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Comparing the Effect of Pre-Biopsy Rectal Cleaning Together with Biopsy Needle Disinfection to Each Technique Alone on Hospitalization Rates because of Post-Biopsy Infections

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Keywords
Prostate biopsy · Formalin disinfection · Infectious complications · Povidone-iodine

Abstract

Introduction: To compare the effects of three techniques: biopsy needle disinfection with 10% formalin solution, povidone-iodine rectal cleaning, and the use of both methods to decrease hospitalization due to infectious complications after transrectal prostate biopsy. ***Methods:*** A total of 827 patients were divided into 3 groups. Group 1 patient data were analyzed retrospectively, while patients of groups 2 and 3 were followed up prospectively. Group 1 included 361 patients who underwent biopsy needle disinfection with a 10% formalin solution. Group 2 included 235 patients who underwent biopsy needle disinfection and povidone-iodine rectal cleaning. Group 3 included 231 patients who underwent povidone-iodine rectal cleaning only. The outcome scale was the number of patients hospitalized for biopsy-related infection 30 days after the date of transrectal prostate biopsy. ***Results:*** The hospitalization rates due to biopsy-related infectious complications were 3.0%, 0%, and 1.7% in groups 1, 2, and 3, respectively. The only statistically significant difference was found between groups 1 and 2. ***Conclusion:*** Biopsy needle disinfection and rectal cleaning with povidone-iodine seem to have greater potential to reduce infectious complications when applied together. Further prospective studies are required to confirm these findings.

Introduction

Prostate cancer (PCa) is the second most common malignancy in the male population, and transrectal ultrasound-guided prostate biopsy (TRUS-PB) is the standard for the diagnosis and treatment planning of PCa [1, 2]. Although targeted biopsy with the guidance of multiparametric prostate magnetic resonance imaging (mpMRI) is supposed to reduce the number of biopsy cores and unnecessary biopsies, the European Association of Urology (EAU) guidelines recommend both targeted and systematic biopsies in cases of suspicious lesions on mpMRI [3].

Despite antibiotic prophylaxis (AP), which is accepted as the gold standard to prevent infectious complications (ICs), TRUS-PB may still cause severe ICs, such as sepsis. These ICs and sepsis rates range from 0.1 to 7% and 0.3–3%, respectively [4]. Moreover, these ICs increased in

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recent years to the overuse of fluoroquinolones (FQs). It is associated with increased colonization of fluoroquinolone-resistant (FQR) microorganisms in the rectal flora, resulting in an increased rate of ICs [5, 6].

Rectal culture-based AP [7] or transperineal prostate biopsy (TP-PB) [8], which does not use the rectal route, are strategies to inhibit ICs. A different method involves rectal cleaning with povidone-iodine (PI) before the biopsy procedure to decrease the bacterial content of the rectal mucosa [9]. Antiseptic solutions for biopsy needle disinfection (BND) are also employed for this purpose [10]. The EAU guidelines recommend rectal cleaning with PI [3]; however, there are limited studies on BND with antiseptic solutions in the literature.

The main aim of this study was to compare the effects of three different techniques: BND with 10% formalin solution, PI rectal cleaning, and the use of both methods together to prevent ICs due to TRUS-PB. The secondary aim was to estimate the risk factors of hospitalization due to ICs.

Materials and Methods

Although this was a retrospective study, only group 1 patients' data were collected retrospectively, whereas group 2 and group 3 patients were followed prospectively. Data from 1,009 patients were analyzed between January 2014 and March 2023. The biopsy criteria were prostate-specific antigen >4.0 ng/mL, suspicious digital rectal examination, suspicious lesions on mpMRI, and a high risk of PCa with previous negative biopsies. The study inclusion criteria included patients who used a pre-biopsy enema and the same augmented AP with a negative pre-biopsy urine culture. The study eliminated patients with urethral catheters and those receiving empiric antibiotics for any purpose. The augmented prophylactic antibiotics ciprofloxacin (500 mg) and ornidazole (500 mg) were administered orally for 5 days, beginning the day before the procedure. A 135-mL sodium phosphate-containing enema was applied 2–3 h before the biopsy procedure.

The groups were built in accordance with our different biopsy strategies. Group 1 consisted of 361 patients who underwent BND with a 10% formalin solution between January 2014 and October 2020. After that date, due to high post-biopsy ICs and according to EUA guidelines, we changed our biopsy protocol and added rectal cleaning with PI. In group 2, from November 2020 to March 2022, 235 patients underwent both BND with formalin solution and rectal cleaning with PI. Since no patients were hospitalized because of ICs in group 2, we thought that PI rectal cleaning was adequate to decrease ICs, and in April 2022, we stopped applying BND. Therefore, group 3, which included 231 patients treated from April 2022 to March 2023, used only PI rectal cleaning.

The parameters analyzed were age, prostate-specific antigen level, prostate volume, number of biopsy cores, previous biopsies performed within 12 months after the first biopsy date, pathology results, previous last 6 months' antibiotic history, and diabetes mellitus. In addition, urinary retention, fever, macroscopic hematuria, hematospermia, rectal bleeding, dysuria, microscopic hematuria, leukocyturia, and urine culture results 1 week after the biopsy procedure were also analyzed in group 2 and group 3 patients. All transrectal 10–12 core biopsy procedures, including PI rectal cleaning and BND, were performed by the same urology doctor (C.B.) with the same ultrasonography equipment and an 18-gauge single-use disposable automatic biopsy gun using 2% lidocaine gel as a local anesthetic in the left decubital position in the same outpatient room.

In groups 2 and 3, rectal cleaning was performed as described by Bostancı et al. [9]. In groups 1 and 2, BND was applied, as described by Issa et al. [10]. In addition, we cleaned the formalin-disinfected biopsy needle after each core by whistling it in a sterile saline solution. In group 3, the biopsy core was placed on sterile gauze and placed in a pathology cup with the help of another needle.

On the third day of the biopsy, all patients in groups 2 and 3 were phoned and asked about complaints. Additionally, patients were requested to return to the hospital 1 week after the biopsy date for urine analysis and culture, regardless of their symptoms.

The endpoint of this study was the number of patients hospitalized because of ICs 30 days after the biopsy date. ICs were defined as acute prostatitis, epididymo-orchitis, urinary tract infection (UTI) with fever (>38°C), and sepsis. UTI was defined as urinary frequency, urgency, suprapubic discomfort, and dysuria.

Statistical analysis was conducted using version 22.0 of the Statistical Package for Social Sciences (SPSS). The Mann-Whitney U test was employed to compare non-normally distributed variables between the two groups, while Kruskal-Wallis and Dunn tests were used to compare the three groups. The Shapiro-Wilk test confirmed that the numerical variables were normally distributed. Categorical variables were compared using the χ^2 test, and multiple comparisons were performed using the Bonferroni test. Binary logistic regression analysis was used to determine hospitalization risk factors for post-biopsy IC. Statistical analysis yielded a confidence interval (CI) of 95%, with a significance threshold set at $p < 0.05$.

Results

The main patient characteristics are summarized in Table 1. Fifteen of the 827 patients (1.8%) required hospitalization due to ICs. Fourteen patients (1.7%) were diagnosed with UTI accompanied by fever, and only 1 patient (0.12%) in group 1 had epididymo-orchitis. Eleven patients in group 1, four in group 3, and none in group 2 were hospitalized. The hospitalization rates were 3%, 0%, and 1.7% in groups 1, 2, and 3, respectively. The only statistically significant difference was observed between groups 2 and 1 ($p = 0.004$).

Our secondary aim was to establish which parameters were predictors of hospitalization, and multivariate analyses showed that only the last 6 months of FQ use (OR: 3,126 [1,037–9,424] 95% CI) was the only predictor for hospitalization due to post-biopsy ICs (online suppl.

Table 1. Main characteristics of the groups

Parameters	Total	Group 1	Group 2	Group 3	*p* value
Patients, *N*	827	361	235	231	
Age (mean, SD), years	66.8±6.93	66.12±6.83	67.59±7.09	67.05±6.82	**0.017***
PSA (mean, SD), ng/mL	16.67±41.23	16.15±31.4	15.91±39.58	18.25±54.44	0.101*
PV (mean, SD), cc	64.62±35.1	63.34±36.72	63.82±29.77	67.45±37.44	0.151*
PCa, *n* (%)	349 (42.2)	147 (40.7)	103 (43.8)	99(42.9)	0.733**
PB, *n* (%)	93 (11.2)	29 (8)	41 (17.4)	23 (10)	**0.001****
No. of cores (mean, SD)	11.51±1.65	11.7±1.38	11.41±1.75	11.31±1.89	**0.007***
DM, *n* (%)	255 (30.8)	99 (27.4)	76 (32.3)	80 (34.6)	0.151**
Last 6 m FQ use, *n* (%)	301 (36.4)	148 (41)	73 (31.1)	80 (34.6)	**0.039****
Hospitalization, *n* (%)	15 (1.8)	11 (3.0)	0 (0)	4 (1.7)	**0.004****

Group 1, January 2014–October 2020, only BND with 10% formalin solution was applied. Group 2, November 2020–March 2022, pre-biopsy PI rectal cleaning used together with BND by 10% formalin solution. Group 3, April 2022–March 2023, applied only pre-biopsy PI rectal cleaning. PSA, prostate-specific antigen; PV, prostate volume; FQ, fluoroquinolone; PB, previous biopsy; DM, diabetes mellitus; PCa, prostate carcinoma; m, month. *Kruskal-Wallis and Dunn tests. **χ^2 and Bonferroni analysis ($p < 0.05$).

Table 1; for all online suppl. material, see https://doi.org/10.1159/000535033). *Escherichia coli* (*E. coli*) was the only microorganism grown in the urine culture of 11 of 15 hospitalized patients (73.3%). In group 1, 7 of the 11 patients (63.6%) showed bacterial growth in urine cultures. Two patients were found to have FQR *E. coli* producing extended-spectrum beta-lactamase in the urine culture. Although no bacterial growth was sustained in the urine cultures of 4 patients in group 1, the patients were hospitalized for UTI with fever. In group 3, all 4 hospitalized patients (100%) had bacterial growth in their urine cultures and three had extended-spectrum beta-lactamase-producing FQR *E. coli*.

The mean hospital administration time was 1.9 days, the mean hospital stay was 6.9 days, and all patients were treated appropriately. Carbapenem group antibiotics were given to 8 patients (53.3%), while piperacillin-tazobactam group antibiotics were given to three (20%). The remaining 4 patients (26.6%) were administered different parenteral antibiotics.

In groups 2 and 3, all patients completed phone interviews, while 6 patients in group 2 and seven in group 3 did not return for urine analysis 1 week after the biopsy date. None of the patients required hospitalization due to non-ICs, such as gross hematuria or rectal bleeding. Macroscopic hematuria was the most common complaint (44.1%) followed by hematospermia (21.6%). Three patients in group 2 and two in group 3 had asymptomatic bacteriuria. They were treated with oral antibiotics, despite being asymptomatic. The only statistically significant difference between group 2 and group 3 was observed in leukocyturia (>5 white blood cells per high-power field), which was higher in group 3. Detailed information on the complaints of the patients in groups 2 and 3 is summarized in online supplementary Table 2.

Discussion

The overall hospitalization rate due to ICs was 1.8%, the highest in group 1 (3%) and lowest in group 2, with no hospitalization. The ICs due to TRUS-PB are thought to be caused by direct inoculation of rectal mucosa bacteria into the prostatic tissue by the contaminated biopsy needle [11]. PI rectal cleaning, which has been demonstrated in numerous studies [12, 13], is intended to reduce the bacterial load on the rectal mucosa. In group 3, where only PI rectal cleaning was performed, the hospitalization rate was 43% less than that in group 1, where only BND was performed (1.7% vs. 3%).

However, our best results were observed in group 2 where BND and PI rectal cleaning applied together. Our hypothesis for the best results in group 2 is that PI rectal cleaning might not decrease the bacterial load by 100% because the PI must dry to show total efficiency, and the rectal vault never dries because of mucosal secretions [14, 15]. In addition, since it is a closed area, PI may not reach every part of the prostate tissue, and BND may be critical in inhibiting bacterial transfer into the prostate tissue in patients with inappropriate rectal cleaning.

In our study, only the last 6 months of FQ use was associated with hospitalization. Similarly, a study by Roberts et al. identified prior FQ use (OR = 4.12; 95% CI, 2.3–7.37) and recent UTI (OR = 2.56; 95% CI, 1.13–5.79)

as significant risk factors for the development of FQR rectal flora [15], which significantly predicted ICs. Another study demonstrated that patients who received antibiotics within 3 months and prophylaxis before the procedure had a significantly higher level of antibiotic resistance in their fecal flora [16]. Therefore, selecting prophylactic antibiotics based on the local antimicrobial resistance pattern is recommended and switching to other antibiotics if FQR strains locally exceed 20% of uropathogens [17, 18]. Moreover, the meta-analysis pointed out that targeted AP based on rectal swab culture, which was also recommended by the EUA guidelines [3], resulted in an 84% lower infection rate than augmented AP [19].

Because of the contamination risks of FQR strains in the transrectal way, there is a tendency toward TP-PB in which there is no contact with the rectal mucosa. Although cancer detection rates are similar, TP-PB has been shown to be superior in detecting anteriorly localized cancers [20]. However, its most important advantage is that it has lower post-biopsy ICs compared to TRUS-PB. A recent meta-analysis found that TP-PB had a lower risk of sepsis (0–1%) than TRUS-PB (0.4–9.8%) [21]. Another meta-analysis demonstrated a similar result that TP-PB was associated with significantly reduced ICs, 3.2% versus 5.6% (OR = 0.55; 95% CI, 0.33–0.92) compared to TRUS-PB [22]. In recent years, studies have shown that TP-PB can be done without AP. A study comparing the TP-PB group without AP to the TRUS-PB group with AP demonstrated that UTIs with fever rate were 1.1% and 5.1%, respectively (RD 4.0, 95% CI, 1.0–7.9, $p = 0.010$) [23]. Kohl et al. [24] demonstrated no sepsis in 550 patients who underwent TP-PB without AP. In a meta-analysis, Castellani found that no significant difference in infection rate, fever, sepsis, or readmission rate after TP-PB between patients with AP and patients without AP [25]. However, due to the lengthy learning curve, further equipment requirements, and lack of tolerating with local anesthetic, TP-PB is still not as common as TRUS-PB. The major limitation of the present study was that it was a single-center retrospective study, and although all patients of groups 2 and 3 followed prospectively, data of group 1 patients were collected retrospectively.

Conclusion

In patients for whom TRUS-PB is planned, applying BND and PI rectal cleaning together seems more effective than using each method individually to decrease ICs. In patients with a history of 6 months of FQ use, prophylactic antibiotics should be chosen according to local antimicrobial resistance patterns or after rectal swab culture results. However, further prospective studies are warranted.

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Statement of Ethics

All procedures performed in studies involving human participants were under the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Written informed consent was obtained from all patients in this study. This study protocol was reviewed and approved by the Ethics Committee of the Karabük University with the approval number of 2023/1205.

The authors declare that the consent to participate form was obtained from all patients and kept in patient files. The authors also confirm that the participation form was obtained from all subjects and/or their legal guardian(s). Ethical Review Board: 2023/1205 Ethics Committee of the University Karabuk, 2023/1205 on January 13, 2023; all the procedures being performed were part of the routine care. Informed consent: https://www.uroturk.org.tr/urolojiData/Document/155201415214-trans_ultr.pdf.

Conflict of Interest Statement

The authors declare that there is no conflict of interest.

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Author Contributions

Coşkun Bostanci: conceptualization (lead), data curation (lead), formal analysis (equal), investigations (lead), methodology (equal), project administration (lead), and writing – original draft preparation (lead). Salih Bürlukkara: conceptualization (supporting), formal analysis (equal), methodology (equal), and writing – review and editing (supporting).

Data Availability Statement

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

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