Poster No.

P0326

Prevalence of multidrug resistance among bacterial pathogens obtained from patients in hospitals and the role of tigecycline: results of the PEG 2013 study

Michael Kresken[1,2*] Barbara Körber-Irrgang[1], Dieter Hafner[3], Martin Kaase[4], Yvonne Pfeifer[5], Franziska Layer[5], Ingo Klare[5], Guido Werner[5], Harald Seifert[6], and Working Party "Antimicrobial Resistance" of the Paul-Ehrlich-Society for Chemotherapy[§]

[1] Antiinfectives Intelligence GmbH, Rheinbach, Germany; [2] University of Applied Sciences, Cologne, Germany; [3] Institute of Pharmacology and Clinical Pharmacology, Heinrich-Heine-University, Düsseldorf, Germany; [4] Ruhr University Bochum; Faculty of Medicine; Department for Medical Microbiology, Bochum, Germany; [5] Robert Koch Institute; Wernigerode Branch, Wernigerode, Germany; [6] Institute of Medical Microbiology, Immunology and Hygiene; University of Cologne, Cologne, Germany

*Contact information (presenting author)

Michael Kresken, PhD
Antiinfectives Intelligence GmbH
Campus of the University of Applied Sciences
Von-Liebig-Straße 20
53359 Rheinbach
Germany

Telefon: + 49-2226-908-912
Fax: +49-2226-908-918

E-mail: michael.kresken@antiinfectives-intelligence.de

26th ECCMID
Amsterdam, Netherlands
9–12 April 2016

Background

The treatment of infectious diseases has increasingly been threatened by multidrug-resistant (MDR) pathogens such as extended-spectrum β-lactamase (ESBL)-producing *Escherichia coli* (ECO) and *Klebsiella* species, carbapenem-resistant (CR) Enterobacteriaceae, *Pseudomonas aeruginosa* (PAE), and *Acinetobacter baumannii* (ABA) as well as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant (VR) *Enterococcus* species (1, 2). Tigecycline has been shown to be active against many Gram-negative and Gram-positive bacteria, except PAE and *Proteeae* (3-5). The objectives of the present study were i) to determine the prevalence of MDR pathogens among clinical isolates obtained from hospital patients in 2013, and ii) to assess the activity of tigecycline against these MDR pathogens.

Material/methods

In a surveillance study conducted by the Paul-Ehrlich-Society (PEG) between October and December 2013, 25 laboratories across Germany (n=22), Switzerland (n=2) and Austria (n=1) were requested each to collect 240 non-duplicate isolates. Isolates were identified by MALDI -TOF. Minimum inhibitory concentrations (MICs) were determined by broth microdilution (BMD) according to ISO 20776-1 (6). Breakpoints (BP) approved by EUCAST (v. 5.0) were applied, if available (7). ESBL testing was performed according to CLSI criteria (8). CR in Gram-negative bacteria was defined as resistance to imipenem and/or meropenem. Molecular methods were those described previously (9-13). Data from the following bacterial species was evaluated: ABA, *A. pittii*, ECO, *Klebsiella oxytoca* (KOX), *K. pneumoniae* (KPN), PAE, *Proteus mirabilis* (PMI), *Enterococcus faecalis* (EFS), *E. faecium* (EFM), and *S. aureus* (SAU).

Results

The data of 3.646 isolates was analyzed. Twenty-four percent derived from patients in intensive care units (ICU). Fifty-eight percent of the patients were male. Data on the prevalence of MDR pathogens among the bacterial species analyzed is given in **Table 1** and data on the prevalence of resistance determinants or epidemiological subtypes is shown in the **Figure**. Susceptibility data to tigecycline for the MDR pathogens of nine species is given in **Table 2**.

§ Members of the Working Party

The list of members is shown on the website of the Paul-Ehrlich-Society for Chemotherapy (http://www.p-e-g.org/econtext/resistenzdaten).

Acknowledgements

The authors are grateful to Pfizer Pharma GmbH for supporting the study by a grant.

Conclusions

In comparing the results from the present surveillance with those from the PEG study conducted in 2010, the rate of ESBL-ECO decreased (-2.5%), while the rate of ESBL-KPN increased (+2.7%). CR was still low in Enterobacteriaceae species, >10% in PAE (-6%), and nearly 30% in ABA (+10%) (14). As for the Gram-positive species, VR increased in EFM (+3.9%), while the prevalence of MRSA decreased (-3.2%). The resistance situation of tigecycline did not change for any of the tested species.

References

1. Izadpanah M and Khalili H. 2015. J Res Pharm Pract. 4:105-14.
2. Basak S et al. 2016. J Pathog. 2016:4065603. doi: 10.1155/2016/4065603.
3. Simner PJ et al. 2011. Diagn Microbiol Infect Dis. 69: 326-334.
4. Sader HS et al. 2011. Diagn Microbiol Infect Dis. 69: 223-227.
5. Kresken M et al. 2011. Eur J Clin Microbiol Infect Dis. 30: 1095-103.
6. ISO 20776-1: 2006. German version EN ISO 20776-1:2006. Beuth-Verlag, Berlin.
7. European Committee on Antimicrobial Susceptibility Testing (EUCAST). 2015. Breakpoint tables v 5.0.
8. Clinical and Laboratory Standards Institute (CLSI). 2015. CLSI document M100-S25. Wayne, PA, USA.
9. Eller C et al. 2013. J Antimicrob Chemother. 68:1978-1981.
10. Kaase M et al. 2014. J Clin Microbiol. 52:1893-1897.
11. Maurya AP et al. 2014. Indian J Med Res. 140:565-567.
12. Strommenger B et al. 2008. J. Clin Microbiol. 46:574-581.
13. Werner G et al. 2007. Int J Med Microbiol. 298:515–527.
14. Kresken M et al. 2013. Antiinfectives Intelligence GmbH, Rheinbach, Germany

Disclosures

MK is a partner and CEO of Antiinfectives Intelligence GmbH, a research organization providing services to pharmaceutical companies. BK-I is head of laboratory of Antiinfectives Intelligence GmbH. DH, MKa, YP, FL, IK and GW declare no competing interests. H.S. has received grants or research support from the Bundesministerium für Bildung und Forschung (BMBF), Germany, the German Centre for Infection Research (DZIF), Basilea, Novartis and Pfizer, has been a consultant for Astellas, AstraZeneca, Basilea, Cubist, Novartis, Pfizer, Tetraphase, and The Medicines Company, and has received payments for lectures from MSD, Novartis and Pfizer. S.R. has received payments for lectures from Pfizer and MSD Sharp & Dohme, as well as travel support from Astellas and MSD Sharp & Dohme.

Table 1: Prevalence of resistance phenotypes

Bacterial species (no. tested)	Resistance phenotype % (n)			
	ESBL	Resistant to cabapenems	MRSA	VR
E. coli (596)	14.9 (89)	0 (0)		
K. pneumoniae (304)	17.4 (53)	1.3 (4)		
K. oxytoca (132)	8.3 (11)	0 (0)		
P. mirabilis (216)	2.3 (5)	0 (0)		
A. baumannii (88)	n.d.	30.7 (27)[a)]		
A. pittii (85)	n.d.	1.8 (1)		
P. aeruginoasa (733)	n.d.	11.3 (83)		
S. aureus (748)			13.5 (101)	
E. faecium (320)				16.6 (53)
E. faecalis (424)				0.2 (1)

Abbreviations: n.d., not determined. [a)] Revised data compared to abstract

Table 2: *In vitro* activity of tigecycline against MDR bacterial pathogens

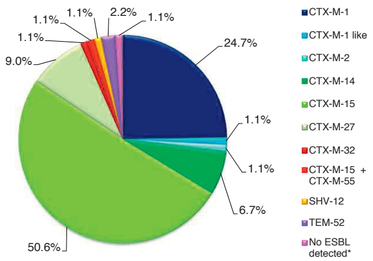
Bacterial species, phenotype (no. tested)	MIC_{50} (mg/L)	MIC_{90} (mg/L)	%-S	%-I	%-R
E. coli, ESBL+ (89)	0.25	0.5	100	0	0
K. oxytoca, ESBL+ (11)	0.5	1	100	0	0
K. pneumoniae, ESBL+ (53)	0.5	1	94.3	3.8	1.9
P. mirabilis, ESBL+ (5)	4	8	0	20.0	80.0
K. pneumoniae, CR (4)	1	1	100	0	0
A. baumannii, CR (27)[a)]	1	2	No EUCAST BP available		
P. aeruginoasa, CR (83)	Not determined				
S. aureus, MR (101)	0.125	0.25	100	–	0
E. faecium, VR (53)	0.063	0.125	96.2	1.9	1.9
E. faecalis, VR (1)	–	–	100	0	0

Abbreviations: ESBL+, ESBL phenotype; CR, carbapenem-resistant; MR, methicillin-resistant; VR, vancomycin-resistant; BP, breakpoint; [a)] Revised data compared to abstract

Figure: Prevalence of resistance determinants or epidemiological subtypes among most common resistance phenotypes

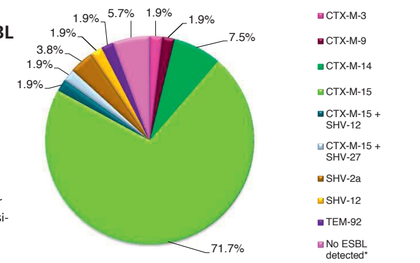
Dissemination of ESBL variants among *E. coli* isolates with an confirmed ESBL phenotype (n=89)

* An ESBL of the CTX-M-, SHV- or TEM-type according to Bush classification could not be detected.



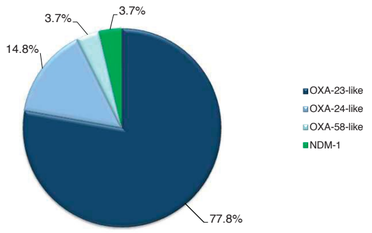
Dissemination of ESBL variants among *K. pneumoniae* isolates with an confirmed ESBL phenotype (n=53)

* An ESBL of the CTX-M-, SHV- or TEM-type according to Bush classification could not be detected.

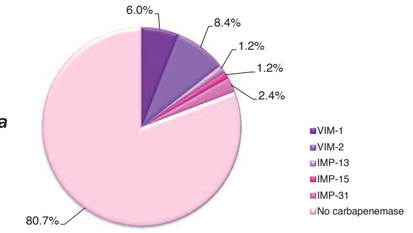


Dissemination of carbapenemase variants among cabapenem-resistant *A. baumannii* isolates (n=27*)

* Revised data compared to abstract

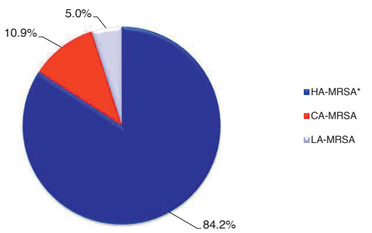


Dissemination of carbapenemase variants among cabapenem-resistant *P. aeruginosa* isolates (n=83)



Dissemination of epidemiological subtypes among MRSA isolates (n=101)

All MRSA harboured the *mecA* gene. * Most prevalent *spa*-types were t003 (37.6%) and t032 (27.1%).



Dissemination of epidemiological subtypes among VR *E. faecium* (n=53)