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Tayfur DEMİRAY[1]
Kerem YILMAZ[2]
Özlem AYDEMİR[1]
Mehmet KÖROĞLU[2]
Ahmet ÖZBEK[2]
Fikret HALİS[3]
Mustafa ALTINDİŞ[2]

Correspondance

Mehmet KÖROĞLU
Sakarya University, Faculty of Medicine, Department of Medical Microbiology, SAKARYA

Phone: 0264 295 66 30
e-mail: mkoroglu@sakarya.edu.tr

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[1] Sakarya University Trainig and Research Hospital, Department of Medical Microbiology, SAKARYA
[2] Sakarya University, Faculty of Medicine, Department of Medical Microbiology, SAKARYA
[3] Sakarya University, Faculty of Medicine, Department of Urology, SAKARYA

RESEARCH

MICROBIOLOGICAL EVALUATION OF URINARY TRACT INFECTIONS IN ELDERLY MEN WITH BENIGN PROSTATIC HYPERPLASIA

ABSTRACT

Introduction: Elderly men with benign prostatic hyperplasia have a higher risk of urinary tract infections. With advanced age, an increased prostate gland results in altered bladder emptying and increased urine retention and rates of urinary tract infections. Here, we aimed to determine the uropathogens and their antimicrobial susceptibility isolated from elderly men with benign prostatic hyperplasia to create baseline data for active surveillance and empiric antimicrobial regimens.

Materials and Method: Urine cultures from 506 elderly men with benign prostatic hyperplasia were retrospectively evaluated. Distribution of the bacteria causing urinary tract infections and their antimicrobial susceptibility test results were examined using automated identification and antimicrobial susceptibility testing system.

Results: No growth was reported in 69.8% (n=353) of the whole cultures. Contamination constituted 13.6% (n=69) of the reports. Urinary tract infection was reported in 16.6% (n=84) of the samples. Gram-negative bacteria (79.8%) were the major cause of urinary tract infection among elder men with benign prostatic hyperplasia; *Escherichia coli* (53.4%) was the most common cause. Among the elderly men, contamination rates in the >85 years group was significantly higher (p<0.005). The most susceptible antimicrobials were determined as carbapenems for the Gram-negative bacteria and glycopeptides for the Gram-positive bacteria, which are the last resort and parenteral only antibiotics.

Conclusion: Gram-negative bacteria, predominantly *Escherichia coli*, are the major causes of urinary tract infections in elderly men with benign prostatic hyperplasia. High resistance to frequently used drugs such as first generation cephalosporins and quinolones is an alerting situation. Also, contamination rates increase with advancing age; thus, urine sampling from these patients should be revised. Antimicrobial treatment should depend on local antimicrobial susceptibility testing results.

Key Words: Aged; Urinary Tract Infection; Prostatic Hyperplasia; Drug Resistance, Microbial; *Escherichia coli*

ARAŞTIRMA

BENİGN PROSTAT HİPERPLAZİLİ YAŞLI ERKEKLERDE ÜRİNER SİSTEM ENFEKSİYONLARININ MİKROBİYOLOJİK YÖNDEN DEĞERLENDİRİLMESİ

ÖZ

Giriş: Benign prostat hiperplazili yaşlı erkeklerde idrar yolu enfeksiyonlarının görülme riski daha yüksektir. İlerleyen yaş ile birlikte, büyüyen prostat bezi idrar retansiyonunda artışa, mesane boşaltımında değişikliklere ve sonuçta üriner sistem enfeksiyonlarında artışa neden olur. Bu çalışmada, aktif sürveyansa ve ampirik antimikrobiyal rejimlerine temel veri oluşturmak için, benign prostat hiperplazili yaşlı erkeklerden izole edilen üropatojenlerin ve bunların antimikrobiyal duyarlılıklarının belirlenmesi amaçlanmıştır.

Gereç ve Yöntem: Benign prostat hiperplazisi olan 506 yaşlı erkek hastanın idrar kültürleri retrospektif olarak değerlendirildi. İdrar yolu enfeksiyonlarına yol açan bakteriler ve bunlara ait antibiyotik duyarlılık test sonuçlarını otomatize identifikasyon ve antimikrobiyal duyarlılık tespit sistemi kullanılarak incelendi.

Bulgular: Değerlendirmeye alınan kültürlerden %69.8'i (n=353), üreme saptanmadı olarak rapor edildi. Kültürlerin %13.6'sı (n=69) kontaminasyon olarak değerlendirildi. Numunelerin %16.6'sında (n=84), üriner sistem enfeksiyonu etkeni saptandı. Gram-negatif bakteriler (%79.8), benign prostat hiperplazili yaşlı erkek hastalarda üriner sistem enfeksiyonlarının en sık nedeniydi. Bunların içinde *Escherichia coli* (%53.4) en fazla tespit edilen bakteri oldu. Yaşlı erkeklerde arasında, 85 yaş üstü grubunda kontaminasyon oranları anlamlı derecede yüksek bulundu (p <0.005). En duyarlı antibiyotikler tedavide son seçenekler olan ve parenteral uygulanabilen gram-negatif bakteriler için karbapenemler, gram-pozitifler için glikopeptidler olarak saptandı.

Sonuç: Gram negatif bakteriler, bunların arasında da *Escherichia coli* benign prostat hiperplazisi olan hastalarda üriner sistem enfeksiyonlarının en sık saptanan nedenleridir. Sıklıkla kullanılan birinci kuşak sefalosporinlere ve kinolonlara direnç oranlarının yüksekliği düşündürücü bir durumdur. Ayrıca yaşla birlikte kontaminasyon oranları artmaktadır; bu nedenle bu hastalardan idrar örneklerinin alınması dikkatle gözden geçirilmelidir. Antimikrobiyal tedavi o bölgeye ait antimikrobik duyarlılık test sonuçlarına göre planlanmalıdır.

Anahtar Sözcükler: Yaşlı; Prostat Büyümesi; Üriner Sistem Enfeksiyonu; Antibiyotik Direnci; *Escherichia coli.*

Introduction

Urinary tract infections (UTI) have been determined to be the most prevalent cause of infection in elderly populations (1, 2). In particular, obstruction of the normal urine flow due to benign prostatic hyperplasia (BPH) is a common cause of urinary retention in elderly men (3). BPH is briefly defined as the proliferation of smooth muscle cells and epithelial cells located in the prostate gland, which is primarily related to testosterone levels (4). It is so common that >70% of the men aged between 60 and 69 years have BPH, and its prevalence rises up to 80% in men >70 years of age (5). Increasing age is associated with decreased resistance to bacterial colonization, altered bladder emptying, poor perianal hygiene and urinary incontinence, which enhances the likelihood of developing a UTI. The high amount of post-void residual urine and urinary retention are additional risk factors for UTI in elderly men (3).

The most common isolated bacteria responsible for both community-acquired and healthcare-associated UTI are members of the *Enterobacteriaceae* family. *Escherichia coli* is the most commonly associated bacteria, followed by other enteric bacilli, such as *Klebsiella pneumoniae, Enterobacter species, Pseudomonas aeroginosa, Proteus mirabilis* and *Providencia* species, in elderly population (3, 6). Gram-positive bacteria are less commonly isolated from the urine samples of elderly patients, but they are reported with a higher frequency as a result of increased hospitalization and increased use of indwelling catheters within this population. *Staphylococcus* and *Enterococcus* species constitute the major Gram-positive uropathogens (7). However, most clinicians fail to prescribe appropriate antimicrobial treatment for UTI in elderly populations. It is remarkable that 40%–75% of antimicrobials used to treat such infections are inappropriate (6, 8). Because elderly patients can easily deteriorate and are more prone to complications, inadequate treatment may lead to more complicated conditions, such as urosepsis, or the overuse of antimicrobials that may cause liver and renal insufficiencies in this population. Inappropriate antimicrobial treatment may also cause difficult-to-treat circumstances, such as *Clostridium difficile* infection and the emergence of multi-drug resistance microorganisms. Thus, the assessment of urine cultures with reliable reporting, together with accurate identification and susceptibility testing is particularly important for the elderly (3).

In this surveillance study, we evaluated the contamination rates, possible causes of UTI and their antimicrobial susceptibilities, isolated from outpatients >65 years of age with BPH, to provide a baseline data for experts dealing with forementioned elderly men for setting appropriate empirical treatments in such patients in our region.

Materials and Method

Patients

The study was conducted at in 750-bed Sakarya University Research and Training Hospital, serving patients from mainly Sakarya province and Eastern Marmara region, during a one-year period from January 2015 to December 2015. We retrospectively evaluated the urine cultures of outpatients with BPH >65 years of age with the preliminary diagnosis of UTI. Patients without the preliminary diagnosis of UTI were excluded. Patients were grouped into the following three groups: 1) 65–74, 2) 75–84 and 3) >85 to compare the urine culture results according to age group. The patients' data were obtained from the hospital records. The study was approved by Sakarya University Non-Invasive Ethics Committee with the acceptance number 050.01.04.87.

Determination of the Isolates

Clean-catch, mid-stream urine samples from the patients were obtained and processed within 2 h of collection. The samples were inoculated onto the Tryptic Soy agar containing 5% sheep blood and Eosin Methylene Blue agar plates using standardized 10 mL loops. The plates were incubated at 35°C for 18–24 h. The predominant growth of the microorganisms ($>10^4$ CFU/mL) was further evaluated as a possible cause of infection. When three or more types of bacterial colonies, without predominance of one kind were detected, these samples were considered as contaminated. A *VITEK® 2* automated system (*bioMerieux, Marcy l'Etoile, France*) was used for identification and antimicrobial susceptibility testing. The results were interpreted according to the CLSI 2015 criteria (9).

Statistical Analyses

Comparisons between groups were made using *Chi-square* or *Fisher's exact test* for categorical variables. A p value<0.05 was considered to be significant. Comparisons between age groups and urine culture reports were analysed. Statistical evaluations were performed using commercial statistical software *SPSS* version 21.0 (*SPSS Inc., Chicago, IL, USA*).

Results

The total numbers of 506 urine samples from male geriatric patients with BPH were evaluated during the study

Table 1— Urine Culture Results of the Elderly Geriatric Patients with BPH According to Age Group

Results	65-74 years		75-84 years		>85 years		Total	
	n	%	n	%	n	%	n	*p*
No growth	235	74.8	106	63.9	12	46.2	353	**0.008**
Contamination	37	11.8	26	15.7	6	23.1	69	
UTI	42	13.4	34	20.5	8	30.8	84	
Total	314		166		26		506	

Table 2— Distribution of Pathogens Causing UTI in Elderly Patients with BPH

Isolate	n	%
Escherichia coli	44	52.4
Klebsiella pneumoniae	10	11.9
Acinetobacter baumanni	2	2.4
Serratia marcescens	1	1.2
Proteus vulgaris	1	1.2
Enterobacter cloaca complex	4	4.8
Pseudomonas aeruginosa	3	3.6
Citrobacter freundii	2	2.4
Enterococcus faecalis	9	10.7
Staphylococcus epidermidis	4	4.8
Staphylococcus haemolyticus	1	1.2
Streptococcus agalactiae	3	3.6
Total	**84**	**100.0**
Gram negatives	67	79.8
Gram positives	17	20.2
Total	**84**	**100.0**

period. The patients were aged between 65 and 90 years, and the mean age of the patients was 73.5 years. *No growth* was reported in 69.8% (n=353) of the whole cultures included in the study. *Contamination* was present in 13.6% (n=69) of the reports. A positive UTI was reported in 16.6% (n=84) of the samples. When the overall urine culture reports were evaluated according to age group, significant differences were determined for the age groups and the culture reports (p<0.05) (Table 1). The significant difference emerged from the rates in the >85 age group. Contamination and UTI rates were significantly higher in the >85 age group (p<0.05). Gram-negative bacteria (79.8%) were isolated more frequently than gram-positive bacteria (20.2%). *E. coli* was identified as the most predominant microorganism (52.4%), followed by *K. pneumoniae* (11.9%) and *E. faecalis* (10.7%). The list of the pathogens causing UTI according to the age groups in elderly patients with BPH is presented in Table 2. Antimicrobial susceptibility testing results of the uropathogens revealed that some susceptible isolates were lower for the commonly used empiric antimicrobials for UTI (e.g. ciprofloxacin, trimethoprim–sulfamethoxazole, gentamicin, ampicillin and cephazolin). The majority of the susceptible antimicrobials were determined to be carbapenems for the Gram-negative bacteria and glycopeptides for the Gram-positive bacteria as expected (Table 3).

Discussion

Socioeconomic advances and developments in medical fields have enabled longer life expectancies in humans. The relative population of elderly individuals is constantly increasing; thus, problems regarding medical issues due to ageing are also increasing. Physiological and anatomical changes inevitably occur with increasing age. These changes, together with decrease in immunity, increase the risk of infections for elderly populations (10).

UTI are common in elderly populations, and they are commonly misdiagnosed because of prevalent asymptomatic bacteriuria (11). When UTI becomes complicated with bacteremia, mortality increases up to 33% (12). Diagnosis of UTI in elderly is particularly challenging and primarily depends on the presence of bacteria together with classical symptoms of the genitourinary system (e.g. fever, frequency, urgency, dysuria and pain) (11, 13). Men with BPH also suffer from urinary frequency and urgency that mimic UTI (14). Aging men have an additional risk for UTI because of the increasing volume of prostate gland-*BPH*, which causes an obstruction of the urinary pathway. In this study, we attempted to select BPH patients pre-diagnosed to have UTI. Nevertheless, we did not detect any bacterial growth in 69.8% of the urine cultures of these selected patients. One of the remarkable findings of this study was a high rate of contamination among

Table 3— Antibiotic Susceptibility Test Results of the Uropathagens in Elderly Patients with BPH

Gram Negative	Number of Susceptible Isolates												
Bacteria	n	AMP	KZ	GN	AK	AMC	CFX	CRO	CIP	IMP	MEM	SXT	NF
E. coli	44	23	24	35	36	34	30	34	29	44	44	30	37
K. pneumoniae	10	4	7	8	9	7	7	7	8	10	10	8	7
A. baumanni	2	-	-	1	1	1	1	1	1	2	2	-	1
S. marcescens	1	1	1	1	1	1	1	1	1	1	1	1	1
P. vulgaris	1	1	1	1	1	1	1	1	1	1	1	-	1
E. cloaca complex	4	-	1	4	4	1	2	3	4	4	4	4	3
P. aeruginosa	3	-	-	2	3	2	1	1	2	3	3	-	1
C. freundii	2	1	-	1	2	2	2	2	1	2	2	1	1
Gram Positive	**Number of Susceptible Isolates**												
Bacteria	**n**	**P**	**AMP**	**OX**	**E**	**CIP**	**GN**	**HLAR**	**FOS**	**SXT**	**LNZ**	**VA**	**TEC**
E. faecalis	9	NA	9	NA	-	3	1	9	7	NA	9	9	9
S. epidermidis	4	-	NA	3	4	1	4	NA	NA	4	4	4	4
S. haemolyticus	1	-	NA	1	1	-	1	NA	NA	1	1	1	1
S. agalactiae	3	-	3	3	3	3	3	NA	NA	3	3	3	3

AMP: Ampicillin; KZ: Cefazolin; GN: Gentamicin; AK: Amikacin; AMC: Amoxicillin clavulonate, CFX: Cefuroxime; CRO: Ceftriaxone; CIP: Ciprofloxacin; IMP: Imipenem; MEM: Meropenem; SXT: trimethoprim-sulfamethoxazole; NF: Nitrofurantain; P: Penicillin; OX: Oxacillin; E: Erythromycin; HLAR: High-level aminoglycoside resistance; FOS: Fosfomycin LNZ: Linezolid; VA: Vancomycin; TEC: Teicoplanin; NA: Not available

the patients in the >85 years age group. Poor self-hygiene and diminished cognitive abilities may contribute to the increased rate of contamination among the very elderly population. Highly descriptive information together with special and proper precautions regarding urine sampling should be provided to such patients to obtain optimal clean catch midstream urine samples. An increase in the UTI rates through the increasing age groups was an expected finding because of an enlargement of the prostate gland, which in turn causes a high amount of post-void residual urine and urinary retention (3, 15).

Gram-negative bacteria, *most probably because of faecal contamination and poor self-hygiene of the elderly population*, are commonly detected in elderly people (10, 14, 15). We also found that the gram-negative bacteria (79.8%) were the most common causative agents of UTI ($p<0.05$). In addition, uropathogenic *E. coli* was the most common gram-negative bacterial species isolated from elderly men and women, responsible for 80%–90% of the cases (15). In one recent study, *E. coli* was the most commonly isolated uropathogen among elderly men living in nursing homes (30.6%) and living at home (39.9%) (16). We determined the rate of *E. coli* to be as high as 52.4%, followed by other enteric bacilli, such as *K. pneumoniae* (11.9%) and *E. cloaca complex* (4.8%). Gram-positive bacteria are less commonly isolated, with rates of approximately 10%–20%. *Enterococcus* spp. and *Staphylococcus* spp. are interchangeably detected as the most prevalent Gram-positive bacteria in several different studies (8, 15-17). *E. faecalis* (10.7%) and *Staphylococcus* spp. (6.0%) were detected in concordance with previous studies (8, 15-17).

Antimicrobial susceptibility results obtained in this study revealed that quinolones, first generation cephalosporins and trimethoprim–sulfamethoxazole, which were commonly prescribed for UTI, may be questioned because of a relative decrease in susceptibility rates. Other words, first generation cephalosporins were ineffective in half of the gram negative isolates and quinolones were useless in one third of the isolates. On the other hand, nitrofurantoin appears to be a good choice. However, its use is very limited and should be very carefully ordered because it is not suitable for the patients with a glomerular filtration rate <60 mL/min. Third and fourth generation cephalosporins and carbapenem are used via the intravenous route (except cefixime) and should be reserved for more complicated infections. In addition, ciprofloxacin resistance was remarkable for *E. faecalis*; therefore, quinolones should be prescribed cautiously in cases of UTI caused by *E. faecalis*.

Turkey is under particular risk for multi-drug and pan-drug resistant microorganisms. Well-documented studies ha-

ve demonstrated that our country is a reservoir for various types of extended spectrum beta-lactamases such as AmpC and CTX-M and many carbapenamases such as OXA-48 and NDM-1 (18, 19). Distribution of pathogens causing UTI in elderly may not change over time, but it is obvious that their resistance patterns do change. This results in treatment failures and unsuccessful patient management, which in turn causes emerge and spread of antimicrobial resistance. We even struggle with pan-resistant microorganisms where we have no antibiotics as a treatment choice. We can overcome this unfavourable condition by successful antibiotic stewardship and the first step towards this way is the knowledge of the distributions and resistance patterns of the microorganisms causing infections, namely the surveillance studies aimed at specific patient groups.

As a limitation, we have retrospectively evaluated the causative microorganisms and their susceptibility test results, so comorbidities and other risk factors in the elder population were not assessed in this study, but such factors may be subject of future multidisciplinary prospective studies.

As a result, the domination of Gram-negative bacteria in UTI in elderly patients is the cornerstone of empirical treatment. Inadequate treatment for UTI among elderly patients is often associated with worsened clinical outcomes, and empirical antimicrobial therapy may have a positive effect on prognosis (8). First line drugs *(i.e. quinolones, aminoglycosides and trimethoprim–sulfamethoxazole)* may alternately be used to avoid further development of resistance among elderly patients with BPH. Urine cultures and antimicrobial susceptibility testing should be requested in case of UTI in the elderly for the correct diagnosis and appropriate antimicrobial treatment.

Conflict of Interest

The authors declare that they have no conflict of interest.

Financial Disclosure

The authors declare that this study has received no financial support.

Ethical Committee Approval

Sakarya University Non-Invasive Ethics Committee, 050.01.04.87

Declaration

All the authors declare that they have obeyed the rules in "Helsinki Declaration", "Good Medical Practice Guidelines", and "Good Laboratories Practice Guidelines".

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