Session: 3b. Resistance surveillance and epidemiology: Gram-negatives
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Multidrug resistance to oral antibiotics among *Escherichia coli* urine isolates from patients at outpatient departments in Germany and *in vitro* activity of nitroxoline, Germany, 2010-2019

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Third party affiliation:
Study Group ‘Antimicrobial Resistance’ of the Paul-Ehrlich-Society for Chemotherapy

Disclosures

- The authors declare the following real or perceived conflicts of interest during the last 3 years in relation to this presentation: MK is a partner and CEO of Antiinfectives Intelligence GmbH (AI), a research organisation providing services to pharmaceutical companies; EW is an employee of AI.
- This study was funded in part by MIP Pharma GmbH.

32nd European Congress of Clinical Microbiology & Infectious Diseases (ECCMID)
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Background

Escherichia coli is the leading pathogen of urinary tract infections (UTI).[1] Resistance to oral antibiotics in *E. coli* and the emergence of extended-spectrum beta-lactamases (ESBLs) have complicated the management of UTI.

Nitroxoline (5-nitro-8-hydroxyquinoline) is an antibiotic used in the treatment of acute or recurrent UTI caused by *E. coli*.

The objectives of this study were to evaluate i) the development of multidrug-resistant strains among uropathogenic *E. c*oli from outpatients and ii) the susceptibility of these isolates to nitroxoline.

Methods

Isolates were collected prospectively at 21 laboratories, in each case over a 3 to 6 month period of four surveillance studies.

Verification of species identification and susceptibility testing were performed at a reference laboratory.

MICs were determined by broth microdilution according to the ISO-standard, and interpreted by EUCAST criteria (v.12.0).[2]

Antibiotics tested were amoxicillin, amoxicillin-clavulanic acid, cefuroxime, cefpodoxime, ciprofloxacin, trimethoprim, fosfomycin, nitrofurantoin, nitroxoline.

Isolates with a confirmed ESBL phenotype were characterized by PCR amplification and sequencing of beta-lactamase genes.[3]

References

1. Naber KG et al., Eur Urol 2008;54(5):1164-75
2. The European Committee on Antimicrobial Susceptibility Testing (EUCAST). 2022. Breakpoint tables for interpretation of MICs and zone diameters, Version 12.0
3. Schuster CF et al., J Antimicrob Chemother 2021; https://doi.org/10.1093/jac/dkab407

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Results

1.673 isolates were collected, of which 33 (7.9%), 13 (3.1%), 32 (7.6%) and 46 (11.0%) produced an ESBL in 2010/11, 2013/14, 2016/17, and 2019/20, respectively.

For each study interval, about half of the isolates were fully susceptible, while 6.4%, 2.7%, 6.2% and 3.6% showed combined resistance to amoxicillin, cefuroxime, ciprofloxacin and trimethoprim. Individual resistance rates are given in the Table.

Genes encoding CTX-M-ESBLs were confirmed for 32, 13, 31 and 46 isolates, respectively.

Nitroxoline was tested against 891 isolates, including the total number of isolates collected in 2010/11, and a subset of isolates, comprising all isolates from men and women aged 18-45 yrs, and the resistant isolates from women >45 yrs, each collected in 2013/14 (n=224) and 2019/20 (n=248).

Resistance to nitroxoline was not observed.

Table: Resistance rates (%) of *E.coli* isolates

Antibacterial agent	Breakpoint (mg/L) [1]	Study interval				Trend [2]
		2010/11 (n=419)	2013/14 (n=414)	2016/17 (n=420)	2019/20 (n=420)	
Resistance to at least one drug	Not applicable	52.3	48.1	51.9	52.4	0.5423
Amoxicillin	> 8	44.2	41.5	42.1	44.8	0.7471
Amoxicillin-clavulanic acid	> 8	33.2	34.5	15.0	18.3	< 0.0001
Cefuroxime	> 8	10.0	5.1	9.8	12.4	0.0031
Cefpodoxime	> 1	8.4	4.3	9.5	12.1	0.0008
Ciprofloxacin	> 0,5	21.0	14.5	17.9	11.2	0.0008
Trimethoprim	> 4	34.1	25.8	27.9	29.8	0.0565
Fosfomycin	> 8	5.0	3.4	6.7	7.4 [3]	0.0569
Nitrofurantoin	> 64	0.7	1.0	1.2	1.2	0.8874
Nitroxoline [4]	> 16	0	0	Not tested	0	Not calculated

[1] EUCAST breakpoints for all orally administered antibiotics. [2] Chi-squared-test for trend. [3] Resistance was confirmed by agar dilution. [4] See text for the isolates tested.

Conclusions

- Overall, the degree of resistance to oral antibiotics in uropathogenic *E. coli* from outpatients remained stable between 2010 and 2019.
- The frequency of resistance to the individual drugs, however, varied over time.
- Resistance rates were low for fosfomycin and nitrofurantoin, and there were no isolates with resistance to nitroxoline.

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