P0243
Poster Session I
Antibacterial drug activity and interactions in Gram-negative bacteria

IN VITRO ACTIVITY OF NITROXOLINE AGAINST UROPATHOGENS OTHER THAN ESCHERICHIA COLI AND IMPACT OF PH

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Objectives: Against the background of rising antimicrobial resistance (R) in E. coli (ECO) and other uropathogens, nitroxoline (5-nitro-8-hydoxyquinoline, NTX) has become an attractive drug for the treatment of acute and recurrent urinary tract infections (UTI). In a previous study, NTX showed uniform in vitro activity against a German collection of ECO urine isolates, irrespective of the R profile (Kresken & Körber-Irrgang, 23th ECCMID, Berlin, Germany, April 27-30, 2013: O311). The objectives of the present study were i) to evaluate the in vitro activity of NTX in comparison to nitrofurantoin (NIT) against various other uropathogens and ii) to define the relationship between pH and the in vitro activity of NTX.

Methods: Susceptibility testing was performed according to the broth microdilution method according to the standard ISO 20776-1. Using the standard susceptibility testing conditions, the activites of NTX and NIT were determined against a panel of 201 organisms belonging to 5 bacterial species: P. mirabilis (PMI, n=101), K. pneumoniae (KPN, n=30), M. morganii (MMO, n=30), P. vulgaris (PVU, n=20), and S. saprophyticus (SSA, n=20). In addition, MICs of NTX and NIT were determined against 27 selected strains (including ECO) at pH values of 5.5, 7.4 and 8.0 (see Table).

Results: MIC-50/90 values (mg/L) of NTX and NIT for PMI, KPN, MMO, PVU, and SSA were 8/8 and 128/128, 4/8 and 64/128, 4/8 and 32/32, 4/4 and 64/64, and 8/8 and 16/16, respectively. The highest observed MICs were 8 mg/L for NTX and 512 mg/L for NIT. MICs of both drugs determined at the three pH values are given in the Table. NTX activity was increased at the acidic pH and slightly decreased at the alkaline pH, compared to activity at pH 7.4. However, the magnitude of difference in activity varied between species, with the greatest shift seen in PMI and staphylococci. NIT also tended to be most active at the acidic pH.

Conclusions: NTX showed almost identical in vitro activity against the 5 bacterial species tested, was up to 16-fold more active than NIT, and exhibited optimal antibacterial activity at low pH.

Table: MICs of NTX and NIT at pH 5.5, 7.4 and 8.0 (mg/L)

Species (n)	pH 5.5		pH 7.4		pH 8.0	
	NTX	NIT	NTX	NIT	NTX	NIT
E. coli (9)	0.5 – 4 (2)*	16 – 128 (16)	2 – 8 (2)	16 – 256 (16)	2 – 8 (4)	16 – 256 (32)
*K. pneumo*niae (9)	2 – 32 (4)	16 – 512 (64)	2 – 32 (8)	16 – 512 (64)	2 – 32 (8)	32 – 512 (64)
K. oxytoca (1)	4	32	8	32	16	64
P. mirabilis (3)	0.25 – 0.5	32 – 64	8	128	8 – 16	256
S. aureus (2)	0.5 – 2	16	2 – 8	16	8	32
S. saprophyticus (3)	1 – 4	16	8 – 16	16	16 – 32	16

*median MIC in parentheses