Comparison between ciprofloxacin and trimethoprim-sulfamethoxazole in antibiotic prophylaxis for transrectal prostate biopsy

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ABSTRACT

Objective: The aim of this study was to compare the efficacies of oral ciprofloxacin administration and oral trimethoprim-sulfamethoxazole (TMP-SMX) regimens in preventing infectious complications following transrectal ultrasound guided biopsy of the prostate.

Material and methods: Between 2011-2013, the medical records of 391 (mean age 64.62 ± 7.64 years; range 40 to 87 years) patients who underwent transrectal prostate biopsies, due to suspicion of prostate cancer were retrospectively reviewed. While 500 mg ciprofloxacin was given orally twice daily starting one day before the procedure, continued for 3 days in the first 174 patients (group 1); was given orally twice daily starting one day before the procedure, continued for 3 days in the remaining 217 patients (group 2) for prophylaxis. Urine samples were obtained for urine culture before the procedure. The two groups were compared with respect to findings of urine cultures performed before and after the procedure and complications.

Results: In the ciprofloxacin and groups, any positive urine culture before the procedure was not observed. Complications occurred in 93 patients (37 in group 1 and 56 in group 2), after the procedure. Twenty-two (5.6%) (11 in group 1 and 11 in group 2). patients were admitted to our clinic because of high fever occurring after biopsy. Nine ciprofloxacin-treated (5.2%) and 16 TMP-SMX-treated (7.4%) patients had severe dysuria after the procedure. Twenty-one ciprofloxacin recipients (12.1%) and 40 TMP-SMX recipients (18.4%) had macroscopic hematuria. In the ciprofloxacin and TMP-SMX groups, the incidences of new culture positivity were 4% (n=7) and 2.8% (n=6) after the procedure, respectively. All of the isolated bacteria was *Escherichia coli*. While 11 patients were hospitalized due to signs of complicated urinary tract infections, and 2 patients were treated as outpatients. Rectal bleeding that did not require any intervention was observed in a patient 8 hours after biopsy. SIRS findings were detected in two patients. There were no significant differences between the two groups with respect to age, prostate volume, prostate specific antigen (PSA) levels, and results of urine culture performed after the procedure ($p>0.05$).

Conclusion: Despite the increasing resistance to antibiotics, ciprofloxacin and TMP-SMX are effective prophylactic treatment modalities for transrectal prostate biopsy. Both three-day ciprofloxacin and TMP-SMX regimens seem to be equally effective in the antibiotic prophylaxis for transrectal prostate biopsy.

Keywords: Ciprofloxacin; prophylaxis; prostate biopsy; trimethoprim-sulfamethoxazole; urinary tract infection.

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Submitted:
25.12.2013

Accepted:
09.12.2014

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Introduction

With the development of transrectal ultrasonographic (TRUS) techniques, TRUS-guided prostate biopsy has become currently a standard method in the diagnosis of prostate cancer. With time prostate biopsy technique has undergone important modifications after TRUS-guided systemic 6 core (sextant) prostate biopsies described firstly in 1989 by Hodges et al.^[1] Especially with the development of transrectal ultrasonographic (TRUS) probes, as a standard

technique TRUS-guided biopsies have been applied. This method is generally tolerable, however because of application of this invasive method through transrectal route, it carries risk of various complications.^[2-4] Despite its lower serious complication rates, simple complications are frequently encountered.^[5] Studies performed revealed that antibiotic prophylaxis applied before biopsy considerably have decreased risks of high fever, bacteremia, and urinary infection.^[6] Many prophylactic protocols have been reported in the literature.

In the Guidelines of European Association of Urology, as the first-line antibiotics, fluoroquinolone group or trimethoprim-sulphamethoxazole are recommended, however various studies have reported development of resistance to these drugs. In the last years gradually increasing resistance to therapy with quinolone group of antibiotics which has been initiated before the procedure, and used 1-3 days after the procedure in many clinics should be taken into consideration.^[7,8] In this study, we compared 500 mg ciprofloxacin with trimethoprim-sulphamethoxazole initiated one day before 12-core TRUS-guided prostate biopsy procedure in our clinic with respect to their efficacies, and infectious complications.

Material and methods

The medical files of the patients who had undergone transrectal prostate biopsies in our clinic between February 2011, and December 2013 were retrospectively investigated. A total of 391 patients with a mean age of 64.62 ± 7.64 (range, 40-87 years) years who had undergone prostate biopsies were included in the study. The patients were divided into 2 groups. Group 1 (n=174) patients received oral doses of 500 mg twice daily doses of ciprofloxacin for 3 days starting from the day before the procedure. Group 2 (n=217) patients were prescribed oral doses of 160 mg trimethoprim- 800 mg sulphamethoxazole twice daily for 3 days starting from the day before the procedure. Before the biopsy, rectal cleansing with enema was not applied. Viking 2400 brand ultrasonograph (B-K Medical, Herlev, Denmark) with biplanar transrectal ultrasonographic probe was used. Prostatic anatomy was evaluated while the patient was laid in the left lateral decubitus position. Then following periprostatic nerve blockage applied using 2% lidocaine (6 mL), 12- core prostate biopsies were performed. The patients were informed about postprocedural complications, and conditions requiring hospital admissions, The patients of two groups were called for control on 10. days after biopsy, and their urine cultures, and histopathological reports were comparatively evaluated.

Statistical analysis

For statistical evaluation Statistical Package for the Social Science (SPSS Inc., Chicago, IL, USA) 18.0 statistical package program was used. For the comparison of measurable values Student t-test, and Mann-Whitney U test, and for the comparison of numerical values *chi*-square, and Fisher's exact test were used. $P < 0.05$ was accepted as the level of significance.

Results

Mean age of a total of 391 patients included in the study was 64.62 ± 7.64 years, mean serum prostate- specific antigen (PSA) level, and prostate volume were 14.43 ± 6.7 ng/mL, and 53.47 ± 11.3 mL, respectively. Mean age, serum prostate- spe-

cific antigen level, and prostate volume in Group 1 patients who received ciprofloxacin were 64.53 ± 7.47 years, 15.93 ± 3.83 ng/mL, and 57.1 ± 4.7 mL, respectively. Mean age, serum prostate-specific antigen level, and prostate volume in Group 2 patients who received TMP-SMX were 64.69 ± 7.79 years, 13.24 ± 1.27 ng/mL, and 50.54 ± 14.2 mL, respectively. A significant difference was not detected between both groups as for mean age, serum PSA level, and prostate volume ($p > 0.05$, Table 1).

Among biopsized patients 292 (74.7%) cases with BPH, and 99 cases (25.3%) with prostate cancer were detected.

In 37 (21.3%) patients in Group 1, and 56 (25.8%) patients in Group 2, complication(s) developed after biopsy procedure. Following biopsy procedures 22 patients (Group 1, n=11; 6.3%, and Group 2, n=11; 5.1%) consulted to our clinic because of high fever. Twenty-five patients presented to our clinic with complaints of severe dysuria (Group 1, n=9, and Group 2, n=16; 7.4%). Patients also complained of macroscopic hematuria not requiring transfusion (Group 1, n=21; 12.1%, and Group 2, n=40; 18.4%). Post-biopsy urine culture positivity was detected in 7 (4%) patients in Group 1, and 6 (2.8%) patients in Group 2. Only *Escherichia coli* was isolated from all urine cultures. Eleven (2.8%) patients with complicated urinary infection whose urine cultures demonstrated bacterial growth were hospitalized, while 2 patients were sufficiently treated on daycare basis. In one patient severe rectal bleeding was observed, while in 2 patients, Systemic Inflammatory Response Syndrome (SIRS) was detected. A significant difference was not detected between two groups as for infective complications ($p > 0.05$, Table 2).

Discussion

Nowadays, transrectal US-guided prostate biopsy is widely used, and it is considered as one of the standardized procedures in the histopathological diagnosis of prostate cancer. Serious complication rates are very low. Though it is generally accepted as a safe method, it can lead to hemorrhagic, and infective complications because of its invasive nature.^[3,4] Generally infective complications which encounter us as asymptomatic bacteriuria can progress to urinary infection or sepsis.^[9]

Recently, thanks to developments of prebiopsy preparation of the patient, and biopsy technique, serious complication rates are at low levels. However, currently simple complication rates are still at considerable levels.^[5,10] Before the biopsy procedure, as is the case with pre-colonoscopy preparation, in addition to rectal cleansing, bowel cleansing is applied to decrease infective complications which may develop secondary to biopsy.^[11]

The major culprit bacteria responsible for the development of symptoms after biopsy is *E. coli* which normally colo-

nizes in the rectal flora, however anaerobic microorganisms as *Proteus* spp., *Bacteriodes* spp., and *Enterococcus* spp. are also held responsible.^[12] An appropriate prophylaxis should be made using an antimicrobial effective on both urinary system, and intestinal flora which can also reach high concentrations in the prostate tissue. Ciprofloxacin which contains all these characteristic features is the most frequently used agent. However because of increasing resistance to quinolone group of antibiotics, different antibiotherapy regimens are also preferred.^[13-15]

Potential post-biopsy complications have different clinical pictures changing from asymptomatic bacteriuria to the development of urinary infection, from bacteremia to fever, prostatitis, epididymitis, and sepsis. On the other hand development of Fournier's gangrene, periprostatic abscess, osteomyelitis, and meningitis have been also reported in the literature.^[16,17] Therefore, previously debatable prophylactic antibiotherapy can be accepted as a standard practice.^[18] However, a consensus has not been reached about the selection of the antibiotic, its dose, and duration of antibiotherapy, usage of mono-, or combination therapy.

When post-biopsy antibiotherapy is not applied, bacteremia (16-78%), urinary infection (32%), and febrile episodes (33%) have been reported in indicated incidence rates.^[6,19] In an investigation, antibiotic prophylaxis was prescribed for 614 out of 1018 biopsized cases, while the remaining 404 patients were biopsized without antibiotic prophylaxis. In a group of patients who received antibiotic prophylaxis median complication rate was 3.7%, while in patients without antibiotic prophylaxis it was detected as 10.3 percent. In this study, serious infectious complications were reported to be 24.4% in the group of patients who received prophylaxis, and in 75.6% of the patients who were not under prophylactic antibiotherapy.^[20]

It has been demonstrated that single-dose ciprofloxacin prophylaxis obviated the need for hospitalization with the indication of febrile urinary infection, and decreases in infective complications, and hence treatment costs after prostate biopsy have been reported with ciprofloxacin prophylaxis.^[21] In a prospective study, Aron et al.^[22] indicated lack of any significant difference between a single dose, and 3 daily oral doses of ciprofloxacin therapy.^[22] In a study where infective complications were evaluated, the authors had achieved comparable outcomes with single dose 500 mg ciprofloxacin prophylaxis, twice daily doses of 500 mg ciprofloxacin, and a single dose parenteral ceftriaxone prophylaxis.^[23]

Presence of urinary infection before biopsy carries a risk for infective complications. Therefore, prebiopsy urinalysis can reveal risk of infection.^[24] In our study, in the presence of abnor-

Table 1. Demographic data, and clinical findings

	Group 1	Group 2	p
Patients (n)	174	217	>0.05
Age	64.53±7.47	64.69±7.79	>0.05
Prostate-specific antigen (PSA) ng/mL	15.93±3.83	13.24±1.27	>0.05
Prostate volume (cm ³)	57.1±4.7	50.54±14.2	>0.05

Table 2. Comparison of complication rates

	Group 1	Group 2	p
All-cause complications	37 (21.3%)	56 (25.8%)	>0.05
High fever	11 (6.3%)	11 (5.1%)	>0.05
Urine culture (+)	7 (4%)	6 (2.8%)	>0.05
Severe dysuria	9 (5.2%)	16 (7.4%)	>0.05
Urethrorrhagia	21 (12.1%)	40 (18.4%)	>0.05
Rectal bleeding	1 (0.5%)	0	>0.05

mal complete routine urinalysis findings, and leukocyturia before biopsy, urine cultures were obtained to rule out bacteriuria. If bacterial growth was detected in prebiopsy urine cultures of the patients, then appropriate antibiotherapy was applied, and biopsy was postponed.

Aus et al.^[25] compared the results of a single dose, and one-week norfloxacin prophylaxis in patients carrying risks for infectious complications including cases with diabetes, indwelling urethral catheters, and urinary infection, and detected significantly lower complication rates in the long-term prophylaxis group. However in the group without any risk factor, a statistically significant difference was not detected between these two protocols. Starting from this point, especially in cases with risk factors longer prophylactic antibiotherapy had been recommended.^[25]

E. coli is the most frequently isolated bacteria from positive urine cultures.^[21,23] In our study, in all cases with urine culture positivity *E. coli* was isolated. Though fluoroquinolones were effective in the prophylaxis of prostate biopsy, increased resistance to fluoroquinolone therapy has been also detected. In our study, in all patients with urine culture positivity, we identified resistant strains to quinolones. In these patients initiation of empirical treatment with cephtriaxone, ceftazidime or amikacin have been recommended till antibiotherapy based on antibiotic susceptibility test results can be started.^[26]

Cormio et al.^[27] compared ciprofloxacin, and piperacillin/tazobactam, and despite its parenteral administration, and higher cost, piperacillin/tazobactam was found to have higher prophylactic efficacy when compared with ciprofloxacin.^[27]

Hodge et al.^[28] reported complication rate of 2.4% in their 251 patients, while they had to hospitalize their 2 patients because of high fever. Also they indicated that they had encountered rectal bleeding requiring intervention in 3 patients.^[28] Besides, in many studies less than 1% major complication rates were reported.^[2]

In our study, we detected febrile episodes in 6.3% of the patients in the ciprofloxacin, and 5.1% of the cases in the TMP-SMX group. Severe dysuria was observed in 5.2% of ciprofloxacin treated patients, while it was seen in 7.4% of the patients in the TMP-SMX group. Similarly, a statistically significant difference was not detected between both groups as for other infective complications.

Lack of a control group who didn't receive antibiotic prophylaxis was a limitation of our study. However, when previous studies were evaluated, a consensus has been reached which asserts that refraining from prescribing prophylactic antibiotic therapy leads to a marked increase in complication rates, and thus necessity for prophylaxis arises. If we consider that most of the post-biopsy infections become manifest within the first 3 days, and urine culture results are available on postprocedural 10. days, conceivably some of the probable infections may be overlooked. Since long-term antibiotherapy is still frequently prescribed before the biopsy with the intention to reduce PSA values, inability to inquire use of recent long-term antibiotherapy in patients who developed resistant *E. coli* strains can be evaluated as one of the limitations of our study.

In conclusion, despite the developments in preprocedural patient preparation, biopsy technique, ease of application, and better tolerability still simple complications occur. In recent years increased antibiotic resistance has manifested itself especially with development of resistance against ciprofloxacin, and TMP-SMX used in the treatment of urinary tract infections. However, 3-day-treatment with ciprofloxacin, and TMP-SMX regimens are effective as a prophylactic modality in transrectal prostate biopsy procedures. As a prophylactic therapy against development of urinary system infections, and other complications after transrectal prostate biopsy ciprofloxacin was not superior to TMP-SMX and vice versa.

Ethics Committee Approval: This study was conducted retrospectively therefore Ethical committee approval was not received.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - D.A.; Design - D.A., Y.G.; Supervision - D.A., B.S.P.; Funding - D.A., Y.G., E.K., Ş.K.; Materials - D.A.; Data

Collection and/or Processing - D.A., Y.G., E.K., Ş.K.; Analysis and/or Interpretation - D.A., N.U., F.E.; Literature Review - D.A., Y.G., Ş.K.; Writer - D.A., Y.G.; Critical Review - D.A., B.S.P., F.E., N.U.

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

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

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