The patterns of aminoglycoside and fluoroquinolones resistance among uropathogenic *Escherichia coli* isolates

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Abstract

Introduction: In the study we sought to determine the patterns of regional antibiotic resistances among uropathogenic *Escherichia coli* (UPEC) isolates. Our finding could be useful for better recognition of regional antibiotic resistances and scheduling a program to control this condition.
Materials and methods: In the study, 270 nonduplicate UPEC isolates were examined from urine samples of outpatients with urinary tract infections (UTIs). All isolates were identified by gram staining and standard conventional biochemical tests. Antimicrobial susceptibility test was performed by disk diffusion (Kirby–Bauer) method. The commercial antibiotics disks (PADTAN TEB Co., Iran) were applied in the study, included amikacin (30 µg), gentamycin (10 µg), ciprofloxacin (5 µg), and nalidixic acid (30 µg).
Results: Most of the patients were female (221, 81.9%). The highest resistance was observed for nalidixic acid (56%), followed by ciprofloxacin 39.64%. In contrast, the lowest resistance was seen for amikacin (3.90%) and gentamicin (10.04%). Moreover, 19.62% of the isolates were multidrug-resistant (MDR).
Conclusion: Amikacin and gentamicin could be chosen as first line antibiotics in treatment of UTIs. Continuous monitoring studies recommended for acquire a suitable regional antibiotic resistance pattern.

Keywords: *Escherichia coli***,** UTIs, Antimicrobial susceptibility

Introduction

Antimicrobial resistances are responsible for many patients' morbidity and mortality in worldwide and approximately 700,000 deaths are reported annually by this phenomenon (1). It also causes increase treatment cost, doses of antibiotics administration and length of hospitalization (2). Nowadays, antimicrobial resistance is growing among bacteria, especially in gram-negative bacterium (3). *Escherichia coli (E.*

coli) as a gram-negative bacterium can be isolated from different infection diseases (4). Uropathogenic *E. coli* (UPEC) isolates are an economic burden for both communities and hospital resources by annually about $6 billion cost in worldwide (5). But current studies have been showed that antibiotic resistances in UPEC isolates have an upward trend (6). So that, our study was carried out to evaluate the patterns of regional antibiotic resistances among UPEC isolates collected from patients with UTIs in Ilam Province, Iran.

Materials and methods

Patients and collecting samples

A total of 270 UPEC isolates were collected from urine samples of outpatients with UTIs that admitted in Khorshid Clinical Laboratory (affiliated to Ilam University of Medical Sciences) from March 2016 to January 2020. All process of study was done in Khorshid Clinical Laboratory.

Bacterial isolates

For bacterial diagnosis, firstly urine samples were cultured on blood agar (BA agar) and MacConkey agar (MC agar) media (Merck, Germany). After an overnight incubation at 37°C, all suspicious colonies were identified by gram staining and also standard conventional biochemical tests including triple-sugar iron (TSI), Simmons citrate, sulfide indole motility (SIM), urea, Voges-Proskauer (VP) and Methyl Red (MR) tests (7). An organism known as *E. coli*, when it was gram negative bacilli, lactose fermentative, grows on the MC agar, motile, indole and MR positive and also was negative for oxidase, H_2S, VP, urea, and citrate utilization (8).

Antimicrobial susceptibility testing

The Kirby–Bauer method was used to investigate antibiotics susceptibility on the Mueller–Hinton (MH) agar (Merck, Germany). For each isolate, we prepared 0.5 MacFarland (1.5×10^8 CFU/ml) suspension. Then all disks of antibiotics were placed on surface of MH agar and incubated at 37 °C for overnight. The commercial antibiotics disks (PADTAN TEB Co., Iran) were included amikacin (30 µg), gentamycin (10 µg), ciprofloxacin (5 µg), and nalidixic acid (30 µg). *E. coli* ATCC 25922 used as quality-control.

Statistical analysis

For statistical analysis, data firstly enrolled to SPSS 16.0 software. Then, by using x^2 and Fisher's exact tests all data were analyzed. A P value less than 0.05 was also considered as significant statistical differences.

Results

A total of 270 UPEC were collected from outpatients with UTIs. Majority of patients were female (221, 81.9%) and only 18.1% (n=49) were males. *E. coli* was responsible for UTIs in 62.07% cases, but prevalence of gram-positive cocci and other gram-negative bacilli had 11.72% and 26.20%, respectively. We found that nalidixic acid had maximum rate of resistance (56%), but amikacin had minimum resistance (3.90%) (Table 1).

Table 1. The results of antimicrobial susceptibility among Uropathogenic *E. coli* (UPEC) isolates.

Antibiotic	Sensitive	Intermediate	Resistance
Ciprofloxacin	56.81%	3.55%	39.64%
Nalidixic acid	39.81%	4.19%	56%
Gentamicin	64.39%	25.57%	10.04%
Amikacin	69.53%	26.57%	3.90%

Our finding did not show any significant association between patient's genera an antibiotic resistance (P >0.05). The patterns of multidrug-resistances (MDR) among UPEC isolates were also studied. Our results were as follow: 17.40% (n= 47) isolates had resistance against two antibiotics, 1.85% (n= 5) isolates had resistance against three antibiotics and 0.37% (n= 1) isolates had resistance against four antibiotics. Therefore, 19.62% of the isolates were MDR.

We also studied association between presences of antibiotic resistance among different antibiotics. We observed that there are significant associations between pattern of resistance among gentamicin with amikacin (P <0.05) and also ciprofloxacin with nalidixic acid (P <0.05).

Discussion

E. coli is introduced as responsible for 80–90% of UTIs in worldwide (9). So, we firstly studied its prevalence among patients. Our results showed that this bacterium is the dominant responsible agent for UTIs in our region. This result was consistent with Esmaili *et al*. (2018) who reported *E. coli* is the main bacterial responsible for UTIs in Ilam province (10). Anvari *et al*. (2014) similarly demonstrated that *E. coli* has higher prevalence among UTIs patients (Tehran, Iran) (11).

Here, we examined the patterns of aminoglycosides (gentamicin and amikacin) and fluoroquinolones (ciprofloxacin and nalidixic acid) resistances. Because mentioned antibiotics are inexpensive and easily available to patients and also our physicians are willing to prescribe these antibiotics. Additionally, we had not information about patterns of aminoglycosides and fluoroquinolones resistances among UPEC isolates in our region.

Here, the rates of resistance were as gentamicin (10.04%), amikacin (3.90%), ciprofloxacin (39.64%) and nalidixic acid (56%). However, in some parts of country, the mean of resistance has been reported as gentamicin 17.9% (from 3.63% to 36.45%) (12-16), amikacin 12.73% (from 2.7% to 36%) (12, 13, 15-18), ciprofloxacin 31.29% (from 8.3%- 52.1%) (8, 12, 14-16, 19) and nalidixic acid 48.15% (from 11.18%-71.9%) (8, 12, 14-16, 20). Fortunately, our rates of antibiotic resitance often were less than the country mean, except nalidixic acid.

Importantly note, antibiotics with resistance higher than 10–20% led to increased risk of treatment failure and selection of resistant strains (21). Based on patient's condition, therefore, we suggested that amikacin or gentamicin can choose as first line antibiotics to treatment of UTIs.

In addition, 19.62% of the isolates were MDR and most isolates were resistance to two antibiotics. However, these results were different from such reported by Dehbanipour *et al*. (2016, Isfahan, Iran) (22). This different was due to variation in geographical region, patient's condition, antibiotics type and others.

Notably, some antimicrobial agents have similar antibiotic resistance mechanisms or co- resistance mechanisms with other antibiotics that cause increase resistant bacteria (23). Here, we observed that there are significant associations between pattern of resistance among gentamicin with amikacin (P <0.05) and also ciprofloxacin with nalidixic acid (P <0.05).

Finally, inattention to antimicrobial resistance phenomenon will lead to an increase in the healthcare complications in society. Because of regionally a standard treatment guideline for empirical therapy, the continuous monitoring of antimicrobial agents will be necessary (22).

Because of our financial limitations, current study was carried out in a small number of

antibiotics. Secondly, it was better we used from molecular method to study antibiotic resistances among UPEC isolates.

Conclusion

Our study was a regional investigation about the prevalence of *E. coli* isolates among UTIs patients and also determination their antibiotic resistance patterns. Our results can be being very important to scheduled a standard regional treatment guideline. Moreover, current study was the first step from a continuous route and we will extend more investigations in future.

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