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Original Article

Should we review our prophylaxis approach for increased antibiotic resistance in transrectal prostate biopsy?

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Abstract

Introduction: This study aims to show the bacteriologic picture of acute prostatitis and bacteremia caused by infective agent after transrectal ultrasound-guided prostate biopsy (TRUSBx) and to determine the resistance rates of the infections in patients undergoing transrectal biopsy and to guide prophylaxis approach before biopsy.

Methodology: The retrospective data of 935 patients who underwent TRUSBx between January 2010 to January 2019 were reviewed. Pre-biopsy urine cultures and antimicrobial susceptibility were obtained. Subsequently, patients admitted to the hospital with any complaint after biopsy were examined for severe infection complications.

Results: Of the 430 (61.7%) patients who underwent urine culture before the procedure, 45 (10.5%) had growth; 30 (66.7%) of the growing microorganisms were *Escherichia coli*. Twenty (44.4%) of all Gram-negative agents in pre-biopsy urine culture were susceptible to quinolone. Post TRUSBx bacteremia was present in 18.2%, urinary system infection in 83.6%, and hospitalization in 61.8% of 55 patients who were admitted to the hospital. In the isolated gram-negative microorganisms, fluoroquinolones resistance in urinary system infections was seen in 40% and bacteremia was seen in 70% of the cases. ESBL-producing Gram-negative bacteria were determined in 40% of infections in blood and 38.5% of urinary system infections in the post biopsy period in the current study.

Conclusions: These high antibiotic resistance rates suggest that we better review our pre-procedure prophylaxis approaches.

Key words: Antibiotic resistance; fluoroquinolone; prophylaxis; prostate biopsy.

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Introduction

Transrectal ultrasound-guided prostate biopsy (TRUSBx) is associated with a severe infection risk [1,2]. Although antibiotic prophylaxis usually with fluoroquinolones is routinely used, the infection rate after TRUSBx is increasing due to antibiotic resistance [1,3].

Increased prevalence of antibiotic resistance in microorganisms coupled with colonization of rectal flora with extended-spectrum beta-lactamases (ESBL) positive and fluoroquinolone-resistant bacteria are increasing the possibility of infection after prostate biopsy [2]. Previous studies have shown prophylactic practices fail due to antibiotic resistance; application of antimicrobial stewardship programs is emphasized [4-7]. Because of the post-biopsy severe infection, pre-procedure prophylaxis approaches should be reviewed. The development of new antibiotic prophylaxis approaches for TRUSBx should include antibiotics that reduce infection rates, have a wide spectrum of activity against urogenital flora pathogens, and have also low resistance and selection pressure [3].

This study aims to show a bacteriologic picture of acute prostatitis and bacteremia caused by infective agents after TRUSBx to determine the resistance rate of the infections in patients undergoing TRUSBx and to guide prophylaxis approach before biopsy.

Methodology

Patients who underwent TRUSBx in Ankara Numune Research and Education Hospital between January 2010 to January 2019 were reviewed (Ethics committee approval no: E-19-2650).

Patients who received TRUSBx due to abnormal digital rectal examination finding or increased prostate-specific antigen (PSA) levels (≥ 2.5 ng/mL) were

included in the study. Patients' demographic characteristics, comorbidities, history of hospitalization, and antibiotic use prior to three months were retrieved from the hospital system. Pre-biopsy urine cultures and antimicrobial susceptibility were obtained. All patients included in the study received antibiotic prophylaxis (Table 1). Subsequently, patients admitted to the hospital with any complaint after biopsy were examined for infection complications.

Biopsy Procedure

The biopsy procedure was performed with the patients in the left decubitus position by using a Hitachi EUB 420 scanner with a 7.5 mHz bi-planar probe attached (Hitachi, Tokyo, Japan) and a rectal povidone-iodine preparation was used in each patient. The transrectal ultrasound probe was disinfected by using a 3.2% glutaraldehyde solution. A standard condom was placed on the distal part of the transrectal ultrasound probe, after which the disposable needle guide was placed over the probe and the first condom. A second condom was attached to these items. 5 mL of 2% lidocaine was injected into the periprostatic area for analgesia before the biopsy. 10-12 cores of prostatic tissue were obtained with an 18-gauge biopsy needle and a biopsy gun.

Data Processing and Statistical Analysis

Data were analyzed by using Statistical Package for Social Sciences (SPSS) for Windows 20.0 (Armonk, NY, USA). Data were expressed as means and standard deviation, and median (min and max) values for continuous variables, while as percentages for categorical variables. Pearson Chi-square was used for the comparison of categorical variables in independent groups, if the variables didn't meet the Pearson Chi-square criteria (in more than 20% of cases expected value is < 5 or the observed value is < 2) Fisher's Exact test was used. The p value of less than 0.05 ($p < 0.05$) was considered statistically significant.

Ethics statement

The present study protocol was reviewed and approved by the Ethical Board of Ankara Numune Research and Education Hospital (approval number: E-19-2650). Informed consent was obtained from all subjects when they were enrolled.

Results

Six hundred ninety seven out of 935 patients who received prostate biopsy with complete medical history were included. The mean age of them was 63 years (range 43 to 75 years). Three hundred seven patients (44%) had at least one comorbidity. Of the 430 (61.7%) patients who underwent urine culture prior to the procedure, 45 (10.5%) had growth; 30 (66.7%) of the growing microorganisms were *Escherichia coli.* The distribution of microorganisms is given in Table 2.

Twenty (44.4%) of all Gram-negative agents in pre-biopsy urine culture were susceptible to quinolone. Six hundred sixty-two patients received prophylactic antibiotics prior to TRUSBx intervention; the most used prophylactics were quinolones alone, followed by quinolone and metronidazole combination. Five hundred twenty-seven (75.4%) patients received quinolone or quinolone-containing prophylaxis (Table 1).

Post TRUSBx intervention, 7.9% (n = 55) of patients were admitted to the emergency room (ER) with high fever complaints. The median admission was 2 days post-intervention; the earliest admission was on the first day and the latest was 3 months post TRUSBx intervention. Sixty percent (n = 33) of the admissions happened in the post 72-hour period. *E. coli* growth was observed in 76.1% (n = 35) of patients from a total of 46 patients' urine cultures. The distribution of the microorganisms and susceptibility profile is summarized in Table 3.

From all 55 admissions to the hospital, 34 patients (61.8%) were hospitalized. All of them received parenteral antibiotic treatment. Median hospitalization was 7 days, ranging from 1 to 14 days. Blood culture

Table 1. Prophylactic antibiotics classification given in pre-biopsy.

Antibiotics class	n	%
Quinolone	369	52.9
Cephalosporin	116	16.6
Quinolone + metronidazole	158	22.7
Cephalosporin + metronidazole	17	2.4
Betalactamine + beta-lactamase inhibitor*	2	.3
No information	35	5.0
Total	697	100.0

*: amoxycilline clavulonate, ampicilline sulbactam.

Table 2. The distribution of microorganisms in pre-biopsy culture.

Microorganisms	n	%
E.coli	30	66.7
Other Gram negative*	3	6.7
CNS	6	13.3
Other Gram positive**	6	13.3
Total	45	100.0

CNS: Coagulase-negative staphylococcus; *: *Acinetobacter lwoffii*, *Edwingella* spp., *Klebsiella* spp.; **: *Streptococcus* spp. and *Enterococcus* spp.

was taken from 15 of 34 hospitalized patients (44.1%); growth was detected in 10 of them (18.2%). Growing active microorganisms were quinolone susceptible *E. coli* in 3, quinolone-resistant – ESBL (-) *E. coli* in 3, quinolone-resistant – ESBL (+) *E. coli* in 3, and quinolone-resistant – ESBL (+) *Klebsiella pneumoniae* in 1 out of 10 patients.

Discussion

During the TRUSBx, bacteria from the rectum wall and periprostatic tissue affect the prostate parenchyma and reach the blood circulation; [3]. The role of antibiotics prophylaxis for infection prevention is well established for this kind of procedure [8]. The rate of infectious complications post TRUSBx is around 5-7%. One to three percent of serious infections require hospitalization and the mortality rate is 0.1-1.3% [4,9]. The rate of infections caused by resistant microorganisms post TRUSBx intervention has increased in recent years. Fluoroquinolones resistance has increased remarkably, which is advised to be used in TRUSBx intervention in the guidelines of the American Urology Association and European Association of Urology [4,8,10] Due to increased resistance and infection rate necessitates a review of prophylactic approaches in the current widespread use of fluoroquinolones for prophylaxis in TRUSBx patients [3,4,11,12].

In this study, for the prophylaxis, fluoroquinolones were the most widely (75.4%) used antibiotics in line with the literature [4,13]. In the isolated gram-negative microorganisms, fluoroquinolones resistance in urinary system infections was seen in 40% and bacteremia was seen in 70% of the cases. ESBL positivity rate was 15/39 and 4/10 in urinary system infections and bacteremia respectively. In many studies, *E. coli* is the mostly isolated microorganism where infectious complications occur in post TRUSBx period [3,4,14]. Fluoroquinolone resistance colonization rate was shown to be between 10-20% in rectal cultures prior to biopsy [4,9]. On the other hand, increased fluoroquinolone usage increases the risk of selection of ESBL-positive bacteria. ESBL-producing Gram-negative bacteria was determined in 40% of infections in blood and 38.5% of urinary system infections in the post-biopsy period in this study. Serious infections caused by ESBL-positive bacteria can result in treatment failure, increased morbidity, mortality, and cost [1-3]. The use of FQ or third-generation cephalosporins induces ESBL production in Gram-negative bacteria [15]. In our study, while approximately half of gram-negative bacteria growth in prebiopsy urine culture were FQ resistant, the fact that 75.4% of pre-procedure prophylaxis regimens contained FQ, would reduce the effectiveness of prophylaxis and caused the development of post-biopsy resistant infections. If FQ resistance to *E. coli* is greater than 20%, other antibiotics should be chosen for prophylaxis [11]. Our study found that bacteria grown in prebiopsy urine cultures showed very high rates (55.6 %) of FQ resistance, suggesting that the use of FQ as a prophylactic would not be appropriate. Prophylactic approaches based on urinary culture prior to biopsy decrease the risk of post-biopsy infection [4,14]. Therefore, the development of new prophylactic approaches based on nation's epidemiologic resistance map and individual-level prophylaxis based on risk factors are necessary.

Table 3. Distribution of microorganisms and susceptibility profiles in urine culture.

Active microorganism	n	%
E.coli	**35**	**76.1**
Quinolone susceptible	11	
Quinolone resistant	10	
ESBL (+), Quinolone susceptible	4	
ESBL (+), Quinolone resistant	10	
Other Gram negative	**4**	**8.7**
Quinolone susceptible	3	
Quinolone resistant	0	
ESBL (+), Quinolone susceptible	0	
ESBL (+), Quinolone resistant	1	
CNS	**2**	**4.3**
Other Gram positive*	**1**	**2.2**
No growth	**4**	**8.7**
Total	**46**	**100**

CNS: Coagulase negative staphylococcus.

Global surveys done by the Global prevalence study of infections in urology (GPIU) about TRUSBx showed increased infectious complications such as urinary tract infection, bacteriemia, and sepsis [13]. In this study, post TRUSBx bacteremia was present in 18.2%, urinary system infection in 83.6%, and hospitalization in 61.8% of 55 patients who were admitted to ER.

Many factors may contribute to the development of infectious complications. Prebiopsy urinary culture and proof of rectal carriage may be a guide in the determination of prophylactic approaches. Additionally, in the presence of individual risk factors against FQ resistant and ESBL-positive isolates, single-dose carbapenem applications such as ertapenem are useful in the prevention of post Bx infection complications [16,17]. FQs are mostly used antibiotics in urinary interventions, contrary to the advisory publication of the European Medical Agency (EMA) [18]. In a meta-analysis, the effectiveness of antibiotics such as cephalosporins, aminoglycosides, and fosfomycin trometamol on TRUSBx has been already

demonstrated [19]. In our study, the use of cephalosporins and fluoroquinolones for prophylactic purposes was not preferred in practice because of high resistance rates. In a study, the use of single-dose ertapenem as a prophylactic agent significantly reduced the incidence of infection, rate of bacteremia, antibiotic consumption, and hospitalization length due to post TRUSBx infections [16]. Recent papers showed prophylactic use of ertapenem has not showed antibiotic resistance problems [16,20,21]; use of ertapenem is advised in literature and guidelines [8,17,22]. FQs are widely used in TRUSBx [3,4,23]. Oral multidose use of ciprofloxacin reached higher concentration in the faeces than in parenteral ertapenem application, thus the presence of resistant pathogens was observed in faecal microbiota [23-25]. Ciprofloxacin as an antimicrobial agent has more potential in the development of resistance than ertapenem. Where CPE is not usually seen, based on the local epidemiologic information and individual evaluation, single-dose ertapenem use would decrease post TRUSBx complications [21]. In our study, the rate of resistance to antibiotics used for prophylaxis before the procedure and ESBL bacteria rate were found to be high. Therefore, we conclude that an agent such as ertapenem, which is effective against ESBL-positive bacteria and has a low potential to increase antibiotic resistance, can be used as a single dose, also providing ease of use.

Conclusions

Antibiotic resistance epidemiology of our region and special risk factors of the patient should be taken into consideration and new prophylaxis protocols should be established in TRUSBx. Instead of standard ciprofloxacin and cephalosporin regimen, the use of broad-spectrum antibiotics such as single-dose carbapenems like ertapenem will reduce infectious complications after biopsy

Authors' Contributions

Adalet Altunsoy: Conceptualization, Methodology, Writing-Reviewing and Editing, Supervision; Şeref Coşer: Investigation and resources; Nizamettin Kemirtlek: Investigation and resources; Melih Balcı: Investigation and resources; İ. Can Aykanat: Investigation and resources; Hürrem Bodur: Investigation; Altuğ Tuncel: Methodology and Visualization, Reviewing and Editing.

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