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Antimicrobial Susceptibility Profiles of Key Intra-abdominal (IAI) Bacterial Isolates from Western Europe: TEST 2014-2016

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Revised Abstract

Background: Evolving resistance in gram-negative bacilli commonly found in intra-abdominal infections (IAI) requires careful monitoring importantly on a country specific basis. Surveillance studies are critical in assessing both resistance rates and trends in resistance over time for antimicrobials commonly used to treat IAIs. *Enterobacteriaceae*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii* are common causes of serious infections, particularly among hospitalized patients, and are increasingly difficult to treat, due in part to increased dissemination of extended-spectrum β-lactamases (ESBLs). In this analysis, data from the Tigecycline European Surveillance Trial (TEST) were used to evaluate the *in vitro* activity of several key drugs against recent intra-abdominal isolates from western European countries. **Methods:** A total of 1646 IAI isolates collected from 16 western European countries during 2014-2016 were identified and tested locally using supplied broth micro dilution panels. Susceptibility testing was performed following CLSI guidelines and interpreted using EUCAST clinical breakpoints. **Results:** The ESBL rates for 502 *Escherichia. coli* and 302 *Klebsiella pneumoniae* were 12.5% and 23.8%, respectively. The activities of the various drugs according to organism group are provided in the table below.

	Enterobacteriaceae (1422)			ESBL+* (137)			*P. aeruginosa* (158)			*A. baumannii* (66)		
Drug	%S	MIC_{50}	MIC_{90}	%S	MIC_{50}	MIC_{90}	%S	MIC_{50}	MIC_{90}	%S	MIC_{50}	MIC_{90}
Tigecycline	93.3	0.25	1	89.78	0.5	2	na	8	>8	na	1	2
Amikacin	95.4	2	4	94.16	4	8	91.8	4	8	27.3	>64	>64
Cefepime	77.0	≤ 0.5	32	6.57	32	>32	82.3	4	16	na	>32	>32
Ceftazidime	67.7	≤1	>16	8.03	16	>16	79.8	2	>16	na	>16	>16
Levofloxacin	76.5	0.06	>8	29.2	8	>8	69.6	0.5	>8	16.7	>8	>8
Meropenem	95.4	≤ 0.06	0.25	92.7	≤0.06	1	73.4	1	16	21.2	>16	>16
Pip -Tazo	76.9	2	128	61.31	8	>128	76.6	4	128	na	>128	>128

E. coli (63), *K. pneumoniae* (72), K. oxytoca (2)
na: no EUCAST breakpoints available

Conclusions: Tigecycline, amikacin, and meropenem were the most active agents against *Enterobacteriaceae* from IAI, with % susceptible ≥93% with only slightly reduced activity against ESBL producers. Amikacin was the most active agent against *P. aeruginosa* with >90% susceptible. Tigecycline had the lowest MIC_{90} against *A. baumannii* at 2 mg/L and was 4-64 fold more active based on MIC_{90} than other agents tested. Decreasing antimicrobial susceptibilities and the increasing prevalence of ESBLs in western European countries substantiate the need for continued monitoring of resistance trends among these clinically important organism groups.

Introduction

Enterobacteriaceae and other gram-negative bacilli cause serious infections among hospitalized patients, including intra-abdominal infections (IAI). Tigecycline European Surveillance Trial (TEST) program data were used to evaluate the *in vitro* activity of several key drugs against pathogens causing IAI among patients in Western European countries. The species included in this study were from the following groups: *Enterobacter* spp., (five species), *Klebsiella* spp., (two species), *Citrobacter spp.*, (two species), *Serratia* spp., (two species), *E. coli*, *P. aeruginosa* and *A. baumannii.*

Materials & Methods

- Between 2014 and 2016 hospital sites in 16 Western European countries participated in the TEST program. A total of 1422 *Enterobacteriaceae* as well as 158 *P. aeruginosa* and 66 *A. baumannii* isolates were identified to the species level and MICs determined at each participating laboratory using supplied broth microdilution panels. All isolates were derived from intraabdominal infections (IAI) from hospitalized patients. Only one isolate per patient was accepted into the study.
- 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.
- Minimum inhibitory concentrations (MICs) were determined by the Clinical and Laboratory Standards Institute (CLSI) recommended broth microdilution testing method using MicroScan (Beckman Coulter, West Sacramento, CA) panels [1]. All antimicrobics were supplied by the panel manufacturers.
- MIC interpretive criteria followed EUCAST guidelines [2]. Multi-drug resistance (MDR) was defined using the following drug classes: glycylcyclines, β-lactam/β-lactamase-inhibitors, cephems, carbapenems, penicillins (ampicillin), quinolones, and aminoglycosides.
- Quality control (QC) was 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 [3].

Results

Figure 1. MIC Distributions of Tigecycline and Comparators Against 66 *A. baumannii* Isolates

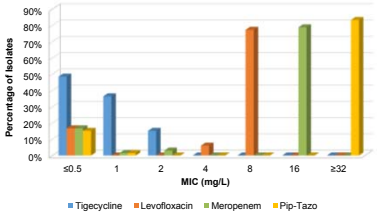

Figure 2. MIC Distributions of Tigecycline and Comparators Against 1422 *Enterobacteriaceae* Isolates

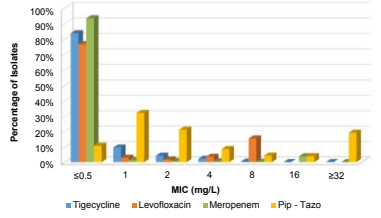

Figure 3. MIC Distributions of Tigecycline and Comparators Against 502 *E. coli* Isolates

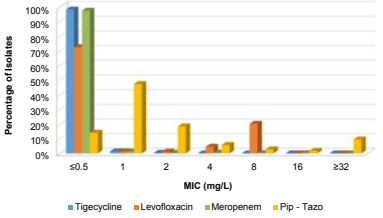

Figure 4. MIC Distributions of Tigecycline and Comparators Against 302 *K. pneumoniae* Isolates

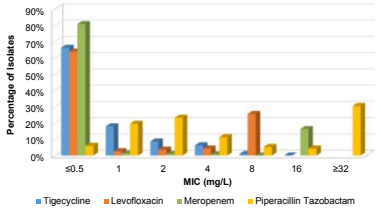

Table 4. Activity of Tigecycline and Comparators Against 52 Carbapenem Resistant (Meropenem) Isolates[a]

Drug	%S	%I	%R	MIC_{50}	MIC_{90}	MIC Range
Tigecycline	61.5	23.1	15.4	1	4	0.25 - >8
Amikacin	21.2	53.9	25	16	32	1 - 64
Cefepime	0	0	100	>32	>32	32 - >32
Levofloxacin	1.9	0	98.1	>8	>8	0.25 - >8
Meropenem	0	0	100	>16	>16	16 - >16
Pip - Tazo	0	0	100	>128	>128	>128 - >128

[a]CRE: 49 *K. pneumoniae*, 2 *Citrobacter spp.*, 1 *E. coli*

Table 1. Activity of Tigecycline and Comparators Against All and MDR *Enterobacteriaceae*[a]

	All (N=1422)		All MDR (N=434)		MDR=3 (N=239)		MDR=4 (N=130)		MDR≥5 (N=65)	
Drug	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}
Tigecycline	93.3	1	83.4	2	92.9	1	81.5	2	52.3	4
Amikacin	95.4	4	85.7	16	95.0	4	96.9	8	29.2	32
Cefepime	77.0	32	32.0	> 32	51.5	32	12.3	> 32	0	> 32
Levofloxacin	76.5	>8	40.8	> 8	71.1	> 8	4.6	> 8	1.5	> 8
Meropenem	95.4	0.25	84.8	> 16	98.7	0.25	92.3	2	18.5	> 16
Pip - Tazo	76.9	128	34.6	> 128	45.2	> 128	31.5	> 128	1.5	> 128

[a]MDR ; Multi-Drug Resistant: MDR=3, resistant to three drug classes; MDR=4, resistant to four drug classes; MDR≥5, resistant to five or more drug classes.

Table 2. Activity of Tigecycline and Comparators Against All and MDR *E. coli*[a]

	All (N=502)		All MDR (N=95)		MDR=3 (N=49)		MDR=4 (N=45)		MDR≥5 (N=1)	
Drug	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}
Tigecycline	99.6	0.25	99.0	0.5	98.0	0.5	100	0.5	100	0.25
Amikacin	98.4	4	93.7	8	93.9	4	95.6	8	0	16
Cefepime	83.5	8	34.7	> 32	63.3	> 32	4.4	> 32	0	> 32
Levofloxacin	72.5	> 8	7.4	> 8	14.3	> 8	0	> 8	0	> 8
Meropenem	99.0	≤0.06	94.7	1	98.0	0.12	93.3	2	0	> 16
Pip - Tazo	88.7	16	59.0	128	69.4	128	48.9	128	0	> 128

[a]MDR ; Multi-Drug Resistant: MDR=3, resistant to three drug classes; MDR=4, resistant to four drug classes; MDR≥5, resistant to five or more drug classes.

Table 3. Activity of Tigecycline and Comparators Against All and MDR *K. pneumoniae*[a]

	All (N=302)		All MDR (N=128)		MDR=3 (N=37)		MDR=4 (N=35)		MDR≥5 (N= 56)	
Drug	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}
Tigecycline	84.1	2	70.3	4	89.2	2	77.1	2	53.6	4
Amikacin	85.1	16	64.8	32	91.9	8	97.1	8	26.8	32
Cefepime	58.9	>32	7.0	>32	18.9	>32	5.7	>32	0	>32
Levofloxacin	63.9	>8	23.4	>8	75.7	8	2.9	>8	1.8	>8
Meropenem	83.1	>16	60.2	>16	94.6	1	100	1	12.5	>16
Pip - Tazo	65.2	>128	28.1	>128	67.6	>128	28.6	>128	1.8	>128

[a]MDR ; Multi-Drug Resistant: MDR=3, resistant to three drug classes; MDR=4, resistant to four drug classes; MDR≥5, resistant to five or more drug classes.

Conclusions

- Based on susceptibility percentages, tigecycline, meropenem, and amikacin were the most active drugs against all *Enterobacteriaceae* isolated from intra-abdominal infections in Western European countries (Table 1).
- Tigecycline was among the most active agents against MDR *Enterobacteriaceae,* including those resistant to five or more drugs and including carbapenem resistant *Enterobacteriaceae* spp. (Tables 1-4).
- Monitoring variation in antimicrobial susceptibilities among clinically significant *Enterobacteriaceae* from IAIs in Europe helps to establish antibiotic treatment guidelines in many European countries. Therefore monitoring of susceptibility in IAI isolates should be continued on an ongoing basis.

References

1. Clinical Laboratory Standards Institute (CLSI), 2015. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standards – Tenth Edition. CLSI document M07-A10 (ISBN 1-56238-987-4). CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA.
2. The European Committee on Antimicrobial Susceptibility Testing – EUCAST Clinical Breakpoints 2017; http://www.eucast.org/clinical_breakpoints/
3. Clinical and Laboratory Standards Institute (CLSI), 2017. Performance Standards for Antimicrobial Susceptibility Testing – Twenty-Seventh Informational Supplement. CLSI Document M100S (ISBN 1-56238-923-8). CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA.

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