Original Article

DOI: 10.4274/uob.galenos.2022.2022.1.1

Bull Urooncol 2022;21(4):130-133

Fluoroquinolone Resistance Level in Rectal Swab Taken Before Transrectal Ultrasound Prostate Biopsy

Hüseyin Saygın[1], Abuzer Öztürk[1], Aydemir Asdemir[1], İsmail Emre Ergin[1], Arslan Fatih Velibeyoğlu[1], Emre Kıraç[1], Mürşit Hasbek[2], Caner Öksüz[3], Seyit Ali Büyüktuna[3], Esat Korgalı[1]

[1]*Sivas Cumhuriyet University Faculty of Medicine Research and Application Hospital, Clinic of Urology, Sivas, Turkey*

[2]*Sivas Cumhuriyet University Faculty of Medicine Research and Application Hospital, Clinic of Medical Microbiology, Sivas, Turkey*

[3]*Sivas Cumhuriyet University Faculty of Medicine Research and Application Hospital, Clinic of Infectious Diseases and Clinical Microbiology, Sivas, Turkey*

Abstract

Objective: It has been shown that antibiotic prophylaxis before transrectal ultrasound prostate biopsy (TRUS-Bx) reduces the incidence of post-biopsy infectious complications. Without the superiority of a particular antibiotic regimen, there are differences in the antibiotic regimens used by clinics. However, recently, there have been serious concerns about TRUS-Bx-related infectious complications due to the increase in fluoroquinolone (FQ)-resistant bacterial strains. To overcome this global problem, alternative antibiotic prophylaxis should be investigated and appropriate antibiotic management should be applied in patients who will undergo TRUS-Bx. This study aimed to determine the antibiotic susceptibility of the rectal flora based on rectal cultures before TRUS-Bx, to systematically determine the basic prevalence of FQ resistance, to investigate the relationship between FQ resistance and the risk of infection after TRUS-Bx, and to determine the susceptibility of Fosfomycin and trimethoprim-sulfamethoxazole (TMP-SMX) as an alternative to the FQ group.

Materials and Methods: Rectal swab cultures were taken from each patient to undergo TRUS-Bx two days before the procedure. Two daily doses of 500 mg ciprofloxacin were given orally for one week, starting one hour before the procedure. All patients underwent 12 core biopsies.

Results: Antibiograms obtained from rectal swabs showed sensitivity to FQ in 78 patients (89.7%), to Fosfomycin in 85 patients (97.7%), to TMP-SMX in 78 patients (89.7%).

Conclusion: Although different antibiotic prophylaxis methods are discussed due to FQ resistance in today's medical practices, FQ sensitivity continues at a high rate of 89.7% in our region and still seems to be a viable prophylaxis method.

Keywords: Antibiotic prophylaxis, antibiotic resistance, fluoroquinolones, image-guided biopsy, prostate

Introduction

Prostate cancer is the most common cancer in men over 50 years of age in Europe and the USA and is responsible for 225,000 new cases in Europe and 240,000 in the USA each year (1). Transrectal ultrasound prostate biopsy (TRUS-Bx) is the most commonly used method for the histological diagnosis of prostate cancer. Besides being a procedure that can be performed safely without hospitalization and is easily tolerated by patients, TRUS-Bx may have complications such as hematuria, rectal bleeding, acute urinary retention, prostatitis, urinary system infection, and sepsis (2).

Antibiotic prophylaxis reduces the incidence of infectious complications after TRUS-Bx (3). There are differences in the antibiotic regimens used by clinics, without the predominance of a particular regimen (4). Among these antibiotic regimens, the fluoroquinolone (FQ) group is the most commonly used prophylactic agent and is recommended by the North American, European, and other international urology societies (5,6,7).

However, recently, there have been serious concerns about TRUS-Bx-related infectious complications due to the increase in bacterial strains resistant to FQ (8,9). In a population-based study of 75,190 men undergoing TRUS-Bx in Canada, hospital readmission rates within 30 days increased from 1.0% (1996) to 4.1% (2005). More than 70% of readmissions in this study were due to infection-related complications (10). In addition to the TRUS-Bx-related morbidity experienced by patients, post-TRUS-Bx infection also has significant negative economic consequences on healthcare systems (11).

Cite this article as: Saygın H, Öztürk A, Asdemir A, Ergin İE, Velibeyoğlu AF, Kıraç E, Hasbek M, Öksüz C, Büyüktuna SA, Korgalı E. Fluoroquinolone Resistance Level in Rectal Swab Taken Before Transrectal Ultrasound Prostate Biopsy. Bull Urooncol 2022;21(4):130-133

Address for Correspondence: İsmail Emre Ergin, Sivas Cumhuriyet University Faculty of Medicine Research and Application Hospital, Clinic of Urology, Sivas, Turkey
Phone: +90 505 252 68 68 **E-mail:** emreergin55@hotmail.com **ORCID-ID:** orcid.org/0000-0002-3115-0533
Received: 03.01.2022 **Accepted:** 10.04.2022

FQs are traditionally used for antibiotic prophylaxis, but overuse and misuse of FQs have increased FQ resistance. The European Medicines Agency has implemented strict regulatory requirements for the use of FQ, resulting in the suspension of the indication for perioperative antibiotic prophylaxis, including TRUS-Bx (12).

Alternative prophylaxis methods that can be used instead of traditional FQ prophylaxis before TRUS-Bx, which is also mentioned in the European urology guideline, can be examined under three procedures. The first procedure was targeted prophylaxis. It is the initiation of appropriate antibiotic prophylaxis with a rectal swab or stool culture to be made before TRUS-Bx. The second procedure is the application of extended antibiotic prophylaxis by adding aminoglycoside or cephalosporin group antibiotics to the FQ group to be administered with two or more antibiotic groups. The last procedure is the use of fosfomycin, cephalosporin, or aminoglycoside antibiotics instead of the FQ group (13).

The increasing rate of FQ resistance and infective complications following TRUS-Bx pose a significant challenge for urologists. To overcome this global problem, alternative antibiotic prophylaxis should be investigated and appropriate antibiotic management should be applied in patients who will undergo TRUS-Bx.

It has been reported that prophylaxis with antimicrobial agents, based on the rectal culture results obtained before the biopsy, reduces infections and morbidity after TRUS-Bx and reduces hospital readmission (14,15).

In this study, infective complications and antibiotic susceptibility of rectal flora were prospectively investigated in patients who underwent empirical FQ treatment before TRUS-Bx in the urology clinic of Sivas Cumhuriyet University approximately 2019-2021. This study aimed to determine the antibiotic susceptibility of the rectal flora based on rectal cultures before TRUS-Bx, to systematically determine the basic prevalence of FQ resistance, to investigate the relationship between FQ resistance and the risk of infection after TRUS-Bx, and to determine the susceptibility of fosfomycin and trimethoprim-sulfamethoxazole (TMP-SMX) as an alternative to the FQ group.

Materials and Methods

Patients who underwent TRUS-Bx in the urology clinic of Sivas Cumhuriyet University between March 2019 and March 2021 were included in this prospective study. Patients who underwent urological surgery in the last three months had significant growth in the last urine culture, had a history of acute or chronic prostatitis in the three last months and had a history of antibiotic use in the three last weeks were excluded from the study. Secondary biopsies were excluded from the study. TRUS-Bx indication was elevated serum prostate-specific antigen (PSA) and/or rectal digital examination positivity. Two days before the procedure, cultures were obtained from each patient with a rectal swab. Informed consent was obtained from each patient. A 135 cc rectal enema was applied to all patients for rectal cleansing two hours before the procedure. 500 mg ciprofloxacin was given orally in two daily doses for one week, starting one hour before the procedure.

The procedure was performed in the left lateral decubitus position. A Viking 2400 model (B-K Medical, Herlev, Denmark) ultrasonography device and a biplanar transrectal ultrasonography (TRUS) probe were used for imaging. The TRUS probe was covered with a latex condom and ultrasound gel was used to eliminate the rectal air artifact. No povidine iodine was used as a rectal preparation. Only enema was used. Local anesthesia was provided with lidocaine gel applied rectally before the biopsy. Then, periprostatic local anesthesia was performed with a 22-G Chiba needle inserted through the disposable biopsy needle guide channel attached to the TRUS probe. Prostate volume (cc) was calculated by measuring prostate dimensions (length x width x height x 0.5236). A biopsy gun and 18-G biopsy needles (GTA Medical Product and Service, Quistello, Italy) were used for the biopsies. All patients underwent 12 core biopsies. After the procedure, the patients were informed that they should reapply to the hospital in case of possible signs of infection. Age, serum PSA levels, prostate volume, presence of diabetes, biopsy pathology results, rectal swab culture results, and antibiogram sensitivity of the cases were analyzed.

Statistical Analysis

The data obtained from the study were evaluated with the SPSS 23.0 program. Mean and standard deviation parameters were used as descriptive statistics. Analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk's test) were used to determine the normal distribution of the variables. Parametric tests were used for normally distributed data, and non-parametric tests were used for non-normally distributed data. The student's t-test was used to compare normally distributed data, and the Kruskal-Wallis test was used for non-normally distributed data. The chi-square test was used to compare categorical values. The error level was taken as 0.05.

All subjects gave their informed consent for inclusion before participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Cumhuriyet University ethics committee (decision no: 2019-03/02, date: 19.03.2019).

Results

The mean age of 87 patients included in the study was 64.4 (±7.7). The mean PSA value was 12.31 (±11.6). Mean prostate volume was 59.46ccs (±21.7). Twelve of the patients (13.8%) had previously undergone TRUS-Bx. 22 patients (25.3%) were diagnosed with diabetes mellitus. The pathological result of 22 patients (25.3%) was malignant (Table 1).

In rectal swab cultures, *Escherichia coli* in 77 patients (88.5%), *Staphilococcus epidermidis* in 6 patients (6.8%), *Klebsiella pneumoniae* in 1 patient (1.1%), *Enterobacter cloacae* in 1 patient (1.1%), *Corynebacterium* in 1 patient (1.1%), *Enterococcus faecalis* in 1 patient (1.1%) were grown (Table 2).

Antibiogram susceptibilities of rectal swabs were evaluated according to FQ, TMP-SMX, and fosfomycin. FQ susceptibility was observed in 78 (89.7%) patients, fosfomycin susceptibility was observed in 85 (97.7%) patients, and TMP-SMX sensitivity was observed in 78 (89.7%) patients (Table 3).

Table 1. Mean age, PSA, and prostate volumes and percentage of diagnosis of diabetes mellitus, and malignant pathology	
	Number (± standard deviation), (%)
Age	64.4 (±7.7)
PSA	12.31 (±11.6)
Prostat volume (cc)	59.46 (±21.7)
Diabetes mellitus	22 (25.3%)
Malignant pathology	22 (25.3%)
PSA: Prostate-spesific antigen	

Table 2. Bacteria growth in rectal swab culture		
	Number	**%**
Escherichia coli	77	88.5
Staphilococcus epidermidis	6	6.8
Klebsiella pneumoniae	1	1.1
Enterobacter cloacae	1	1.1
Corynebacterium	1	1.1
Enterococcus faecalis	1	1.1

Table 3. Antibiogram susceptibilities		
	Sensitive patient (n)	**%**
Fluoroquinolone	78	89.7
Trimethoprim - sulfamethoxazole	78	89.7
Fosfomycin	85	97.7

No statistically significant relationship was found between FQ resistance and patients' age, diagnosis of diabetes, and malignancy of pathology ($p>0.05$). Of 9 patients with FQ resistance, 8 were Fosfomycin sensitive and 6 were TMP-SMX sensitive.

Urinary system infection, sepsis, severe hematuria, and rectal bleeding were not observed in any patient.

Discussion

TRUS-Bx is a method that is frequently used in the urology outpatient clinic for the diagnosis of prostate cancer and is considered safe. Despite bowel cleansing and antibiotics used, it can cause complications such as asymptomatic bacteriuria, urinary tract infections, and sepsis.

With the increasing use of antibiotics, multi-drug resistant (MDR) infections have become an important health problem. Recently, the number of infective complications after TRUS-Bx has been increasing worldwide. It has been observed that 50% resistance has developed in some regions to FQs used for prophylactic purposes (14). It is recommended to perform transperineal biopsies after surgical cleaning of the perineal skin due to the lower risk of infection (15).

To prevent urinary infections from developing after TRUS-Bx due to MDR infections, giving antibiotic prophylaxis according to the results of rectal swab culture taken before the procedure will reduce the morbidity and mortality rates that may occur due to urinary infections, as well as reduce the treatment costs resulting from infectious complications.

In the study of Cook et al. (16), infectious complications were seen at a rate of 0.41% in the group of 244 patients who were given appropriate antibiotics according to the swab, whereas infectious complications were observed at a rate of 2.65% in the control group of 264 patients, and the difference was significant between the two groups ($p<0.05$). In this study, many bacteria, especially *Escherichia coli*, were produced in rectal swab cultures examined before TRUS-Bx. In the antibiotic susceptibility tests, FQ sensitivity was 89.7%, fosfomycin sensitivity was 97.7%, and TMP-SMX sensitivity was 89.7%. None of the 87 patients who underwent TRUS-Bx had complications, such as urinary tract infection, fever, and sepsis. This may be due to the success of prophylactic antibiotics applied in our clinic and the low level of antibiotic resistance in the region.

Antibiotic prophylaxis by performing a rectal swab culture before the procedure is an ideal method for widespread antibiotic resistance. In the study of Knaapila et al. (17), the rate of antibiotic-resistant bacteria in rectal swab culture was 11%, while the rate of infectious complications was 0.7%. While Fosfomycin resistance was not found in the study, FQ resistance was detected in 12% of the patients (17). In our study, 10.3% resistance to the antibiotic used was observed according to the rectal swab culture, but no infectious complications were observed. In our study, fosfomycin resistance was seen as 2.3%, and although fosfomycin is a good option for prophylaxis, it has also been shown that fosfomycin resistance may occur.

In the study by Taylor et al. (15) on 457 male patients, infectious complications were observed at a significantly lower rate ($p=0.12$) in the group that received targeted antimicrobial prophylaxis by taking rectal swab compared with the group that received empirical prophylaxis (16). Because of the cost of infectious complications caused by FQ-resistant organisms, the targeted antibiotic prophylaxis group was found to be more cost-effective than the empirical prophylaxis group. In our study, all prophylaxis were empirical FQ and no infection was observed. The use of empirical FQ seems to be cost-effective, but the small sample size of our study with 87 patients should also be considered.

Although different antibiotic prophylaxis methods are discussed in today's medical practice due to FQ resistance, rectal swab removal from patients before TRUS-Bx is a method that prolongs the procedure and involves difficulties in applying for the patient. Although FQ sensitivity is as high as 89.7% in our region, it is still a cost-effective prophylaxis method.

Study Limitations

There are several limitations to this study. The most important one is the limited number of patients.

Another limiting factor is that direct quinolone prophylaxis was used, not prophylaxis for the culture results obtained before biopsy. Although prophylaxis was not changed according to the culture results, no infective complications were observed after biopsy.

Conclusion

Although different antibiotic prophylaxis methods are discussed due to FQ resistance in today's medical practices, FQ sensitivity

continues at a high rate of 89.7% in our region and still seems to be a viable prophylaxis method.

Acknowledgements

Publication: The results of the study were not published in full or in part in form of abstracts.

Contribution: There is not any contributors who may not be listed as authors.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

Ethics

Ethics Committee Approval: The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Cumhuriyet University ethics committee (decision no: 2019-03/02, date: 19.03.2019).

Informed Consent: Informed consent was obtained from each patient.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: A.A., İ.E.E., C.Ö., S.A.B., Design: A.A., A.F.V., Supervision: A.A., İ.E.E., E.K., Data Collection or Processing: A.Ö., A.F.V., Analysis-Interpretation: A.A., İ.E.E., Literature Review: H.S., M.H., S.A.B., Writing: H.S., A.A., C.Ö., S.A.B., Critical Review: H.S., A.A., M.H., E.Ko., Funding: A.Ö., E.K., E.Ko.

References

1. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. CA Cancer J Clin 2005;55:74-108.
2. Loeb S, Carter HB, Berndt SI, et al. Complications after prostate biopsy: data from SEER-Medicare. J Urol 2011;186:1830-1834.
3. Bootsma AM, Laguna Pes MP, Geerlings SE, Goossens A. Antibiotic prophylaxis in urologic procedures: a systematic review. Eur Urol 2008;54:1270-1286.
4. Yang M, Zhao X, Wu Z, et al. Meta-analysis of antibiotic prophylaxis use in transrectal prostatic biopsy. Zhong Nan Da Xue Xue Bao Yi Xue Ban 2009;34:115-123.
5. Wolf JS Jr, Bennett CJ, Dmochowski RR, et al. Best practice policy statement on urologic surgery antimicrobial prophylaxis (published correction appears in J Urol 2008;180:2262-2263). J Urol 2008;179:1379-1390.
6. Pilatz A, Dimitropoulos K, Veeratterapillay R, et al. Antibiotic Prophylaxis for the Prevention of Infectious Complications following Prostate Biopsy: A Systematic Review and Meta-Analysis. J Urol 2020;204(2):224-230.
7. El-Hakim A, Moussa S. CUA guidelines on prostate biopsy methodology. Can Urol Assoc J 2010;4:89-94.
8. Borghesi M, Ahmed H, Nam R, et al. Complications After Systematic, Random, and Image-guided Prostate Biopsy. Eur Urol 2017;71:353-365.
9. Wagenlehner FM, van Oostrum E, Tenke P, et al. Infective complications after prostate biopsy: outcome of the Global Prevalence Study of Infections in Urology (GPIU) 2010 and 2011, a prospective multinational multicentre prostate biopsy study. Eur Urol 2013;63:521-527.
10. Nam RK, Saskin R, Lee Y, et al. Increasing hospital admission rates for urological complications after transrectal ultrasound guided prostate biopsy. J Urol 2013;189:S12-S17.
11. Batura D, Gopal Rao G. The national burden of infections after prostate biopsy in England and Wales: a wake-up call for better prevention. J Antimicrob Chemother 2013;68:247-249.
12. European Medicine Agency. Disabling and potentially permanent side effects lead to suspension or restrictions of quinolone and fluoroquinolone antibiotics. 2019 (access date March 2021). Available from: https://www.ema.europa.eu/en/news/disabling-potentially-permanent-side-effects-lead-suspension-restrictions-quinolone-fluoroquinolone
13. EAU Guidelines. Edn. presented at the EAU Annual Congress Amsterdam 2022. Available from: https://uroweb.org/guideline/prostate-cancer/#note_308
14. Duplessis CA, Bavaro M, Simons MP, et al. Rectal cultures before transrectal ultrasound-guided prostate biopsy reduce post-prostatic biopsy infection rates. Urology 2012;79:556-561.
15. Taylor AK, Zembower TR, Nadler RB, et al. Targeted antimicrobial prophylaxis using rectal swab cultures in men undergoing transrectal ultrasound guided prostate biopsy is associated with reduced incidence of postoperative infectious complications and cost of care. J Urol 2012;187:1275-1279.
16. Cook I, Angel JB, Vera PL, et al. Rectal swab testing before prostate biopsy: experience in a VA Medical Center urology practice. Prostate Cancer Prostatic Dis. 2015;18:365-369.
17. Knaapila J, Gunell M, Syvänen K, et al. Prevalence of Complications Leading to a Health Care Contact After Transrectal Prostate Biopsies: A Prospective, Controlled, Multicenter Study Based on a Selected Study Cohort. Eur Urol Focus 2019;5:443-448.