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Evaluation of Microbial Resistance Pattern in Children with Urinary Tract Infection in Bushehr between 2017 and 2018

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Abstract

Background and Aim: Urinary tract infection is one of the most common childhood illnesses that can lead to complications such as hypertension and kidney failure. The aim of this study was to evaluate microbial resistance and sensitivity and to determine the relationship between urinary tract abnormalities and prior antibiotic use with microbial resistance.

Methods: This is a descriptive-analytic study on 90 patients with a positive urine culture. Urine culture samples were taken using one of the sampling methods (midstream clean catch, catheterization, urine bag, suprapubic aspiration) and ultrasonography was requested for all patients to evaluate urinary system abnormalities. Also, a history of prior antibiotic use was asked and recorded.

Results: Of all patients, 55.6% showed E.coli and 44.4% showed other bacteria in urine culture. 97.7% of patients' cultures were sensitive to imipenem, 82.2% to nitrofurantoin, and 77.8% to cefixime. 65% of patients' cultures showed resistance to nalidixic acid, 56.7% to co-trimoxazole, and 38.9% to ceftriaxone. There was a significant relationship between cefixime and amikacin antibiotic resistance with abnormal ultrasound and there was a significant relationship between antibiotic resistance to cefixime, ceftriaxone, co-trimoxazole, and duration of prior antibiotic use (p-value <0.05).

Conclusion: The most common pathogen in UTI was E.coli. The highest sensitivity was to imipenem, nitrofurantoin, and cefixime, and the highest resistance was to nalidixic acid, co-trimoxazole, and ceftriaxone. There was a relationship between urinary tract abnormalities and prior antibiotic use with microbial resistance, so it is suggested to use kidney ultrasound in all patients with urinary tract infection.

Keywords: Urinary tract infection; Microbial resistance; Microbial sensitivity; Child.

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Introduction

Urinary tract infection is one of the most common childhood diseases (1) and has been described since ancient times, with the first document describing a urinary tract infection dating back to 1550 BC (2). The prevalence of this disease is reported to be 3% to 8% in girls and 1% to 2% in boys (3-5). The most common microorganism in urinary tract infection is gram-negative intestinal bacteria, especially Escherichia coli (4-6). Other microorganisms involved in UTI include Pseudomonas, Proteus, Enterobacter and Klebsiella (6). Urinary tract infection may be limited to the bladder, called cystitis, or spread to the renal parenchyma, called pyelonephritis (5, 6). The manifestations of the disease in pyelonephritis and cystitis are quite

different. In pyelonephritis, there are symptoms such as high grade fever, weakness, lethargy, abdominal and flank pain, nausea and vomiting, but in cystitis, restlessness, dysuria, frequency and urinary incontinence are seen. Laboratory findings vary, but in both, urine culture is positive (4-6). Delayed treatment, especially in renal tissue involvement, can lead to prolonged illness and long-term complications. Currently, the third generation of cephalosporins, aminoglycosides and ampicillin intravenously and co-trimoxazole, nitrofurantoin and cefixime orally are used to treat urinary tract infection (5). Due to the over-prescribing and misuse of antibiotics, microbial resistance in all infections, including urinary tract infections, is practically seen in dealing with these patients (7). If this happens, the available antibiotics will not control the infection, and other medications must be used to control the infection and prevent long-term complications (8, 9). Therefore, we decided to identify microbial resistance to control the infection as soon as possible in critically ill patients using an appropriate antibiotic.

Methods

This is an analytical descriptive study. The study population included all children less than 14 years of age with urinary symptoms and positive urine culture and fever of unknown origin on outpatient basis or in the pediatric ward of Shohaday-e-Khalij-e-Fars Hospital in Bushehr. In all patients, after obtaining informed consent from the patient's guardian, complete history was taken and physical examination was done. Urine culture sample was taken by one of these methods: urinary bag, midstream clean catch, catheterization or suprapubic aspiration. The choice of sampling method varied according to the child's age and physical and general condition. The sample was sent to the laboratory for urinalysis and urine culture. For urine culture and antimicrobial susceptibility test, standardized mediums and antibiogram disks containing third and fourth generation cephalosporins, aminoglycoside, co-trimoxazole, nitrofurantoin and nalidixic acid were used. Finally, after 48 hours, the urine culture result was reported to be negative or positive, along with the number of bacterial colonies and the sensitivity or resistance to antibiotics. In urinary bag sampling and midstream clean catch method, the colony counts more than 100,000 with urinary symptoms (fever, dysuria, pain, foul-smelling urine, urinary incontinence, and flank or suprapubic pain) was considered positive. In catheter or suprapubic sampling, the colony counts more than 50,000 of a single pathogen, or 10,000 if the patient was symptomatic, was assumed to be positive. In all patients with a first-time urinary tract infection, an ultrasound was performed to evaluate the urinary tract. In all patients with suspected urinary tract infections, after sending a urine sample, treatment with a third-generation cephalosporin with or without an aminoglycoside was started. Antibiotic treatment was continued until the culture result was reported. After that, according to the patient's condition and the antibiogram result, a decision was made whether to change the antibiotic regimen or not. After collecting the information, all data were entered into SPSS software version 16 and analyzed by descriptive statistics and chi-square test.

Results

Of the 90 patients, 57 (63.3%) were female and 33 (36.7%) were male. 44 patients (48.8%) were 1 to 5 years, 29 patients (32.3%) were less than one year and 17 patients (18.9%) more than 5 years. All patients included in this study had a positive urine culture. In 50 patients (55.6%), the pathogen was E.coli. Other pathogens included: Klebsiella, Proteus and Pseudomonas.

In this study, 9 antibiotics (imipenem, gentamicin, nitrofurantoin, cefixime, ceftriaxone, co-trimoxazole, ciprofloxacin, amikacin, and nalidixic acid) were selected and the susceptibility and resistance to them were investigated. The highest sensitivity was found to imipenem (97.7%), nitrofurantoin (82.2%) and cefixime (77.8%) and the highest resistance was seen in nalidixic acid (65%), co-trimoxazole (56.7%) and ceftriaxone (38.9%) (Table 1).

Table 1. Sensitivity and resistance of studied antibiotics

Antibiotic	Sensitivity	Resistance
Imipenem	97.7 %	2.3 %
Nitrofurantoin	82.2 %	17.8 %
Cefixime	77.8 %	22.2 %
Gentamicin	75.6 %	24.4 %
Amikacin	74.4 %	25.6 %
Ciprofloxacin	73.3%	26.7 %
Ceftriaxone	61.1 %	38.9 %
Co-trimoxazole	43.3 %	56.7 %
Nalidixic acid	35 %	65 %

The susceptibility of each UTI pathogen to each antibiotic is summarized in Table 2. According to our studies, the highest sensitivity of E.coli is to imipenem (98%) and its highest resistance is to co-trimoxazole (64%). Proteus is sensitive to most of the antibiotics and only 40% of cases are resistant to nalidixic acid. All cases of klebsiella were sensitive to imipenem and gentamicin, and most resistance was to nalidixic acid (75%). All the Pseudomonas aeruginosa cases were sensitive to imipenem, gentamicin, amikacin, and nalidixic acid, and half were resistant to cefixime and co-trimoxazole.

Table 2. Sensitivity of each selected antibiotic according to UTI pathogens

Antibiotic	E.coli	Klebsiella	Proteus	Pseudomonas
Imipenem	98 %	87.5 %	100 %	100 %
Nitrofurantoin	84 %	75 %	71.4 %	-
Cefixime	75 %	50 %	100 %	50 %
Gentamicin	82 %	87.5 %	71.4 %	100 %
Amikacin	74 %	87.1 %	100 %	100 %
Ciprofloxacin	76 %	62.5 %	100 %	50 %
Ceftriaxone	51 %	37.5 %	100 %	-
Co-trimoxazole	36 %	50 %	71.4 %	50 %
Nalidixic acid	39.5 %	25 %	60 %	100 %

Of these 90 patients, 79 (87.7%) had taken antibiotics for less than 30 days and 11 (12.3%) for more than 30 days. Accordingly, the relationship of microbial resistance to each of the selected antibiotics with the duration of antibiotic use in the past was evaluated. The results of this analysis showed that resistance to 3 antibiotics including cefixime, ceftriaxone and co-trimoxazole had a significant relationship with the duration of prior antibiotic use (p-value <0.05).

In 80 patients (88.8%), the findings of the ultrasound were normal and 10 patients (11.2%) had abnormality in ultrasound. Accordingly, the relationship of microbial resistance to each of the selected antibiotics with abnormal ultrasound findings was evaluated. The results showed that resistance to cefixime and amikacin had a significant relationship with abnormal ultrasound findings (p-value <0.05).

Discussion

The aim of this study was to determine microbial resistance and sensitivity in urinary tract infection and evaluate the relationship between urinary tract abnormalities and prior antibiotic use with microbial resistance. Other goals of our study were to determine the type of pathogens that causes UTI and the prevalence of urinary tract infection in both genders and different age groups.

In our study, the prevalence of urinary tract infections was higher in females (63.3%) and in the age group of 1-5 years (48.9%). E.coli was the cause of 55.6% of urinary tract infections. Other common pathogens included klebsiella, proteus, and pseudomonas.

In our study, out of a total of 90 urine cultures, 97.7% were sensitive to imipenem, 82.2% to nitrofurantoin, and 77.8% to cefixime, and 65% were resistant to nalidixic acid, 56.7% to co-trimoxazole, and 38.9% to ceftriaxone. There was a significant relationship between the duration of prior antibiotic use and microbial resistance to cefixime, ceftriaxone, and co-trimoxazole, and between abnormal ultrasound finding and microbial resistance to cefixime and amikacin.

In a study of 77,783 cases of children and adolescents aged from 5 to 17 years with positive E. coli culture. Similar to our study, E.coli was identified as the most common cause of UTI (8, 10). A 2016 study by Ashley Bryce at the University of Briston found that in developed countries, 53% of urinary tract infections are resistant to amoxicillin, 25% to co-trimoxazole and 8% to amoxicillin-clavulanate. The rate of resistance is higher in developing countries, with 80% resistance to amoxicillin, 60% to amoxicillin-clavulanate, 25% to ciprofloxacin and 17% to nitrofurantoin (7).

In our study, 9 antibiotics were selected and their sensitivity and resistance were assessed. Unlike Ashley Bryce's study, amoxicillin and amoxicillin-clavulanate antibiotics were not selected. In our study, resistance was reported to be 56.7%, to co-

trimoxazole, 26.7% to ciprofloxacin and 17.8 % to nitrofurantoin and the numbers are very similar to the previous study, as can be seen (7).

In another study of 533 patients between 2001 and 2006, Paschke et al. showed that antibiotic resistance in pediatric urinary tract infections, between the ages of 6 months and 6 years who received prior antibiotics, is seen more with ampicillin and amoxicillin (12).

A study by Stephanie et al. on 361 children aged less than 18 years with positive urine culture was performed for 5 years at Milwaukee Children's Hospital from 1997 to 2001. In patients on antibiotic prophylaxis, 27% had resistance to cefotaxime. Increased percentage of infections with enterococci and pseudomonas was associated with decreased sensitivity to cefotaxime. Patients with vesicoureteric reflux also had higher antibiotic resistance. Even with antibiotic prophylaxis, resistance to aminoglycosides was less reported. In this study, the antibiotic of choice was cefotaxime, which was not among the antibiotics of our choice. However, this study showed that there was a significant relationship between the rate of cefotaxime consumption and abnormal ultrasound findings. In our study, the relationship between resistance to cefixime, ceftriaxone and co-trimoxazole, and prior antibiotic therapy was significant. Also, this relationship was seen between cefixime and amikacin resistance and abnormal ultrasound finding (13).

A study of multidrug resistance by Yaakow Diskstein was conducted in northern Israel from 2011 to 2015 on 4,409 children with a urinary tract infection. The results of this study showed that there is multidrug resistance in microorganisms causing urinary tract infections (14). A study by Mesut Kocak et al. on 142 patients less than 3 years of age, from 2009 to 2014, showed an increase in multidrug resistance of 49.3% to the 3rd generation cephalosporins. The third generation of cephalosporins includes cefixime, ceftriaxone, ceftazidime, and ceftizoxime (15). In our study, resistance to cefixime was 22.2 % and to ceftriaxone was 38.9%. Ceftriaxone was one of the three antibiotics that showed the highest resistance, and our study reported the highest resistance to nalidixic acid.

In the study by Moloud Barzan on 1349 cases of hospitalized and outpatient children with positive urine culture, the highest resistance was reported to cephalothin and the highest sensitivity to amikacin and piperacillin. In our study, the highest resistance was reported to nalidixic acid, co-trimoxazole, and ceftriaxone, respectively (16).

According to our data and the previous studies, urinary tract infections are more common in females and the most common pathogen is E. coli. This microorganism has the highest sensitivity to imipenem (98 %) and nitrofurantoin (84 %) and the highest resistance to co-trimoxazole (64 %) and nalidixic acid (60.5 %).

Conclusion

The overall results of this study showed that due to the sensitivity of 50% and higher, aminoglycosides and ceftriaxone are still the first choice for treatment of UTI. Despite the high sensitivity to imipenem (97.7%), this medication should not be used as the first line of treatment.

According to our study, there is a significant relationship between prior antibiotic use and urinary tract abnormalities and microbial resistance, so it is recommended that a history of antibiotic use and its duration be taken from the patient's guardian, before starting antibiotic therapy. Also, due to the relationship between urinary system abnormalities and antibiotic resistance, which was significant with cefixime and amikacin in our study, it is recommended that the child with urinary tract infection to undergo ultrasonography and if there is an abnormality in the ultrasound, it is best not to use cefixime. Raising awareness and educating the parents and physicians about antibiotics as major medications in the treatment of infections to prevent serious resistance is necessary.

Conflict of Interest

The author declares no conflicts of interest.

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Ethics

Not declared.

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