Original Article

DOI: 10.4274/haseki.galenos.2023.9205
Med Bull Haseki 2023;61:199-205

Comparison of the Efficacy of Fosfomycin Trometamol and Ciprofloxacin in Transrectal Ultrasound-Assisted Prostate Biopsy Prophylaxis: Clinical Results of A Tertiary Referral Center

Mehmet Hamza Guktekin*, Goktug Kalender*, Kadir Can Sahin*, Sami Berk Ozden*, Ilker Inanc Balkan**, Muhammed Fatih Simsekoglu*, Bulent Onal*, Ahmet Erozenci*

*Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Department of Urology, Istanbul, Turkey

**Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Istanbul, Turkey

Abstract

Aim: Although infectious complications after a prostate biopsy are uncommon, they may have fatal outcomes. An efficient prophylaxis plan has not been defined in the current literature to reduce these problems. In this study, we aimed to compare the use of ciprofloxacin (CIP) and fosfomycin trometamol (FT) for prophylaxis in terms of infectious complications and morbidity-related parameters in patients who underwent transrectal ultrasound-guided prostate biopsy (TRUSPB).

Methods: The study included 104 patients who received FT for TRUSPB prophylaxis (group 1) between May 2021 and May 2022 and 113 patients who received CIP for TRUSPB prophylaxis between April 2020 and April 2021 (group 2). All patients were instructed to visit our hospital if they had any complaints relevant to the procedure, and outpatient control visits were scheduled one month after the procedure. Post-procedure infectious or non-infectious complications within one month were identified by screening the patients' electronic records and medical charts belonging to their inpatient, outpatient, or emergency department visits.

Results: After the biopsy procedures, the rates of lower urinary tract symptom development, positive urine cultures, and the requirement of hospitalization for parenteral antibiotic treatment were found to be significantly lower in group 1 than in group 2 (p=0.048). In the analyses performed independently of the prophylaxis regimen, it was observed that an increase in the Charlson Comorbidity Index of the patients caused a significant increase in the rates of both urosepsis (p=0.024) and the requirement of hospitalization for parenteral antibiotic treatment (p<0.001).

Conclusion: We observed that the use of FT for prophylaxis in TRUSPB was superior to the use of CIP in terms of reducing infectious complications.

Keywords: Complications, hospitalization, mortality, prophylaxis, prostate biopsy

Introduction

Prostate cancer is the second most common cancer in men worldwide and occurs mostly when men are active in their lives (1,2). Prostate biopsy is currently the gold standard diagnostic tool for prostate cancer diagnosis, and it can be performed via the transperineal or transrectal approach (3). Although over 2 million procedures are performed annually in the United States and Europe, complications, some of which can be life-threatening, continue to be a significant challenge (4). Frequent complications of transrectal biopsies have been defined as hematospermia, hematuria, and rectal bleeding. A minority of patients who have undergone transrectal ultrasound-guided prostate biopsy (TRUSPB) face infectious complications, including

Address for Correspondence: Mehmet Hamza Guktekin, Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine, Department of Urology, Istanbul, Turkey
Phone: +90 505 244 49 62 E-mail: dr.mhgultekin@gmail.com ORCID: orcid.org/0000-0001-6111-2987
Received: 16.04.2023 **Accepted:** 20.06.2023

cystitis, epididymitis, orchitis, prostatitis, and urosepsis (5). Mortality after a prostate biopsy is extremely rare and is mostly due to urosepsis (4). Various antibiotic prophylaxis protocols are used to reduce infectious complications, and clinics regularly update their antibiotic preferences according to the published results of the new regimens. Fluoroquinolones have been traditionally used for the antibiotic prophylaxis of TRUSPB. However, the overuse and misuse of fluoroquinolones have increased fluoroquinolone resistance (6). A systematic review and meta-analysis on antibiotic prophylaxis for the prevention of infectious complications following prostate biopsy concluded that in cases of fluoroquinolone resistance or augmented prophylaxis (combination of two or more different classes of antibiotics), the common recommendation in the literature was targeted therapy (7). However, no standard antibiotic prophylaxis protocol is used worldwide because of regionally different antibiotic resistances. A meta-analysis of three randomized clinical trials reported that fosfomycin trometamol (FT) was superior to fluoroquinolones (relative risk: 0.49, 95% confidence interval: 0.27-0.87) (7), but the routine general use of this agent remains controversial due to the infectious complications reported to date (8).

The aim of this study was to compare FT prophylaxis with ciprofloxacin (CIP) prophylaxis in terms of their efficacy in preventing infectious complications.

Methods

Compliance with Ethical Standards

The present study was approved by the Ethics Committee of Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine (approval number: 488788, date: 22.09.2022).

Study Design

The records of all patients who underwent TRUSPB with two different prophylactic antibiotic regimes (FT and CIP) in our institution between April 2020 and May 2022 were retrospectively evaluated. Group 1 consisted of patients who received 3 g of oral FT 12 h before and 24 h after TRUSPB. Group 2 consisted of patients who received oral CIP for three days prophylactically, starting the day before TRUSPB. Only patients who were followed up for more than three months were included in the study. Patients who had used fluoroquinolones or FT for any reason within the last three months, had known resistance or allergies, had missing data, or did not attend follow-up visits were excluded from the study. To assess the data more homogenously, we also excluded patients who underwent TRUSPB under parenteral antibiotic prophylaxis due to resistant susceptibility testing results. Patients who were admitted to the hospital with conditions unrelated to the biopsy procedure were excluded from the final analysis.

Biopsy Procedure

Biopsies were performed in the endoscopy suite of our institution by experienced urologists with more than five years of experience in prostate biopsies. Antibiotic prophylaxis was started for the patients in both groups one day before the procedure, and the patients were instructed to apply a self-administered sodium phosphate enema the evening before the procedure. Before the procedure, the patients' comorbidities, urine culture results, prophylaxis status, blood coagulation parameters, antiaggregant or anticoagulant drug use, and the presence of specific symptoms of infection (i.e., fever, chills, urgency, frequent urination, or suprapubic tenderness) were questioned in detail by urologists. For the patients whose antiaggregant or anticoagulant therapy was not regulated, those who had symptoms of urinary tract infection (UTI), and those with positive urine culture results, the biopsy procedures were postponed. Patients with positive urine cultures were treated with antibiotics, and a negative microbiological control after therapy was required before biopsy. 3 g FT was administered prophylactically before and within 24 to 48 h after the procedure, as specified in the prostate biopsy prophylaxis section of the current European Association of Urology (EAU) prostate cancer guideline (3). Patients who received CIP for prophylaxis received a three-day prophylactic course of medication beginning the day before their procedure. The patients were placed in the left lateral decubitus position, and lubricant sterile gel with lidocaine (Lubagel Plus, Yasemin Medika, Istanbul, Turkey) was applied via the rectal route. A digital rectal was examined, and the findings were recorded in the patient's file. A 6.5-MHz transrectal ultrasound probe (Siemens Medical Systems, Inc., Issaquah, WA, USA). Prostate volume was calculated using the prostate ellipsoid formula: volume (V)=0.52 (L x W x H), where L is the cephalocaudal diameter, W is the width, and H is the anteroposterior diameter. A periprostatic block was applied with a combination of lidocaine and bupivacaine using a 20-cm-long, 22-gauge needle (Chiba Biopsy Needle with Echogenic Tip, Argon Medical Devices Inc., Dallas, USA) for both sides under the guidance of transrectal ultrasonography. Transrectal ultrasound-guided prostate biopsy was performed using a disposable 18-gauge × 25-cm biopsy needle (Argon Pro-Mag Biopsy Needle, Argon Medical Devices Inc., Dallas, USA). According to the standard biopsy protocol, 12 core biopsies were taken. If the calculated prostate volume was larger than 60 cc, four additional cores were added. If a suspicious lesion was detected on multiparametric prostate magnetic

resonance imaging (MRI) before the procedure, three subsequent additional core biopsies per lesion were taken using an MRI fusion biopsy device (UroNav, Invivo-Philips, Gainesville, FL, USA).

Follow-up

All patients were advised to present to our hospital if there were any severe rectal or urinary bleeding, urinary retention, fever, chills, or lower urinary tract symptoms. We scheduled visits within one month after TRUSPB as a cut-off to capture only infections that could be related to the prostate biopsy. Any events that occurred more than one month after the prostate biopsy were considered unlikely to have been related to TRUSPB. All symptomatic patients who presented to the hospital underwent a physical examination and urinalysis. Similar to the criteria described by Fahmy et al. (9), urine cultures were taken from the patients who presented with fever, fatigue, any lower urinary tract symptom (i.e., urgency, frequency, dysuria, or suprapubic tenderness), bacteriuria [$\geq 10^4$ colony-forming units (CFUs)/mL], and pyuria (>5 leucocytes/high-power field). Hemocultures and blood tests were collected from the patients with a body temperature of >38 °C and/or in the presence of a septic status. Patients who were considered to have febrile UTIs and required parenteral antibiotics were admitted to the inpatient clinic. In our study, we screened for sepsis using the quickSOFA (qSOFA) score, in which each of the following three criteria is assigned one point: A low systolic blood pressure (≤100 mmHg), a high respiratory rate (≥22 breaths per minute), or altered mental status (Glasgow Coma Scale score <15). (10) Those who scored two out of three in the screening were further evaluated by an infectious diseases specialist in terms of sepsis.

Statistical Analysis

SPSS v. 20 (IBM Corp. Released 2011, IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.) statistical program was used for the evaluation of the data. The assumption of normality was tested using the Shapiro-Wilk test. The two groups were compared with the Independent sample t-test and the Mann-Whitney U test. The relationship between categorical variables was analyzed with Fisher's exact and chi-square tests. P<0.05 was considered significant.

Results

Patient characteristics for both groups are shown in Table 1. Group 1 consisted of 104 (47.92%) patients, and group 2 consisted of 113 (49.77%) patients. The two groups were similar in terms of median age, prostate volume, the number of biopsy cores, and presence of urethrorrhagia and rectorrhagia. The median Charlson Comorbidity Index (CCI) and prostate-specific antigen (PSA) values of the patients in group 2 were significantly higher than those of the patients in group 1 (p=0.004). The median number of biopsy cores was significantly higher in group 1 than in group 2 (p=0.007). The number of patients presenting with lower urinary tract symptoms after the biopsy was 16 (15.38%) in group 1 and 39 (34.51%) in group 2 (p<0.001). We detected six (5.76%) post-procedure positive urine cultures in group 1 and 20 (17.69) in group 2 (p=0.007). Eight (30.76%) of these patients were treated with oral antibiotics (Table 2). In group 1, five patients were hospitalized for parenteral antibiotic treatment. Extended-spectrum beta-lactamase (ESBL)-positive *Escherichia coli (E. coli)* > 100.000 CFU/mL was detected in the urine cultures of four of these patients, and meropenem was administered in accordance with susceptibility testing. We detected *Pseudomonas aeruginosa* in the remaining patient and treated it with amikacin monotherapy according to the susceptibility testing results. In group 2, ESBL (+) *E. coli* >100.000 CFU/mL was detected in the urine cultures of 11 of the 13 patients, of whom nine were treated with meropenem and two with ertapenem in line with susceptibility testing. In the remaining patient, *Enterococcus* spp. >100.000 CFU/

Table 1. Patient characteristics

	FT (group 1)	CIP (group 2)	p value
Patients, n (%)	104 (47.92)	113 (52.07)	
Age, median (IQR25-IQR75)	65 (58-71.75)	65 (59-69.5)	0.581♠
Diabetes mellitus, n (%)	32 (30.76)	41 (36.28)	0.39♥
CCI, median (IQR25-IQR75)	3 (1-5)	4 (2-5)	**0.004**#
PSA, ng/mL, median (IQR25-IQR75)	7.5 (5.2-12)	10 (6.24-26)	**0.007**#
Prostate volume, cm^3, median (IQR25-IQR75)	50 (37.63-65.75)	50 (35-65)	0.901#
Number of biopsy cores, mean (IQR25-IQR75)	16 (15-18)	14 (12-16)	**0.000**#
Urethrorrhagia, n (%)	16 (15.38)	16 (14.15)	0.799♥
Rectorrhagia, n (%)	16 (15.38)	27 (23.89)	0.108♦

♠Independent samples t-test, #Mann-Whitney U test, ♦Fisher's exact test, ♥Chi-square test
FT: Fosfomycin trometamol, CIP: Ciprofloxacin, CCI: Charlson Comorbidity Index, PSA: Prostate-specific antigen

mL ampicillin resistant were detected in urine cultures, and teicoplanin treatment was started according to susceptibility testing (Table 3). Two patients, both in group 2 and both with CCI >7, were evaluated for urosepsis according to the qSOFA screening criteria. ESBL (+) *E. coli* >100.000 CFU/mL was detected in the first patient's urine culture 14 days after the biopsy. Empirical meropenem treatment was started as soon as blood cultures were obtained when clinical signs appeared. Blood cultures remained sterile, and meropenem was continued based on urine culture results. In the second patient, *Enterococcus spp.* >100.000 CFU/mL were detected in the urine culture 8 days after the biopsy, while his blood cultures were sterile. Teicoplanin was initiated empirically upon Gram staining results and continued according to susceptibility testing. Due to the development of urosepsis, both patients were transferred to the intensive care unit. Despite timely and prompt parenteral antibiotics and vasopressor therapy, the patients succumbed to urosepsis.

Discussion

The results of our study showed that FT prophylaxis was superior to CIP prophylaxis in terms of lower urinary tract symptoms, urine culture positivity, infections requiring hospitalization, and urosepsis after TRUSPB. Although TRUSPB is generally considered a safe outpatient procedure, infectious complications carry the risk of death. The incidence of bacteriuria and urosepsis following transrectal prostate biopsy was reported to be 17.1% and 5.7%, respectively, in a recent study (11). This circumstance appears to be very extraordinary and concerning. Also, with the increasing number of men on active surveillance worldwide, there has also been an increase in the number of repeat biopsies that have a higher risk of infectious complications than primary biopsies. To prevent infectious complications, fluoroquinolones, which are effective in the *Enterobacteriaceae* family, are commonly used in patients undergoing TRUSPB worldwide. However, due to increasing fluoroquinolone resistance in recent years, fluoroquinolones are no longer the most effective alternative for prophylaxis (12-14). In particular, the European Commission has imposed stringent limits on fluoroquinolones and prohibited their use for prostate biopsy prophylaxis (6). Other alternatives to CIP include parenteral antibiotics, which are not endorsed as prophylaxis according to the EAU guidelines. Despite the increasing resistance to CIP in Turkey, this antibiotic is still widely used for various clinical cases, and yet there is no regulatory rule to limit its use for prophylaxis. Since we encountered challenging infective complications under CIP prophylaxis more frequently, we started to use FT prophylaxis, recommended by the EAU guidelines, in our clinical practice and compared the outcomes of these two prophylaxis agents in the current study. A study by Ongün et al. (15) compared the outcomes for 620 patients under FT- or fluoroquinolone-based TRUSPB prophylaxis, and the results showed that FT prophylaxis reduced the rates of fluoroquinolone-resistant infections requiring hospitalization. In a meta-analysis published by Pilatz et al. (7) in 2020, data obtained from 59 randomized controlled trials and 14,153 patients were examined, and it was emphasized that FT prophylaxis was a good alternative for prophylaxis with low infection rates, especially in countries where the use of CIP was restricted. In comparison to fluoroquinolone, a recent meta-analysis suggested that

Table 2. Patients were treated with oral antibiotics

	FT (group 1)	CIP (group 2)	p value
Presence of LUTS symptoms after biopsy, n (%)	16 (15.38)	39 (34.51)	**<0.001**♥
Positive urine culture, n (%)	6 (5.76)	20 (17.69)	**0.007**♥
Treatment with oral antibiotics, n (%)	1 (0.96)	7 (6.19)	0.067♦
Hospitalization and treatment with parenteral antibiotics, n (%)	5 (4.8)	13 (11.5)	**0.048**♥
Urosepsis, n (%)	0 (0)	2 (1.76)	0.49♦
Mortality, n (%)	0 (0)	2 (1.76)	0.49♦

♦Fischer's exact test, ♥Chi-square test
FT: Fosfomycin trometamol, CIP: Ciprofloxacin, LUTS: Lower urinary tract symptoms

Table 3. Urine culture results of the patients treated with parenteral antibiotics

	FT (group 1)	CIP (group 2)
Escherichia coli (ESBL), n (%)	4 (80)	11 (84.6)
Pseudomonas aeruginosa, n (%)	1 (20)	0
Staphylococcus aureus, n (%)	0	1 (7.7)
Enterococcus spp. *n (%)*	0	1 (7.7)

FT: Fosfomycin trometamol, CIP: Ciprofloxacin, ESBL: Extended-spectrum beta-lactamase

FT or the combination of FT and fluoroquinolone may have a similar preventive impact on UTIs after TRUSPB, and FT may be a good option considering the increase in fluoroquinolone resistance (16). However, Carignan et al. (8), who examined the data of 9,391 patients who had undergone TRUSPB in a nested case-control non-randomized study, reported that the risk of infection increased with FT prophylaxis compared to CIP prophylaxis and that this risk could not be reduced by administering a second dose of FT. Similar to the studies of Ongün et al. (15) and Pilatz et al. (7), we found fewer infective complications in our FT prophylaxis group. Urosepsis development after TRUSPB is a serious, life-threatening complication. When the current literature is reviewed in terms of urosepsis rates, Morin et al. (12) examined the results of prostate biopsies performed in Canada between 2012 and 2015 and found that only 1.1% (12/1090) of patients who received CIP prophylaxis and 0.2% (2/1197) of those who received CIP + FT prophylaxis developed urosepsis, and the rate of urosepsis development was lower in the CIP + FT combination. In a study conducted in Italy in 2015, Cai et al. (17) retrospectively evaluated the data of 1,109 patients who underwent TRUSPB and found that 0.3% (2/632) of the patients in the FT group and 1.8% (9/477) of those in the CIP group developed urosepsis. We evaluated our patients for urosepsis according to the qSOFA criteria as recommended by the EAU urological infection guidelines (10,3). We found the rate of urosepsis to be 1.76% in the CIP group, whereas urosepsis was not observed in any of the patients in the FT group. Our results seem to be consistent with the literature. Positive urine culture results, with or without systemic findings of infection requiring hospitalization after TRUSPB are becoming a more significant problem in current medical practice. When our series was examined, ESBL (+) *E. coli* growth was detected in 83.33% of our hospitalized patients, and *Staphylococcus aureus, Enterococcus spp.*, and *Pseudomonas aeruginosa* growth was observed in one patient each. In the current literature, ESBL (+) *E. coli* growth is reported in a wide range from 56% to 100% (18-20). According to the risk distribution map of the 2019 global antimicrobial resistance evaluation study, the rate of fluoroquinolone-resistant *E. coli* in the general population of Turkey was 40-50%, and the rate of third-generation cephalosporin-resistant *E. coli* was 20-30% (21). In light of these data, the rate of multidrug resistance reflects current epidemiology. Comorbidities often lead to poor outcomes, and therefore patients' comorbidities should be evaluated before TRUSPB. Charlson Comorbidity Index is widely used to evaluate patients' comorbidities and assess mortality risks. In our study, an increase in CCI increased both the requirement for hospitalization for parenteral antibiotic treatment and the rate of urosepsis. However, CCI is rarely used in studies comparing different prophylaxis protocols in the literature. In a 2016 study, Cai et al. (17) compared FT and CIP in TRUSPB prophylaxis and found that a CCI of more than 1 increased the likelihood of symptomatic UTIs. Based on our similar results, we consider that CCI should be evaluated before the procedure and that more effective prophylaxis protocols should be applied for prophylaxis in patients with a CCI of more than 1. Mortality is rarely seen after TRUSPB. In a large-scale population-based study evaluating mortality rates within the first four months after TRUSPB, the data of 22,175 patients was evaluated, and it was reported that 279 (1.3%) patients died during this period (22). In addition, the mortality rate was found to be 0.7% in patients with a CCI of 0 and 2.2% in those with a CCI of 3 or 4. In our study, there was no patient loss in the FT group, but two (1.7%) patients who underwent prophylaxis with CIP died due to urosepsis and related complications after the procedure. The first of these patients was a 71-year-old male who had no known additional disease but had metastatic disease of an unknown primary on admission. The CCI for this patient was determined to be 9. Since his total PSA was 15 ng/dL, a transrectal prostate biopsy was performed. He presented with chills and a fever four days after the biopsy. Extended-spectrum beta-lactamase positive *E. coli* was detected in the urine culture, and his qSOFA score was 3 on clinical assessment. The patient was transferred to the intensive care unit and followed up with positive inotropes for 5 days, but died despite all efforts. The second patient was a 72-year-old man with diabetes mellitus, mitral valve regurgitation, and congestive heart failure. He had a CCI value of seven. Considering that the total PSA level was 16 ng/mL, a transrectal prostate biopsy was performed. One day after the biopsy, he presented to our clinic with a deterioration in his general condition. The qSOFA score was calculated to be 3, and he was transferred to an intensive care unit. *Enterococcus spp.* >100.000 CFU/mL were detected in his urine culture, and teicoplanin was started empirically and continued as targeted therapy according to susceptibility testing. He died after six days of follow-up in the intensive care unit. There was no patient loss in the FT group. The high CCI scores of both patients who died indicate the importance of evaluating patient comorbidities before TRUSPB.

Study Limitations

There are some limitations to our study. Rectal swab cultures to screen for multidrug resistance in the rectal flora were not obtained from the patients before the biopsy procedure. A controversial issue emphasized in the literature is that different patterns of resistance may exist among the rectal flora of the same patient and

may be overlooked in screening cultures. Routine rectal washing with povidone-iodine was also not undertaken during the procedure. Lack of randomization in assigning patients to the prophylaxis groups and the higher mean CCI score of the patients in the CIP arm are among the major limitations of our study. Laboratory analyses for control were also not requested for patients who did not develop any symptoms during the follow-up period. The number of fusion biopsies performed was higher in the FT group. Finally, it should be noted that Germany has withdrawn the use of FT for prostate biopsies because its manufacturers failed to provide the required pharmacokinetic data (3).

Conclusion

It was observed that the use of FT for prophylaxis in TRUSPB was superior to the use of CIP in terms of reducing infectious complications. We recommend that more effective prophylaxis protocols be applied to lower the rates of infectious complications related to TRUSPB.

Ethics

Ethics Committee Approval: The present study was approved by the Ethics Committee of Istanbul University-Cerrahpasa, Cerrahpasa Faculty of Medicine (approval number: 488788, date: 22.09.2022).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.H.G., M.F.S., Concept: M.H.G., S.B.O., Design: M.H.G., I.I.B., M.F.S., B.O., A.E., Data Collection or Processing: G.K., K.C.S., Analysis or Interpretation: M.H.G., G.K., K.C.S., Literature Search: M.H.G., G.K., S.B.O., Writing: M.H.G., S.B.O., I.I.B., M.F.S., B.O., A.E.

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

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

References

1. Culp MB, Soerjomataram I, Efstathiou JA, Bray F, Jemal A. Recent Global Patterns in Prostate Cancer Incidence and Mortality Rates. Eur Urol 2020;77:38-52.
2. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394-424. Erratum in: CA Cancer J Clin 2020;70:313.
3. EAU Guidelines. Edn. presented at the EAU Annual Congress Milan 2023. ISBN 978-94-92671-19-6.
4. Borghesi M, Ahmed H, Nam R, et al. Complications After Systematic, Random, and Image-guided Prostate Biopsy. Eur Urol 2017;71:353-65.
5. Udeh EI, Amu OC, Nnabugwu II, Ozoemena O. Transperineal versus transrectal prostate biopsy: our findings in a tertiary health institution. Niger J Clin Pract 2015;18:110-4.
6. European Medicines Agency. Disabling and potentially permanent side effects lead to suspension or restrictions of quinolone and fluoroquinolone antibiotics. 2018 EMA/175398/2019. [Access date March 2022]. https://www.ema.europa.eu/en/documents/press-release/disabling-potentially-permanent-sideeffects-lead-suspension-restrictions-quinolone-fluoroquinolone_en.pdf
7. 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;204:224-30.
8. Carignan A, Sabbagh R, Masse V, et al. Effectiveness of fosfomycin tromethamine prophylaxis in preventing infection following transrectal ultrasound-guided prostate needle biopsy: Results from a large Canadian cohort. J Glob Antimicrob Resist 2019;17:112-6.
9. Fahmy A, Rhashad H, Mohi M, Elabbadie A, Kotb A. Optimizing prophylactic antibiotic regimen in patients admitted for transrectal ultrasound-guided prostate biopsies: A prospective randomized study. Prostate Int 2016;4:113-7.
10. Vincent JL, de Mendonça A, Cantraine F, et al. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. Working group on "sepsis-related problems" of the European Society of Intensive Care Medicine. Crit Care Med 1998;26:1793-800.
11. Islam MA, Alam SM, Reza AM. Urosepsis and Bacteriuria in Patients Undergoing TRUS-Guided Prostate Biopsy. Mymensingh Med J 2023;32:330-7.
12. Morin A, Bergevin M, Rivest N, Lapointe SP. Antibiotic prophylaxis for transrectal ultrasound-guided prostate needle biopsy: Compared efficacy of ciprofloxacin vs. the ciprofloxacin/fosfomycin tromethamine combination. Can Urol Assoc J 2020;14:267-72.
13. Zaytoun OM, Vargo EH, Rajan R, Berglund R, Gordon S, Jones JS. Emergence of fluoroquinolone-resistant Escherichia coli as cause of postprostate biopsy infection: implications for prophylaxis and treatment. Urology 2011;77:1035-41.
14. Kapoor DA, Klimberg IW, Malek GH, et al. Single-dose oral ciprofloxacin versus placebo for prophylaxis during transrectal prostate biopsy. Urology 1998;52:552-8.
15. Ongün S, Aslan G, Avkan-Oguz V. The effectiveness of single-dose fosfomycin as antimicrobial prophylaxis for patients undergoing transrectal ultrasound-guided biopsy of the prostate. Urol Int 2012;89:439-44.

16. Gu HM, Gu JS, Chung HS, et al. Fosfomycin for Antibiotic Prophylaxis in Men Undergoing a Transrectal Prostate Biopsy: A Systematic Review and Meta-Analysis. Medicina (Kaunas) 2023;59:911.
17. Cai T, Gallelli L, Cocci A, et al. Antimicrobial prophylaxis for transrectal ultrasound-guided prostate biopsy: fosfomycin trometamol, an attractive alternative. World J Urol 2017;35:221-8.
18. Lange D, Zappavigna C, Hamidizadeh R, Goldenberg SL, Paterson RF, Chew BH. Bacterial sepsis after prostate biopsy--a new perspective. Urology 2009;74:1200-5.
19. Kutluhan MA, Toprak T, Topaktaş R. Evaluation of the Patients with Urinary Tract Infection after Transrectal Ultrasound-guided Prostate Biopsy. Haydarpasa Numune Med J 2020;60:422-5.
20. Young JL, Liss MA, Szabo RJ. Sepsis due to fluoroquinolone-resistant Escherichia coli after transrectal ultrasound-guided prostate needle biopsy. Urology 2009;74:332-8.
21. Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet 2022;399:629-55. Erratum in: Lancet 2022;400:1102.
22. Gallina A, Suardi N, Montorsi F, et al. Mortality at 120 days after prostatic biopsy: a population-based study of 22,175 men. Int J Cancer 2008;123:647-52.