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O0124 Dissemination of carbapenem-resistant, carbapenemase non-producing and carbapenemase-producing Pseudomonas aeruginosa in Germany

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Background: *Pseudomonas aeruginosa* (PAE) is a leading nosocomial Gram-negative pathogen, which is often multi-drug resistant. Carbapenems (e.g., imipenem [IPM], meropenem [MEM]) are used commonly to treat infections caused by PAE. Mechanisms of resistance to carbapenems include production of a carbapenemase (CP) (mostly a metallo-beta-lactamase [MBL]), overproduction of the efflux pumps, overproduction of the AmpC BL, and reduced porin expression. We aimed to determine i) the dissemination of carbapenem-resistant, CP non-producing and CP-producing isolates among PAE, and ii) the in vitro activity of ceftolozane/tazobactam (C/T) against carbapenem-resistant isolates.

Materials/methods: 986 PAE collected in 20 laboratories in Germany from January 2016 to April 2017 were included. Isolates were recovered from patients with bloodstream infections, lower respiratory tract infections, intraabdominal infections or urinary tract infections. Susceptibility testing was performed with the broth microdilution method according to the standard ISO 20776-1 at a central laboratory. Microtitre plates containing the antibiotics in a dehydrated form were purchased from Merlin Diagnostika (Bornheim, Germany). EUCAST breakpoints (v. 7.1) were applied for interpretation of MICs. Genetic testing on the CP was performed at the German National Reference Laboratory for Multidrug-resistant Gram-negative Bacteria.

Results: 34% of the isolates were obtained from patients on intensive care wards. Susceptibility and resistance rates of IPM, MEM, C/T and other antipseudomonal drugs are presented in the Table. 679/986 (68.9%) PAE were susceptible to both IPM and MEM, while 174 (17.6%) were carbapenem-resistant (i.e. resistant to either drug or both drugs). 75/986 (7.6%) isolates showed resistance to IPM and MEM. A CP was detected in 25 isolates. Among these, 24 expressed one CP and one isolate two CPs. MBLs detected were VIM-1 (n=4), VIM-2 (n=12), VIM-11 (n=1), NDM-1 (n=2), IMP-1 (n=1), IMP-7 (n=2) and an unknown MBL (n=1). Three isolates harbored a GES variant. C/T at 4 mg/l inhibited 142 of the 174 (81.6%) carbapenem-resistant isolates, 140 of the 149 (94.0%) carbapenem-resistant, CP non-producing isolates, but none MBL-producing isolate, as expected.

Conclusions: Overall, 2.5% of the PAE harbored a CP, while 15.1% were carbapenem-resistant, CP non-producing isolates. Based on these findings, C/T seems to be useful for empiric treatment of PAE infections.

Table: Susceptibility of *Pseudomonas aeruginosa* isolates towards antipseudomonal agents (n=986)

Antibacterial agent	Isolates inhibited at MIC (mg/l)										%S	%R
	≤0.12	0.25	0.5	1	2	4	8	16	32	>32		
Imipenem	4	19	200	376	106	45	110	85	19	22	76.1	12.8
Meropenem	84	214	207	120	95	69	74	76	20	27	73.0	12.5
Ceftolozane/ tazobactam		48	582	246	56	18	3	2	2	29	96.3	3.7
Ceftazidime		3	10	123	416	199	81	51	45	58	84.4	15.6
Cefepime	1	2	8	128	342	224	138	83	34	26	85.5	14.5
Ciprofloxacin	388	215	117	65	51	36	30	34	35	15	73.0	27.0
Amikacin		12	45	253	452	138	44	15	9	18	95.7	2.7
Tobramycin	259	534	89	29	10	7	12	12	11	23	94.1	5.9
Colistin			12	186	665	106	10	4	1	2	87.5	12.5*

*Determination of the colistin MIC was repeated for 24 isolates with frozen microtitre plates containing the antibiotics. Repeated MICs were almost always one dilution step lower when compared with the MICs of plates containing the antibiotics in a dehydrated form. Hence, the rate of colistin resistance is more likely <2%.