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Antimicrobial Susceptibility of Enterobacteriaceae Causing Intra-Abdominal Infections (IAI) in Adult and Pediatric Patients in France, Germany, Italy, and Spain: Results from the TEST program 2012-2016

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Revised Abstract

Background: The Tigecycline European Surveillance Trial (TEST) monitors the in vitro activity of tigecycline and other antimicrobials against clinically-relevant pathogens collected globally from pediatric and adult patients. This study reports on the activity of tigecycline and comparators against IAI isolates collected in France, Germany, Italy, and Spain analyzed by age groups.

Methods: Non-duplicate clinical *Enterobacteriaceae* (2334) isolates from medical centers in France, Germany, Italy, and Spain were collected during 2012-2016 from IAI specimens. Pediatric patients were those ≤16 years and adults were ≥17. Organism identification and antibiotic susceptibility testing was performed by the local laboratories. Susceptibility testing was performed using supplied broth micro-dilution panels according to CLSI guidelines and categorical interpretation of results was done using EUCAST breakpoints.

Results: The table provides MIC_{90} (%S) data for tigecycline and comparators.

	MIC_{90}/%S					
	Tigecycline	Amikacin	Cefepime	Levofloxacin	Meropenem	Pip-Tazo
Spain (766)	0.5/95.7	4/99.1	2/86.7	8/79	0.25/99.2	32/84.6
Pediatrics (35)	2/88.6	2/88.7	2/88.8	2/88.9	2/88.10	2/88.11
Germany (520)	1/95.4	4/98.7	8/82.7	4/81.9	0.12/99.2	64/82.7
Pediatrics (59)	0.5/98.3	4/98.3	8/81.4	0.5/91.5	0.25/100	64/79.7
France (473)	1/94.3	4/98.5	16/77.4	8/80.8	0.12/99.8	64/81.4
Pediatrics (37)	0.5/94.6	4/100	4/86.5	1/89.2	≤0.06/100	8/91.9
Italy (410)	2/85.4	16/79	>32/52	>8/46.6	>16/79.3	>128/51.2
Pediatrics (34)	1/97.1	8/91.2	>32/64.7	8/82.4	0.12/94.1	32/76.5

Conclusions: Tigecycline, amikacin and meropenem had *in vitro* activity (>85%) susceptible against pediatric *Enterobacteriaceae* IAI isolates in all countries. Adult patient *Enterobacteriaceae* isolates were generally less susceptible to all agents tested. Country specific monitoring of susceptibility patterns among common *Enterobacteriaceae* IAI pathogens provides useful information for determining if changes in treatment strategies based on patient age should be considered.

Introduction

The Tigecycline European Surveillance Trial (TEST) program monitors the *in vitro* activity of tigecycline and other antimicrobials against clinically-relevant pathogens collected globally from pediatric and adult patients. This study reports on the activity of tigecycline and comparators against IAI isolates collected in France, Germany, Italy, and Spain analyzed by age groups.

Materials & Methods

- Between 2012 and 2016 medical centers in France, Germany, Italy, and Spain collected isolates from intraabdominal infections (IAI) in the TEST program. A total of 165 *Enterobacteriaceae* isolates from pediatric patients and 2169 isolates from adult patients were identified to the species level.
- 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. (Schaumburg, IL, USA).
- Minimum inhibitory concentrations (MICs) were determined at each participating laboratory by the Clinical and Laboratory Standards Institute (CLSI) recommended broth microdilution testing method [1,3] using MicroScan (Beckman Coulter, West Sacramento, CA) [1]. MIC interpretive criteria followed EUCAST guidelines [2].
- 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 [3].

Results

Fig 1. Species Distribution of *Enterobacteriaceae* Isolates collected from Pediatric and Adult Patients in France

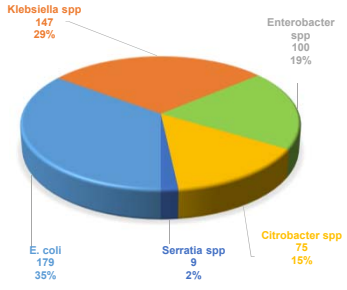

Fig 2. Species Distribution of *Enterobacteriaceae* Isolates collected from Pediatric and Adult Patients in Germany

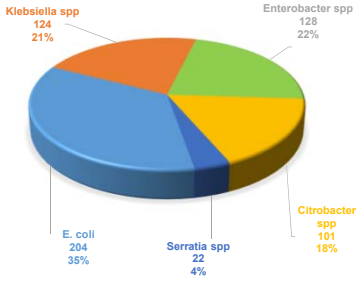

Fig 3. Species Distribution of *Enterobacteriaceae* Isolates collected from Pediatric and Adult Patients in Italy

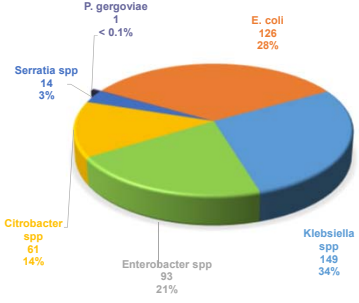

Fig 4. Species Distribution of *Enterobacteriaceae* Isolates collected from Pediatric and Adult Patients in Spain

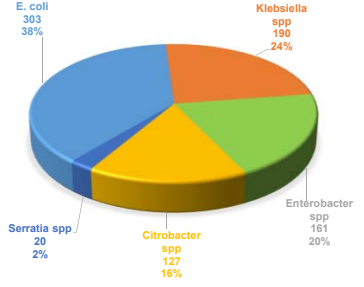

Table 1. *In Vitro* Activity of Tigecycline and Comparator Agents Tested Against Isolates from Adult Patients with IAI in Spain, Germany, France and Italy. Values ≥90% are shaded.

Region	Drug	% S	% I	% R	MIC_{50}	MIC_{90}
Spain	Tigecycline	95.7	3.0	1.3	0.25	0.5
(n=766)	Amikacin	99.1	0.8	0.1	2	4
	Cefepime	86.7	5.7	7.6	≤0.5	2
	Levofloxacin	79.0	2.2	18.8	0.06	8
	Meropenem	99.2	0.4	0.4	≤0.06	0.25
	Pip-Tazo	84.6	3.4	12.0	2	32
Germany	Tigecycline	95.4	2.7	1.9	0.25	1
(n=520)	Amikacin	98.7	1.0	0.4	2	4
	Cefepime	82.7	6.9	10.4	≤0.5	8
	Levofloxacin	81.9	4.0	14.0	0.06	4
	Meropenem	99.2	0.4	0.4	≤0.06	0.12
	Pip-Tazo	82.7	4.2	13.1	2	64
France	Tigecycline	94.3	3.6	2.1	0.25	1
(n=473)	Amikacin	98.5	1.3	0.2	2	4
	Cefepime	77.4	7.8	14.8	≤0.5	16
	Levofloxacin	80.8	2.3	16.9	0.06	8
	Meropenem	99.8	0	0.2	≤0.06	0.12
	Pip-Tazo	81.4	3.4	15.2	2	64
Italy	Tigecycline	85.4	8.1	6.6	0.5	2
(n=410)	Amikacin	79.0	12.2	8.8	2	16
	Cefepime	52.0	7.6	40.5	1	>32
	Levofloxacin	46.6	1.7	51.7	4	>8
	Meropenem	79.3	3.2	17.6	≤0.06	>16
	Pip-Tazo	51.2	5.4	43.4	8	>128

Table 2. *In Vitro* Activity of Tigecycline and Comparator Agents Tested Against Isolates from Pediatric Patients with IAI in Spain, Germany, France and Italy. Values ≥90% are shaded.

Country	Drug	% S	% I	% R	MIC_{50}	MIC_{90}
Spain	Tigecycline	88.6	8.6	2.9	0.25	2
(n=35)	Amikacin	100	0	0	2	4
	Cefepime	82.9	2.9	14.3	≤0.5	8
	Levofloxacin	85.7	5.7	8.6	0.03	1
	Meropenem	100	0	0	≤0.06	0.12
	Pip-Tazo	88.6	2.9	8.6	1	16
Germany	Tigecycline	98.3	0	1.7	0.25	0.5
(n=59)	Amikacin	98.3	1.7	0	2	4
	Cefepime	81.4	8.5	10.2	≤0.5	8
	Levofloxacin	91.5	1.7	6.8	0.03	0.5
	Meropenem	100	0	0	≤0.06	0.25
	Pip-Tazo	79.7	5.1	15.3	1	64
France	Tigecycline	94.6	5.4	0	0.12	0.5
(n=37)	Amikacin	100	0	0	2	4
	Cefepime	86.5	5.4	8.1	≤0.5	4
	Levofloxacin	89.2	2.7	8.1	0.03	1
	Meropenem	100	0	0	≤0.06	≤0.06
	Pip-Tazo	91.9	2.7	5.4	1	8
Italy	Tigecycline	97.1	2.9	0	0.5	1
(n=34)	Amikacin	91.2	8.8	0	2	8
	Cefepime	64.7	5.9	29.4	≤0.5	> 32
	Levofloxacin	82.4	2.9	14.7	0.12	8
	Meropenem	94.1	5.9	0	≤0.06	0.12
	Pip-Tazo	76.5	11.8	11.8	2	32

Conclusions

- **Regardless of country, tigecycline, amikacin and meropenem demonstrated *in vitro* activity against pediatric *Enterobacteriaceae* IAI isolates while the activity of cefepime and levofloxacin was considerably less.**
- **Adult patient *Enterobacteriaceae* also demonstrated the highest susceptibility to tigecycline, amikacin and meropenem. The other tested agents had susceptibility rates that were generally less than 86% against the enteric species, particularly in Italy.**
- **Country specific monitoring of susceptibility patterns among common gram-negative IAI pathogens provides useful information for determining if changes in treatment strategies based on patient age should be considered.**

References

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