

# Antimicrobial Susceptibility of *Stenotrophomonas maltophilia* Isolates from a Korean Tertiary Care Hospital

Hae-Sun Chung,<sup>1</sup> Seong Geun Hong,<sup>2</sup> Yangsoon Lee,<sup>1</sup> Myungsook Kim,<sup>1</sup> Dongeun Yong,<sup>1</sup>  
Seok Hoon Jeong,<sup>1</sup> Kyungwon Lee,<sup>1</sup> and Yunsop Chong<sup>1</sup>

<sup>1</sup>Department of Laboratory Medicine and Research Institute of Bacterial Resistance, Yonsei University College of Medicine, Seoul;

<sup>2</sup>Department of Laboratory Medicine, CHA Bundang Medical Center, CHA University, Seongnam, Korea.

Received: July 1, 2011

Revised: August 8, 2011

Accepted: August 8, 2011

Corresponding author: Dr. Kyungwon Lee,  
Department of Laboratory Medicine and  
Research Institute of Bacterial Resistance,  
Yonsei University College of Medicine,  
50 Yonsei-ro, Seodaemun-gu,  
Seoul 120-752, Korea.  
Tel: 82-2-2228-2446, Fax: 82-2-313-0908  
E-mail: leekcp@yuhs.ac

The authors have no financial conflicts of interest.

We determined the antimicrobial susceptibility of 90 clinical isolates of *Stenotrophomonas maltophilia* collected in 2009 at a tertiary care hospital in Korea. Trimethoprim-sulfamethoxazole, minocycline, and levofloxacin were active against most of the isolates tested. Moxifloxacin and tigecycline were also active and hold promise as therapeutic options for *S. maltophilia* infections.

**Key Words:** *Stenotrophomonas maltophilia*, antimicrobial susceptibility, trimethoprim-sulfamethoxazole, levofloxacin, minocycline

*Stenotrophomonas maltophilia* is one of several opportunistic pathogens of growing significance and is the third most common nonfermentative Gram-negative bacillus that has been isolated from clinical specimens.<sup>1-3</sup> Differentiation between *S. maltophilia* colonization and infection may be difficult. Despite its relatively low virulence, *S. maltophilia* can cause a wide variety of infections including bacteremia and pneumonia, especially in debilitated or immunocompromised patients. Risk factors for colonization and infection include mechanical ventilation, use of central venous catheters, and broad-spectrum antibiotic prophylaxis and treatment.<sup>1,4</sup>

Antimicrobial susceptibility testing methods of *S. maltophilia* are not clearly standardized, and there is poor correlation between disk diffusion and agar dilution results for some agents.<sup>2,5</sup> The British Society for Antimicrobial Chemotherapy (BSAC, version 10.2, 2011) recommends disk diffusion and dilution testing for trimethoprim-sulfamethoxazole only,<sup>6</sup> while the Clinical and Laboratory Standards Institute (CLSI) recommends dilution testing for trimethoprim-sulfamethoxazole, ceftazidime, chloramphenicol, levofloxacin, minocycline, and ticarcillin-clavulanate, and disk diffusion testing for only trimethoprim-sulfamethoxazole, levofloxacin, and minocycline.<sup>7</sup>

Infections caused by *S. maltophilia* are particularly difficult to manage because they show resistance to many classes of antimicrobial agents. However, few studies have focused on the susceptibility of *S. maltophilia* in Korea.<sup>8,9</sup> The aim of this study was to determine the antimicrobial susceptibility of recent clinical *S. malto-*

## © Copyright:

Yonsei University College of Medicine 2012

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

*philia* isolates from Korea.

A total of 90 non-duplicate clinical isolates of *S. maltophilia* were collected during 2009 from patients at a tertiary care hospital in Seoul, Korea. Sources of the isolates were respiratory specimens (n=46), urine (n=15), blood (n=11), body fluid (n=9), and pus (n=9). The species were identified using conventional methods and/or the ATB 32GN system (bioMerieux, Marcy l'Etoile, France). Antimicrobial susceptibility was tested by the CLSI agar dilution method.<sup>7</sup>

The antimicrobial agents used were trimethoprim and sulfamethoxazole (Dong Wha, Seoul, Korea), levofloxacin (Daiichi, Tokyo, Japan), minocycline (SK Chemicals Life Science, Seoul, Korea), ticarcillin and clavulanate (Dong-A, Yongin, Korea), ceftazidime, amikacin, and gentamicin (Sigma Chemical, St. Louis, MO, USA), chloramphenicol and tetracycline (Chong Kun Dang, Seoul, Korea), moxifloxacin (Bayer Korea, Seoul, Korea), tigecycline (Wyeth Research, Pearl River, NY, USA), cefepime (Bristol-Myers Squibb, Syracuse, NY, USA), imipenem (Choongwae, Seoul, Korea), piperacillin and tazobactam (Yuhan, Seoul, Korea). For the combinations of ticarcillin-clavulanate and piperacillin-tazobactam, constant amounts of clavulanate (2 µg/mL) and tazobactam (4 µg/mL) were added to ticarcillin and piperacillin, respectively. The breakpoints recommended by CLSI for *S. maltophilia* were applied to interpret the minimum inhibitory concentrations (MIC).<sup>7</sup> *Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853 were used as controls.

Table 1 shows the MICs of antimicrobial agents and the resistance rates of the *S. maltophilia* isolates tested. Among

the six drugs recommended by CLSI, the relatively more active agents were trimethoprim-sulfamethoxazole, levofloxacin and minocycline.

Trimethoprim-sulfamethoxazole showed the lowest MIC<sub>90</sub> (1 µg/mL) and the isolates showed a high susceptibility rate of 94% to this agent. All but five isolates were inhibited at ≤2 µg/mL. Resistance rates to trimethoprim-sulfamethoxazole have been reported to vary geographically,<sup>1,2,10,11</sup> but were generally less than 20%, as was also seen in this study. However, isolates from cystic fibrosis patients and from some Asian countries, such as Taiwan and Turkey, showed high resistance rates (31.3-100%).<sup>5,12-14</sup> Trimethoprim-sulfamethoxazole alone, or in combination with other agents, is still considered the treatment of choice for suspected or culture-proven *S. maltophilia* infections.

The MIC of levofloxacin ranged from 0.25 to 16 µg/mL, and the MIC<sub>50</sub> and MIC<sub>90</sub> were 1 and 8 µg/mL, respectively. The resistance rate was 13%, which was slightly higher than the rates of 3 to 11% seen in a previous study.<sup>1</sup> The new fluoroquinolone, moxifloxacin, is more active *in vitro* than ciprofloxacin and levofloxacin.<sup>4</sup> In this study, the MIC<sub>50</sub> and MIC<sub>90</sub> of moxifloxacin were 0.5 and 4 µg/mL, respectively, which were two-fold lower than those of levofloxacin. These results indicated that moxifloxacin could be suggested as an alternative to levofloxacin. Further clinical studies are necessary to evaluate the effectiveness of moxifloxacin in treating *S. maltophilia* infections, as there is little data published on the clinical efficacy of moxifloxacin.

In this study, all *S. maltophilia* isolates were inhibited by ≤4 µg/mL of minocycline, and the MIC<sub>90</sub> was 2 µg/mL,

**Table 1. Antimicrobial Activity of Various Antimicrobial Agents Tested Against *S. maltophilia* Using the Agar Dilution Method**

Drug	MIC (µg/mL)			% Susceptibility		
	Range	50%	90%	S	I	R
Amikacin	4 - >128	>128	>128	-	-	-
Cefepime	2 - 128	64	64	-	-	-
Ceftazidime	2 - >128	64	>128	23	8	69
Chloramphenicol	4 - 64	16	32	43	36	21
Gentamicin	1 - >128	128	>128	-	-	-
Imipenem	16 - >128	>128	>128	-	-	-
Levofloxacin	0.25 - 16	1	8	81	6	13
Minocycline	0.12 - 4	0.5	2	100	0	0
Moxifloxacin	≤0.06 - 16	0.5	4	-	-	-
Piperacillin-tazobactam	16 - >256	>256	>256	-	-	-
Tetracycline	8 - >128	32	32	-	-	-
Ticarcillin-clavulanate	2 - >256	32	256	23	44	32
Tigecycline	0.25 - 8	1	2	-	-	-
Trimethoprim-sulfamethoxazole	≤0.06 - 64	0.5	1	94	0	6

-Not applicable.

which was 16 times lower than that of tetracycline. No isolates were resistant to minocycline. This data was similar to that of Taiwan, Brazil, Spain, and the USA.<sup>5,15-17</sup> MICs of tigecycline ranged from 0.25 to 8 µg/mL, and MIC<sub>50</sub> and MIC<sub>90</sub> were 1 and 2 µg/mL, respectively, which were similar to those in other studies.<sup>1,11</sup> The tetracycline derivatives minocycline and tigecycline have shown good *in vitro* activity against clinical isolates of *S. maltophilia*; however, there is little clinical data to support this claim.

The isolates showed low rates of susceptibility (23-43%) to ceftazidime, ticarcillin-clavulanic acid and chloramphenicol, which were slightly higher than those in other studies.<sup>1</sup> In general, β-lactams and/or β-lactamase inhibitor combinations show little activity against *S. maltophilia*, because the organism has a high intrinsic resistance to most penicillins and cephalosporins, as well as to all carbapenems.

Aminoglycosides show poor activity against *S. maltophilia* because of high intrinsic resistance and, therefore, are not useful in monotherapy.<sup>1,4</sup> Despite a lack of clinical trials, treatment of *S. maltophilia* infections with a combination of two or three antimicrobials has become current practice where trimethoprim-sulfamethoxazole therapy is contraindicated.

In conclusion, trimethoprim-sulfamethoxazole, minocycline, and levofloxacin showed good *in vitro* activity against *S. maltophilia* isolates from Korea. Moxifloxacin and tigecycline were also active and hold promise as therapeutic options for *S. maltophilia*.

## ACKNOWLEDGEMENTS

This research was supported by the Happy Tech. Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (grant number 20110004679).

## REFERENCES

- Looney WJ, Narita M, Mühlemann K. *Stenotrophomonas maltophilia*: an emerging opportunist human pathogen. *Lancet Infect Dis* 2009;9:312-23.
- Sader HS, Jones RN. Antimicrobial susceptibility of uncommonly isolated non-enteric Gram-negative bacilli. *Int J Antimicrob Agents* 2005;25:95-109.
- Jones RN, Sader HS, Beach ML. Contemporary *in vitro* spectrum of activity summary for antimicrobial agents tested against 18569 strains non-fermentative Gram-negative bacilli isolated in the SENTRY Antimicrobial Surveillance Program (1997-2001). *Int J Antimicrob Agents* 2003;22:551-6.
- Nicodemo AC, Paez JI. Antimicrobial therapy for *Stenotrophomonas maltophilia* infections. *Eur J Clin Microbiol Infect Dis* 2007;26:229-37.
- Wang WS, Liu CP, Lee CM, Huang FY. *Stenotrophomonas maltophilia* bacteremia in adults: four years' experience in a medical center in northern Taiwan. *J Microbiol Immunol Infect* 2004;37:359-65.
- BSAC Methods for antimicrobial susceptibility testing. Available at <http://www.bsac.org.uk/Susceptibility+Testing/GUIDELINES+Standardized+Disc+Susceptibility+Testing+Method>. [access on June 2011]
- Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing; twenty-first informational supplement, M100-S21. Wanye, PA: Clinical and Laboratory Standards Institute; 2011.
- Song JH, Sung JY, Kwon KC, Park JW, Cho HH, Shin SY, et al. Analysis of acquired resistance genes in *Stenotrophomonas maltophilia*. *Korean J Lab Med* 2010;30:295-300.
- Seol SY, Jang KS, Jeong OG, Cho ER, Kim NH, Yu HS, et al. Antimicrobial resistance and molecular epidemiologic characteristics of *Stenotrophomonas maltophilia* isolated from clinical specimens. *J Korean Soc Microbiol* 2000;35:239-50.
- Livermore DM, Hope R, Brick G, Lillie M, Reynolds R; BSAC Working Parties on Resistance Surveillance. Non-susceptibility trends among *Pseudomonas aeruginosa* and other non-fermentative Gram-negative bacteria from bacteraemias in the UK and Ireland, 2001-06. *J Antimicrob Chemother* 2008;62 Suppl 2:ii55-63.
- Farrell DJ, Sader HS, Jones RN. Antimicrobial susceptibilities of a worldwide collection of *Stenotrophomonas maltophilia* isolates tested against tigecycline and agents commonly used for *S. maltophilia* infections. *Antimicrob Agents Chemother* 2010;54:2735-7.
- Cantón R, Valdezate S, Vindel A, Sánchez Del Saz B, Maíz L, Baquero F. Antimicrobial susceptibility profile of molecular typed cystic fibrosis *Stenotrophomonas maltophilia* isolates and differences with noncystic fibrosis isolates. *Pediatr Pulmonol* 2003;35:99-107.
- Gülmez D, Hascelik G. *Stenotrophomonas maltophilia*: antimicrobial resistance and molecular typing of an emerging pathogen in a Turkish university hospital. *Clin Microbiol Infect* 2005;11:880-6.
- Valenza G, Tappe D, Turnwald D, Frosch M, König C, Hebestreit H, et al. Prevalence and antimicrobial susceptibility of microorganisms isolated from sputa of patients with cystic fibrosis. *J Cyst Fibros* 2008;7:123-7.
- Galles AC, Jones RN, Sader HS. Antimicrobial susceptibility profile of contemporary clinical strains of *Stenotrophomonas maltophilia* isolates: can moxifloxacin activity be predicted by levofloxacin MIC results? *J Chemother* 2008;20:38-42.
- Valdezate S, Vindel A, Loza E, Baquero F, Cantón R. Antimicrobial susceptibilities of unique *Stenotrophomonas maltophilia* clinical strains. *Antimicrob Agents Chemother* 2001;45:1581-4.
- Vartivarian S, Anaissie E, Bodey G, Sprigg H, Rolston K. A changing pattern of susceptibility of *Xanthomonas maltophilia* to antimicrobial agents: implications for therapy. *Antimicrob Agents Chemother* 1994;38:624-7.