EV0522

Comparison of Susceptibility Patterns Among *Enterobacteriaceae* from European and North American ICU and Non-ICU Wards: TEST 2014-2016

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Revised Abstract

Background: Higher resistance rates have been reported in *Enterobacteriaceae* from intensive care units (ICUs) than observed in non-ICU settings limiting treatment options in ICU patient management. Using data from the Tigecycline European Surveillance Trial (TEST), the susceptibility of *Enterobacteriaceae* to tigecycline and comparators was analyzed according to ICU and non-ICU wards in Europe and North America.

Methods: 20,011 *Enterobacteriaceae* (*E. coli*, *Klebsiella* spp., *Citrobacter* spp., *Enterobacter* spp., and *Serratia* spp.) isolates from multiple specimen sources were collected in 22 countries in Europe and North America (Canada and the United States) from ICU and non-ICU wards in 2014-2016. MICs were determined at each site using supplied broth micro dilution panels following CLSI methodology and interpreted according to EUCAST guidelines. Isolates were categorized as multi-drug resistant (MDR) if resistant to ≥3 of the tested drug classes (glycylcyclines, β-lactam/inhibitor, cephems, penems, penicillins [ampicillin], quinolones, and aminoglycosides). Differences in susceptibility and MDR rates between patient locations and geographic regions were assessed for statistical significance with the chi-square test.

Results: Susceptibility to a selected subset of the tested agents and % MDR are shown below.

	Europe		North America	
	ICU	non-ICU	ICU	non-ICU
Tigecycline	**90.7**	**92.5***	**92.9**	**92.7**
Amikacin	**95.8**	**97.3***	**98.7**	**99.2**
Amox-Clav	**37.4**	**43.5***	**45.0**	**55.5***
Cefepime	**75.2**	**78.5***	**88.8**	**89.1**
Ceftriaxone	**67.6**	**71.2***	**80.5**	**84.1***
Levofloxacin	**79.1**	**76.3****	**87.1**	**82.0****
Meropenem	**96.1**	**97.8***	**98.9**	**99.0**
Pip-Tazo	**76.9**	**81.3***	**85.3**	**89.6***
MDR	**32.5**	**30.0***	**20.5**	**18.6**
Number	**4541**	**11245**	**1132**	**3093**

* Significantly lower susceptibility or higher MDR rate in ICU than non-ICU (p<0.05)
** Significantly higher susceptibility in ICU (p<0.05)

Comparing regions, isolates from ICUs were less susceptible in Europe than in North America (p<0.05) to all agents; isolates from non-ICU wards were significantly less susceptible in Europe than in North America to all agents except tigecycline.

Conclusions: In Europe, *Enterobacteriaceae* isolates from ICUs were significantly less susceptible than those from non-ICU wards to the majority of agents, but not in North America. Of the tested agents, only tigecycline, meropenem, and amikacin maintained susceptibility >90% against *Enterobacteriaceae* in both settings and both regions. Knowledge of resistance patterns across geographic regions and hospital settings is crucial both for infection control efforts and patient treatment decisions.

Introduction

Higher resistance rates have been reported in *Enterobacteriaceae* from intensive care units (ICUs) compared to general hospital wards. Furthermore, ICU admission has been identified as a risk factor for extended-spectrum β-lactamase (ESBL) infections, especially in *Klebsiella pneumoniae*, further limiting treatment options in this setting. Using data from the Tigecycline European and Surveillance Trial (TEST) program susceptibility of *Enterobacteriaceae* to tigecycline and comparators as well as MDR rates were analyzed according to ICU and non-ICU wards in Europe and North America.

Materials & Methods

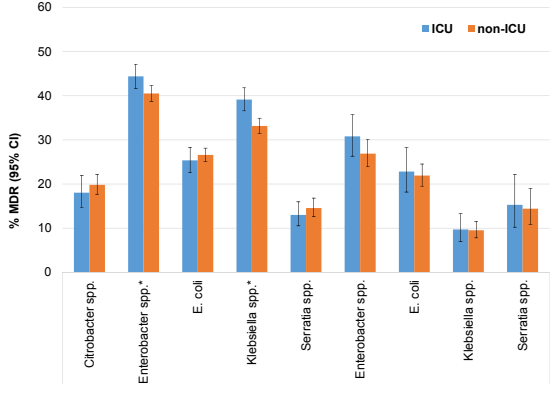
- 20,011 *Enterobacteriaceae* (*Escherichia coli*, *Klebsiella* spp., *Citrobacter* spp., *Enterobacter* spp., and *Serratia* spp.) isolates from various specimen sources were collected in 20 countries in Europe and 2 countries in North America from ICU and non-ICU wards in 2014-2016. Laboratories were assigned collection quotas for each species. MICs were determined at each site using CLSI broth microdilution methodology [1, 3] and interpreted according to EUCAST guidelines [2].
- Isolates were categorized as multi-drug resistant (MDR) if resistant to ≥3 of the tested drug classes (glycylcyclines, β-lactam/inhibitor, cephems, penems, penicillins [ampicillin], quinolones, and aminoglycosides). Differences in susceptibility and MDR rates between patient locations and geographic regions were assessed for statistical significance with the chi-square test.

Results

Table 1. Distribution of *Enterobacteriaceae* species collected for this study.

	n (% of *Enterobacteriaceae* in each subset)				
	EU-NA	Europe		North America	
	Overall	ICU	non-ICU	ICU	non-ICU
***Citrobacter* spp.**	**1665 (8.3%)**	**432 (9.5%)**	**1230 (10.9%)**	**1 (0.1%)**	**2 (0.1%)**
E. coli	**5335 (26.7%)**	**906 (20.0%)**	**3224 (28.7%)**	**267 (23.6%)**	**1044 (33.8%)**
***Enterobacter* spp.**	**5441 (27.2%)**	**1270 (28.0%)**	**2899 (25.8%)**	**370 (32.7%)**	**796 (25.7%)**
***Klebsiella* spp.**	**5480 (27.4%)**	**134 (29.5%)**	**2822 (25.1%)**	**350 (30.9%)**	**967 (31.3%)**
***Serratia* spp.**	**2090 (10.4%)**	**592 (13.0%)**	**1070 (9.5%)**	**144 (12.7%)**	**284 (9.2%)**
Enterobacteriaceae	**20011 (100%)**	**4541 (100%)**	**11245 (100%)**	**1132 (100%)**	**3093 (100%)**

Figure 1. Percent MDR *Enterobacteriaceae*; by patient location, region, and *species*.



* Significantly higher MDR rate in ICU than non-ICU (p<0.05)

Table 2. Susceptibility of *Enterobacteriaceae*; by patient location and region. Values ≥90% are shaded.

	Europe		North America	
	ICU	non-ICU	ICU	non-ICU
***Enterobacteriaceae* (n)**	4541	11245	1132	3093
Tigecycline	90.7	92.5*	92.9	92.7
Amikacin	95.8	97.3*	98.7	99.2
Amox-Clav	37.4	43.5*	45.0	55.5*
Cefepime	75.2	78.5*	88.8	89.1
Ceftriaxone	67.6	71.2*	80.5	84.1*
Levofloxacin	79.1	76.3**	87.1	82.0**
Meropenem	96.1	97.8*	98.9	99.0
Pip-Tazo	76.9	81.3*	85.3	89.6*
***Citrobacter* spp. (n)**	432	1230	1	2
Tigecycline	99.1	99.3	na	na
Amikacin	99.1	99.8	na	na
Amox-Clav	57.4	53.4	na	na
Cefepime	91.9	93.3	na	na
Ceftriaxone	80.8	80.5	na	na
Levofloxacin	93.1	91.5	na	na
Meropenem	99.3	99.7	na	na
Pip-Tazo	87.3	86.8	na	na
***E. coli* (n)**	906	3224	267	1044
Tigecycline	99.5	99.5	97.8	98.0
Amikacin	97.8	97.8	97.8	99.2*
Amox-Clav	66.3	69.7	71.9	75.7
Cefepime	75.2	78.8*	85.8	85.5
Ceftriaxone	76.3	77.5	84.3	84.8
Levofloxacin	68.1	63.8**	67.8	64.7
Meropenem	99.7	99.8	100	99.9
Pip-Tazo	87.0	89.9*	93.3	93.3

	Europe		North America	
	ICU	non-ICU	ICU	non-ICU
***Enterobacter* spp. (n)**	1270	2899	370	796
Tigecycline	92.7	91.3	91.9	93.0
Amikacin	98.3	98.1	99.2	99.6
Amox-Clav	3.6	4.0	3.0	4.2
Cefepime	73.8	77.2*	86.0	88.2
Ceftriaxone	56.0	61.0*	67.3	74.8*
Levofloxacin	86.0	84.2	96.0	94.1
Meropenem	98.0	99.0*	99.2	99.5
Pip-Tazo	67.7	71.8*	74.1	81.0*
***Klebsiella* spp. (n)**	1341	2822	350	967
Tigecycline	85.8	86.5	93.7	91.0
Amikacin	90.6	94.3*	98.3	98.6
Amox-Clav	58.0	63.8*	86.6	90.3
Cefepime	62.6	67.0*	92.0	91.5
Ceftriaxone	60.5	65.3*	90.0	90.4
Levofloxacin	69.7	70.7	92.6	90.1
Meropenem	89.3	92.9*	97.7	97.8
Pip-Tazo	68.9	74.8*	89.4	91.5
***Serratia* spp (n)**	592	1070	144	284
Tigecycline	78.0	82.6*	85.4	78.5
Amikacin	96.8	98.3*	100	99.7
Amox-Clav	4.6	7.0*	2.1	6.7*
Cefepime	94.8	94.3	94.4	96.5
Ceftriaxone	85.6	85.1	84.7	85.9
Levofloxacin	92.1	89.9	86.8	84.2
Meropenem	99.7	99.6	98.6	98.2
Pip-Tazo	92.1	92.2	90.3	93.7

*Susceptibility in ICU significantly lower than non-ICU (p<0.05).**Susceptibility in ICU significantly higher than non-ICU (p<0.05). na, % susceptible not calculated if n<10.

Comparing regions, *Enterobacteriaceae* from ICUs were significantly less susceptible in Europe than in North America (p<0.05) to all studied agents; isolates from non-ICU wards were significantly less susceptible in Europe than in North America to all agents except tigecycline.

Conclusions

- In Europe, *Enterobacteriaceae* isolates from ICUs were significantly less susceptible than those from non-ICU wards to the majority of agents, but not in North America.
- For most agents, isolates from Europe were less susceptible and MDR rates were higher than in isolates from North America, regardless of patient location.
- Of the tested agents, only tigecycline, meropenem, and amikacin maintained susceptibility >90% against *Enterobacteriaceae* in both settings and both regions.
- Knowledge of resistance patterns across geographic regions and hospital settings is crucial both for infection control efforts and patient treatment decisions.

References

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