Journal Of Harmonized Research (JOHR)

Journal Of Harmonized Research in Medical & Health Sci.
2(2), 2014, 31-36

ISSN 2395 – 6046

Original Research Article

ANTIBIOTIC RESISTANCE RATES OF *ESCHERICHIA COLI* AND *KLEBSIELLA SPP.* STRAINS ISOLATED FROM URINARY TRACT INFECTIONS

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Abstract: Introduction: The aim of this study is to investigate the resistance profiles of *E.coli* and *Klebsiella* spp. isolates which constitute a major part of uropathogen gram-negative bacteria isolated from urine cultures, examining by distinguishing inpatients and outpatients. **Methodology:** Urine samples were incubated in aerob conditions for 18-24 hours in 35 ºC by spreading blood agar and Eosin Methylene Blue agar with quantative method. Single type colonies of 10^5 CFU/mL and above were regarded as positive. Antibiotic sensitivity tests were made by VITEK 2 Compact (BioMerieux-France) system identification and antibiogram cards. **Result:** In 3.777 of 15.000 urine samples (25.1%), the most isolated among the reproduced gram-negative bacteria were 52.1% *E.coli*, 13.74% *Klebsiella* spp. isolates. Antibiotics *E.coli* and *Klebsiella* spp. isolates taken from inpatient and outpatients are most sensitive to were determined as imipenem (IPM) and amikacin (AMC). Phosphomycine and Nitrofurantoin were determined as the antibiotics in which the sensitivity was highest after IPM and AMC in especially *E.coli* isolates. **Conclusion:** Phosphomycine and nitrofurantoin usage in urinary system infections caused by these isolates was considered as appropriate choice. While the empirical treatments of these infections were made valid, regional resistance rates should be considered separately for policlinic and service patients.

Keywords: *E.coli*, *Klebsiella spp.*, Antimicrobial sensitivity

Introduction

Although urinary tract infections (USI) caused by gram-negative bacteria from the Enterobacteriaceae family mostly show a clinically asymptomatic transfer, they may also cause very severe conditions. *E. coli* and *Klebsiella* spp. isolates constitute an important part of these uropathogen gram-negative bacteria. These infections which belong to the infection group commonly seen in almost all parts of the society cause severe labour force and economical loss in the society in addition to the mortality and morbidity they cause [1-3]. In

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Received on: May 2015
Accepted after revision: June 2015

order to minimalize the effects which may be caused by these infections on both the patient and the society, appropriate use of antibiotics which are among the keystones of treatment is vital. Antibiotic resistance profiles of uropathogen isolates of policlinic and service patients differ. In such a period in which antibiotic resistance increases due to using broad spectrum antibiotics inappropriately and widely, it is important to evaluate the valid changes in regional antibiotic selection which can be used in the empirical treatment of these patients [4-6]. Antibacterials to be preferred by clinicians according to these resistance results would contribute to prevent resistance problems which might develop in the future in addition to being more successful in treatment.

In order to provide more current data aim of this study is to investigate the resistance profiles of E.coli and Klebsiella . isolates which constitute a major part of uropathogen gram-negative bacteria isolated from urine cultures, examining by distinguishing inpatients and outpatients.

Material and Methods

Inpatients and outpatients who were sent to Amasya University Sabuncuoglu Serafettin Education and Research Hospital Microbiology laboratory between 2013 and 2014 with USI fore-diagnosis and bacteria culture reproduction results of the urinary samples sent were retrospectively evaluated. Culture results of 15.000 patients were examined in the study. After the urinary samples were accepted to the laboratory, blood agar and Eosin Methylene Blue agar were spread by the quantative method. The plates were incubated in aerob conditions in 35 ºC for 18-24 hours. At the end of the incubation bacteria belonging to one type of colonies of 10^5 cfu/ml and over were defined by conventional methods in the plates examined. Defining the undefinable micro organisms by these methods and antibiotic sensitivity tests were made by using VITEK 2 Compact (BioMerieux-France) system identification and antibiogram cards. Sensitivity results were evaluated according to Clinical and Laboratory Standards Institute (CLSI) criteria.

Results

A significant reproduction was detected in 3.777 of 15.000 urine samples included in the study (25.1%). 2313 of the samples these reproductions were present belonged to female (61.2%) and 1464 belonged to (38.8%) male patients. 995 (26.4%) of the samples in which significant reproduction was detected were isolated from service patients and 2782 from policlinic patients (73.6%). 3053 of these reproductions (80.8%) belonged to gram-negative bacteria and these reproducing gram-negative bacteria were detected as 1968 of *E.coli* (52.1%), 519 *Klepsiella* spp. (13.7%), 176 of *Pseudomonas spp*. (4.65%), 77 of *Proteus* spp. (2%), 125 of *Enterobacter* spp. (3.30%) and 54 of *Acinetobacter* spp. (1.4%) in order according to their isolation frequency (**Table 1).**

Table 1: Isolation frequencies of gram negative bacteria isolated from urine samples

Kinds of bacteria	(n)	%
E.coli	1968	%52.1
Klebsiella spp.	519	%13.7
Pseudomonas spp.	176	%4.7
Enterobacter spp.	125	%3.3
Proteus spp.	77	%2
Acinetobacter spp.	54	%1.4
Other gram negatives	134	%3.5
	3053	%80.8

n:number of isolates , %: Percentage

The antibiotics which have the least resistance for *E.coli* isolates isolated from the policlinic patients were determined as imipenem (IPM) (0%) and amikacin (AN) (0.2%), phosphomycine (FM) (1.26%) and nitrofurantoin (F) (235%) in order. And in *E.coli* isolates isolated from inpatients, no resistance against carbapenems and amikacin and phosphomycine (FM) resistance was found (2.6%) and nitrofurantoin (F) resistance was found (2.9%)(**Table 2).**

Table 2: Evaluating the antibiotic resistances of *E.coli* isolates.

Distrubution of patients	AMC (%)	AMP (%)	TPZ (%)	CXM (%)	CAZ (%)	GN (%)	AN (%)	CIP (%)	LEV (%)	SXT (%)	FM (%)	F (%)	IPM (%)
Outpatients(1563)	19.5	60.1	11.4	38.5	32.5	11.7	0.2	29.9	26.2	47.5	1.3	2.4	0
Inpatients (405)	19.6	64.9	7.4	42.8	42	15.4	0	41.4	33.3	48.1	2.6	2.9	0

N:number of isolates, %: Percentage, AMP:Ampisilline, AMC:Amoxicillin/clavulanic acid, TZP: Piperasillin/tazobactam,GN:Gentamycine,CXM:Cefuroxime,CAZ:Ceftazidime, IMP:Imipenem, AN:Amikacin, LEV:Levofloxacin, CIP:Ciprofloxacin, SXT:Trimethoprim/sulfamethoxazole, F:Nitrofurontoin FM:Phosphomycine

Antibiotics with lowest resistance ratios for *Klebsiella* spp. isolates isolated from policlinic patients were found AN (0%), IMP (0.1%) and levofloxacin (LEV) (2%) and antibiotics with lowest resistance ratios detected after AMC (2.6%) and IPM (3.3%) for *Klepsiella* spp. isolates isolated in inpatients were piperacillin/tazobactam (TPZ) (13.5%) and FM (13.2%)(**Table-3).**

Table 3: Evaluating the antibiotic resistances of Klebsiella spp. isolates.

Distrubution of patients	AMC (%)	AMP (%)	TPZ (%)	CXM (%)	CAZ (%)	GN (%)	AN (%)	CIP (%)	LEV (%)	SXT (%)	FM (%)	F (%)	IPM (%)
Outpatients(389)	22.2	99.2	22.9	28.3	29.9	10.8	0.0	10.1	2	22.8	13.2	16.1	0.1
Inpatients(130)	22.6	99.1	14.5	39.5	41.7	19.2	2.6	26.1	47.6	27.5	18.3	28.6	3.3

N:Number of isolates**, %:** Percentage**,** N:number of isolates, %: Percentage, AMP:Ampisilline, AMC:Amoxicillin/clavulanic acid, TZP: Piperasillin/tazobactam, GN:Gentamycine, CXM:Cefuroxime, CAZ:Ceftazidime, IMP:Imipenem, AN:Amikacin, LEV:Levofloxacin, CIP:Ciprofloxacin, SXT:Trimethoprim/sulfamethoxazole, F:Nitrofurontoin FM:Phosphomycine

Discussion:

Urinary tract infections which are among the most commonly seen infection groups on earth and most of which are caused by gram-negative bacteria are seen frequently in our country too. In our study regeneration was present in 25.1% of samples taken from patients who are considered to have USI. In addition to this, it was determined that 80.8% of the uropathogens we isolated belonged to gram-negative bacteria. It was observed that *E. coli* (52.1%) and *Klebsiella* spp (13.7%) isolates constitute an important part of the detected gram-negative bacteria. In a study made in Cerrahpasa Medical Faculty Hospital the isolated bacteria as infection factor from the urines of the patients were detected as 50.1% *E. coli*, 9.7% *Klebsiella spp*, 7.2% *Proteus* spp, 2.2% *Pseudomonas aeruginosa* and 2.2 *Enterobacter* spp. [7]. In a study by Sanlı *et al*. on urine cultures, the isolation ratios were detected *E.coli* (68.7%), *Klebsiella* spp.(12.5%) and *Proteus* spp.(2.7%) [8]. In our study, *E.coli* in 52.1%, *Klebsiella* spp. in 13.7%, *Proteus* spp. in 2%, *Pseudomonas aeruginosa* in 4.7% and *Enterobacter* spp. in 3.3% of the isolates were detected. In different studies made in our country, results similar to the factor frequency we detected in our study were found.

Due to using antibiotics containing SXT, CIP, ciprofloxacin, cephalosporins and beta-lactam/beta beta-lactamase inhibitor combinations for a long time as the first choice

in urinary tract infections which are among the common reasons for applying to clinics, the resistance development towards these antibiotics gradually increase and cause negative results in the treatments [9-12]. In our study, the resistance ratios of *E. Coli's* isolated in inpatients and outpatients against these antibiotics were detected 60.1% and 64.9% for AM; 19.5% and 15.6% for AMC; 47.5% and 48.1% for SXT; 38.5-42.8% for CXM, 29.9% and 41.4% for CIP and 26.2% and 33.3% for LEV. Pullukcu *et al.* found these ratios in inpatients and outpatients for *E. coli* as 16% and 21.6% for AMC, 58.7% and 76.1% for AMP, 44.6% and 58.4% for SXT and 30.2% and 47% for CIP [13]. Gulcan *et al.* [14] determined the resistance rates as 22.2%-38.6% for AMC, 60.9-79% for AMP, 21.9%-59% for CXM; 29,7% - 62,2% for LEV, 45.9% and 55.4 % for SXT. Gazi *et al.* [15] detected 57% and 65.2% for AM; 11.1% and 14.6% for AMC; 37.8% and 38.8% for SXT. As it can also be seen in these results, high resistance ratios against antibiotics used in empirical treatment frequently, draw the attention. The resistance ratios we detected are similar to the ratios found in other studies made in our country. We detected the resistance ratios of *Klebsiella* spp. strains we isolated in our study in inpatients and outpatients as 22.2% and 22.6% for AMC; 2.% and 47.6% for LEV; 22.84% and 27.5% for SXT and 28.3% and 39.5% for CXM. Gulcan *et al.* [14] detected the resistance ratios in uropathogen *Klebsiella* strains in inpatients and outpatients as 24-64.9% for AMC; 25-45.5% for LEV; 30.2-72.7% for SXT and 28.3-72.7% for CXM in order. While Gazi *et al.* [15] detected 20.3% and 11.1% for AMC, 27.8% and 36.7% for SXT and 25.3% and 36.7% for CXM, Temiz *et al.* [16] detected 59-64.9% for AMC; 26.2-31.5% for CİP; 44.2-49.1% for SXT and 55.7-71.9% for CXM in order. Albayrak *et al.* [17] detected the resistance ratios in isolated *Klebsiella* spp. isolates as 56% for AMC, 30.7% for SXT, 5.5% for CİP and 32.9% for CXM. The fact that the resistance ratios of *Klebsiella* spp. isolates taken from inpatients and outpatients show against levofloxacin are so different makes us consider that this is because of levofloxacin, which is a high-spectrum antibiotic, being preferred in empirical treatment of urinary system infections and the treatment of many infections. This resistance difference in outpatients and inpatients makes us consider that the isolates taken from service patients may be the hospital based infection factor.

In the recent studies, using the antibiotics the resistance ratio of which reach 20% is not recommended in empirical treatment [18]. As seen above and study and other studies made in our country showed that the resistance ratios of many antibiotics we frequently use are much above the recommendable border. As new alternative antibiotics at hand are limited, use of antibiotics which are used very rarely today and were used frequently before come up. The most interesting among these are FM and F. F which is a specific antibacterial for urinary tracts is absorbed quickly orally and shows effect in a short time [18,19]. The fact that nitrofurantoin and FM resistance levels are detected low in *E.coli* and *Klebsiella* spp. kinds in inpatients and outpatients in our study is a proof of this. Although FM showing low resistance ratios in different studies made in our country especially is in use for many years, it is preferred for showing rather low resistance ratios, usability in pregnancy, low toxicity, cost efficiency, easy usability and presence in urine in high concentration for a long time [12,20].

There were differences in the resistance results in outpatient and inpatients and resistance profiles developing against antibiotics used frequently in these two bacterial groups in the same bacterial family and constituting a large part of gram-negative isolates isolated from urine. This difference draw the attention in especially the quinolon group antibiotics, while LEV resistance was found 2% in *Klebsiella* spp. isolates we isolated from policlinic patients, this ratio was found 47.6% in *Klebsiella*. We isolated in inpatients. Coming across different

resistance ratios in strains isolated from inpatients and outpatients who are considered to have USI also showed us the importance of studies made by categorizing inpatients and outpatients together with regional studies in planning the treatments. The contribution of laboratory is important for a successful antibiotic control program [5].

As a result the resistance ratios of many antibiotic groups used frequently in urinary tract infections caused by Gram-negative bacteria, especially *E.coli,* in our region, are over 20% level which is shown as the critical threshold or getting close to this level. It was observed that the sensitivity of *E.coli* and *Klebsiella* spp. isolates against FM and F was in higher ratios compared to most of the antibiotics used frequently. Especially the fact that the resistance ratios of the *E.coli* strains consisting most of uropathogen isolates against FM and F is about 2% gives us the idea that the usage of these agents in empirical treatment may be appropriate. The results of our study have shown that there are differences in antibiotic resistance between not only the areas but also the outpatient and inpatients in the same area. The doctor's part here is considering resistance difference rates between the inpatients and outpatients in addition to the resistance of the area when arranging the empirical treatment. Our study which may be a guide to the clinicians in empirical studies has also shown that due to high resistance ratios which are seen in cephalosporin group, quinolon group SXT and Beta-lactam and beta-lactamase inhibitor antibiotics, antibiotic sensitivity test should certainly be followed and evaluated and the treatment should be intervened if necessary.

Acknowledgement: No

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