















Selection for antimicrobial prophylaxis in emergency and elective transurethral procedures: Susceptibility pattern in Türkiye

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ABSTRACT

BACKGROUND: In this study, we aimed to determine the most appropriate antimicrobial agents for prophylactic antibiotic use during emergency and elective transurethral procedures.

METHODS: The study was conducted in five hospitals located in five different geographical regions of Türkiye. The microorganism cultured in urine before emergency and elective transurethral procedures in these centers between March 2021 and March 2022 were reviewed retrospectively from the hospital records. Demographic data (age and gender) of the patients, comorbid disorders, previous urological procedures, anomalies of the urogenital tract, use of urethral catheters (permanent or clean intermittent catheterization), cultured microorganisms, and antibiotic susceptibilities were noted. The patients hospitalized or had antibiotics for any reason in the previous 1 month were excluded from the study.

RESULTS: A total of 1450 patients, 742 men (51.2%) and 708 women (48.8%), were included in the study. The mean age of the patients was 55.3±19.36 (1–98) years. Diabetes mellitus was evident in 271 (18.7%) patients. The five most common microorganisms cultured in urine, in order of frequency, were: ESBL (-) *Escherichia coli* in 418 (28.8%), ESBL (+) *E. coli* in 309 (21.3%), *Klebsiella pneumoniae* in 183 (12.6%), *Enterococcus faecalis* in 124 (8.6%), and *Pseudomonas aeruginosa* in 89 (6.1%). The susceptibility rates to antimicrobial agents recommended for prophylaxis by the American Urology Association and the European Association of Urology guidelines were found as follows: cefepime 87.1%, ampicillin+sulbactam 84%, TMP-SMX 71.6%, amoxicillin+clavulanate 63.5%, cefoxitin 59%, ceftazidime 58.6%, cefuroxime 43.5%, ceftriaxone 43%, and cefixime 38.4%.

CONCLUSION: We found that currently recommended antimicrobials provide poor coverage for the most common pathogens isolated. Urologists should consider patient-based antibiotic prophylaxis in endoscopic urethral procedures, follow appropriate protocols, and consider local antibiotic resistance.

Keywords: Antimicrobial prophylaxis; susceptibility pattern; transurethral procedures.

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INTRODUCTION

The transurethral route has become the most preferred surgical approach in the majority of urological procedures with several hundred thousand procedures being performed annually in the USA.^[1] A growing number of transurethral procedures pose a great risk of infection in the patients who have these procedures. Therefore, antimicrobial prophylaxis has been recommended to diminish the risk of infectious complications in patients undergoing diagnostic or invasive transurethral procedures.^[2]

The most common infectious agent related to transurethral procedures is *Escherichia coli*, followed by *Pseudomonas aeruginosa*, *Enterococcus faecalis*, *Klebsiella*, *Proteus mirabilis*, and *Staphylococci*.^[3,4] A suitable antimicrobial prophylaxis may decrease the postoperative infection rate in certain transurethral procedures. However, there are some drawbacks including misuse of antibiotics and antibiotic resistance. Over and misuse of antibiotics raise the problem of antibiotic resistance in uropathogens and also threaten public health. Rational use of antibiotics improves surgical outcomes, and reduces the risk for antimicrobial resistance as well as the infections resistant to multiple antibiotics.^[5]

Prophylaxis with a single-dose cephazolin or trimethoprim-sulfamethoxazole has been advised by The American Urology Association (AUA) guidelines.^[6] The European Association of Urology (EAU) guideline recommends trimethoprim/trimethoprim sulfamethoxazole or cephalosporin group 2/3 or aminopenicillin + a beta-lactamase inhibitor.^[7]

In this study, we examined antibiotic susceptibility tests all across Türkiye, and investigated optimal empirical antimicrobial prophylaxis regimens for transurethral urologic procedures, presuming that greater coverage of possible microorganisms causing infection may improve outcomes.

MATERIALS AND METHODS

This study was conducted in accordance with the ethical standards specified in the Declaration of Helsinki (1964) and was approved by Local Ethics Committee (Approval number: E2-22-1718).

The study was conducted in five medical centers located in five different geographical regions of Türkiye. The microorganism cultured in urine before emergency and elective transurethral procedures in these centers between March 2021 and March 2022 were reviewed retrospectively from the electronic hospital records. Demographic data (age and gender) of the patients, comorbid disorders, previous urological procedures, anomalies of the urogenital tract, use of urethral catheters (permanent or clean intermittent catheterization), cultured microorganisms, and antibiotic susceptibilities were noted. To prevent the confounding effect of hospital-originated infectious agents, urine culture samples were taken from all patients before hospitalization for the operation. The pa-

tients hospitalized or had antibiotics for any reason in the previous 1 month were excluded from the study.

Statistical Analysis

Statistical Package for Social Sciences (SPSS) v. 20.0 for Windows (SPSS Inc., Chicago, IL) software was used for statistical analysis. The mean, median, standard deviation, minimum and maximum values of the included quantitative data were calculated. The distribution of qualitative data was described using absolute values and percentages.

RESULTS

A total of 1450 patients 742 men (51.2%) and 708 women (48.8%) were included in the study. Of the 1450 transurethral procedures, 1416 (97.7%) were elective and 34 (2.3%) were emergency cases. The mean age of the patients was 55.3 ± 19.36 (1–98) years. Diabetes mellitus was evident in 271 (18.7%) patients. There was a history of previous urological surgery in 365 (25.2%) patients. It was observed that 11.4% of the patients were being followed up for a malignancy (three most common malignancies were bladder tumor [5.9%], colorectal cancer [2%], and prostate cancer [1.4%]). One or more pathological conditions of the urinary tract were present in 900 patients (62.1%) (in order of frequency: urinary system stone diseases [30.2%], benign prostate hyperplasia [25.8%], bladder tumor [12.4%], prostate cancer [4.7%], and urethral stricture [3.7%]). Thirty-one patients (2.1%) were on systemic chemotherapy, 11 patients (0.8%) were on radiotherapy, and 3 patients (0.2%) were on systemic chemotherapy + radiotherapy. A urethral catheter was present in 230 patients (15.9%).

The microorganisms cultured in urine, in order of frequency, were: ESBL (-) *E. coli* in 418 (28.8%), ESBL (+) *E. coli* in 309 (21.3%), *Klebsiella pneumoniae* in 183 (12.6%), *E. faecalis* in 124 (8.6%), *P. aeruginosa* in 89 (6.1%), *Candida albicans* in 53 (3.7%), *Enterobacter* in 43 (3%), *Staphylococcus spp.* (CNS) (*Staphylococcus epidermidis*) in 33 (2.3%), *Enterococcus faecium* in 31 (2.1%), *Streptococci* in 27 (1.9%), *Acinetobacter baumani* in 24 (1.7%), *Klebsiella oxytoca* in 18 (1.2%), *P. mirabilis* in 16 (1.1%), *Pseudomonas spp.* in 11 (0.8%), *Proteus spp.* in 8 (0.6%), *Acinetobacter spp.* in 9 (0.6%), *Morganella morganii* in 9 (0.6%), MSSA in (%) 0.6, *Citrobacter* in 6 (0.4%), *Serratia* in 5 (0.3%), *Providencia* in 3 (0.2%), and other microorganisms in 22 (1.5%) patients (Table 1).

Antibiotic susceptibility results indicated that the cultured microorganisms were the most sensitive to following antibiotics: vancomycin (100%), teicoplanin (100%), linezolid (98.3%), aztreonam (96.9%), meropenem (92.5%), imipenem (92.2%), amikacin (92%), ertapenem (88.7%), fosfomicin (87.5%), cefepime (87.1%), nitrofurantoin (86.9%), Pip-Taz (86.1%), gentamicin (85.6%), tigecycline (85.1%), ampicillin + sulbactam (84%), levofloxacin (76%), TMP-SMX (71.6%), amoxicillin + clavulanate (63.5%), ceftazidime (59%), ciprofloxacin (58.7%), ceftazidime (58.6%), cefuroxime (43.5%), ceftriaxone (43%),

Table 1. Microorganisms grown in urine culture and antibiotic susceptibility rates in order of frequency

Bacterium	Antimicrobial	Total		Patients with foley catheter	
		n	Susceptibility (%)	n	Susceptibility (%)
ESBL (-) E. coli	Penicillin Combination	385	76.1	48	58.3
	2nd generation Cephalosporins	214	87.9	29	79.3
	3rd generation Cephalosporins	334	79.9	41	53.7
	Fluoroquinolones	355	73	41	58.5
	TMP-SMX	349	77.9	35	65.7
	Fosfomycin	261	94.6	42	88.1
	Nitrofurantoin	271	97	38	92.1
	Aminoglycosides	399	94.5	51	86.3
	Pip-taz	264	91.7	40	82.5
ESBL (+) E. Coli	Penicillin Combination	288	30.6	30	43.3
	2nd generation Cephalosporins	271	45.4	27	51.9
	3rd generation Cephalosporins	275	20	29	24.1
	Fluoroquinolones	290	34.5	29	62.1
	TMP-SMX	275	66.9	28	71.4
	Fosfomycin	273	97.4	30	96.7
	Nitrofurantoin	298	94.6	32	96.9
	Aminoglycosides	296	90.9	29	93.1
	Pip-taz	167	86.2	16	93.8
Klebsiella pneumonia	Penicillin Combination	108	39.8	23	43.5
	2nd generation Cephalosporins	187	48.3	19	52.6
	3rd generation Cephalosporins	174	90.5	22	36.4
	Fluoroquinolones	160	66.2	30	40
	TMP-SMX	159	75.5	30	43.3
	Fosfomycin	64	95	20	57.8
	Nitrofurantoin	103	61.2	26	61.5
	Aminoglycosides	176	94.3	32	100
	Pip-taz	127	78	19	36.8
Enterococcus faecalis	Penicillin Combination	139	89.7	8	87.5
	Fluoroquinolones	114	64.9	18	38.9
	TMP-SMX	108	56.5	17	29.4
	Nitrofurantoin	94	97.9	12	100
	Tigecycline	99	98	14	100
	Vancomycin	107	100	15	100
	Linezolid	109	97.2	15	100
	Teicoplanin	103	100	15	100
Pseudomonas aeruginosa	3rd generation Cephalosporins	174	90.5	6	100
	Fluoroquinolones	81	42	29	62.1
	Aminoglycosides	185	98.8	28	100
	Pip-taz	165	95.4	27	92.6
Proteus	Penicillin Combination	23	82.6	3	66.7
	2nd generation Cephalosporins	18	77.8	2	50
	3rd generation Cephalosporins	61	90.5	3	33.3
	Fluoroquinolones	44	91.7	3	100
	Fosfomycin	19	89.5	2	50
	Aminoglycosides	24	91.7	3	100
	Pip-taz	17	94.1	2	50
Enterobacter	Penicillin Combination	34	0	6	0
	2nd generation Cephalosporins	32	0	6	0
	3rd generation Cephalosporins	43	46.5	7	71.4

Table 1. Cont.

	Fluoroquinolones	43	67.4	7	71.4
	TMP-SMX	43	67.4	7	71.4
	Fosfomycin	30	26.7	4	50
	Nitrofurantoin	34	58.8	6	66.7
	Aminoglycosides	43	90.7	7	71.4
	Pip-taz	43	48.8	7	100
Acinetobacter	3rd generation Cephalosporins	20	80	7	85.7
	Fluoroquinolones	19	63.2	2	50
	TMP-SMX	29	68.9	6	83.3
	Aminoglycosides	23	73.9	7	85.7
	Pip-taz	25	84	7	85.7
Staphylococcus	Penicillin Combination	11	18.2	3	0
	2nd generation Cephalosporins	9	77.8	1	100
	Fluoroquinolones	29	86.2	4	75
	TMP-SMX	14	100	1	100
	Fosfomycin	11	90.9	3	100
	Nitrofurantoin	11	100	1	100
	Aminoglycosides	25	92	5	100
	Clindamycin	20	80	3	66.7
	Daptomycin	10	90	3	100
	Tetracycline	24	58.3	3	33.3
	Vancomycin	25	100	4	100
	Linezolid	17	100	4	100
	Teicoplanin	10	100	3	100

ESBL: Extended-spectrum beta-lactamase, E. coli: Escherichia coli, TMP-SMX: Trimethoprim-sulfamethoxazole, Pip-taz: Piperacillin-tazobactam

Table 2. Antibiotic susceptibility rates in patients with and without foley catheter

Antimicrobial	Patients without foley catheter		Patients with foley catheter	
	n	Susceptibility (%)	n	Susceptibility (%)
Penicillin Combination	442	54.2	67	47.5
1st generation Cephalosporins	11	16.9	1	12.5
2nd generation Cephalosporins	349	60.4	54	54
3rd generation Cephalosporins	497	60.5	91	57.2
Fluoroquinolones	606	59.8	110	57
TMP-SMX	688	73.3	94	61.4
Fosfomycin	505	87.7	98	86.7
Nitrofurantoin	642	88.2	108	80
Aminoglycosides	892	92.5	172	89.6
Clindamycin	27	71.1	2	50
Daptomycin	20	71.4	4	100
Tetracycline	22	51.2	2	50
Tigecycline	157	84.4	20	90.9
Pip-taz	536	86.9	112	82.4
Vancomycin	165	100	22	100
Linezolid	151	98.1	21	100
Teicoplanin	139	100	20	100
Aztreonam	184	98.4	35	89.7
Metronidazole	119	100	4	100

TMP-SMX: Trimethoprim-sulfamethoxazole; Pip-taz: Piperacillin-tazobactam.

Table 3. Antibiotic susceptibility rates in female and male patients

Antimicrobial	Female patients		Male patients	
	n	Susceptability (%)	n	Susceptability (%)
Penicillin combination	216	50.9	293	55
1st generation Cephalosporins	2	7.1	10	22.2
2nd generation Cephalosporins	161	55.3	242	62.5
3rd generation Cephalosporins	280	59.2	308	60.6
Fluoroquinolones	357	57.4	359	61.5
TMP-SMX	363	69.7	419	73.4
Fosfomycin	236	81.4	367	92
Nitrofurantoin	315	81	435	91.8
Aminoglycosides	499	89.4	565	94.5
Clindamycin	16	61.5	13	81.2
Daptomycin	19	76	5	71.4
Tetracycline	10	38.5	14	66.7
Tigecycline	110	86.6	67	82.7
Pip-taz	313	81.9	335	90.3
Vancomycin	133	100	54	100
Linezolid	124	97.6	48	100
Teicoplanin	118	100	41	100
Aztreonam	128	95.5	91	98.9
Metronidazole	55	100	68	100

TMP-SMX: Trimethoprim-sulfamethoxazole; Pip-taz: Piperacillin-tazobactam.

cefixime (38.4%), and ampicillin (27.4%) (Table 2).

When the patients were divided into 2 groups as male and female; antibiotic susceptibility results in female patients indicated that the cultured microorganisms were the most sensitive to the following antibiotics: vancomycin (100%), teicoplanin (100%), linezolid (97.6%), aztreonam (95.5%), aminoglycosides (89.4%), tigecycline (86.6%), Pip-Taz (81.9%), fosfomycin (81.4%), nitrofurantoin (81%), and TMP-SMX (69.7%). The antibiotics to which the cultured microorganisms are most sensitive in male patients are as follows: vancomycin (100%), teicoplanin (100%), linezolid (100%), aztreonam (98.9%), aminoglycosides (94.5%), tigecycline (82.7%), Pip-Taz (90.3%), fosfomycin (92%), nitrofurantoin (91.8%), and TMP-SMX (73.4%) (Table 3). There was no significant difference between male and female gender in terms of antibiotic susceptibility rates.

DISCUSSION

In our study, the most frequent bacteria causing infection were *E. coli*, *K. pneumoniae*, *E. faecalis*, *P. aeruginosa*, and *Proteus*, in rank order. The results of our study indicated that current first-line guideline recommendations for antimicrobial prophylaxis provide insufficient antimicrobial coverage. When we take the two most commonly cultured bacteria, *E. coli* and *Klebsiella*, the mean coverages were 72.4% and 75.5%

for trimethoprim-sulfamethoxazole, 67% and 48.3% for second-generation cephalosporins, 50% and 90.5% for third-generation cephalosporins, and 53% and 40% for penicillin combinations, respectively. Our results based on bacterial susceptibility highlight the superiority of other antimicrobials: aminoglycosides, piperacillin-tazobactam, nitrofurantoin, and fosfomycin provided significantly better *E. coli* coverage compared to other antibiotics studied. It must be noted that ESBL (–) *E. coli* is highly sensitive to almost all antibiotics while ESBL (+) strains are resistant. For *Klebsiella*, aminoglycosides, third-generation cephalosporins, and fosfomycin are better options compared to other antimicrobials. Penicillin combinations and nitrofurantoin are significantly better options for *Enterococcus*. For *Pseudomonas*, aminoglycosides, third-generation cephalosporins, and piperacillin-tazobactam are better than fluoroquinolones. For *Proteus*, aminoglycosides, third-generation cephalosporins, penicillin combinations, fluoroquinolones, and fosfomycin are the best. Although the susceptibility rates decrease slightly in patients with a Foley catheter, susceptibility rates were similar. Resistance to vancomycin or teicoplanin was not determined in our study population, and the coverage was 98% for linezolid, 97% for aztreonam, 91% for carbapenems, 91% for aminoglycosides, 88% for fosfomycin, 87% for cefepime, 87% for Nitrofurantoin and 86% for piperacillin-tazobactam.

Antibiotic prophylaxis has been defined as administering suitable antibiotics for a certain period before surgery. This may reduce the postoperative infection risk. However, the choice and use of antibiotic prophylaxis may vary depending on the type of surgery, the patient's health status and local infection control protocols. Therefore, specific protocols and guidelines should be followed for each condition. One point to remember is that antibiotic prophylaxis should not be abused or prolonged unnecessarily.^[8] Increasing prevalence of antibiotic resistance is an important issue emphasizing appropriate use of antibiotics. Antimicrobial resistance is particularly prevalent in the principal pathogens of the urogenital tract.^[9] This has been explained in part by the overuse and often prolonged use of prophylactic antibiotics in standard urological procedures.^[10] Therefore, the conditions that need antibiotic prophylaxis should be carefully determined, and appropriate antibiotics should be administered to the patients who have a high risk for infection. Cai et al.^[11] reported that antimicrobial prophylaxis was necessary. A protocol was formed for adherence to the EAU guidelines, and data of 2,619 urological procedures (open, laparoscopic, and endoscopic) before implementation of this protocol and 3,529 urological procedures after implementation of the protocol were compared. Postoperative infection was defined as the presence of symptoms related to urinary tract infection and confirmed by microbiological methods, or infection in the site of surgery. No significant difference was observed between before and after protocol implementation groups for symptomatic postoperative infection (5.1% vs. 4.5%). The ciprofloxacin resistance rate of *E. coli* decreased significantly (32.3% vs. 19.1%) after introduction of the protocol.^[11]

Due to increasing resistance to aminoglycosides, an important issue is Carbapenem resistance of *E. coli* in the future. It has been known that, resistance to fluoroquinolones has increased greatly today and particularly in recent years, reaching alarming levels.^[12] In our study, fluoroquinolone resistance was quite high and resistance to carbapenems and aminoglycosides was around 8–9%. Therefore, care should be taken in the selection of the antibiotic agent for prophylaxis. However, it is difficult to come up with a universal preferred regimen since antibiotic resistance varies greatly in different geographic regions. Overall, this is a complicated picture, and the AUA best-practice statement recommends urologists to consider patient, procedure and environmental factors when selecting an antimicrobial regimen. EAU guidelines suggested that the urologist should have the knowledge of local diversity in microbial resistance. Therefore, our results are important for our country and region. The limitations of our study are its retrospective nature and antibiogram differences among the centers.

CONCLUSION

We found that currently recommended antimicrobials provide poor coverage for the most common pathogens isolated. Aminoglycosides, fosfomycin, nitrofurantoin, and piperacil-

in-tazobactam are generally superior to current first-line recommendations and provide a good coverage. Very broad-spectrum antimicrobials such as carbapenems were also found to have excellent efficacies. Urologists should consider patient-based antibiotic prophylaxis in endoscopic urethral procedures, follow appropriate protocols, and consider local antibiotic resistance.

Ethics Committee Approval: This study was approved by the University of Health Sciences Ankara City Hospital Ethics Committee (Date: 27.04.2022, Decision No: E2-22-1718).

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Authorship Contributions: Concept: T.K., M.B., Ü.E., A.Y.Ö.; Design: T.K., M.B., Ü.E., A.Y.Ö.; Supervision: Ş.G., S.B., T.K., M.B.; Resource: K.T., A.E., Ü.E., A.Y.Ö.; Materials: Ç.Ş., R.S., A.E., Ş.C.; Data collection and/or processing: S.B., K.T., A.E., Ç.Ş.; Analysis and/or interpretation: Ş.C.S.B., K.T., R.S.; Literature search: Ö.G., Y.A., R.S., A.T., A.A.; Writing: Ö.G., T.K., Y.A., A.T., M.B., A.A.; Critical review: Ö.G., Y.A., T.K., A.T., M.B., A.A.

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ORİJİNAL ÇALIŞMA - ÖZ

Acil ve elektif transüretal prosedürlerde antimikrobiyal profilaksi seçimi: Türkiye'deki duyarlılık durumu

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AMAÇ: Bu çalışmada, acil ve elektif transüretal girişimler sırasında profilaktik antibiyotik kullanımı için en uygun antimikrobiyal ajanların tespit edilmesi amaçlanmıştır.

GEREÇ VE YÖNTEM: Çalışma Mart 2021-Mart 2022 tarihleri arasında Türkiye'nin farklı coğrafi bölgelerinde yer alan beş hastanede gerçekleştirildi. Acil ve elektif transüretal işlemler öncesinde alınan idrar kültürlerinde üreme tespit edilen hastalara ait veriler retrospektif olarak hastanelerin veri kayıt sistemlerinden elde edildi. Hastaların demografik verileri (yaş ve cinsiyet), eşlik eden hastalıkları, geçirilmiş ürolojik işlemler, ürogenital sistem anomalileri, üretral kateter kullanımı (kalıcı veya temiz aralıklı kateterizasyon), kültürde üreyen mikroorganizmalar ve antibiyotik duyarlılıkları not edildi. Son 1 ay içinde herhangi bir nedenle hastaneye yatırılan veya antibiyotik kullanan hastalar çalışma dışı bırakıldı.

BULGULAR: Çalışmaya 742 erkek (51.2%) ve 708 kadın (48.8%) olmak üzere toplam 1450 hasta alındı. Hastaların ortalama yaşı 55.3±19.36 (1-98) yıl idi. En sık görülen komorbidite diabetes mellitus olarak saptandı (18.7%). İdrar kültürlerinde en sık izole edilen mikroorganizmalar, sıklık sırasına göre: ESBL (-) *E. coli* 418 hasta (28.8%), ESBL (+) *E. coli* 309 hasta (21.3%), *Klebsiella pneumoniae* 183 hasta (12.6%), *Enterococcus faecalis* 124 hasta (8.6%) ve *Pseudomonas aeruginosa* 89 hasta (6.1%) olarak tespit edildi. Amerikan Üroloji Derneği ve Avrupa Üroloji Derneği klavuzlarının profilaksi için önerdiği antimikrobiyal ajanlara karşı duyarlılık oranları: Sefepim %87.1, Ampisilin+Sulbaktam %84, TMP-SMX %71.6, Amoksisilin + Klavulanat %63.5, Sefoksitin %59, Sefotazidim %58.6, Sefuroksim %43.5, Seftriakson %43 ve Sefiksım %38.4 olarak bulundu.

SONUÇ: Çalışmamızın sonuçlarına göre güncel kılavuzlar tarafından profilaksi için tavsiye edilen antimikrobiyal ajanlar idrar kültürlerinde en sık izole edilen patojenlere karşı yeterli koruma sağlamamaktadır. Ürologlar endoskopik üretral girişimler sırasında antibiyotik profilaksisini hasta bazında düşünmeli, uygun protokollerini takip etmeli ve yerel antibiyotik direncini göz önünde bulundurmalıdır.

Anahtar sözcükler: Antibiyotik profilaksisi; antibiyotik duyarlılığı; transüretal girişim.

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