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The effect of povidone-iodine rectal cleansing on post-biopsy infectious complications

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ABSTRACT

Objective: To evaluate the effect of pre-biopsy povidone-iodine rectal cleansing on post-biopsy hospitalization rates due to prostate biopsy-related infectious complications.

Material and methods: In this retrospective study, we reviewed 552 patients who underwent ultrasonography-guided transrectal prostate biopsy between 2014 and 2022. Group 1, 361 patients (January 2014–October 2020) were not applied povidone-iodine rectal cleansing, and group 2, 191 patients (November 2020–January 2022) were applied povidone-iodine rectal cleansing since we changed our biopsy protocol. All patients were given the same antibiotic prophylaxis, ciprofloxacin 500 mg, and ornidazole 500 mg twice daily starting 24 h before the biopsy and lasting a total of 5 days. Sodium phosphate enema was applied to all patients in the biopsy morning. The outcome was the hospitalization rates of patients because of infectious complications a month after the biopsy.

Results: No patients were hospitalized in the povidone-iodine rectal cleansing group because of biopsy related complications. The hospitalization rate of group 1 was 3% and there was a statistical difference between groups.

Conclusion: The povidone-iodine solution is cheap, safe and easy to apply. The povidone-iodine rectal cleansing method seems to decrease infectious complications related to prostate biopsy procedure, but we need a randomized controlled trial to confirm our study.

Trial registration: We got permission for this retrospective study from the Karabuk university ethics council with the number 2021/649 on 1 October 2021.

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Introduction

Although the increased use of new methods such as magnetic resonance imaging (MR) fusion prostate biopsy and transperineal biopsy, ultrasonography-guided transrectal prostate biopsy (TRUS-P) is still the most widely used diagnostic tool to diagnose prostate carcinoma. While it is a diagnostic tool, it is invasive. It may result in several infectious complications ranging from asymptomatic bacteriuria, febrile urinary tract infection, acute prostatitis, cystitis, and epididymo-orchitis to sepsis at a rate of 0.1–7% [1]. Prophylactic antibiotic use still is the most effective method to prevent these biopsy-related infectious complications [2]. However, there is no consensus on the type, starting time, and duration of prophylactic antibiotics. The two other attempts related to antibiotic prophylaxis are augmented [3] and targeted antibiotic prophylaxis with rectal swab culture [4]. The non-antibiotic strategies were also developed to decrease these complications. In recent years, the use of multiparametric prostate magnetic resonance imaging (mpMRI) before the prostate biopsy is strongly recommended since this screening method may decrease unnecessary biopsies by up to 25% [5]. Another way is a transperineal prostate biopsy in which infectious complications are very low compared to

TRUS-P since there is no contact with rectal flora during the biopsy [6]. The other non-antibiotic strategies are pre-biopsy sodium phosphate enema (SPE) [7], prostate biopsy needle disinfection using 10% formalin solution (FD) [8], and pre-biopsy povidone-iodine rectal cleansing (PIRC) [9].

Here in this study, we want to evaluate the effect of PIRC on hospitalization rates due to biopsy-related infectious complications.

Materials and methods

In this retrospective study on our hospital's electronic media, we reviewed 552 patients who underwent TRUS-P from 2014 to 2022. Age, prostate-specific antigen (PSA) level, prostate volume, repeat biopsies, pathology results, the existence of diabetes mellitus (DM), use of SPE, pre-biopsy urine culture, type of prophylactic antibiotics, last six months of FQ usage, number of biopsy cores and presence of urethral catheter were studied. We reviewed DM, the number of biopsy cores, and the last six months of FQ usage history since these parameters may increase the risk of post-biopsy infectious complications. After November 2020, as a new strategy, we started applying PIRC to our prostate biopsy patients in our hospital. We started to recall the patients on routine control

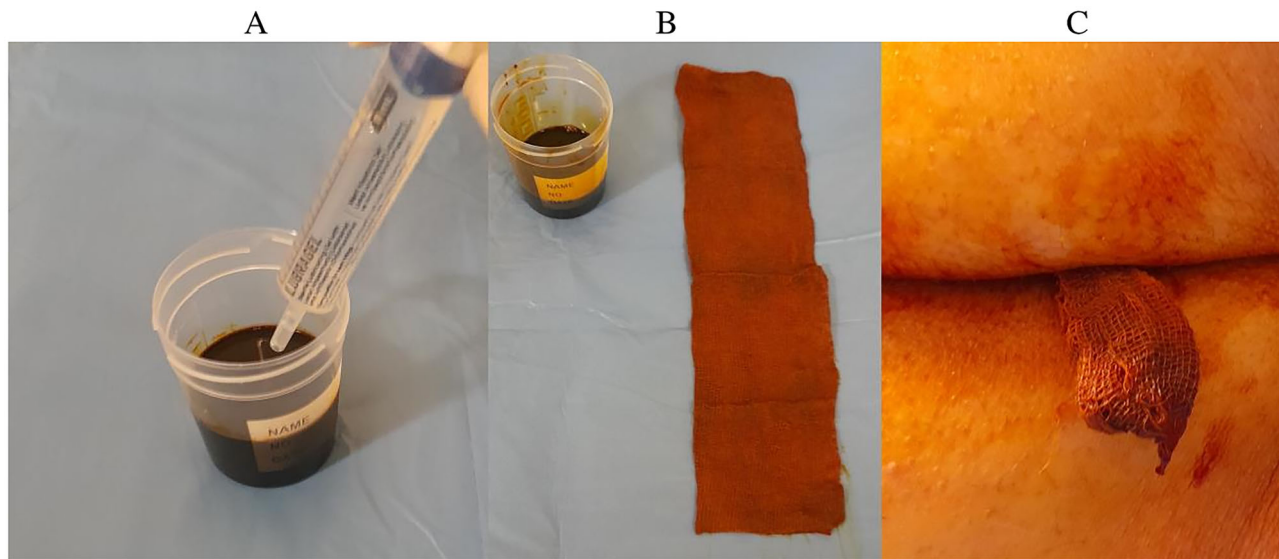


Figure 1. Application of sterile gauze soaked with povidone-iodine and lidocaine gel. (A) 11 ml lidocaine gel 2% added into 40 ml povidone-iodine solution. (B) Sterile gauze soaked with that mixture. (C) Manual insertion of that gauze into the rectum, only 2 or 3 cm left outside and waited 2 min.

7–10 days after the biopsy to see their urine analysis and urine culture.

Our biopsy indications were a PSA level higher than 4.0 ng/ml, abnormality on the digital rectal examination, positive mp-MRI results, and suspicious biopsy results of previous biopsies. The inclusion criteria were ciprofloxacin + ornidazole (CIP + ORN) augmented antibiotic as prophylaxis and negative urine culture before the biopsy. CIP + ORN antibiotic prophylaxis (500 mg ciprofloxacin twice daily and 500 mg ornidazole twice daily) started 24 h before the biopsy procedure and lasted five days. All patients were given SPE in the biopsy morning. This study did not include patients with positive pre-biopsy urine cultures, patients who had undergone biopsy procedures under antibiotic suppression, and patients with urethral catheters. Anticoagulation drugs were stopped seven days before the procedure, and low molecular weight heparin started subcutaneously in patients using that kind of drug.

All biopsy procedures were performed in the same outpatients' room using the same ultrasonography device (Aloka ProSound 5500SV) and probe with the same 18-gauge single-use spring-loaded biopsy needle gun (Geotek Medical, Turkey). The biopsy procedure was performed in a left decubital position, and routinely 12 core biopsy was performed on each patient. As local anesthesia, 2% lidocaine gel (11 ml) was applied to all patients ten minutes before the biopsy.

We made two groups according to our changed prostate biopsy protocol. Group 1, including 361 patients (January 2014–October 2020), was given CIP + ORN prophylaxis 24 h before the biopsy, lasting five days; SPE was applied on the biopsy morning. Group 2, 191 patients (November 2020–January 2022), was the same as group 1; additionally, PIRC was applied just before the biopsy procedure as a new strategy.

In group 1 and group 2, after each core was taken, the outer sheath of the biopsy needle withdrew, and the biopsy needle was swished into the cup containing 10% formalin solution to remove the biopsy core. The biopsy needle was

swished into the sterile saline cup after each core biopsy to prevent the harmful effects of the formalin solution. In group 2, before the biopsy, the perianal region was cleaned with povidone-iodine (PI) soaked sterile gauze first. After that, new sterile gauze (4 × 16 cm), soaked with the mixture of 40 ml PI solution and 11 ml sterile 2% lidocaine gel, was located in the anterior rectum wall, covering the prostate tissue manually, only letting 2 or 3 cm outside the rectum (Figure 1). After two minutes, we dislocated this gauze, waited 5 min to dry the biopsy area, and then started the biopsy procedure.

All patients were alerted to readmit to the hospital if they had severe hematuria, hematochezia, dysuria, fever, or chill. They were also given a phone number to call if these symptoms happened. Additionally, all group 2 patients were phoned on the third day and recalled to the hospital 7–10 days after the biopsy procedure to ask for complications and obtain urine analysis and urine culture, although they had no symptoms.

Our only outcome was the hospitalization rate of the patients due to biopsy-related infectious complications a month after the biopsy procedure.

The statistical package for social sciences (SPSS) 25.0 was used for statistical analysis. Mann Whitney u test was used to compare PV, number of biopsy cores, and PSA values. Independent samples t-test was used to age. Chi-square analysis was performed to compare the groups and ratio of DM, previous biopsy, last six months' FQ usage, and pathology outcomes. Fisher exact test was used to compare the results of hospitalization rate due to biopsy-related infectious complications between groups. Logistic regression test Forward LR method was used as multivariate analysis. The confidence interval was determined as 95%, and $p < 0.05$ values were considered significant.

We get permission for this retrospective study from our university ethics council with the number 2021/649 on 01 October 2021.

Table 1. Demographic data of groups.

Parameters	Group 1	Group 2	p-Value
Number of patients	361	191	
Age (years, mean \pm SD)	66.1 \pm 6.9	67.4 \pm 7.1	0.035*
PSA (ng/ml, median, range)	7.3 (1.2–323)	6.6 (0.9–456)	0.036**
PV (cc, median, range)	55 (20–300)	55 (10–192)	0.964**
DM (n, %)	99 (27.4%)	67 (35.1%)	0.062***
Last six months FQ use (n, %)	148 (40.9%)	70 (36.6%)	0.320***
Biopsy cores were taken (median, range)	12 (8–14)	12 (4–12)	0.197**
Previous biopsy (n, %)	61 (16.9%)	48 (25.1%)	0.021***
Pathology of prostate cancer (n, %)	147 (40.7%)	83 (43.5%)	0.535***

Group 1, January 2014–October 2020, no povidone-iodine was used for perineal and rectal cleansing. Group 2, November 2020–January 2022, povidone-iodine used before prostate biopsy for perineal and rectal cleansing. *Independent samples t-test; **Mann–Whitney U test; ***Chi-square analysis. PSA: prostate-specific antigen; PV: prostate volume; DM: diabetes mellitus; FQ: fluoroquinolones.

Results

The demographic data of the groups are shown in Table 1. There is no difference between groups according to prostate volume, diabetes, last six months of FQ use, number of biopsy cores, and carcinoma detection rates. The age and previous biopsy rates were higher in group 2. Nevertheless, the PSA value was higher in group 1. We could not explain why the age of group 2 was higher and the PSA value was lower than group 1. The mean age was 66.1 in group 1 and 67.4 in group 2; the mean PSA values were 16.15 and 16.20, respectively. A previous biopsy rate is also higher in group 2, which includes patients from November 2020 to January 2022. We thought that since our hospital is the biggest in our region, all patients who had previously suspicious biopsy results were referred to us again, and that increased repeat biopsies.

In group 1, eleven out of 361 patients (3.0%) were hospitalized because of biopsy-related infectious complications. In group 2, no patient was hospitalized because of infectious complications. The difference was statistically significant ($p = 0.015$) (95% CI).

In group 1, one patient (0.2%) was hospitalized with the diagnosis of acute orchitis, and the remaining ten patients (2.7%) were hospitalized with febrile urinary tract infection diagnoses. Seven out of 11 (63%) patients had positive urine cultures; all were *Escherichia coli* 100,000 colony forming units/ml (CFU/ml). Only two patients had *E. coli* that produces extended-spectrum beta-lactamase [ESBL (+)], resistant to FQ in their urine culture.

All patients in group 1 recovered with appropriate antibiotic treatment [seven patients (63%) were given carbapenem group of antibiotics] without any sequel. The mean hospital stay was six days.

In group 1, ten patients had the story of FQ antibiotic use in the last six months, and 3 of them had DM, meaning that 90% of hospitalized patients were in a group called potentially risk group (DM, FQ use in last six months).

In group 2, no patient was hospitalized for infectious complications. All patients were phoned and asked for complications, but three patients (1.5%) did not readmit to the hospital for routine control 7–10 days after the biopsy since they declared that they had no complaints on a phone call. The remaining 188 patients were closely followed up, and no other doctor gave them any medication. Hematuria lasting

1–2 days was the most common complaint of group 2 patients. Nearly half of the patients, 89 patients (46.5%), answered that they had hematuria, 38 patients (19.8%) complained of hematospermia, 34 patients (17.8%) complained of dysuria. Only five out of 34 patients who complained about dysuria had leucocyturia on urine analysis. There was no bacterial growth on the urine cultures of these 34 patients. Thirty patients complained of rectal bleeding (15.7%). No patient complained of fever. Three patients (1.5%) were readmitted to the hospital for acute urinary retention the next day after the biopsy. On urine analysis, 62 patients (32.9%) had only microscopic hematuria (5 or more red blood cells per high-power field), and 21 patients (11.1%) had both microscopic hematuria and leucocyturia (5 or more white blood cells per high-power field).

Three patients (1.5%) have positive urine cultures. ESBL (+) *E. coli* resistant to FQ was the only microorganism grown on the urine cultures of these three patients (two patients had 50,000 CFU/ml, and one patient had 100,000 CFU/ml *E. coli*). When we reanalyzed these three patients with positive urine cultures, we saw that one had a positive urine culture two months ago and was treated with FQ (although no bacterial growth was obtained three days before the biopsy date). The other two patients also had a story of FQ use during the last six months. One patient also had DM. They were all asymptomatic and were treated with appropriate antibiotics without any sequelae.

Although it was not the primary goal of this study, with the use of univariate and multivariate studies, we want to see which parameters have potential risk for hospitalization because of infectious complications. The multivariate analysis showed that only the use of FQ in the last six months affected hospitalization because of infectious complications. The other parameters have no effect. The explanatory power of the model was found to be 19.5% (Table 2).

Discussion

In our retrospective study, we found that no patient was hospitalized because of infectious complications. Although 3 patients had positive urine cultures, they were all asymptomatic and recovered without hospitalization. The main reason for infectious complications of TRUS-P is probably due to the translocation of rectal flora microorganisms into the highly vascular prostate tissue, directly into the urinary system or

Table 2. Results of multivariate logistic regression analysis of parameters.

Variables	OR (95% CI)	p-Value
Age	0.983 (0.887–1.089)	0.983
Prostate-specific antigen	0.998 (0.940–1.060)	0.998
Prostate volume	1.004 (0.987–1.021)	0.659
Diabetes mellitus	1.014 (0.244–4.219)	0.985
Last six months FQ use	6.804 (1.431–32.337)	0.013
Previous biopsy	0.0 (0.0)	0.996
Biopsy core number	1.472 (0.637–3.402)	0.365
Pathology of prostate cancer	0.325 (0.059–1.791)	0.325

CI: confidence interval OR: odds ratio.

bloodstream by the biopsy needle during the TRUS-P procedure [10]. According to the EUA guidelines [11], which strongly recommend PIRC, we started to apply this method to our patients in our hospital in November 2020. Because after PIRC, it is shown that bacterial density was very low in rectal mucosa covering prostate tissue [12,13], and this low bacterial density may not cause systemic infection, instead only local infection. However, there is no standard PIRC application method; in the literature, we see different forms of PI (solution, suppository, gel) usage and different ways of application.

These studies are summarized in Table 3 [12–19]. In all these studies, PIRC was shown to be superior to control groups and highly effective in preventing these infectious complications. Our study also showed that no patient was hospitalized because of infectious complications.

Although TRUS-P is supposed to be a safe procedure as a diagnostic tool, it may lead to many infectious complications. *Escherichia coli* is the most common microorganism causing it. In recent years FQ-resistant *E. coli* has been increasing [20,21], which leads to increased rates of infectious complications [22].

Unfortunately, no data shows the rate of FQ-resistant *E. coli* in our region and hospital, and we do still use CIP + ORN as a prophylactic antibiotic before the biopsy. Because FQs are easy to use and ideally penetrate blood, urine, and prostate tissue. They are very effective against *E. coli* and anaerobes that cover the colon flora. As an augmented antibiotic prophylaxis strategy, ornidazole was added, which is effective against *Klebsiella*, *Clostridium*, and *Bacteroides fragilis* strains. They were commonly seen in patient's blood and urine cultures after TRUS-P [23]. Other than augmented antibiotic prophylaxis, targeted antibiotic prophylaxis with rectal swab culture is another method to decrease biopsy-related infectious complications. In some studies [24,25], it has been shown that targeted antibiotic prophylaxis significantly reduces sepsis and infectious complication rates. On the other hand, some publications [26,27] reported that, although appropriate antibiotics were given to patients before the biopsy procedure, it was not superior to augmented antibiotic prophylaxis. Both authors of these studies [26,27] recommended a transperineal prostate biopsy.

Since there is no contact with rectal flora at transperineal prostate biopsy, in studies performed in recent years, sepsis and infectious complications were found to be very low compared to transrectal prostate biopsy [6], and transperineal prostate biopsy was updated as a strong recommendation in the EUA guidelines and preferred over transrectal biopsies. One of the latest studies showed that transperineal prostate biopsy could be done even without antibiotic prophylaxis [28]. In this prospective study, including 553

patients, in both groups, no patient required hospitalization because of urinary tract infection or sepsis. In the antibiotic prophylaxis group, only one patient out of 277 developed a urinary tract infection not requiring hospitalization, and three out of 276 were in the non-antibiotics prophylaxis group. Its cancer detection rate is similar to TRUS-P and superior to detecting anteriorly located prostate cancers [29]. However, it has not yet become widespread among urologists since it needs additional instruments. Nevertheless, it should be kept in mind because of lower post-biopsy infection rates and superiority to detecting anteriorly located prostate cancers.

The main goal of prostate biopsy should be to detect clinically significant prostate cancers with a high accuracy rate and minimal complications. However, our cancer detection rate is under 50%. Our low cancer detection rate is probably due to it being small-sized and a single-center study. Also, anteriorly located prostate cancers are probably missed by TRUS-P. Another possible reason is that we have lately started to use mp-MRI as a triage before the biopsy procedure, which might avoid unnecessary biopsies [5]. Some studies showed that the clinically significant cancer detection rate of TRUS-P is lower than targeted MR fusion biopsies [30], and TRUS-P has more significant post-biopsy infection risks. EAU guidelines recommend both mpMRI before the biopsy procedure and targeted MR fusion biopsy together with systematic biopsy for any suspicious lesion on mpMRI [11].

The main limitation of our study is that, since it is a retrospective study, no routine control was asked from patients of group 1 after the biopsy procedure, which started in 2014. However, all group 2 patients phoned on the third day and were recalled to the hospital 7–10 days after the biopsy for urine analysis and urine culture. So, only symptomatic patients who applied to our hospital could be reached in group 1, which means that the actual number of mildly infected patients might be higher in group 1. However, all patients in both groups were advised to apply to our hospital, and all were given a phone number to call if they had complications such as hematuria, dysuria, fever, chill, or urinary retention.

Conclusion

The povidone-iodine solution is cheap, safe and easy to apply. Our cleansing method with povidone-iodine seems to decrease infectious complications related to prostate biopsy procedure, but we need a randomized controlled trial to confirm our study.

Ethical approval

All procedures performed in studies involving human participants were in accordance with 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. Ethical approval was waived by the local Ethics Committee of the University Karabuk, given the retrospective nature of the study with the number 2021/649, on the date of 1 October 2021, and all the procedures being performed were part of the routine care.

Table 3. Main characteristics of studies including povidone-iodine usage for rectal cleansing.

Study	Year	Method	Total no. of patients	No. of PI applied patients	PI form	PI application method	Outcome measures	Infectious complications no. (%)
Huang et al. [14]	2006	RS	222	157	PI solution 100 ml	Direct rectal injection of PI solution together with enema	UTI, hospitalization	0 (0%)
Park et al. [12]	2009	RCT	481	360	PI Suppository Form (200 mg)	200 mg PI suppository form	Infectious complications, bacterial colony counts	1 (0.3%)
Gil-Yernet Sedo et al. [15]	2012	RCT	530	530	PI gel (30 g)	Intra-rectal administration of PI gel	Post-biopsy urine culture, UTI	1 (0.2%)
Abughosh Z et al. [16]	2013	RCT	865	421	PI soaked gauze	Direct manual cleaning of an anterior rectal wall over prostate with PI-soaked gauze	Fever, UTI, sepsis	11 (2.6%)
Gyorfi et al. [13]	2014	RS	570	114	PI solution together with lidocaine gel-soaked gauze	Rectal vault swabbed with PI-soaked gynecologic swab	Culture-positive febrile infection	0 (0%)
Park et al. [17]	2018	RS	1007	303	PI solution together with lidocaine gel-soaked gauze	Rectal vault swabbed with PI-soaked gynecologic swab	UTI, bacteremia, hospital admission, ICU admission	2 (0.7%) UTI 1 (0.3%) B.emi 2 (0.7%) HA 1 (0.7%) ICU 13 (11.2%)
Lee et al. [18]	2020	RCT	451	116	PI solution (0.1 gr/ml)	Injection of PI solution into anal and lower rectal canals	Asymptomatic bacteriuria, UTI, prostatitis, fever, sepsis, hospitalization, mean length of hospital stay	11 (6.5%)
Ramedani et al. [19]	2021	RS	1181	355	PI soaked gauze	Direct manual cleansing of the mucosal surface of the anus and lower rectum using forceps and PI cotton balls Direct cleaning of the rectal vault by PI-soaked gynecologic swab	Asymptomatic bacteriuria, UTI, prostatitis, fever, sepsis, hospitalization, mean length of hospital stay Clinical infections, hospital admission, ICU admission, bacteremia	4 (1.1%) CI 2 (0.6%) HA

RS: retrospective study; RCT: randomized controlled trial; PI: povidone-iodine; UTI: urinary tract infection; B.emi: bacteremia; HA: hospital admission; ICU: intensive care unit; CI: clinical infections.

Patient consent

The authors declare that 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).

Authors' contributions

BOSTANCI Coşkun: Project development, Data management, Manuscript writing. BOZKURT Ufuk: Project development, Data management

Disclosure statement

No potential conflict of interest was reported by the author(s).

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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