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Paper Poster Session V

Recent epidemiological data on carbapenem-resistant Enterobacteriaceae

Current status of carbapenem-resistant Enterobacteriaceae (CRE) in Europe

K. Kazmierczak[1], M. Hackel[1], M. Estabrook[1], H. Li[1], D. Biedenbach[1], B. Johnson[1], H. Leister-Tebbe[2]

[1]*International Health Management Associates- Inc., Schaumburg- IL, USA*

[2]*Pfizer- Inc., Collegeville- PA, USA*

Objectives: Worldwide dissemination of Gram-negative bacteria producing extended-spectrum b-lactamases (ESBLs) has led to increased use of carbapenems and, in turn, the emergence of carbapenem-resistant *Enterobacteriaceae* (CRE). The Tigecycline European Surveillance Trial (TEST) monitors the activity of tigecycline and other antimicrobials against clinically-relevant pathogens collected globally. This study reports the incidence of CRE in TEST isolates collected in Europe in 2013 and the b-lactamase content of a subset of organisms.

Methods: Non-duplicate clinical isolates were collected from defined infection sites (e.g. respiratory tract, urine, skin, wound) and identified to the species level. Antibiotic susceptibility testing was performed by the local laboratory using CLSI broth microdilution and supplied panels and interpreted using EUCAST breakpoints. Isolate identification and meropenem non-susceptibility were confirmed at IHMA, Inc. Meropenem non-susceptible (MEM-NS; MIC > 2 mg/L) isolates were molecularly characterised for genes encoding ESBLs, carbapenemases and AmpC b-lactamases.

Results: 9712 *Enterobacteriaceae* were collected from sites in 13 European countries in 2013. Of these, 291 isolates (3.0%) were MEM-NS. A subset of 136 isolates (7 *Citrobacter* spp., 25 *Enterobacter* spp., 2 *Escherichia coli*, 3 *Klebsiella oxytoca*, 97 *K. pneumoniae*, and 2 *Serratia marcescens*) collected in Belgium (6), Croatia (4), Germany (8), Ireland (2), Italy (91), Portugal (3), Romania (1), and Spain (21) were molecularly characterised. The susceptibilities of CRE isolates carrying serine carbapenemases (KPC or OXA-48), metallo-b-lactamases (MBLs), or ESBLs, plasmid-encoded/ inducible AmpC b-lactamases, and presumed changes in membrane permeability are shown below.

	TGC (%S|I|R; MIC_{90})[1,2]	MEM (%S|I|R; MIC_{90})	TZP (%S|I|R; MIC_{90})	LVX (%S|I|R; MIC_{90})
All (9712)	92.3|5.3|2.5; 1	97.0|0.9|2.1; 0.25	80.2|4.3|15.5; 64	77.1|2.0|20.9; >8
MEM-NS (291)	66.3|26.8|6.9; 2	0|28.5|71.5; >16	7.6|3.1|89.4; >128	16.2|3.1|80.8; >8
KPC (82)	61.0|29.3|6.1; 2	0|2.4|97.6; >16	0|0|100; >128	6.1|2.4|91.5; >8
OXA-48 (7)	57.1|14.3|28.6	0|71.4|28.6	0|0|100	14.3|0|85.7
MBL (21)	57.1|28.6|14.3; 4	0|71.4|28.6; 16	0|0|100; >128	23.8|4.8|71.4; >8
MBL+OXA-48 (1)	0|100|0	0|0|100	0|0|100	0|0|100
ESBL (6)	83.3|0|16.7	0|83.3|16.7	0|0|100	0|0|100
AmpC (19)[3]	89.4|5.3|5.3; 2	0|73.7|26.3; >16	31.6|15.8|52.6; >128	47.4|5.3|47.4; >8

[1]TGC, tigecycline; MEM, meropenem; TZP, piperacillin-tazobactam; LVX, levofloxacin; %S|I|R; percent of isolates susceptible|intermediate|resistant to the indicated agent. MIC_{90} not provided if n<10.

[2]EUCAST 2014 S|I|R breakpoints: TGC (1≤|2|≥4), MEM (2≤|4-8|≥16), TZP (8≤|16|≥32), LVX (1≤|2|≥4).

[3]Includes *Citrobacter* spp., *Enterobacter* spp., and *S. marcescens* with intrinsic inducible chromosomal AmpC enzymes but no detected plasmid-encoded b-lactamase.

Conclusions: Tigecycline was more active *in vitro* against CRE than MEM, TZP, or LVX, with 66% of MEM-NS isolates inhibited at ≤1 mg/L. Isolates carrying carbapenemases (81.6% of those characterised) displayed decreased susceptibility to TGC relative to those harboring other b-lactamases in combination with presumed alterations in permeability – however, TGC was still more potent against these isolates than other agents tested. Tigecycline continues to display significant *in vitro* activity against *Enterobacteriaceae* that are increasingly difficult to treat using other classes of agents.