P0800

Paper Poster Session IV

Urinary tract infection

Susceptibility of Gram-negative pathogens isolated from patients with community-acquired urinary tract infections in three European countries

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Objectives: Ceftibuten, an oral third-generation cephalosporin (3GC) licensed in the 1990ies, has been shown to possess *in vitro* activity against Gram-positive and Gram-negative pathogens including *Escherichia coli* (ECO) and other Enterobacteriaceae. Since the introduction of ceftibuten into the market, increased rates of acquired resistance to a variety of antibiotics (including 3GC) have complicated the management of community-acquired UTI (CA-UTI). It is therefore of interest to investigate the current prevalence of resistance to ceftibuten among Gram-negative pathogens causing CA-UTI. As the resistance epidemiology may differ between regions and countries, the study aimed to investigate the occurrence of resistant isolates in three European countries.

Methods: Six laboratories, two each in Belgium, Germany and Spain, participated in the study. Each site was requested to send 200 clinical isolates. These were 90 ECO, 40 *Klebsiella* spp., 40 *Proteus* spp., and 30 other *Enterobacteriaceae*. Only first isolates obtained from patients with CA-UTI were included. MICs were determined using broth microdilution according to the standard EN ISO 20776-1:2006. Breakpoints were those defined by EUCAST (Version 4.0, 2014).

Results: From August 2013 to January 2014 a total of 1,190 isolates were collected. 96% of the isolates were obtained from patients in ambulatory care. Patients' mean age was 56.8 years (range <1-96 years). 937 (78.7%) isolates were obtained from females.

The in vitro activity of ceftibuten against ECO (n=538, $MIC_{50/90}$ ≤0.25/0.5 mg/l) was comparable to ceftriaxone ($MIC_{50/90}$ ≤0.25/≤0.25 mg/l). Highest resistance rates in ECO were observed for amoxicillin-clavulanic acid (46.8%), the fluoroquinolones (ciprofloxacin, 23.4%) and trimethoprim-sulfamethoxazole (21.4%), while resistance to fosfomycin and nitrofurantoin was rare (<1.5%). Ceftibuten (MIC_{90} ≤0.25 mg/l) showed also good activity against *Proteus mirabilis* (PMI, n=234) and *Klebsiella pneumoniae* (KPN, n=196). 7.1%, 5.6% and 0.4% of the ECO, KPN and PMI isolates, respectively, showed an ESBL phenotype.

In general, resistance was most common in isolates from men and elderly women. Resistance to ciprofloxacin in ECO isolates from women gradually increased with age. In all age groups, resistance in ECO to ceftibuten (3.5-6.6%) was less frequent than resistance to other cephalosporins.

Resistance to 3GC, fluoroquinolones and trimethoprim-sulfamethoxazole in ECO were lowest among isolates from Belgium (**Table**), while geographical variations in the prevalence of resistance among KPN were noted only for fosfomycin. Resistance to fluoroquinolones in PMI was more frequently distributed among isolates from Belgium than Germany or Spain.

Conclusion: Resistance to oral antibiotics that are commonly used as first-line treatment of UTI in the ambulatory sector, seems to be widespread in Gram-negative pathogens from patients with CA-UTI. However, regional differences as well as variations in the prevalence of resistance between patient subgroups must be considered when empirical treatment of UTI is prescribed. Ceftibuten retained excellent activity against the majority of Enterobacteriaceae isolates, with resistance rates below 7% for ECO, KPN and PMI.

Table: Susceptbility of ECO to ceftibuten and comparators by country

Antibacterial agent	Belgium (n=178)		Germany (n=179)		Spain (n=181)	
	S (%)	R (%)	S (%)	R (%)	S (%)	R (%)
Amoxicillin-clavulanic acid	62.9	37.1	62.6	37.4	34.3	65.7
Cefuroxime (oral)	94.4	5.6	87.2	12.8	83.4	16.6
Cefixime	96.1	3.9	89.9	10.1	86.7	13.3
Cefpodoxime	95.5	4.5	89.9	10.1	86.2	13.8
Ceftibuten	97.8	2.2	91.1	8.9	92.3	7.7
Ceftriaxone	96.6	3.4	90.5	9.5	89.5	10.5
Ciprofloxacin	87.1	12.9	82.7	17.3	59.7	39.8
Fosfomycin	98.9	1.1	100	0	97.2	2.8
Nitrofurantoin	99.4	0.6	99.4	0.6	100	0
Trimethoprim-sulfamethoxazole	85.4	14.6	80.4	18.4	68.5	30.9