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Effect of Prophylactic Antibiotic Use in the Development of Antibiotic Resistance in Children with Recurrent Urinary Tract Infections

Tekrarlayan İdrar Yolu Enfeksiyonunda Profilaktik Amaçlı Antibiyotik Kullanımının Çocuklarda Antibiyotik Direnç Gelişimine Etkisi

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Abstract

Aim: Although prophylactic antibiotic treatment is still debatable, it is currently in use in recurrent urinary tract infections (UTIs). In the present study, we aimed to observe if prophylactic antibiotic use had any effect on the development of antibiotic resistance in patients with recurrent UTIs who we followed up in our clinic.

Methods: The present study was performed on patients aged between one month and 16 years, who had recurrent UTIs, and were followed up by the Department of Pediatrics at Bülent Ecevit University Medical School. Patient files were retrospectively reviewed, and 50 patients who received antibiotic prophylaxis and 100 patients without prophylaxis were enrolled in the study. Urinary tests, subsequent urinary culture results, and antibiotic resistances were compared between the groups.

Results: The mean age was 42.7±44.2 months. The most frequently cultured isolated bacterium was *Escherichia coli* (*E. coli*) (58.4%). No difference was determined in bacteria in cultures between prophylaxis receivers and non-receivers. Isolation rate of *E. coli* was higher in urinary cultures in females than in males (p<0.001). When antibiotic resistance of all urinary culture-isolated bacteria was compared between the two groups, there was no statistically significant difference. However, an increased resistance against amoxicillin/clavulanic acid, ceftriaxone, and piperacillin was determined in prophylaxis group in whom *E. coli* was grown. In this study, general antibiotic resistance was most frequently observed against ampicillin (71.9%).

Conclusion: In the present study, we observed that prophylaxis did not contribute so much to resistance other than *E. coli*. We recommend not preferring antibiotics which have increased resistance in our institution especially in children receiving prophylaxis for empirical treatment.

Keywords: Childhood, urinary tract infection, prophylaxis, antibiotic resistance

Öz

Amaç: Tekrarlayan idrar yolu enfeksiyonlarında (İYE) antibiyotik proflaksisi günümüzde tartışmalı da olsa kullanılmaya devam edilmektedir. Biz bu çalışmada, kendi kliniğimizde takip ettiğimiz tekrarlayan İYE'de kullanılan profilaksinin antibiyotik direnç gelişimine etkisinin olup olmadığını gözlemlemeyi amaçladık.

Yöntemler: Bu çalışma Bülent Ecevit Üniversitesi Tıp Fakültesi Pediatri Departmanı'nca takip edilen bir ay ile 16 yaş arası tekrarlayan idrar yolu enfeksiyonu olan hastalarda yapılmıştır. Hasta dosyaları retrospektif olarak taranarak antibiyotik proflaksisi alan 50 ve almayan 100 hasta çalışmaya dahil edildi. Hastaların idrar tetkikleri, sonraki kültürlerindeki üremeleri ve bunların antibiyotik dirençleri gruplar arasında karşılaştırıldı.

Bulgular: Hastaların %43,3 erkek, %56,7 kızlardan oluşmaktaydı ve ortalama yaşları 42,7±44,2 ay (1 ay-16 yaş) idi. Tüm kültürlerde en sık üreyen bakteri %58,4 ile *Escherichia Coli (E. coli)* idi. Profilaksi alan ve almayan gruplar arasında kültürde üreyen bakterilerin dağılımı açısından bir fark saptanmadı. Kızlardaki idrar kültürlerinde *E. coli* görülme oranı erkeklerden daha fazlaydı (p<0,001). Her iki grupta idrar kültürlerinde üreyen tüm bakterilerin antibiyotiklere direnci karşılaştırıldığında istatistiksel olarak anlamlı fark görülmedi. Buna karşın profilaksi grubunda idrar kültüründe *E. coli* üreyenlerde amoksisilin/klavulanik asit, seftriakson ve piperasiline karşı artmış direnç saptandı. Bu fark istatistiksel olarak anlamlı bulundu. Bu çalışmada da en sık antibiyotik direnci %71,9 ile ampisiline karşı gözlendi.

Sonuç: Biz bu çalışmada *E. coli* dışındaki ajanlarda proflaksinin dirence çok katkısının olmadığını gözlemledik. Kendi hastanemizde özellikle proflaksi alan bir çocuk için ampirik tedavide direnç artışı saptanan antibiyotiklerin tercih edilmemesini önermekteyiz.

Anahtar Sözcükler: Çocukluk çağı, idrar yolu enfeksiyonu, proflaksi, antibiyotik direnci

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Introduction

Urinary tract infection (UTI) is the second most commonly encountered infectious disease following upper respiratory tract infection in children (1). UTIs is an important cause of morbidity in childhood. Antibiotic therapy is generally initiated empirically because early treatment decreases the rate of morbidity resulting from UTIs (2,3). Although prophylactic antibiotic use for recurrent UTIs is decreasing nowadays, it still is in the use (4-6). However, antibiotic resistance has become an increasingly pressing problem in many countries. Moreover, there are considerable geographic variations in bacterial patterns and resistance properties depending on local antimicrobial prescription practices (3). Additionally, it is believed that prophylactic antibiotic use contributes to drug resistance.

The aim of the present study was to determine causative microorganisms in our institution in recurrent UTI cases in our clinic, etiological factors, and whether prophylactic antibiotic use had any effects on resistance development.

Methods

Design, Setting, and Participants

This was a retrospective case-control study conducted in the Department of Pediatrics, Bülent Ecevit University School of Medicine, between January 2008 and January 2013. A total of 150 patients (100 receiving no prophylaxis, and 50 receiving prophylaxis) aged between one month and 16 years, who were diagnosed with recurrent UTI in our clinic, were enrolled in the study. All patients were investigated for UTI causes. Additionally, all had population-based UTI. Antibiotic resistance rates in later urinary cultures were compared between the groups who satisfied recurrence criteria and was followed up without prophylactic antibiotic use. In addition, other tests and demographic characteristics of the patients were evaluated retrospectively.

Study Content

Urine samples were provided after perineal cleaning in children with urinary control by mid-flow urine sampling, and by catheterization in children without urinary control, and all samples were incubated in appropriate media. Suprapubic aspiration was performed in none of our patients for sampling. For biochemical analysis, non-centrifuged fresh urine samples were used. Acidity, density, leukocyte and neutrophil counts, and nitrite reaction were performed. An insight xpert u500 device was used for these data. In microscopic examination, urine samples were first centrifuged, and examined at x40 magnification there were 5 or more leukocytes in one microscopic field, then it was diagnosed as pyuria; five or more erythrocytes per field was diagnosed as hematuria; and any number of bacteria was diagnosed as bacteriuria. Urine samples were inoculated into blood agar and eosin methylene blue agar (GBL, Turkey), and were incubated at 37°C for 18-24 hours. After the inoculation, grown up bacteria were determined according to classical methods and/or appropriate API® identification system (BioMerieux, France) after colony counting. The level of significance was determined as $\geq 10^5$ colony-forming units (CFU)/mL for mid-flow urine and $\geq 10^4$ CFU/mL for catheter cultures, if children had clinical signs.

Antibiotic sensitivities were determined by using agar disc diffusion technique. After spreading bacterial suspension prepared in 0.5 McFarland over Müller-Hinton agar (GBL, Turkey), antibiotic discs (Bioanalyse, Turkey) were used. Bacterial sensitivities were assessed according to the Clinical and Laboratory Standards Institute criteria. According to antibiogram results, antibiotics were separated into two groups as susceptible and resistant. Trimethoprim-sulfamethoxazole (TMP-SMX), amoxicillin, nitrofurantoin, and cefixime were used according to patient age in antibiotic prophylaxis. Urinary ultrasound, voiding cystourethrogram and Tc-99m Dimercaptosuccinic acid scintigraphy were used as imaging techniques.

Statistical Analysis

Statistical analyses were performed with SPSS 18.0 software (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation and categorical variables as frequency and percent. Continuous variables were compared with the independent samples t-test and categorical variables were compared using the Pearson chi-square test or Fisher's exact test. A p value of less than 0.05 was considered statistically significant for all tests.

The present study was approved on 3rd September 2014 by Local Ethics Committee of Zonguldak Bülent Ecevit University (approval number: 2013/14).

Results

In the present study, 235 culture growths from 150 patients, who had population-based UTIs recurred within approximately five-years, were retrospectively screened in medical files and documented.

Demographic characteristics of the groups: Of the subjects, 65 (43.3%) were male, and 85 (56.7%) were female. The mean age of the patients was 42.7±44.2 months (1 month-16 years). There was no difference between the groups in gender distribution and age (Table 1). The indication for prophylaxis was vesicoureteral reflux (n=11; 22%), neurogenic bladder (n=2; 4%), renal anomalies (n=10; 20%), renal calculus (n=5; 10%), and

voiding dysfunction (n=4; 8%); the other 18 children (36%) had idiopathic recurrent UTI.

Correlation of biochemical examination of urine with cultural positivity: In both groups, *Escherichia coli* (*E. coli*) was the most common (n=137, 58.4%) bacterium among causative agents. In prophylaxis receiving group, *E. coli* was more commonly isolated compared to the other agents in the presence of leukocyte esterase in urine (p=0.017). However, no correlation was determined in other parameters (bacteriuria, pyuria, hematuria, and nitrite). Moreover, there was no similar correlation between urine analysis and culture bacteria isolated in prophylaxis non-receivers. The mean number of cultural growth was 2±2.32 and 1±1.19 in prophylaxis receivers and no-receivers, respectively (p<0.001).

Distribution of isolated bacteria in groups receiving and non-receiving prophylaxis: There was no significant difference in bacterial growth in urine cultures between prophylaxis receivers and non-receivers. The distribution of cultured microorganisms is given in Table 2.

Table 1. Gender distribution of groups

Gender	Prophylaxis		No prophylaxis		Total	p
	n	%	n	%		
Male	22	44	43	43	65	1.000
Female	28	56	57	57	85	
Total	50	100	100	100	150	

Table 2. The distribution of isolated bacteria in the urine cultures

		Prophylaxis		No prophylaxis		Total		p
		n	%	n	%	n	%	
Bacteria	*Escherichia coli*	60	51.3	77	65.3	137	58.4	p>0.05
	Klebsiella pneumoniea	18	15.4	21	17.8	39	16.6	
	Proteus mirabilis	13	11.1	11	9.3	24	10.2	
	Pseudomonas spp.	12	10.2	1	0.8	13	5.5	
	Klebsiella oxytoca	6	5.1	4	3.4	10	4.3	
	Enterobakter auerogenes	6	5.1	3	2.6	9	3.8	
	Morganella morganii	1	0.9	1	0.8	2	0.8	
	Serratia marcescens	1	0.9	0	0.0	1	0.4	
	Total	117	100	118	100	235	100	

In order of frequency, *E. coli*, *Klebsiella* spp., and *Proteus mirabilis* were determined.

Distribution of bacteria among genders in prophylaxis receivers and non-receivers: *E. coli* was the most commonly isolated bacteria both in males and females. Isolation rate of *E. coli* was 34.5% in males and 79.2% in females. Majority of patients with *E. coli* were females, and it was more common than males (p<0.001) (Table 3) (Graphic 1).

Distribution of age range according to gender in children with isolated bacteria: Of patients with UTI, 41.5% (n=27) of males were ≤1 year old; whereas 80% (n=68) of females were ≥13 months old. UTI rate was increased in males younger than one year of age, and in females older than one year of age (p=0.007) (Table 4).

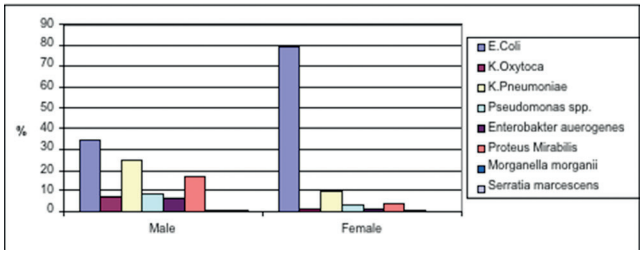
Distribution rate of antibiotics used in prophylaxis: There were a total of 50 patients in the prophylaxis receiving group, and 62.0% of them were receiving TMP-SMX, 28.0% were receiving amoxicillin, 8.0% were receiving nitrofurantoin, and 2.0% were receiving cefixime.

Table 3. Gender distribution of isolated bacteria in the urine cultures

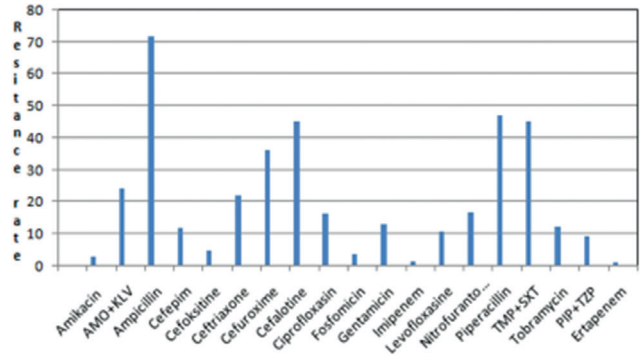
		Male		Female		Total		
		n	%	n	%	n	%	p
Bacteria	*Escherichia coli*	38	34.5	99	79.2	137	58.4	p<0.001
	Klebsiella pneumoniae	27	24.5	12	9.6	39	16.6	p>0.05
	Proteus mirabilis	19	17.3	5	4	24	10.2	
	Pseudomona spp.	9	8.2	4	3.2	13	5.5	
	Klebsiella oxytoca	8	7.3	2	1.6	10	4.3	
	Enterobakter auerogenes	7	6.4	2	1.6	9	3.8	
	Morganella morganii	1	0.9	1	0.8	2	0.8	
	Serratia marcescens	1	0.9	0	0	1	0.4	
	Total	110	100	125	100	235	100	

Table 4. Distribution of age range according to gender in children with urinary culture

Age (years)	Gender				Total		p
	Male		Female				
	n	%	n	%	n	%	
≤1 year	27	41.5	17	20.0	44	29.3	0.007
>1 year	38	58.5	68	80.0	106	70.7	
Toplam	65	100	85	100	150	100	



Graphic 1. Gender distribution of isolated bacteria in the urine cultures



Graphic 2. The over all rate of antibiotic resistance in patients (%) AMO+CLV: Amoxicillin +clavulanic acid, TMX+SXT: Trimethoprim+sulfametaxazole, PIP+TZP: Piperacilline+tazobactam

Mean antibiotic resistance rate in all patients: Total resistance rate of bacteria which were isolated in urine cultures was determined as 71.9% for ampicillin, 47.0% for piperacillin, 45.3% for cefalotin, 45.1% for TMP-SMX, 4.9% for cefoxitin, 3.7% for fosfomycin, 2.9% for amikacin, 1.4% for imipenem, and 1.0% for ertapenem (Graphic 2).

Antibiotic resistance differences in cultures between prophylaxis receivers and non-receivers: When all grown up agents were evaluated together, there was no difference in resistance development for abovementioned antibiotics between prophylaxis receivers, and non-receivers. Namely, having started prophylactic antibiotic treatment did not have any effect on antibiotic resistance development of microorganisms, which were later in urine cultures.

Effects of causative microorganisms in urine culture in antibiotic resistance development: Increased resistance against amoxicillin/clavulanic acid (AMO/CLV) (37.5-8.7%), ceftriaxone (34.6-10.4%) and piperacillin (71.4-39.9%) was determined in patients who had *E. coli* in subsequent urine cultures and were receiving prophylaxis, when compared with prophylaxis non-receivers (Table 5). There was no significant difference in drug resistance between patients having *Klebsiella* spp. in the two groups. As the number of other bacteria grown was fewer, statistical analysis was not performed.

Discussion

Currently, empirical antibiotic treatment is recommended in all patients, who are suspected to have UTI, to start early treatment, and decrease morbidity rate. Treatment and prophylaxis plans should be performed according to regional UTI agents, and antimicrobial resistance patterns (2,7). It has been reported that UTI is more commonly encountered in female gender. (2) In a study on recurrent UTI, the rate of recurrent infection was found to be 68.2% in females and 57.4% in males, and it was determined that 42.9% of male children with the diagnosis of UTI were younger than one year of age; as age increased UTI rate was significantly decreased among these patients (8). Similar to that study, 43.3% of patients in our cohort were male, and 56.7% were female. There was no difference in gender distribution between the groups. Similar to the literature, we detected that UTI rate was increased in male children younger than one year, and in female children older than one year of age (8-11). In the present study, *E. coli* was more frequent than other agents in the presence of leukocyte esterase than in its absence in biochemical examination of urine in prophylaxis receiving group (p=0.034), whereas such a relationship was not found in the prophylaxis non-receiving group.

In a large-scale study, it was shown that resistance developed against prophylactic antibiotics, and chemoprophylaxis could not prevent recurrence of UTI (2,5). We observed that prophylaxis did not decrease the rate of UTI recurrence. The mean number of growth in urinary culture was 2±2.32 in prophylaxis receivers, and 1±1.19 in non-receivers. However, we believe that standardized patient studies (etiological cause, prophylactic antibiotic etc.) are required to clarify this issue.

In studies performed all over the world, *E. coli*, *Klebsiella* spp., and *Proteus* spp. are determined in the first three lines (7,9,12-15). Similar to the literature, it was determined in the present study that *E. coli* (58.4%) was the most commonly isolated microorganism both in females and males in both groups. It was followed by *Klebsiella* spp. (20.9%), and *Proteus* spp. (10.2%). No difference was determined in isolated bacteria between the two groups. Although the most commonly isolated agent was *E. coli* in both genders, majority of patients with *E. coli* were females (Table 3). Frequent empiric treatment of UTI increases the importance of antibiotic susceptibility characteristics of agents (3,16). In many countries, the most common antibiotic resistance in isolated species is against ampicillin. The probability of resistance development against ampicillin was determined as 45%, 50%, and 100% in children living in Canada, Europe, and Africa, respectively (17-20). Ampicillin is not recommended alone in the treatment of UTIs,

Table 5. The comparison of the groups in the breeding of antibiotic resistance in *E. coli*

Antibiotic		*Escherichia coli*						p
	No prophylaxis		Prophylaxis		Total			
		%	n	%	n	%		
Amikacin	Antibiotic-sensitive	64	98.5	25	92.6	89	96.7	0.205
	Antibiotic-resistant	1	1.5	2	7.4	3	3.3	
	Total	65	100	27	100	92	100	
AMO+CLV	Antibiotic-sensitive	42	91.3	10	62.5	52	83.9	0.014
	Antibiotic-resistant	4	8.7	6	37.5	10	16.1	
	Total	46	100	16	100	62	100	
Ampicillin	Antibiotic-sensitive	28	40.6	6	22.2	34	35.4	0.146
	Antibiotic-resistant	41	59.4	21	77.8	62	64.6	
	Total	69	100	27	100	96	100	
Cefepim	Antibiotic-sensitive	56	94.9	19	82.6	75	91.5	0.092
	Antibiotic-resistant	3	5.1	4	17.4	7	8.5	
	Total	59	100	23	100	82	100	
Cefoksitine	Antibiotic-sensitive	68	98.6	24	96.0	92	97.9	0.463
	Antibiotic-resistant	1	1.4	1	4.0	2	2.1	
	Total	69	100	25	100	94	100	
Ceftriaxone	Antibiotic-sensitive	60	89.6	17	65.4	77	82.8	0.012
	Antibiotic-resistant	7	10.4	9	34.6	16	17.2	
	Total	67	100	26	100	93	100	
Cefuroxime	Antibiotic-sensitive	39	81.3	13	59.1	52	74.3	0.094
	Antibiotic-resistant	9	18.8	9	40.9	18	25.7	
	Total	48	100	22	100	70	100	
Cefalotin	Antibiotic-sensitive	37	69.8	11	50.0	48	64.0	0.173
	Antibiotic-resistant	16	30.2	11	50.0	27	36.0	
	Total	53	100	22	100	75	100	
Ciprofloxasin	Antibiotic-sensitive	61	88.4	19	73.1	80	84.2	0.111
	Antibiotic-resistant	8	11.6	7	26.9	15	15.8	
	Total	69	100	26	100	95	100	
Fosfomisin	Antibiotic-sensitive	64	98.5	23	100	87	98.9	1.000
	Antibiotic-resistant	1	1.5	0	0.0	1	1.1	
	Total	65	100	23	100	88	100	
Gentamicin	Antibiotic-sensitive	61	91.0	22	84.6	83	89.2	0.458
	Antibiotic-resistant	6	9.0	4	15.4	10	10.8	
	Total	67	100	26	100	93	100	
Imipenem	Antibiotic-sensitive	67	98.5	27	100	94	98.9	1.000
	Antibiotic-resistant	1	1.5	0	0.0	1	1.1	
	Total	68	100	27	100	95	100	
Levofloxasin	Antibiotic-sensitive	60	87.0	22	84.6	82	86.3	0.747
	Antibiotic-resistant	9	13.0	4	15.4	13	13.7	
	Total	69	100	26	100	95	100	
Nitrofurantoin	Antibiotic-sensitive	67	100	24	100	91	100	-
	Antibiotic-resistant	-	-	-	-	-	-	
	Total	67	100	24	100	91	100	
Piperacilline	Antibiotic-sensitive	37	60.7	6	28.6	43	52.4	0.022
	Antibiotic-resistant	24	39.3	15	71.4	39	47.6	
	Total	61	100	21	100	82	100	

Table 5. Continue								
TMX+SXT	Antibiotic-sensitive	38	55.9	13	48.1	51	53.7	0.650
	Antibiotic-resistant	30	44.1	14	51.9	44	46.3	
	Total	68	100	27	100	95	100	
Tobramycin	Antibiotic-sensitive	47	90.4	17	81.0	64	87.7	0.269
	Antibiotic-resistant	5	9.6	4	19.0	9	12.3	
	Total	52	100	21	100	73	100	
PIP+TZP	Antibiotic-sensitive	44	95.7	15	93.8	59	95.2	1.000
	Antibiotic-resistant	2	4.3	1	6.3	3	4.8	
	Total	46	100	16	100	62	100	
Ertapenem	Antibiotic-sensitive	44	95.7	15	93,8	59	95.2	-
	Antibiotic-resistant	2	4.3	1	6.3	3	4.8	
	Total	46	100	16	100	62	100	

AMO+CLV: Amoxicillin+clavulanicacid, TMX+SXT: Trimethoprim+sulfametaxazole, PIP+TZP: Piperacilline+tazobactam

because of high risk of resistance development (21). In a study conducted in the United Kingdom, it was almost recommended that routine antibiotic prophylaxis should be stopped in children having UTI (5,22).

The rate of resistance against ampicillin ranged between 64.9% and 88% in studies performed in Turkey and in the world (7,9,23-29). When antibiotic resistance in all patients was reviewed in the present study, the resistance rates were determined as 71.9% for ampicillin, 47.0% for piperacillin, 45.1% for TMP-SMX, 24.2% for AMO/CL, and 22.1% for ceftriaxone. We recommend that antibiotics with lower resistance rates should be selected for empiric treatments for UTI in our institution.

Ampicillin resistance of *E. coli* was determined as 50-70%, and TMP+SMX was 31.2-53% in previous studies (3,7,18,30). In a study, cefotaxime resistance in *E. coli* was significantly higher in patients receiving prophylaxis when compared with non-receivers. However, there was no increase in aminoglycoside resistance in these patients (31). Different from the former study, receiving prophylaxis did not change any microorganisms in later cultures in the present study. It was also determined that resistance was more commonly determined for AMO/CLV, ceftriaxone, and piperacillin in patients who had *E. coli* isolated in urine cultures, and received prophylaxis than the non-receivers (Table 5). However, there was no difference in resistance for other antibiotics between the groups. There was no significant difference in antibiotic resistance in patients having *Klebsiella* growth between the two groups. In conclusion, we recommend that these three antibiotics should be selected neither orally nor parenterally as empiric antibiotic in the prophylaxis, since *E. coli* is the most commonly isolated agent.

Currently, there is no consensus in the world on criteria for initiating prophylaxis. Low-dose, long-term prophylaxis is still being recommended in patients with high renal scarring risk (2,5,6,32). However, antimicrobials in prophylaxis may increase the risk of development of resistance (5,22,31,33).

Although there are many data about UTI and antibiotic resistance in the literature, there are limited data indicating that prophylaxis might increase antibiotic resistance. In a study performed in two centers, previous urine culture results in 420 patients who received prophylaxis were compared. It was determined in both hospitals that *E. coli* infection rate was decreased in patients receiving antibiotic prophylaxis when compared with that in those with a previous UTI (23). However, there were significant decreases in susceptibility of all 3rd generation cephalosporins, ciprofloxacin, gentamicin, and amikacin in patients receiving cephalosporins prophylaxis and significant decreases were determined in susceptibility of gentamicin and ciprofloxac in in patients receiving TMP-SXT prophylaxis (23). In the study, initiation of prophylaxis caused neither *E. coli* nor other bacteria in later cultures.

The design of the present study was different from the study mentioned above. We had a total of 50 patients who received prophylaxis. As the number of patients for each prophylactic antibiotic was fewer, we compared groups as prophylaxis receivers and non-receivers. When antibiotic resistances of isolated bacteria in all urine cultures were compared in both groups, there was no statistically significant difference in increase of resistance. Thus, initiation of prophylaxis did not affect antibiotic resistance in later cultures. As there are few such designed studies in the literature, we believe that large-scale prospective studies should be performed to define any correlation between prophylaxis and resistance development.

In a study performed in Iran, it was shown that resistance was developed against antibiotic used for prophylaxis in more than half of patients with resistant UTI, who received previous prophylaxis (28). In the

present study, we did not observe increased resistance against antibiotics used in the prophylaxis in later cultures between the groups. However, resistance rate is generally increasing against prophylactic antibiotics in our institution

Study Limitations

Limitations of our study may be summarized as the patients might have used another antibiotic rather than prophylactic antibiotic previously for an infection other than the urinary system, and this might have affected susceptibility of UTI agent. Patient compliance was not definite for prophylactic antibiotics. Moreover, we did not divide patients into groups according to their underlying etiological factors, as well as we did not divide them according prophylaxis duration. Considering these factors, well-standardized prospective studies are required for the future. Similar to the world, we believe that inappropriate antibiotic use may contribute to increased antibiotic resistance also in our region.

Conclusion

In the present study, on the contrary to the common belief, we observed that prophylaxis did not increase antibiotic resistance in later urine cultures, and the rates were similar between the groups. However, we also determined increased resistance rates against AMO/CLV, ceftriaxone, and piperacillin in the prophylaxis group if *E. coli* was isolated in the culture. We recommend that empiric antibiotics should be selected considering these results and general antibiotic resistance rates in similar patients as in our institution. Consequently, we recommend that resistance studies specific for every regions should be performed and empiric treatments should be designed under the light of the study results.

Ethics

Ethics Committee Approval: The present study was approved on 3rd September 2014 by Local Ethics Committee of Zonguldak Bülent Ecevit University (approval number: 2013/14).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

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