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Comparison of the Effect of Ciprofloxacin and Nalidixic Acid in the Infection of Different Parts of the Urinary Tract

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Abstract

Background: *Urinary tract infection (UTI) is one of the most common bacterial infections. The most common cause is Escherichia coli. This research is done with the aim at compare effect of ciprofloxacin with nalidixic acid in the infection of different parts of the urinary tract.*

Methods: *In this cross-sectional study, 130 patients with symptoms of the urinary tract infection referred to Imam Hossain Hospital of Shahrood were studied. For the all patients, urine samples were collected by standard method and urine analysis and culture was performed. Then, positive culture samples were tested by antibiogram and the resistance rate for the two antibiotics ciprofloxacin and nalidixic acid and MBC and MIC was investigated.*

Results: *Of the 130 patients with symptoms of UTI (fever, flank pain or tenderness and dysuria, urgency or frequency (84 patients had positive urine culture. Of all patients with positive urine, 31 cases had symptoms of pyelonephritis, 25 patients had symptoms of cystitis and 28 patients had symptoms of UTI. In antibiogram for positive urine samples, 21 pieces were resistant to ciprofloxacin and 46 pieces were resistant to nalidixic acid which significantly reduced resistance to ciprofloxacin (P=0.005). There was no significant difference between the two antibiotics in place of clinical symptoms and drug resistance. So there was no significant difference between the two MIC and MBC in place of clinical symptoms and drug resistance.*

Conclusions: *This study showed that ciprofloxacin is more effective in controlling infection of different parts of the urinary tract due to less drug resistance.*

Keywords: Escherichia coli, Ciprofloxacin, Nalidixic acid, Urinary tract infection.
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Introduction

Urinary tract infections (UTI) are a generic term for the replacement and growth of a pathogen in the kidney, bladder, and urethra. The prevalence of urinary tract infection in boys is more common the girls than in the first year of life, and after one year, the prevalence of girls is significantly higher.[1-2] The reason for such a distribution of age and sex can be attributed to the shortness of the urethra in the female genome, which makes it easier for the microbe to go into the urinary tract.[3] The most important symptoms of the disease are including pain, hematuria, dysuria, urinary incontinence, pain in the lower back, fever and abdominal pain.[3-4] Several organisms interfere with the development of urinary tract infections, the most common of which is E. coli. Over 80% are caused by E- coli, a Gram negative bacillus. Other causes of urinary tract infection include Enterobacter agglomerans, Proteus mirabilis, Klebsiella pneumonia, Pseudomonas aeruginosa, Staphylococcus saprophyticus and Enterococcus faecalis.[5-6] E. coli is a large heterogeneous group of gram-negative bacilli in the form of a bar without spores, a part of the natural flora of the intestine. This bacterium is a natural habitat for humans and animals, but if it enters other devices in different ways, it will cause infection.[7-9] Treatment for mild infections is often out-patient and with oral antibiotics but in severe cases, especially in pyelonephritis, treatment is administered as an adjunct to an antibiotic.[10] Appropriate antibiotic selection depends on several factors such as the outcome of urine culture and its antibiogram, the age of the patient and the presence of accompanying illnesses. One of the problems of treatment is the antibiotic-resistant strains.[11-12] This problem occurs as a defensive reaction by infectious agents and from the very beginning, the discovery of antibiotics has also existed.[11] It is also a matter of accelerating and intensifying the process of resistance to mankind and preventing the current self-made process to reduce the occurrence of resistance and control.[12] Factors such as inappropriate diagnosis of illnesses, the supply of counterfeit drugs to the pharmaceutical market, the administration of inappropriate drugs, or inappropriate dosage, inadequate training and the problem of hospital infections all work together and increase drug resistance.[13] Ciprofloxacin and nalidixic acid are increasingly used in the treatment of urinary tract infections but the drug resistance level is not clear.[14-15] The procedure for performing antibiotics is based on the MIC (The lowest amount of antibiotics that can significantly inhibit the growth of an organism after a specific incubation period) and MAC (The lowest concentration of antibiotics, which can reduce the bacterial population by 1000 times after 24 hours) criteria, which, according to the American National Laboratory Standards Committee (NCCLS), is a gold standard for determining antimicrobial susceptibility and resistance.[16] Also, since conventional antibiogram methods based on disk have many problems (lack of reliability and more human error) and quality we decided to test antibiotic ciprofloxacin and nalidixic Acid antibodies against E. coli based on the precise MIC and MBC methods.[16-18] Furthermore, the resistance rates of urinary E. coli to various antimicrobials show large inter-country variability. Only a few studies have shown that E. coli resistance rates differ for hospital-acquired and community-acquired UTI.[9-11] Measuring and comparing the levels of AMR in both hospital- and community-acquired UTI is essential because although effects of AMR are mainly felt in healthcare facilities, the greatest use of antimicrobials occurs in the community.[19] The prevalence of AMR including hospital and

community urinary E. coli resistance levels is not completely known in Iran. Obtaining this information is important because it not only provides knowledge about the health status of a population, but also contributes to disease management decisions.[13] This study was done with the aim of compare effect of ciprofloxacin with nalidixic acid in the infection of different parts of the urinary tract.

Materials and Methods

This is a cross-sectional study with the aim of comparing the effectiveness and resistance rate of two antibiotics ciprofloxacin and nalidixic acid on UTI. In this study, 130 patients admitted to Imam Hossain Hospital of Shahroud with the diagnosis of clinical signs of UTI (upper urinary tract including: fever, flank pain or tenderness and lower urinary tract including dysuria, urgency or frequency), during (March 2015 to February 2016) were selected by convenient method. The initial selection of these patients was based on the positive urine culture test. Then a researcher-made questionnaire containing demographic and clinical data was completed by patients.

Inclusion criteria: having urinary tract infection (pyelonephritis, cystitis and urethritis) and satisfaction of entering the research.

Exclusion criteria, if there was: a history of allergy to nalidixic acid; evidence of renal dysfunction (serum creatinine greater than 130 µmol/L); a history of renal calculi (these patients are known to relapse); or pregnancy. In addition, patients known to be infected with organisms resistant to the study drug or who had antimicrobial therapy less than 72 h before entry were excluded.

The urine sample was taken by the Middle Stream method and sent to the laboratory of Imam Hossain Hospital for urine culture (significant bacteriuria was defined as a midstream urine culture bacterial count of greater than or equal to 105 colony forming units (cfu)/L of urine) and antibiogram tests in EMB and Blood Agar selective environments.[13-15] In the next step, colonies grown on the EMB medium were examined for Enterobacteriaceae type. To do this, the oxidase test was first performed and if the oxidase test was negative, a differential diagnosis of lactose fermentation was performed and a final diagnosis was made.[20]

Determination of antibiotic susceptibility by Disk Agar diffusion (DAD): According to the Clinical and Laboratory Standards Institute (CLSI) instruction,[21] after removing all specimens from the freezer -20° C and their culture at Muller Hinton Agar (3 times), pure bacterial colonies were harvested and the turbidity of 0.5 McFarland was obtained in bacterial serum physiology. Then, a bacterial suspension was inoculated into a Muller Hinton Agar medium (in three different directions) and after a few minutes (to absorb the humidity of the environment), antibiotic discs were placed in the environment and then they were incubated at 35 ° C. The inhibition zone for all antibiotics was measured after 20 to 16 hours.

MIC (Minimum Inhibitory Concentration): based on the CLSI instruction recommendation, antibiotic stoiches were prepared as 10X in the highest concentration.[22] The following formula was used to prepare the antibiotic suitable for preparation of antibiotic stokes. After obtaining the appropriate amounts of antibiotics in milligrams, each antibiotic was dissolved in its proper solvent and reached the appropriate volume. Finally, of Micro Broth Dilution method was used to determine the MIC level of antibiotics. In order to determine the MBC (Minimum bacterial Concentration), 10 µl of wells that were free from turbidity were removed and cultured on the surface of the Muller Hinton Agar and after 18-24 hours incubation at 37 ° C was investigated. The amount of MBC was determined based on the minimum concentration of drug that has a fungal effect on the bacteria. Data were analyzed using SPSS software.

This study has an ethics code number (IR.SHMU.REC.1394.66) from research deputy of Shahroud University of Medical Sciences. The essential information and the objectives of the study were explained to the patients and written consent was obtained for participation in the plan.

Results

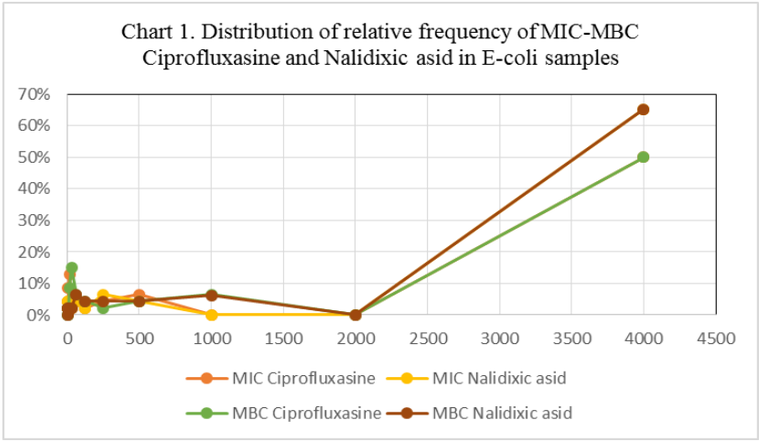
Of the 130 patients with symptoms of UTI, 84 patients (64.6%) had positive urine culture. Among the positive samples of urine culture, 78 cases (92.9%) were E. coli. Three cases (3.6%) were coagulase-negative Staphylococci, two cases (2.4%) were E. agglomerans and one case (1.2%) was K. pneumonias. Of the 84 patients, 64 (76.2%) were female and the rest were male. Of all patients with positive urine, 31 cases (36.9%) had symptoms of pyelonephritis, 25 patients (29.8%) had symptoms of cystitis and 28 patients (33.3%) had symptoms of urinary tract inflammation. The demographic characteristics of patients are shown in table 1. In antibiogram for positive urine samples, 21 pieces (25%) were resistant to ciprofloxacin and 46 pieces (43%) were resistant to nalidixic acid which significantly reduced resistance to ciprofloxacin (P=0.005). The drug resistance levels of ciprofloxacin and Nalidixic acid in terms of the location of the involvement are shown in table 2. As can be seen there was no significant difference between the two antibiotics in place of clinical symptoms and drug resistance (P=0.085). So there was no significant difference between the two MIC and MBC in place of clinical symptoms and drug resistance (P=0.069). Distribution of MIC and MBC ciprofloxacin and nalidixic Acid are shown in Chart 1.

Table 1. Characteristics of the population with positive urine culture

Characteristic (N=84)	Variables Number (Percent) / Mean
Sex	
−Male	20(23.8)
−Female	64(76.2)
Mean Age (years)	38.4±14.2
Age groups	
−<20 years	7(8.3)
−20-40 years	46(54.7)
−41-60 years	23(27.4)
−>60 years	8(9.5)
Mean BMI (kg/m^2)	24.35±4.17
Symptomatic urinary tract area	
−Upper (Pyelonephritis)	31(36.9)
−Lower (Cystitis and Urethritis)	53(63.1)
Marital status	
−Single	23(27.3)
−Married	61(72.7)

Table 2. Frequency distribution of drug resistance according to the location of the conflict (Number (%))

	Kidney & Ureter	Bladder	Urethral duct	Total	P.V
Ciprofloxacin Resistant	6 (28.6)	3 (14.3)	12 (57.1)	21 (100)	0.09
Nalidixic acid Resistant	11 (25.6)	7 (15.2)	28 (60.9)	46 (100)	



Discussion

According to the results of this study, 84 urine samples from patients with urinary tract infection with various microorganism, especially E. coli, among 21 patients (25%) with UTI, were resistant to ciprofloxacin antibiotics, and for nalidixic acid antibiotics, 46 patients (54.7%) were also resistant to nalidixic acid antibiotics. In the Swami study, E. coli resistance to ciprofloxacin antibiotic was 2.7% and the resistance to antibiotic nalidixic acid was 16.22%.[23] This suggests a greater effect of ciprofloxacin antibiotic on E. coli from urine specimens and while nalidixic acid antibiotics are rapidly resistant, this is also mentioned in Hsu and Costelloe studies,[24-25] which emphasizes the use of ciprofloxacin. In this study, MIC was the antibiotic ciprofloxacin was found to be less resistant to the nalidixic acid. According to the findings of this study, in 57.1% of cases, patients with urethral duct, 28.6% of patients with pyelonephritis and 14.3% of them had cystitis was observed resistance to ciprofloxacin, in the case of nalidixic acid, this level of resistance was respectively 28 (60.9%), 11 (25.6%) and 7 (15.2%) which is consistent with Freeman's research findings.[26] In addition 53.48% of these patients had MIC resistant to ciprofloxacin and 61.53% of these patients had nalidixic acid -resistant MIC which is consistent with Sun's research findings but contradicts Adam's results, perhaps because of the size of the sample examined in the two studies above.[27-28] On the other hand, 34.8% of these patients had MBC resistant to ciprofloxacin and 55.6% of these patients had nalidixic acid -resistant MBC which is similar to Cornaglia's research results.[29] Regarding these findings, there was a significant relationship between the antibiogram of ciprofloxacin and nalidixic acid, but no significant relationship was found between the place of infection (the kidney, bladder and urethra). This finding suggests that the location of the infection does not play an important role in antibiotic selection. Also, in the MIC, there was no significant relationship between the two antibiotics that was found with the results of studies and consistency.

Antimicrobial resistance poses grave concerns for antimicrobial effectiveness in treating infections such as UTI. This study demonstrates the increasing resistance of urinary E. coli to commonly prescribed antimicrobials. The antibiogram and MIC of the two antibiotics ciprofloxacin and nalidixic acid showed that nalidixic acid resistance was higher than ciprofloxacin and this should be considered in prescribing for the needy and ciprofloxacin can be used to treat urethritis, cystitis, and pyelonephritis.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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