P0344. Antimicrobial Resistance Patterns of Gram-negative Urinary Tract Pathogens Isolated from Outpatients in Russia

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ABSTRACT

Objectives: To study etiological structure of urinary tract infection (UTI) and antimicrobial resistance of its pathogens isolated from outpatients in 3 geographically distant areas of Russia.

Methods: Bacterial strains: A total of 299 consecutive gram-negative isolates were collected from the urine samples of outpatients with UTI. All participating medical centers in Moscow, Novosibirsk and Smolensk provided an equal number of strains. The reference strains used for susceptibility determination were E.coli ATCC25922 and P.aeruginosa ATCC27853. The MICs were determined by agar dilution method for gentamicin (GM), ampicillin (AM), nitrofurantoin (FT), nitroxoline (NL), trimethoprim (TM), trimethoprim/sulfamethoxazole (TS), pipemidic acid (PA), nalidixic acid (NA), norfloxacin (NX) and ciprofloxacin (CI). Interpretation of susceptibility testing results was performed using the breakpoints currently recommended by NCCLS. Susceptibility to NL was interpreted according to SFM standards.

Results: All isolated strains: E.coli (90.6%), K.pneumonia (6.4%), K.oxytoca (1%), P.mirabilis (1.7%) and P.vulgaris (0.3%) belonged to the Enterobacteriaceae family. The cumulative results of susceptibility testing are represented in the following table:

	GM	AM	FT	NL	TM	TS	PA	NA	NX	CI
% S	93.6	61.9	91.6	5.7	77.3	79.6	94	93	97.7	97.7
% I	0	0.7	3	94.3	0.7	1	0	0	0	0.3
% R	6.4	38	5.4	0.7	22.4	19.7	6.1	7.1	2.4	2

Conclusions: 1) E. coli was identified as the chief causative agents of UTI in outpatients. 2) The fluoroquinolones: NX and CI were the most active antimicrobial agents. 3) The highest percent of resistance was observed for AM and TS which were the most frequently prescribed antibiotics in Russia.

INTRODUCTION AND PURPOSE

Infections of the urinary tract are one of the most common infectious diseases diagnosed in outpatient. These infections are usually caused by Gram-negative bacteria most of which belong to the family *Enterobacteriaceae*. In most cases, the choice of antibiotics for the treatment of UTI is made empirically and should be based on the local antibiotic susceptibility data.

The currently available data on antibiotic susceptibility of uropathogenic strains in Russia are still incomplete. This led us to perform a study with the aim to determine the antimicrobial resistance profile of Gram-negative uropathogenic strains isolated from outpatients with UTI in different regions of Russia.

METHODS

Bacterial isolates collection and identification. In total, 299 gram-negative strains were collected from the urine samples of outpatients with UTI in four medical centers of Smolensk, Novosibirsk and Moscow. The microorganisms were identified using the API 20E system (BioMérieux, France).

Antibiotics. The 10 antibiotics included in the study were: gentamicin, pipemidic acid, nalidixic acid, norfloxacin, ciprofloxacin (KRKA, Slovenia), ampicillin, nitrofurantoin, trimethoprim, trimethoprim/sulfamethoxazole (SIGMA-ALDRICH, Germany) and nitroxoline (ALDRICH, USA).

Susceptibility testing. Minimum inhibitory concentrations (MICs) of antimicrobials were determined by agar dilution method on Mueller-Hinton agar (Becton Dickinson, USA). For each antimicrobial agent, the drug concentration range tested was as recommended by the NCCLS. Quality control was performed by testing *E.coli* ATCC 25922 and *P.aeruginosa* ATCC 27853. The overnight cultures were suspended to achieve an optical density of inoculum equal to 0.5 McFarland standard and inoculated onto the surface of each test plate using the Automated Multipoint Inoculator (Mast Diagnostics, UK). The results were read after 18 h of incubation. Interpretation of results was performed using the breakpoints currently recommended by NCCLS. Susceptibility to NL was interpreted according to SFM standards.

RESULTS

Microorganisms

The species distribution of urinary tract pathogens is represented in Figure 1. The identified species, in order of frequency, were *E.coli* (90.6%), *K.pneumonia* (6.4%), *K.oxytoca* (1%), *P.mirabilis* (1.7%) and *P.vulgaris* (0.3%). All isolated strains belonged to the *Enterobacteriaceae* family.

Activity of antimicrobial agents

Figure 2 shows the cumulative results of susceptibility testing of uropathogens. The antimicrobial activity of fluoroquinolones (NX and CI) was superior to that of all other drugs tested. The corresponding rates of resistance were 2.4% and 2.3% respectively. The early quinolones (NA and PA) were at least 2.5 - 3 times less effective in terms of the percentage of resistance. *In vitro* activity of these drugs was generally comparable to that of GM (6.4% resistance) and FT (8.4% resistance). The following 4 drugs were identified as the least effective against urinary isolates: NL, AM, TM and TS. Approximately 23% of all isolates were resistant to TM. Activity of this drug in combination with sulfamethoxazole was not significantly high with very little (11.8%) of TM-resistant isolates being susceptible to TS. Only 66.8% of *E.coli* isolates were susceptible to AM. The rate of resistance to AM among all tested strains was 38.7%. Interpretation of susceptibility to NL using the SFM standards does no seems to be satisfactory, because the majority of isolates (94.3%) had the MICs corresponding to the intermediate level of resistance.

The data on antimicrobial activity of various tested drugs against *E.coli* isolates as the most frequent cause of UTI are summarised in Table 1.
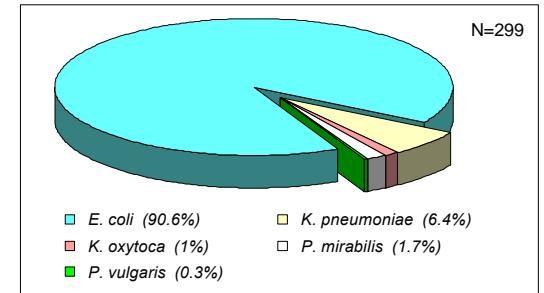

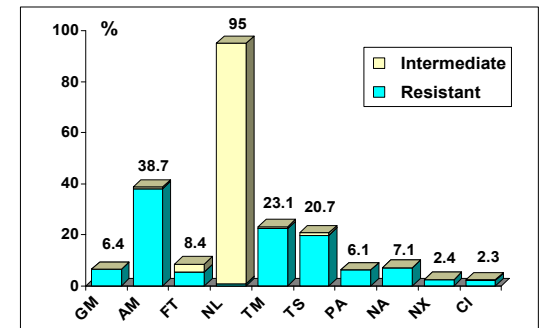**Figure 1.** Species distribution of Gram-negative urinary tract pathogens.

- E. coli (90.6%)
- K. pneumoniae (6.4%)
- K. oxytoca (1%)
- P. mirabilis (1.7%)
- P. vulgaris (0.3%)

N=299

Figure 2. Resistance of urinary tract pathogens to the commonly used antimicrobial agents.

Table 1. Antimicrobial potency of various drugs against urinary *E.coli* isolates.

	GM	AM	FT	NL	TM	TS	PA	NA	NX	CI
Range, mg/L	0.125-16	0.5-64	1-128	0.125-128	0.25-32	0.25-32	0.125-16	0.125-16	0.125-16	0.125-16
% R+I	5.9	33.3	2.9	94.1	20.3	18.4	4.4	5.5	2.6	2.6
MIC$_{50}$, mg/L	0.5	4	16	4	0.5	0.25	2	2	0.125	0.125
MIC$_{90}$, mg/L	1	128	32	8	64	64	4	4	0.25	0.125

CONCLUSIONS

- *E.coli* isolates were the most frequent cause (90.6%) of UTI in outpatients.
- In terms of antimicrobial potency the most troublesome agents were AM (33.3% resistance among *E.coli*) and TS (20.7% resistance).
- The fluoroquinolones: NX and CI were the most active antimicrobial agents.