Tigecycline Susceptibility Trends among Pathogens Isolated from Complicated Skin and Soft Tissue Infections in North and Latin America: 2012-2016

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Revised Abstract

Background: The Tigecycline Evaluation Surveillance Trial (TEST) monitors the activity of tigecycline and other antimicrobials against clinically-relevant pathogens collected globally. This study reports the activity of tigecycline (TGC) against gram-positive and gram-negative isolates collected in North and Latin America from patients with complicated skin and soft tissue infections (cSSTI).
Methods: Hospital sites from North America (NA) and Latin America (LA) collected non-duplicate clinical gram-positive and -negative isolates from various complicated skin and skin structure infection sources during 2012-2016. Organism identification and antibiotic susceptibility (S) testing was performed by the local laboratories. Susceptibility testing was determined using the broth microdilution method according to CLSI guidelines and categorical interpretation of results was done using CLSI or FDA (tigecycline) breakpoint criteria where appropriate. Cefoxitin disk testing was performed for all S. aureus to determine methicillin susceptibility (i.e. MRSA and MSSA).
Results: The table provides %S and MIC_{90} data for TGC against cSSTI isolates:

Region, n, %S, MIC_{90} (µg/ml)

	North America			Latin America		
Organism	**n**	**%S**	**MIC_{90}**	**n**	**%S**	**MIC_{90}**
S. aureus	2272	100	0.12	310	100	0.25
***Enterobacter* spp.**	925	96.4	1	159	92.5	2
P. aeruginosa	758	na*	> 8	165	na	> 8
E. coli	716	99.9	0.25	241	100	0.25
***Enterococcus* spp.**	691	99.3	0.12	135	100	0.12
S. agalactiae	503	100	0.12	58	100	0.06
K. pneumoniae	471	94.9	2	152	91.5	2
S. marcescens	347	96.8	2	67	97.0	2
A. baumannii	310	na*	2	97	na	1
K. oxytoca	204	99.0	0.5	15	100	1

*na = not applicable or no breakpoints available for this species

Conclusions: Based on %S and MIC_{90} data TGC exhibited potent activity against isolates of all organism groups from cSSTI, regardless of the geographic region. However, given the potential many of these organisms have for developing resistance, continued and careful surveillance monitoring is warranted.

Introduction

Bacterial resistance presents a challenge to clinicians with increasing multi-drug resistance worldwide. Early targeted antibiotic therapy is an important factor in managing patient outcomes. The Tigecycline Evaluation Surveillance Trial (TEST) program has been monitoring infections for epidemiologic and antimicrobial susceptibility trends globally since 2004. This study and report was designed to assist clinicians, epidemiologists, and pharmacologists in their assessments of current trends and developments in the susceptibilities of commonly utilized antimicrobial agents prescribed to treat cSSTI.

Materials & Methods

- Between 2012 and 2016, 378 cumulative sites in North America and 133 cumulative sites in Latin America performed identifications to the species level and broth microdilution testing (following CLSI guidelines) on target species isolated from skin and soft tissue specimens [1,2]
- Organism collection, transport, confirmation of organism identification, susceptibility testing, and development and management of a centralized database were coordinated by International Health Management Associates, Inc. located in Schaumburg, IL, USA.
- MIC interpretive criteria followed published guidelines of the CLSI and the recent United States Food and Drug Administration package insert for Tigecycline where applicable [2, 3].

Results

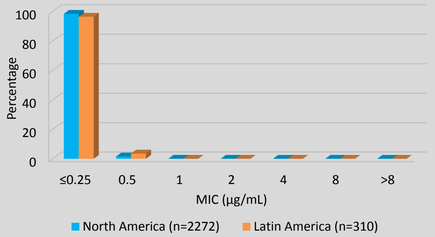
Table 1. *In vitro* activity of tigecycline against cSSTI pathogens isolated in North America

Organism	N	%S	%I	%R	MIC_{90}	Range
A. baumannii	310	N/A	N/A	N/A	2	≤.008-8
Enterobacter spp.	925	96.4	2.4	1.2	1	≤.008->8
Enterococcus spp.	691	99.3	0	0.7	0.12	≤.008-1
E. coli	716	99.9	0.1	0	0.25	≤.008-4
K. oxytoca	204	99.0	1.0	0	0.5	≤.008-4
K. pneumoniae	471	94.9	4.0	1.1	2	≤.008->8
S. marcescens	347	96.8	2.9	0.3	2	≤.008-8
S. aureus	2272	100	0	0	0.12	≤.008-1
S. agalactiae	503	100	0	0	0.12	0.015-0.25

Table 2. *In vitro* activity of tigecycline against cSSTI pathogens isolated in Latin America

Organism	N	%S	%I	%R	MIC_{90}	Range
A. baumannii	97	N/A	N/A	N/A	1	0.03 - 4
Enterobacter spp.	159	92.5	6.3	1.3	2	0.03 - > 8
Enterococcus spp.	135	100	0	0	0.12	0.015 - 0.25
E. coli	241	100	0	0	0.25	≤ 0.008 - 2
K. oxytoca	15	100	0	0	1	0.12 - 2
K. pneumoniae	152	91.5	6.6	2.0	2	0.12 - > 8
S. marcescens	67	97.0	3.0	0	2	0.03 - 4
S. aureus	310	100	0	0	0.25	0.015 - 0.5
S. agalactiae	58	100	0	0	0.06	0.015 - 0.25

Figure 1. MIC distribution of tigecycline against *S. aureus* from cSSTI*



* North America MRSA (n=1196), North America MSSA (n=1076), Latin America MRSA (n=144), and Latin America MSSA (n=166)

Figure 2. MIC distribution of tigecycline against *S. agalactiae* from cSSTI

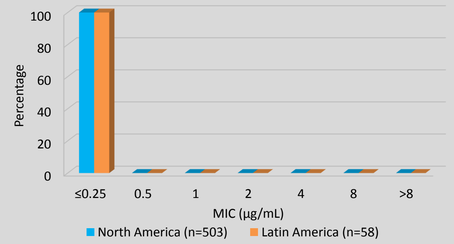


Figure 3. MIC distribution of tigecycline against *Enterococcus* spp. from cSSTI

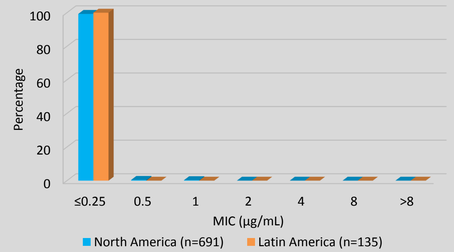


Figure 4. MIC distribution of tigecycline against *Enterobacter* spp. from cSSTI

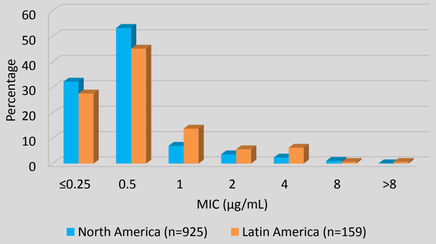


Figure 5. MIC distribution of tigecycline against *E. coli* from cSSTI

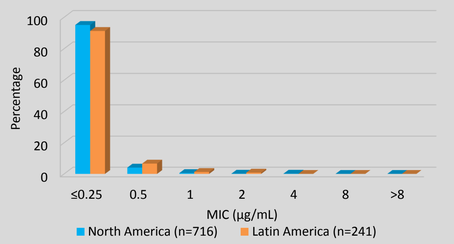


Figure 5. MIC distribution of tigecycline against *K. pneumoniae* from cSSTI

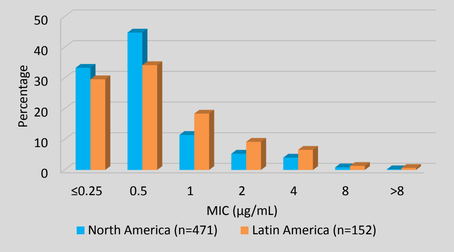
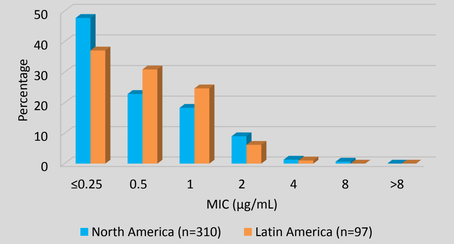


Figure 5. MIC distributions of tigecycline against *A. baumannii* from cSSTI



Conclusions

- Tigecycline demonstrated potent in vitro activity against all organism species and groups based upon MIC_{90} and percent susceptible.
- MIC_{90} and percent susceptible were essentially equivalent between North America and Latin America isolates.
- With increasing antibiotic resistance in cSSTI pathogens globally, continued surveillance is warranted.

References

1. Clinical Laboratory Standards Institute. 2015. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standards-Tenth Edition. CLSI document M07-A10. Wayne, PA.
2. Clinical and Laboratory Standards Institute. 2017. Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Seventh Informational Supplement. CLSI Document M100S. Wayne, PA.
3. Tygacil®, 2016. Tigecycline FDA prescribing information. Pfizer, Inc., Collegeville, PA.

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