    | 1    | 2    | 2    | 5     | 0.27   |
| Mouth               | 2    | 1    | -    | -    | 3     | 0.16   |
| Stool               | 1    | 2    | -    | 8    | 11    | 0.59   |
| Eyes                | -    | 1    | 1    | -    | 2     | 0.11   |
| Other               | 1    | -    | 1    | 1    | 3     | 0.16   |
| Abscess             | -    | -    | 1    | 1    | 2     | 0.11   |
| Gastric fluid       | -    | 1    | -    | -    | 1     | 0.05   |
| Pleural fluid       | -    | -    | 1    | 1    | 2     | 0.11   |
| Prostatic fluid     | -    | -    | 1    | -    | 1     | 0.05   |
| Urine, catheter     | -    | 1    | -    | -    | 1     | 0.05   |
| Total               | 547  | 493  | 455  | 381  | 1876  | 100.00 |

Abbreviations: Bl, Bronchoalveolar lavage; CR, composition ratio.

Table 3. Monitoring of Drug Resistance of Stenotrophomonas maltophilia in Xiangya Hospital from 2016 to 2019

| AD            | 2016 | 2017 | 2018 | 2019 | Total |
|---------------|------|------|------|------|-------|
|               | R    | I    | S    | R    | I    | S    | R    | I    | S    | R    | I    | S    | R    | I    | S    | R    | I    | S    | R    | I    | S    | R    | I    | S    | R    | I    | S    | R    | I    | S    | R    | I    | S    |
| CSL           | 20.8 | 37   | 42.2 | 20.5 | 39.7 | 39.9 | 16.9 | 24.5 | 40.6 | 15.2 | 31.8 | 53.0 | 18.6 | 38.0 | 43.4 |
| LVX           | 7.7  | 6.2  | 86.1 | 9.3  | 2.7  | 88.0 | 9.5  | 4.4  | 86.1 | 8.0  | 1.6  | 90.4 | 8.6  | 3.9  | 87.5 |
| SXT           | 7.9  | 0.5  | 90.6 | 3.5  | 0.4  | 96.1 | 3.9  | 2.8  | 93.3 | 4.5  | 0.3  | 95.2 | 5.3  | 1.0  | 93.9 |
| MNO           | 0.5  | 2.6  | 96.9 | 0.4  | 2.7  | 96.9 | 0.7  | 1.4  | 97.9 | 0.0  | 0.3  | 99.7 | 0.4  | 1.9  | 97.7 |

Abbreviations: AD, antibacterial drugs; CSL, ceftoperazone/sulbactam; LVX, levofloxacin; SXT, trimethoprim-sulfamethoxasole; MNO, minocycline.

otic resistance of these pathogens (15). Stenotrophomonas maltophilia-related nosocomial infections occur in ICU patients due to mechanic ventilation and immunosuppressed patients, who encounter huge morbidity and mortality rates (16). Innate resistance of S. maltophilia to numerous antibiotics applied to Gram-negative pathogens...
S. maltophilia composes of sputum (70.63%) followed by the most prevailing clinical equipment for desolation of basis of research, in the south central region of China, ples along with respiratory samples (26.41%) (23). On the that maximal numbers of strains from blood (61.32%) sam-

to N. maltophilia was chiefly separated from tracheal aspi-

rate (55%), blood (15.0%) and sputum (14.0%) samples from this pathogen was chiefly separated from tracheal aspi-

demonstrated higher antibiotic resistance to cefepime (32.1%), amikacin (42.3%), ce-

ered in 2012 (28). The proportion of strains resistant to SXT was obviously altered from 29.7% in 2005 - 2009 to 47.1% in 2010 - 2014 in Anhui province, China (29).

Twenty-six S. maltophilia isolated from blood were sensitive to ceftazidime (53.9%), ticarcillin/clavulanic acid (80.8%), ciprofloxacin (92.3%), levofloxacin (96.2%), and trimethoprim/sulfamethoxazole (100%) in Warsaws (30). Stenotrophomonas maltophilia demonstrated higher antibiotic resistance to cefepime (32.1%), amikacin (42.3%), cefotaxime (51.5%), ceftazidime (52.3%), gentamicin (55.1%) and meropenem (93.4%), and lower resistance to lev-

In another study, levofloxacin was found to be the most effective antibiotic against S. maltophilia strains with resistance rate of 7.6%. The resistance rates for other antibiotics were as follows: chloramphenicol 18.2%, trimethoprim-sulfamethoxazole 20.3%, and ceftazidime 72% (31). When SXT is not an adequate first-line treatment choice of patients, levofloxacin could be alternately accepted as an applicable medical choice of S. maltophilia infections (32). A study displayed that S. maltophilia is susceptible to various antibacterial drugs in Turkey of 118 strains detached from different clinical samples between 2006 and 2012. The therapy of infections provoked by S. maltophilia should be adopted primitively as TMP-SXT, chloramphenicol, and levofloxacin independently (31). In Najran Saudi
Figure 2. The distribution of clinical departments of *S. maltophilia* in Xiangya Hospital from 2016 to 2019

Figure 3. The total distribution of specimen types of *Stenotrophomonas maltophilia* in Xiangya Hospital; Bl, Broncho-alveolar lavage.

Figure 4. The distribution of specimen types of *Stenotrophomonas maltophilia* in Xiangya Hospital from 2016 to 2019

Figure 5. Monitoring of drug resistance of *Stenotrophomonas maltophilia* in Xiangya Hospital from 2016 to 2019

Arabia, the utmost effective antibiotics were tigecycline (93.7% sensitivity) and trimethoprim/sulfamethoxazole (100% sensitivity) between 2015 and 2016. However, the results of this study indicate that minocycline is considered to be the most effective antibiotic for the treatment of *S. maltophilia* with a drug resistance rate of 0.3%.

In this study, from 2016 to 2019 year, the resistance rate of cefoperazone/sulbactam decreased from 20.8% to 15.2% during four years, the resistance rate of trimethoprim-sulfamethoxazole decreased from 7.9% to 4.5%. The resistance rate of minocycline fluctuate in 0.0% between 0.7%. However, the resistance rate of levofloxacin increased from 7.7% to 8.0%. *Stenotrophomonas maltophilia* is still a troublesome multi-resistant nosocomial bacterium. Trimethoprim/sulfamethoxazole is the most promising antibacterial drugs against *S. maltophilia*. In face of trimethoprim/sulfamethoxazole hypersensitivity, intermediary or resistance, fluoroquinolones are another medical choice. By reason of the low prevalence of levofloxacin resistance, these drugs can be adopted either in high dosage monotherapy or rather in partnership with other antibac-
terial drugs, in the matter of the risk of rapid resistance evolution during monotherapy.

Quinolones are synthetic antibiotics, and the leading reason for resistance to these drugs is mutation of the genes encoding their purposes. Nevertheless, in opposition to the case for other isolates, such mutations have not been detected in quinolone-resistant S. maltophilia strains, in which overabundance of the SmeDEF efflux pump is a dominant source of quinolone resistance (31). The above data indicate that the antibiotic resistance of S. maltophilia isolated from clinical specimens in the central south of China is significantly different from that in other regions. Different antibiotic susceptibility results appear due to different drug sensitivity programs and reference standards used in different places. Early recognition of S. maltophilia is particularly significant. The use of antibiotics to which this microorganism is ingenuous wipes out the infection and alleviates avoid graft failure (30). Exact recognition and susceptibility programs of S. maltophilia are essential for the supervision of infected patients and avoidance of transmit of this nosocomial microorganism (34).

Lacking clinical breakpoints, consent antibiotic susceptibility testing guidelines, and clinical trials make the explanation of antibiotic susceptibility testing outcomes challenging. The foundation of clinical breakpoints for drugs not just SXT is greatly demanded lately. The most trustworthy antibiotic susceptibility testing approach to replaceable options should vigorously be announced. Physicians must hold an opinion that S. maltophilia is a co-colonizer or co-pathogen in polymicrobial infections can have unfavorable influence on the success amount of antibiotic therapy and clinical consequence.

5.1. Limitations

This study was only retrospectively analyzed in a single center in central south China, and the resistance data for the cross-regional multi-center S. maltophilia was more credible.

5.2. Conclusions

The study demonstrated that S. maltophilia can be detected in a variety of specimen types of different clinical departments, with the most detected in ICU patients and sputum specimens. Moreover, S. maltophilia was sensitive to minocycline and levofloxacin, but the situation of cefoperazone/sulbactam resistance was not optimistic. Sometimes we have to consider that it may not be used to treat certain infections caused by S. maltophilia. It is worth noting that we need to prompt clinicians to target the treatment of S. maltophilia based on the results of drug susceptibility testing, and to strengthen its drug resistance monitoring and dynamic changes in drug resistance.

Footnotes

Authors’ Contribution: Study concept and design: Yongwen Yang, Qun Yan, Xia Chen, and Wenen Liu; analysis and interpretation of data: Yongwen Yang, Qun Yan, and Xia Chen; drafting of the manuscript: Yongwen Yang; critical revision of the manuscript for important intellectual content: Yongwen Yang, and Wenen Liu; statistical analysis: Yongwen Yang.

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