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Study of the Resistance of Escherichia Coli Which Creates Community-Acquired Urinary Tract Infections to Ciprofloxacin and Co-Trimoxazole Antibiotics in Sari Hospitals, Iran

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Abstract

Objective: Escherichia coli is the most important etiologic factor in urinary tract infection (UTI), which is becoming resistant to the common antibiotics. The aim of this study was to evaluate the resistance of this bacterium to the antibiotics that are commonly used.

Materials and Methods: A descriptive study conducted in patients with uncomplicated UTI referring to Sari hospitals during 2013-2014. For this purpose, samples that had positive urine culture were selected and evaluated with antibiogram. In addition, E-Test MIC method was used for antibiotics ciprofloxacin and co-trimoxazole. SPSS software was used for data analysis.

Results: Of the 101 patients studied, 83 (82.2%) were females and 18 (17.8%) were male. The mean age of patients was 40.32 ± 3.22 years. The most sensitivity was seen to nitrofurantoin (92.07%), gentamicin (76.23%). Most resistance was also seen to the antibiotics amoxicillin (74.25%), co-trimoxazole (64.35%) and ciprofloxacin (36.63%). In E-Test MIC method, 23.7% were resistant to the ciprofloxacin and 43.5% to co-trimoxazole.

Conclusion: Due to the high antibiotic resistance that was observed to ciprofloxacin and co-trimoxazole in this study, it seems a better alternative antibiotic such as nitrofurantoin should be used for the empirical treatment of patients with UTIs.

Keywords: Antibiotic, Antimicrobial Resistance, Escherichia coli, Urinary Tract Infection

Introduction

Every year 150 million people are affected by urinary tract infections (UTIs) and 7 million people are affected by community-acquired UTIs (CA-UTI), which includes 6 billion of the health costs (1).

The most common bacterial factor in Community-Acquired cystitis in Escherichia coli. In the past, co-trimoxazole was used effectively to cure CA-UTI. Based on Infectious Diseases Society of America guideline (IDSA), in curing UTIs if the regional resistance to this drug is less than 20%, it is still used as the first-line therapy (2). However, nowadays resistance to this drug is increasing every day (from 14% to 65% in different regions of the world) (3-5).

While based on IDSA guideline, the alternative options are nitrofurantoin and phosphomycin (2), quinolones have been quickly replaced as the first-line therapy. Unfortunately, with increasing trend of using this category of drugs, E. coli resistant to quinolone is increasingly reported from many countries, which are becoming a health issue.

The level of resistance to ciprofloxacin in different counties has been reported 1.5%, 18% to 29.2% (3,6).

Dealing with increasing resistance of E. coli to different drugs needs a new strategy. Thus, in treating UTIs, existence of regional studies of resistance is very helpful. Many different studies have been done about

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UTIs in our country (7-9). Of course, none of them were only done on outpatients, and they reported a great deal of resistance anyway. In hospitalized cases, therapy must be guided based on cultivation and antibiogram, but in the case of out-patient knowing the level of resistance can be very helpful in choosing the right drug. Hence, this study was designed to determine the regional resistance of E. coli, which creates CA-UTI against two first-line therapy drugs, which are ciprofloxacin and co-trimoxazole.

Materials and Methods

A descriptive study conducted in patients with CA-UTI referring to Sari hospitals during 2013-2014. In this study, patients with CA-UTI were taken into account. Criteria's out of the study include: diabetes, kidney insufficiency, anatomic disorder of urinary system, continual UTIs (three or more recurrence during recent year), recent use of antibiotic, infection during the recent month, kidney stone, cancer experience, pregnancy, existence of Community-Acquired urinary, human immunodeficiency virus (HIV), kidney transplantation, urinary retention.

Although UTI in men, pregnant women and children is considered as Community-Acquired UTI, but because our purpose was to study the resistance in outpatients, we also included young men that had no UTI experience.

In this study, 101 numbers of the samples that were affected by E. coli and had positive urinary cultivation were extracted and evaluated.

Antibiogram was done using Kirby-Bauer disc diffusion method based on CLSI criteria toward prevalent antibiotics using nitrofurantoin (300 µg), Gentamicin, ciprofloxacin and co-trimoxazole (Hi-media, Mumbai). Counterfoils resistant to ciprofloxacin and co-trimoxazole antibiotics were evaluated with E-Test method one more time.

A questionnaire was designed for each and every patient and personal information including age, sex, urinary cultivation results, and antibiogram were written in the questionnaire.

Statistical analysis

After gathering information, data were registered in SPSS software (version 16.0, SPSS Inc., Chicago, IL, USA) and with the aid of this software, statistical analysis was carried away. In order to describe the data, dispersion indicators (including mean and standard deviation) was put into use. To analyze the qualitative data, chi-square correlation test and Fisher exact test was used and to analyze the quantitative data, t-test was used. In this study, $P < 0.05$ was considered meaningful statistically.

Results

Of the 101 patients studied, 83 (82.2%) were females and 18 (17.8%) were male. The mean age of patients was 40.32 ± 3.22 years.

Antibiogram with disk method

Of the 101 cultivations studied, 75 cases (74.25%) were resistant to amoxicillin, 17 cases (16.83%) were intermediate, and 9 cases (8.91%) were sensitive (Table 1). Among men, 13 cases (72.22%) were resistant to amoxicillin and 5 cases (27.77%) were intermediate; but among women, 62 cases (74.69%) were resistant, 12 cases (14.45%) were intermediate and 9 cases (10.84%) were reported to be sensitive. No meaningful statistical discrepancy was witnessed between the two sexes (P = 0.17).

In studying the sensitivity of E. coli to nitrofurantoin, 93 cases (92.07%) were sensitive, 7 cases (6.93%) were intermediate and only one case (0.99%) was reported to be resistant (Table 1).

18 cases of male cultivations were sensitive to this antibiotic, while of 83 cases of females, 75 cases (89.15%) were sensitive, 7 cases (8.43%) were intermediate and only one case (1.20%) was reported to be resistant (P = 0.39).

About 76.23% of the cultivation of patients (77 cases) was sensitive to Gentamicin and 9.9% of the patients (10 cases) were resistant (Table 1). Taking the two sexes into account, E. coli cultivation of 15 men (83.33%) was sensitive to this antibiotic and 3 men (16.66%) were resistant. Among women, of the 83 cultivations, 62 cultivations (74.69%) were sensitive, 14 cultivations (16.86%) were intermediate and 7 cases (8.43%) were resistant (P = 0.12).

In the case of ciprofloxacin, of the 101 sample, 37 cases (36.63%) were resistance, 10 cases (9.9%) were intermediate and 54 cases (53.46%) were reported to be sensitive to this antibiotic (Table 1).

Of the 18 cultivation cases studied about men, 3 cases (16.66%) were resistant to Ciprofloxacin and 12 cases (66.6%) were sensitive. Among women, 42 cases (50.60%) were sensitive and 34 cases (40.96%) were reported resistant (P = 0.12). After amoxicillin, resistant to co-trimoxazole was more than other antibiotics in this study; and facing this antibiotic, 64.35% of the samples (65 cases) were resistant (Table 1).

Table 1. Results of antibiogram of cultivations studied with disk method

Type of antibiotic	Sensitive (%)	Intermediate (%)	Resistant (%)
Amoxicillin	9 (8.91)	17 (16.83)	75 (74.25)
Nitrofurantoin	93 (92.07)	7 (6.93)	1 (0.99)
Gentamicin	77 (76.23)	14 (13.86)	10 (9.99)
Ciprofloxacin	54 (53.46)	10 (9.90)	37 (36.63)
Co-trimoxazole	29 (28.71)	7 (6.93)	65 (64.35)

Table 2. Results of the antibiogram of discussed cultivations using E-Test (level of sensitivity to each sample)

Type of antibiotic	Sensitive (%)	Intermediate (%)	Resistant (%)
Ciprofloxacin	21 (20.79)	2 (1.98)	24 (23.7)
Co-trimoxazole	24 (23.76)	4 (3.96)	44 (43.5)

Table 3. Comparing the level of resistance in studied cultivations using Disk and E-Test methods

Type of antibiotic	Resistant in disk	Resistant in E-Test
Ciprofloxacin	37 (36.63)	24 (23.7)
Co-trimoxazole	65 (64.35)	44 (43.5)

On the other hand, only 29 cases (28.71%) were reported to be sensitive to this antibiotic. Among men, of the 18 cultivations, 5 cultivations (27.77%) were sensitive to co-trimoxazole, 1 cultivation (5.55%) was intermediate, and 12 cultivations (66.66%) were resistant. Among women, of the 83 cultivations, 24 cultivations (28.91%) were sensitive, 6 cases (7.22%) were intermediate and 53 cases (63.85%) were reported resistant (P = 0.95).

Antibiogram with E-Test MIC method

Ciprofloxacin by Disc method, the sensitivity of E. coli toward ciprofloxacin, which was done on 47 cases, cultivations were reported to be intermediate or resistant. By antibiogram method, 21 cases (44.68%) were sensitive to ciprofloxacin, 2 cases (4.25%) were intermediate and 24 cases (51.06%) were resistant (Table 2) and ultimately the resistance level among 101 cases was (23.7%) (Table 2).

Average density in sensitive cultivations was 0.39 ± 0.33, in intermediate cultivations 2 ± 0 and in resistant cultivations was 51 ± 68.35. Overall, considering Disc and E-Test methods, 75 cases (74.25%) were sensitive to ciprofloxacin, 2 cases (1.98%) were intermediate and 24 cases (23.76%) were resistant.

Co-trimoxazole considering sensitivity toward co-trimoxazole, 24 cases (33.33%) were sensitive, 4 cases (5.55%) were intermediate, and 44 cases (61.11%) were resistant (Table 2), and ultimately the resistance level of the 101 samples was (43.5%).

Average density in sensitive cultivations was 1.07 ± 1.44, in intermediate cultivations 13.33 ± 8.16 and in resistant cultivations was 152.06 ± 84.99.

Overall, considering Disc and E-Test methods, 53 cases (52.47%) were sensitive to co-trimoxazole, 4 cases (3.96%) were intermediate, and 44 cases (43.56%) were resistant (Table 3).

Discussion

UTI is one of the most prevalent infections among patient and after respiratory infection takes in the second position. This illness is one of the reasons that antibiotics are prescribed widely (10). Resistance is an ever increasing phenomenon, and, unfortunately, excessive use of antibiotics in our society makes this issue even worse. Different studies have been done on UTI in our country, but none of them focused on CA-UTI in outpatients (7-9).

Unlike what we see in guideline of Urinary infections treatment, in many regions fluoroquinolones are the first option to be prescribed empirically for these patients. These drugs have a high urinary density and have wide antibacterial effect (11).

Aypak et al. have shown in their study in Turkey that ciprofloxacin was the most commonly prescribed (77.9%) drug. co-trimoxazole (10.7%), phosphomycin (9.2%) and nitrofurantoin (2.1%) were in the next position (12).

As expected, the E. coli samples taken from the patients showed great deal of resistance to most of the outpatient drugs.

In our study, the most sensitivity was toward nitrofurantoin (92.7%) and Gentamicin (73.23%).

In the study of Madani et al. in Tehran, most sensitivity was shown toward Ciprofloxacin (66.7%), cefotaxime and ceftriaxone (62.2%) and nitrofurantoin (48.8%). In their study, sensitivity to gentamicin was only present in 7.3% of the cases (7). Of course in this study, outpatient cases were not separated and the method used was only antibiogram Disk. These situations are effective on analyzing the level of resistance and universalizing it to any case.

In our study, 92.7% of the cases were sensitive to nitrofurantoin, which proves that this drug, as seen in IDSA guideline, in the best option for curing urinary infection. Unfortunately, because of the improper penetration into kidney tissue, in the case of pyelonephritis it is not a good choice.

In the study of Erfani et al**.** in Tehran, most sensitivity was shown toward nitrofurantoin (92%), gentamicin (74%) and ceftazidime (66%) (9).

E. coli levels in the present study have shown 64% resistance using antibiogram disk method and 43.5% resistance using E-Test method to co-trimoxazole; unfortunately due to more than 20% resistance, this drug should be eliminated from first line UTI treatment (2). Of course, if the antibiogram results showed a sensitivity to this level, treatment be done using co-trimoxazole, and hence that other effective drugs are less used.

Ciprofloxacin which seems to be the best choice for curing unitary infections is highly in danger of resistance because it is widely used for respiratory and unitary infections.

E. coli levels in the present study have shown 36% resistance using antibiogram disk method and 23.7% resistance using E-Test method to Ciprofloxacin, which seems according to IDSA guideline this drug is on the edge of being eliminated from first-line therapy and be replaced by new quinolones (2).

In the study of Erfani et al. we also witness great

deal of resistance to co-trimoxazole (43.65%) and ciprofloxacin (23.76%) (9). In this study, due to use of disk method, the level of resistance in too real; on the other hand it is not confined to CA-UTI.

In the study of Madani et al. Ciprofloxacin was the most effective antibiotic, but of course after 7 years, increase in resistance level in not far from reality (7).

Unlike the studies in Iran, the studies have shown less amount of resistance level. Olson et al. in E. coli levels of urinary infections of the students, 29.6% resistance to co-trimoxazole and 6.8% resistance to cypro was reported. No case of resistance to nitrofurantoin was seen in this study (13).

Studies of Nicolle et al. in Switzerland have shown 22% resistance to ciprofloxacin which was close to our study (14).

Kresken et al. have witnessed 30.9% resistance to co-trimoxazole and 19.8% to ciprofloxacin on outpatients (15).

Level of resistance to co-trimoxazole is high most countries and it is above 20% (15-18). The results of this study in close to our study and prove that co-trimoxazole is out of the first-line therapy. Although some regions have reported the low amount of 18% (10).

Surely the main reason of resistance is excessive use of the drug in various infectious deceases.

The level of resistance is different in different regions of the world based on therapy guideline, different demographic and socioeconomic factors and the level of attention of the doctors and patients to correct consumption and is different from the indications of antibiotics. Also, geographic variety in using antibiotics is another reason.

Chen et al. have shown in Taiwan that at least 20% of the doctors do not follow the therapy guideline. This level was witnessed more among older doctors and the doctors working out of the clinic (19).

Kim et al. proved that only 33.96% of the clinicians follow the IDSA guideline in treating UTI, and, unfortunately, their prescription for using antibiotics have been undesirable. Their suggestion was to follow stewardship programs for outpatients in each region (11).

Not following the IDSA guideline in treating UTI and not being informed about regional resistance plan has led to overconsumption of antibiotics, especially Quinolones, but also increased the costs of therapy.

Conclusion

In the end, our study have shown that there is a great deal of resistance to co-trimoxazole and ciprofloxacin in E. coli cultivations of CA-UTI patients in our region. The need for more logical prescription of antibiotics and using more suitable alternative antibiotics like nitrofurantoin to empirically cure UTI is necessary. It seems that co-trimoxazole has exited the first-line therapy and is only usable in situations where high sensitivity is seen in antibiogram results.

CA-UTI can be easily cured with nitrofurantoin, which is more economical and reduces the use of quinolones and resistance to them. Nevertheless, because of the low tissue penetration in pyelonephritis cases, it should be used carefully.

It appears that in addition to knowing the regional resistance plan, existence of therapeutic guidelines in every region and commitment of doctors to these guidelines is the most significant way of preventing this ever increasing phenomenon of resistance.

Ethical issues

In this study was considered ethical issues and all the participant are not be identifiable in any way by a reader of the final report or dissertation.

Conflict of interests

We declare that we have no conflict of interests.

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