Original Article

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Can Urinary Nitrite Results Be Used to Conduct Antimicrobial Option for Urinary Tract Infection in Children?

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Abstract

Objective: This study was performed to determine the relationship between urinary nitrite results and bacterial resistance to antimicrobial drugs in urinary tract infection of children.

Methods: In a cross-section study 119 children younger than 12 years with urinary tract infection were evaluated in Qazvin children's hospital. Patients were divided into negative and positive nitrite groups depending on urinary nitrite test result. Rates of antibiotic resistance in the two groups were compared.

Findings: Sixty seven patients were in the negative nitrite group and 52 in the positive nitrite group. Resistance rates to ceftriaxone, trimethoprim sulfamethoxazole, ampicillin, gentamicin, amikacin, nalidixic acid, cephalothin and nitrofurantoin in the nitrite negative group were 7.5%, 31.3%, 50.7%, 11.9%, 9%, 3%, 14.9% and 11.9%, respectively. These values in the nitrite positive group were 21.2%, 28.8%, 63.5%, 7.7%, 5.8%, 1.9%, 9.6%, and 3.8%, respectively (P>0.05).

Conclusion: This study showed that there is no correlation between urinary nitrite results and bacterial resistance to antimicrobial drugs. Therefore, it seems that physicians should not adjust antibiotic therapy for UTI based on nitrite results.

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Key Words: Urinary tract infections; Nitrite; Anti-bacterial agents; Drug resistance

Introduction

Urinary tract infection (UTI) is a common disease in children. It results from invasion of pathogenic microorganisms (bacteria, viruses, or fungi) to the urinary tract system [1,2]. Incidence of disease in boys and girls has been reported 1% and 3-5%, respectively. The disease manifests in three forms; cystitis, pyelonephritis and asymptomatic bacteriuria [1,2]. *Escherichia coli* is the most common etiologic agent in 70-90% of cases [1,2]. To prevent serious complications of the disease such as renal scar, hypertension and chronic renal failure, early detection, timely and appropriate treatment of the disease is very important [3,4]. Regarding the increased drug resistance of microorganisms causing UTI, appropriate initial drug selection before obtaining the results of urine

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culture and antibiogram is important [1-2,5-9]. The question is whether it is possible to guess microorganism resistance using markers such as nitrite test before preparation of urine culture and antibiogram results? Weiz believes that it is possible to identify resistance to cephalosporin based on the urinary nitrite result [10]. In contrast, other studies are not in accordance with this opinion [11-12]. Considering the controversy, we conducted this study to determine the relationship between the urinary nitrite results and bacterial resistance to antimicrobial drugs in UTI of children in Qazvin children's hospital, Qazvin, Iran.

Subjects and Methods

In a cross-section study, all children with final diagnosis of UTI (119 patients) that were admitted to Qazvin children's hospital during March 2008 – December 2009 were investigated. All patients were younger than 12 years. Qazvin children's hospital is affiliated to Qazvin University of Medical Sciences. Inclusion criteria included: 1) first episode of UTI, 2) positive urine culture (more than 10^5 colonies of one organism per cc of urine by clean catch method or more than 10^3 colonies of one organism per cc of urine by catheterization or presence of any number of colonies of organism in urine culture taken by suprapubic method), 3) performance of urine nitrite test, 4) performance of circumcision in males. Exclusion criteria included: 1) patients with negative urine culture, 2) presence of more than one organism in urine culture, 3) history of recurrent UTI, 4) no performance of urinary nitrite test, 4) hematuria, 5) no performance of circumcision.

Patients were divided into negative and positive nitrite groups depending on urinary nitrite test results. Rates of antibiotic resistance in the two groups were compared. All tests were done in laboratory department of Qazvin children's hospital. Urinary nitrite test was done by Medi-Test Combi11 (Macherey–Nagel, Duren, Germany) and urine culture by blood and MacConkey agars. Antibiogram was performed by disk diffusion method. Patients' data were gathered from medical records. Two groups were compared and analyzed by Chi square and nonparametric test (Mann-Whitney test) using SPSS software. P value <0.05 was considered significant.

All parents were given clear explanations regarding the methodology of the research. The children were included in the study if their parents agreed and signed the consent form.

Findings

Out of 119 cases, 22 (18.5%) were males and 97 (81.5%) females. Minimum and maximum ages of the patients were 15 days and 132 months, respectively with median 24 months (Mann-Whitney test). Five patients (4.2%) were younger than 28 days, 42 (35.5%) between 1 to 12 months, and 72 (60.5%) older than 12 months.

The most common symptoms were fever, dysuria, vomiting, restlessness, anorexia, and frequency. Abnormal urine analysis and leukocytosis were the most common paraclinical findings. Ultrasound and DMSA scan were abnormal in 50 (42.1%) and 16 (39.7%) of patients, respectively. Abnormal ultrasound findings included hydronephrosis, fullness of pyelocalyx system, dilation of pyelocaliceal system and ureter. *Escherichia coli* (84%) was the most common grown microorganism. Other organisms in decreasing frequency were *Entrobacter* (5.8%), *Klebciella* (5%), *Proteus* (4.2%) and coagulase negative *Staphylococcus* (1%).

Of 119 patients, 67 were nitrite negative and 52 nitrite positive. Of 67 nitrite negative cases, 16 were males and 51 females. These values in nitrite positive cases were 6 males and 46 females. There was no significant difference between the two groups regarding sex (P=0.1). In the nitrite negative group minimum and maximum ages were 15 days and 132 months, respectively with median 15 months. These values in the nitrite positive group were 1 and 128 months, respectively with median 34.5 months (Mann-Whitney test). There was no significant difference between the two groups regarding age (P=0.1).

Table 1: Comparison of antimicrobial drug resistance rates in UTI children with negative and positive nitrite test

Antimicrobial drug	Nitrite negative patients (n=67)		Nitrite positive patients (n=52)		*P Value*
	Anti. Res. Cases (%)	95%CI	Anti. Res. Cases (%)	95%CI	
Ceftriaxone	5 (7.5)	2.5-16.5	11 (21.2)	11-34.7	0.055
TMP-SMX	21 (31.3)	20.5-43.8	15 (28.8)	17.1-43	0.8
Ampicillin	34 (50.7)	38.2-63.1	33 (63.5)	48.9-76.3	0.2
Gentamycin	8 (11.9)	5.2-22.1	4 (7.7)	2.1-18.5	0.5
Amikacin	6 (9)	3.3-18.4	3 (5.8)	1.2-15.9	0.7
Nalidixic acid	2 (3)	0.4-10.3	1 (1.9)	0.04-10.2	0.8
Cephalotin	10 (14.9)	7.4-25.7	5 (9.6)	3.2-21	0.4
Nitrofuran-toin	7 (11.9)	4.3-20.3	2 (3.8)	0.5-13.2	0.3

UTI: Urinary tract infection; Antti. Res: Antibiotic Resistance; CI: Confidence Interval

Rate of resistance to antimicrobial drugs are shown in Table 1.

Discussion

In our study, the organisms responsible for UTI resembled those quoted in the medical literature[1,2,13]. Although *Escherichia coli* is known to be nitrate reducing, only 34% of UTIs caused by *Escherichia coli* were nitrite positive[13]. Very limited studies pointed out to the relation between urinary nitrite results and the selection of initial antibiotics. Weiz and colleagues study implies that if the urine nitrite test is negative, it is possible that microorganism is resistant to the first and third-generation of cephalosporins. This author mentioned that nitrite results are a useful indicator of resistance to empiric treatment with first- and third-generation cephalosporins[10]. In contrast, Grant and his colleagues showed that although cases of resistance to first-generation cephalosporins in negative-nitrite group were more than that in positive-nitrate group, there was no significant difference between the two groups. He concluded that detection of urine nitrites should not influence the use of first-generation cephalosporins for urinary tract infection[11]. Larson reported that no significant difference was observed between the rates of TMP-SMX resistance in both negative and positive nitrite groups[12]. In our study the rates of resistance to first and third cephalosporin and TMP-SMX were not significant in two groups, and our findings were similar to the last two studies. In our study the difference between the two groups regarding ceftriaxone was very close (*P*=0.055). Therefore, more evaluation and researches considering the relationship between ceftriaxone and nitrite test results are strongly recommended. Regarding the previous studies, we compared more antibiotics such as gentamycin, amikacin, nalidixic acid, ampicillin and nitrofurantoin in two groups. But the results were not significant. Philosophy of using this test in the diagnosis of UTI is that, large numbers of gram negative bacteria such as Entrobacteriaceae, non-glucose-fermenting gram negative rods and *Moraxella catarrhalis* can change urine nitrate to nitrite and then nitrite is converted to nitrogen. This test has 22-43% sensitivity and 99-100% specificity[10]. Although the positive test could indicate the presence of gram negative bacteria, false positive and negative tests should be considered. Hematuria and no circumcision can cause false positive results. The cause of false positive tests in children who are not circumcised is accumulation of bacteria under the prepuce[2].

Several factors can lead to a false negative nitrite result: short time between urine collection and testing, amount of bacteriuria, urine pH less than 6.0, organisms that further reduce nitrites to ammonia, blood, dilute urine, and presence of urobilinogen, medications, or ascorbic acid[13]. In addition, the sensitivity of this test in the neonates and infants is very low. Because the time required for reduction of nitrate to nitrite is at least 4 hours stay of urine in bladder[2,12,14].

Limitations of this study were single hospital and in vitro practice. In vivo results may unpredictably vary, although recent studies of resistant uropathogens correlate well between laboratory and in vivo outcomes [15,16]. According to results of the present study, we think that

urinary nitrite test should not be used as a marker for bacterial resistance to antimicrobial agents in UTI of children.

Conclusion

This study showed that there is no correlation between urinary nitrite results and bacterial resistance to antimicrobial drugs. Therefore, it seems that physicians should not adjust antibiotic therapy for UTI based on nitrite results

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Conflict of Interest: None

References

1. Elder JS. Urinary tract infections. In: Kliegman RM, Behrman RE, Jenson HB, Stanton BF. *Nelson Textbook of Pediatrics*. 18th ed. Philadelphia: Saunders. 2007; Pp: 2223-8.
2. Hansson S, Jodal U. Urinary tract infection in: Avner ED, Harman WE, Niavdet P. *Pediatric Nephrology*. 5th ed. Philadelphia: Lippincott Williams & Wilkins. 2004; Pp 1007-25.
3. Ayazi P, Moshiri SA, Mahyar A, et al. The effect of vitamin A on renal damage following acute pyelonephritis in children. *Eur J Pediatr* 2011; 170(3):347-50.
4. Ayazi P, Mahyar A, Jahani Hashemi H, et al. Comparison of Procalcitonin and C-reactive protein tests in children with urinary tract infection, *Iran J Pediatr* 2009;19(4):381-6.
5. Yoksel S, Ozturk B, Kavas A, et al. Antibiotic resistance of urinary tract pathogen and evaluation of empirical treatment in Turkish children with urinary tract infections. *Int J Antimicrob Agents* 2006;28(5):413-6.
6. Tseng MH, Lo WT, Lin WJ, et al. Changing trend in antibiogram in antimicrobial resistance of pediatric uropathogens in Taiwan. *Pediatr Int* 2008;5(6):797-800.
7. Muratani T, Matsumoto T. Bacterial resistance to antimicrobials in urinary isolates. *Int J Antimicrob Agents* 2004;24(1):28-31.
8. Hooton TM. Fluoroquinolones and resistance in the treatment of uncomplicated urinary tract infection. *Int J Antimicrob Agents* 2003;22(2):65-72.
9. Muratani T, Matsumoto T. Urinary tract infection caused by fluoroquinolone- and cephem-resistant Enterobacteriaceae. *Int J Antimicrob Agents* 2006; 28(1):10-13.
10. Weiz D, Seabrook JA, Lim RK. Urinary nitrite is a significant predictor of pediatric UTI susceptibility to first and third–generation cephalosporins. *J Emerg Med* 2008;39(1):6-12.
11. Grant DC, Chan L, Waterbrook A. Urine nitrite not correlated with bacterial resistance to cephalosporins. *J Emerg Med* 2005;28(3):321-3.
12. Larson MJ, Brooks CB, Leavy WL, et al. Can urinary nitrite results be used to guide antimicrobial choice for urinary tract infection? *J Emerg Med* 1997;15(4):435-8.
13. Holloway J, Hoshi N, Thomas H. Positive urine test: an accurate predictor of absence of pure enterococcal bacteriuria. *South Med J* 2000; 93(7):681–5.
14. Mahon CR, Manuselis GM. Text Book of Diagnostic Microbiology. 2nd ed. Philadelphia: Saunders. 2000; Pp: 1132-3.
15. Talan D, Stamm W, Hooton T, et al. Comparison of ciprofloxacin (7 days) and trimethoprim-sulfamethoxazole (14 days) for acute uncomplicated pyelonephritis in women: a randomized trial. *JAMA* 2000;283(12):1583-90.
16. Raz R, Chazan B, Kennes Y, et al. Empiric use of trimethoprim-sulfamethoxazole (TMP-SMX) in the treatment of women with uncomplicated UTIs, in a geographical area with a high prevalence of TMP-SMX-resistant uropathogens. *Clin Infect Dis* 2002;34(9):1165-9.