

Revised Abstract

Background: Skin and skin structure infections (SSTIs) are frequently encountered in clinical practice and are among the most common indications for antibiotic therapy and hospital admission. The Tigecycline Evaluation and Surveillance Trial (TEST) has been monitoring susceptibility to tigecycline globally since 2004. This study reports on the activity of tigecycline against clinical isolates from SSTIs in Latin America. **Methods:** A total of 1,970 clinical isolates of key species from SSTI were collected and identified at 54 sites in 9 countries in Latin America in 2007-2010. MICs were determined by broth microdilution using CLSI guidelines. Susceptibility to tigecycline was interpreted using FDA breakpoints. **Results:** Resistant phenotypes were found frequently in SSTI pathogens, with rates in Latin America ranging from 21% for vancomycin-resistant (VR) *E. faecium* (out of all *E. faecium*), 29% for ESBL+ *E. coli*, 43% for ESBL+ *K. pneumoniae*, and 45% for MRSA. Results of tigecycline's *in vitro* activity for 2007-2010 are summarized below:

Organism	n	MIC ₅₀	MIC ₉₀	% S
<i>Acinetobacter baumannii</i>	141	0.5	2	na
<i>Enterobacter cloacae</i>	274	0.5	2	97.1
<i>Enterococcus faecalis</i>	163	0.12	0.25	100
<i>E. faecium</i>	48	0.12	0.25	97.9
<i>E. faecium</i> , VR	10	0.06	0.25	90.0
<i>Escherichia coli</i>	260	0.25	0.5	100
<i>E. coli</i> , ESBL+	75	0.25	1	100
<i>Klebsiella pneumoniae</i>	204	0.5	2	96.1
<i>K. pneumoniae</i> , ESBL+	87	0.5	2	95.4
<i>Pseudomonas aeruginosa</i>	292	8	16	na
<i>Serratia marcescens</i>	116	1	2	95.7
<i>Staphylococcus aureus</i>	394	0.12	0.25	100
<i>S. aureus</i> , MRSA	178	0.12	0.25	100
<i>Streptococcus agalactiae</i>	78	0.03	0.06	100

na - breakpoint not defined; ESBL+ - extended-spectrum β-lactamase positive; MRSA - Methicillin-resistant *S. aureus*.

Conclusions: Tigecycline demonstrated potent *in vitro* activity against gram-negative and gram-positive SSTI pathogens including resistant phenotypes. This is particularly important in Latin America, where rates of resistant phenotypes were high, especially ESBL+ isolates. MIC₉₀ values ranged from 0.25 to 2 mcg/ml for all studied species, except *P. aeruginosa* against which tigecycline is known to have very little activity. Overall between 2007 and 2010, tigecycline susceptibilities were >95% for all studied species for which breakpoints exist.

Introduction

Skin and skin structure infections (SSTIs) are frequently encountered in clinical practice and are among the most common indications for antibiotic therapy and hospital admission as well as a common cause of morbidity in both the community and the hospital [1, 2]. Increases in antibiotic resistance seen in bacteria commonly causing such infections have made selection of appropriate empiric therapy challenging [3].

The Tigecycline Evaluation and Surveillance Trial (TEST) has been monitoring the activity of tigecycline and comparators globally since 2004. For this report, the *in vitro* activity against key species from SSTI collected in Latin America between 2007 and 2010 is evaluated.

Materials & Methods

- A total of 1,970 clinical isolates of key species from SSTI were collected at 54 sites in 9 countries in Latin America in 2007-2010. Only one isolate per patient was accepted into the study. Isolates were identified to the species level and MICs determined at each participating laboratory using sponsor supplied broth microdilution panels.
- Organism collection, transport, confirmation of organism identification, and development and management of a centralized database were coordinated by Laboratories International for Microbiology Studies (LIMS), a division of International Health Management Associates, Inc. located in Schaumburg, IL, USA.
- Minimum inhibitory concentrations (MICs) were determined by the Clinical and Laboratory Standards Institute (CLSI) recommended broth microdilution testing method using MicroScan (Siemens Medical Solutions Diagnostics, West Sacramento, CA) or Sensititre (TREK Diagnostic Systems, Cleveland, OH) panels [4]. All antimicrobics were supplied by the panel manufacturers.
- MIC interpretive criteria followed published guidelines of the CLSI and the most recent United States Food and Drug Administration package insert for tigecycline where applicable [5,6].
- Quality controls (QC) were performed on each day of testing using appropriate ATCC control strains, following CLSI and manufacturer guidelines. Results were included in the analysis only when corresponding QC results were within the acceptable ranges [5].
- The Cochran-Armitage test was used to assess linear trends in percent susceptible over time.

References

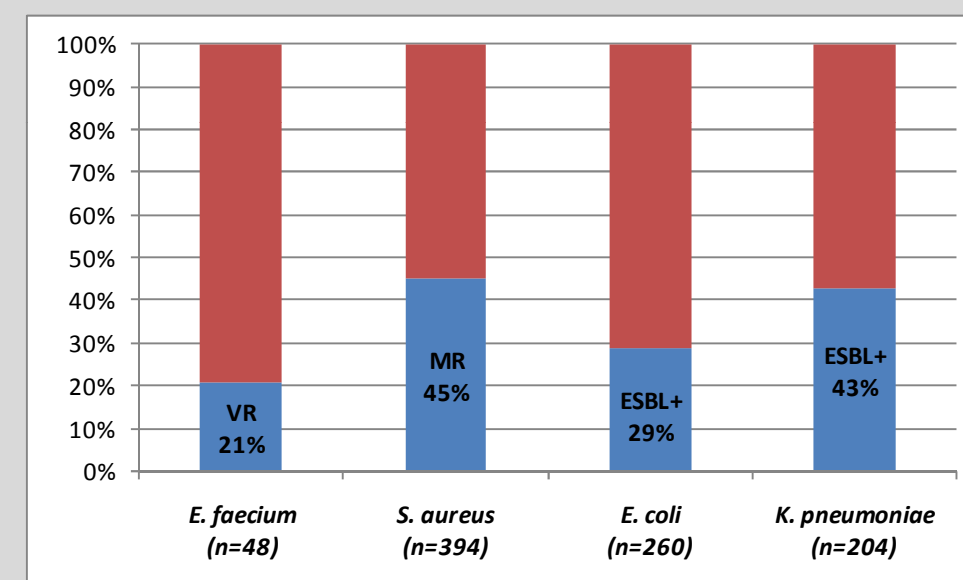
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Acknowledgements

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Results

Figure 1. Proportion of resistant phenotypes in key species from SSTI in Latin America, 2007-2010.



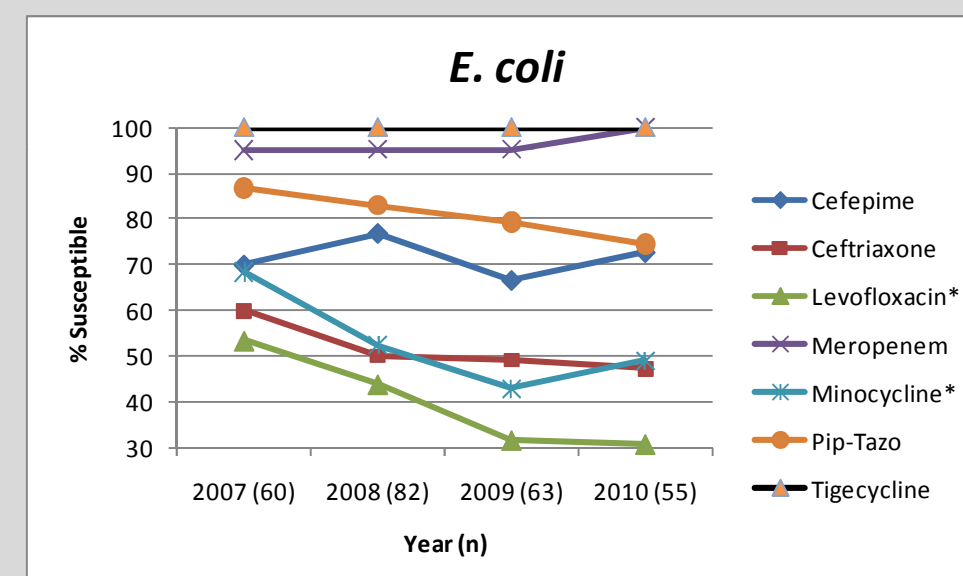
VR - vancomycin-resistant; MR - methicillin-resistant; ESBL+ - extended-spectrum β-lactamase positive.

Table 1. *In vitro* activity of tigecycline against key species from SSTI in Latin America, 2007-2010.

Organism	n	MIC ₅₀	MIC ₉₀	% S	% I	% R
<i>Acinetobacter baumannii</i>	141	0.5	2	na	na	na
<i>Enterobacter cloacae</i>	274	0.5	2	97.1	2.6	0.4
<i>Enterococcus faecalis</i>	163	0.12	0.25	100	0	0
<i>E. faecium</i>	48	0.12	0.25	97.9	0	2.1
<i>E. faecium</i> , VR	10	0.06	0.25	90.0	0	10
<i>Escherichia coli</i>	260	0.25	0.5	100	0	0
<i>E. coli</i> , ESBL+	75	0.25	1	100	0	0
<i>Klebsiella pneumoniae</i>	204	0.5	2	96.1	3.4	0.5
<i>K. pneumoniae</i> , ESBL+	87	0.5	2	95.4	4.6	0
<i>Pseudomonas aeruginosa</i>	292	8	16	na	na	na
<i>Serratia marcescens</i>	116	1	2	95.7	3.5	0.9
<i>Staphylococcus aureus</i>	394	0.12	0.25	100	0	0
<i>S. aureus</i> , MRSA	178	0.12	0.25	100	0	0
<i>Streptococcus agalactiae</i>	78	0.03	0.06	100	0	0

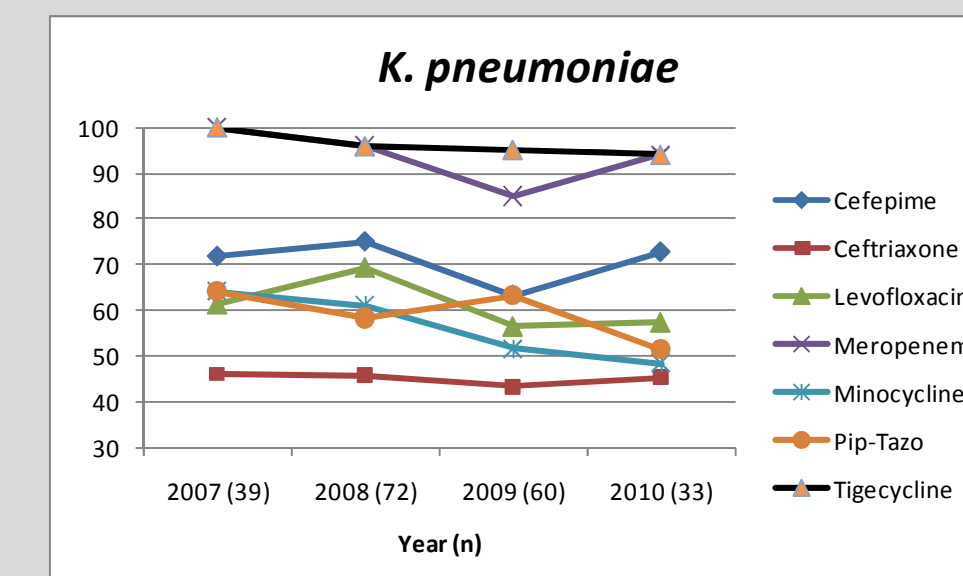
% S/I/R - percent susceptible/intermediate/resistant; na - breakpoint not defined; ESBL+ - extended-spectrum β-lactamase positive; VR - vancomycin-resistant; MRSA - methicillin-resistant *S. aureus*.

Figure 3. Trends in susceptibility of tigecycline and comparators against *E. coli* isolates from SSTI in Latin America, 2007-2010.



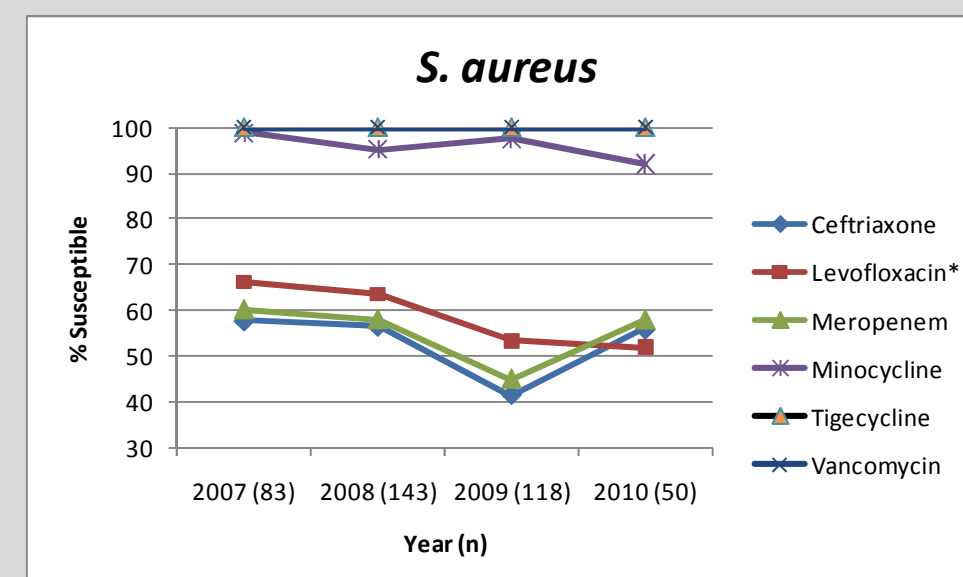
* Statistically significant decreasing trend in % susceptible (p<0.05).

Figure 4. Trends in susceptibility of tigecycline and comparators against *K. pneumoniae* isolates from SSTI in Latin America, 2007-2010.



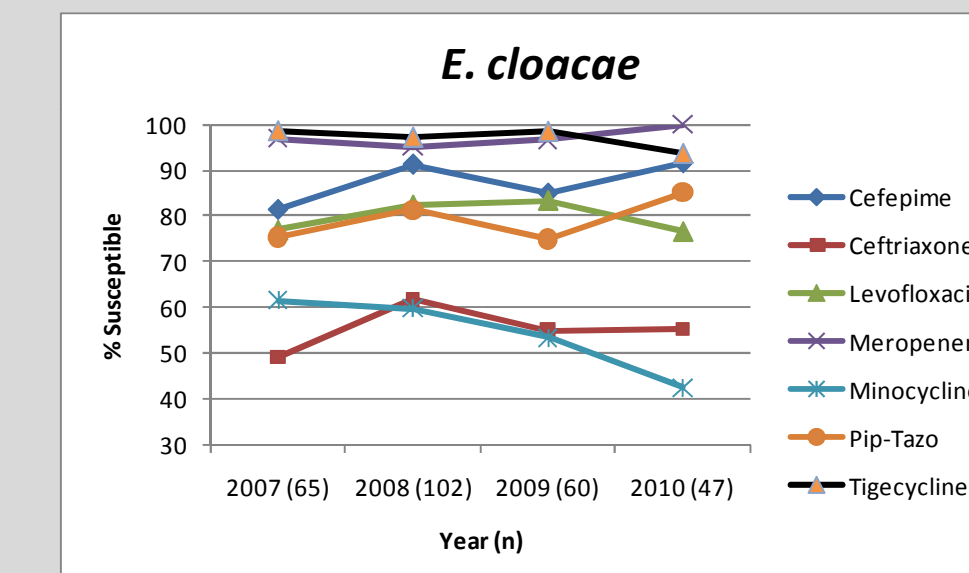
* Statistically significant decreasing trend in % susceptible (p<0.05).

Figure 6. Trends in susceptibility of tigecycline and comparators against *S. aureus* isolates from SSTI in Latin America, 2007-2010.



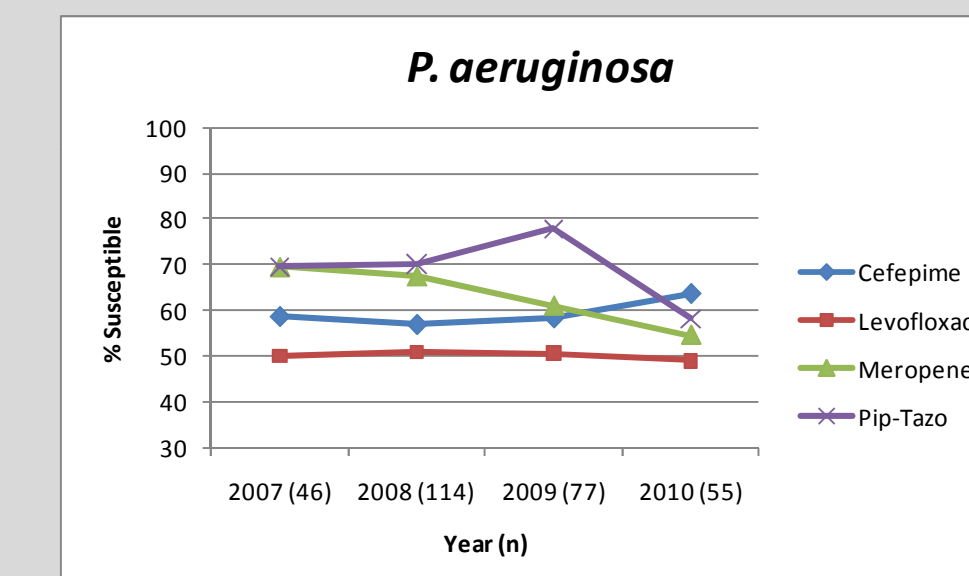
* Statistically significant decreasing trend in % susceptible (p<0.05).

Figure 2. Trends in susceptibility of tigecycline and comparators against *E. cloacae* isolates from SSTI in Latin America, 2007-2010.



* Statistically significant decreasing trend in % susceptible (p<0.05).

Figure 5. Trends in susceptibility of antimicrobial agents against *P. aeruginosa* isolates from SSTI in Latin America, 2007-2010.



Conclusions

- Tigecycline demonstrated potent *in vitro* activity against gram-negative and gram-positive SSTI pathogens including vancomycin-resistant *E. faecium*, MRSA, and ESBL+ *E. coli* and *K. pneumoniae*. This is particularly important in Latin America, where rates of these resistant phenotypes were high, especially ESBL+ isolates.
- Tigecycline MIC₉₀ values ranged from 0.25 to 2 mcg/ml for all studied species, except *P. aeruginosa* against which tigecycline is known to have very little activity.
- Significant decreasing trends in %S (p<0.05) between 2007 and 2010 were found for minocycline (against *E. cloacae* and *E. coli*) and levofloxacin (against *E. coli* and *S. aureus*), as well as a marginally significant trend for meropenem against *K. pneumoniae* (p=0.046). Tigecycline susceptibilities were stable and >93% in each year and for all studied species for which breakpoints exist.
- These *in vitro* results suggest that tigecycline remains a treatment option for SSTI in Latin America.