

A Novel Enema Method Can Prevent Infectious Complications of Transrectal Ultrasound-Guided Prostate Biopsy: A Single-Center Experience

Fatih Gokalp¹, Omer Koras², Didar GURSOY¹, Hakan Sigva¹, Sefa Burak PORGALI¹,
Nezih TAMKAC¹, Bilal Kulak¹, Ferhat Uçurmak¹, and Sadik GORUR¹

¹Hatay Mustafa Kemal University

²Mustafa Kemal University Faculty of Medicine

September 24, 2021

Abstract

Background: Transrectal ultrasound biopsy is the preferred method for diagnosing prostate cancer, but it can cause infectious complications as a result of fluoroquinolone resistance. We aimed to explore the potential protective effect of a second rectal enema before biopsy. **Methods:** Between January 2015 and December 2020, 419 patients were assessed retrospectively. Patients with a history of anticoagulant use, uncontrolled diabetes, urological surgery, prostate biopsy, or recent hospitalization or overseas travel, as well as those with previous prostatitis, were excluded from the study. The patients were subsequently divided into two groups: Group 1 (n=223) had received one enema, on the morning of the biopsy, and Group 2 (n=196) had received two, with the additional enema administered half an hour before the procedure. **Results:** There was no significant difference between the groups in terms of age, BMI, diabetes, prostate-specific antigen (PSA) level, and prostate size (p=0.076, p=0.489, p=0.265, p=0.193, and p=0.661, respectively) or in relation to cancer detection (p=0.428). The median hospitalization date was significantly higher in Group 1 (p=0.003) as was UTI development (p=0.004). However, there was no significant difference in terms of fever and sepsis (p=0.524 and p=0.548, respectively). Additionally, subgroup analysis demonstrated that UTI was significantly lower in patients with diabetes mellitus who had received a second enema (p=0.004), though there was no significant difference in UTI between the groups in those without diabetes mellitus (p=0.215). Multivariable analysis showed that age and diabetes were significant risk factors for the development of UTI (p=0.002 and p=0.003, respectively). Furthermore, the second enema was a significant protective factor for preventing UTI (p<0.001). **Conclusion:** Older age and the presence of diabetes mellitus are independent risk factors for UTI after prostate biopsy. A second enema procedure before biopsy may protect patients from related infectious complications and could therefore be used as an alternative preventative method.

A Novel Enema Method Can Prevent Infectious Complications of Transrectal Ultrasound-Guided Prostate Biopsy: A Single-Center Experience

Abstract

Background: Transrectal ultrasound biopsy is the preferred method for diagnosing prostate cancer, but it can cause infectious complications as a result of fluoroquinolone resistance. We aimed to explore the potential protective effect of a second rectal enema before biopsy.

Methods: Between January 2015 and December 2020, 419 patients were assessed retrospectively. Patients with a history of anticoagulant use, uncontrolled diabetes, urological surgery, prostate biopsy, or recent hospitalization or overseas travel, as well as those with previous prostatitis, were excluded from the study. The patients were subsequently divided into two groups: Group 1 (n=223) had received one enema, on the

morning of the biopsy, and Group 2 (n=196) had received two, with the additional enema administered half an hour before the procedure.

Results: There was no significant difference between the groups in terms of age, BMI, diabetes, prostate-specific antigen (PSA) level, free/total PSA (f/t PSA) ratio, and prostate size ($p=0.076$, $p=0.489$, $p=0.265$, $p=0.193$, $p=0.518$, and $p=0.661$, respectively) or in relation to cancer detection ($p=0.428$). The median hospitalization date was significantly higher in Group 1 ($p=0.003$) as was UTI development ($p=0.004$). However, there was no significant difference in terms of fever and sepsis ($p=0.524$ and $p=0.548$, respectively). Additionally, subgroup analysis demonstrated that UTI was significantly lower in patients with diabetes mellitus who had received a second enema ($p=0.004$), though there was no significant difference in UTI between the groups in those without diabetes mellitus ($p=0.215$). Multivariable analysis showed that age and diabetes were significant risk factors for the development of UTI (OR: 0.074, 95%CI: 1.027-1.130, $p=0.002$ and OR: 1.220, 95%CI: 0.131-0.665, $p=0.003$, respectively). Furthermore, the second enema was a significant protective factor for preventing UTI (OR: -1.794, 95%CI: 2.208-16.389, $p<0.001$).

Conclusion: Older age and the presence of diabetes mellitus are independent risk factors for UTI after prostate biopsy. A second enema procedure before biopsy may protect patients from related infectious complications and could therefore be used as an alternative preventative method.

Keywords: Biopsy, Prostate cancer, Infectious Complication, Enema

What's Already Known?

Transrectal ultrasound-guided biopsy (TRUS-bx) is one of most common modality to diagnose prostate cancer. Infectious complications after prostate biopsy are rising due to antibiotic usage and fluoroquinolone resistance. Reducing risk of complications is the question to must be answered. Previous studies showed that rectal swaps could decrease infectious due to targeted prophylaxis, however, culture sampling several days prior biopsy is cost effective in routine practice. Additionally, rectal enemas, povidone-iodine and antimicrobial lubricant could decrease infectious complications. Literature suggest that preventive effect of rectal enemas is still debatable.

What's New?

Our study showed that a different application of rectal enema prevents urinary tract infection after prostate biopsy. In addition, in our research, it was shown that the second rectal enema administration did not show any difference in urinary tract infection in patients without diabetes, while it reduced urinary tract infection in patients with diabetes. Although, thus, diabetes and advanced age were found to be independent risk factors for urinary tract infection, the second enema was also found to be a protective factor.

Introduction

Prostate cancer is the second most common cancer worldwide. Transrectal ultrasonography-guided (TRUS-bx) and transperineal ultrasonography-guided (TPUS-bx) needle biopsies are well-established methods in diagnosing prostate cancer, with TRUS-bx the traditionally more preferred and more reliable method. However, bacterial sepsis is a severe complication of TRUS-bx, and hospital readmission increases over time due to these infective complications (1).

Effective prebiopsy preparation of the patient is essential; approximately 96% of urologists support preoperative antibiotics and more than 80% promote rectal enemas (2). In TRUS-bx, fluoroquinolones are the most preferred agent because of their excellent tolerability, broad-spectrum efficacy, and good penetration into the prostate tissue, and they can also reduce septic complications. However, in recent years, there has been an increase in fluoroquinolone resistance and infectious TRUS-bx complications as a result because of increased antibiotic use (3, 4). Rectal preparation is another essential stage of the prebiopsy procedure to decrease potential infection with enemas and povidone-iodine administration both effective in preventing infectious complications (5, 6). Most relevant studies suggest that enemas reduce bacterial load and, therefore, the rate of bacteremia (1).

However, conflicting results about the timing of enema administration exist in the literature, and it has also been shown that enemas may even increase infective complications and be ineffective (7, 8). As a result of these findings, the optimal preparation procedure to prevent infection remains unclear (9) although predicting and preventing such issues following TRUS-bx has been gaining increased attention (10). In the current study, we investigated the effect of enema timing on preventing infectious complications.

Materials and Methods

Participants

A total of 419 patients were evaluated retrospectively between January 2015 and December 2020. The patients had undergone TRUS-bx due to prostate cancer suspicion following total prostate-specific antigen (tPSA) of ≥ 4 ng/mL or digital rectal examination and lesions with a PIRADS score of ≥ 3 on multi-parametric MRI. Patients with histories of anticoagulant use, uncontrolled diabetes mellitus, urological surgery, prior TRUS-bx, recent hospitalization, recent overseas travel, or prostatitis were excluded from the study. Uncontrolled diabetes was defined as an HgbA1c level of ≥ 7 (11). Informed consent was obtained from all patients, and all procedures were performed by experienced staff.

Prebiopsy urinary cultures were routinely obtained, and all patients received cephalosporine and aminoglycoside prophylaxis 24 hours before the biopsy which was also continued afterwards for seven days. All biopsies were taken using an 18-gauge prostate biopsy needle with transrectal ultrasound guidance. According to current practice, 12 core samples were obtained in standard fashion. Patients were discharged on the same day in the absence of abnormal rectal or urethral bleeding or urinary retention. Two weeks after the biopsy, patients were called for control, and they were asked to attend the hospital in case of acute symptoms such as high fever, severe rectal bleeding, and general condition disorder.

Study design

The participants were divided into two non-randomized groups with 223 who had received one rectal enema on the morning of their biopsy in Group 1 and 196 who had received an additional enema half an hour before the procedure in Group 2. Medical records, including demographic, clinical, and biochemical data, were collected from the hospital database and each patient's chart. Body temperature of more than 38°C, dysuria, and urinary pyuria were accepted as indicating a urinary tract infection (UTI). A sequential organ failure assessment score of more than 2 and a positive urine culture were considered evidence of sepsis (12). The neutrophile-lymphocyte ratio (NLR) was calculated as the absolute number of neutrophils divided by the lymphocyte count, and the platelet-lymphocyte ratio (PLR) was determined by dividing the number of platelets by the number of lymphocytes. The systemic immune-inflammatory index (SII) was calculated as the platelet count multiplied by neutrophils and divided by lymphocytes.

The primary endpoint of the study was the reduction or prevention of infective complications following prostate biopsy with a secondary goal being the prevention of clinically essential complications that require hospitalization. The local ethics committee approved the study.

Statistical analysis

Statistical Package for the Social Sciences 23.0 (IBM, New York, USA) was used for the analysis with the distribution examined using the Shapiro-Wilk test and Q-Q plots. The continuous variables are expressed as median and interquartile range, and were compared by Mann-Whitney U test, and the categorical variables are expressed as percentage and frequency, and were compared by chi-squared or Fisher's exact test. Logistic regression was used for the correlation, and $p < 0.05$ was considered statistically significant.

Results

Patient characteristics

The median age was 66 (61-72) years, median PSA level was 7.27 (5.13-12.16) ng/ml, and median prostate size was 56 (45-76) cm³. Of the 419 patients, 52.2% were found to have benign prostate hyperplasia with

prostate cancer detected in 23.6%, and 58 (13.8%) developed complications. UTI and sepsis were observed in 36 (8.6%) and 3 (0.7%) patients, respectively. No patients were admitted to the intensive care unit.

Group comparison

Table 2 compares UTI incidence. The age and presence of diabetes were significantly higher in patients with postbiopsy UTI ($p = 0.002$ and $p = 0.005$, respectively), and tPSA and prostate cancer detection were also significantly higher in patients with UTI ($p < 0.001$ and $p = 0.001$, respectively) (Table 2).

When the data was divided according to preoperative rectal preparation, there was no significant difference between the groups in terms of age, BMI, and diabetes ($p = 0.076$, $p = 0.489$, and $p = 0.265$, respectively). PSA level, f/t PSA ratio, and prostate size were also similar between the groups ($p = 0.193$, $p = 0.518$, and $p = 0.661$, respectively) (Table 3). While chronic prostatitis was higher in Group 1, ISUP 1 and 2 pathologies were higher in Group 2. However, there was no statistically significant difference between the groups in terms of pathological evaluation ($p = 0.428$).

The median hospitalization date was significantly higher in Group 1 ($p = 0.003$) as was UTI development ($p = 0.004$). However, there was no significant difference between the groups in terms of fever, epididymitis, and sepsis ($p = 0.524$, $p = 0.521$, and $p = 0.548$, respectively). Subgroup analysis demonstrated that UTI was significantly lower in Group 2 patients with diabetes ($p = 0.004$), but there was no significant difference between the groups in terms of UTI development in non-diabetic patients ($p = 0.215$).

Multivariate analysis showed that age and presence of diabetes was a significant risk factor for the development of UTI (OR: 0.074, 95%CI: 1.027-1.130, $p = 0.002$ and OR: 1.220, 95%CI: 0.131-0.665, $p = 0.003$, respectively; Table 4). Furthermore, the additional enema was found to be a significantly protective factor for preventing UTI in patients with diabetes (OR: -1.794, 95%CI: 2.208-16.389, $p < 0.001$).

Discussion

Prebiopsy preparation with a cleansing rectal enema is a well-tolerated and low-cost process, and our findings show that it significantly reduces UTI after TRUS-bx. We observed that administering two enemas, the first on the biopsy morning and the second half an hour before, significantly decreased infection and related complications.

Prostate cancer is an essential health concern in urology practice, and TRUS-bx remains the most preferred diagnostic method. Unfortunately, however, biopsy-related complications are an important cause of morbidity with three major issues frequently seen: rectal bleeding, difficulty in urination, and infective complications that require treatment (13). A large population-based study comparing TRUS-bx and TPUS-bx found that infections were higher following the rectal approach, with a sepsis rate of 1.35%, although the readmission rate was higher among TPUS-bx patients (14).

Various factors affecting biopsy-related infection have been identified in the literature (4, 15). A nationwide study in Taiwan involving 12,968 TRUS-bx procedures found that 6.59% of patients had infection complications and demonstrated that age, prostate cancer, and hospitalization were significant risk factors for severe infection (13). Elsewhere, a 10-year case-control investigation showed that infectious complications rose in the study period, and that recent hospitalization, diabetes, and chronic pulmonary obstructive disease from smoking were significant risk factors for infection (4). Similarly, our study demonstrates that age, diabetes, and prostate cancer are significantly higher in patients with postbiopsy UTI, and the involvement of both diabetes and age are independent risk factors for biopsy-related infections of this kind.

To prevent subsequent complications, good preoperative planning is crucial. Existing studies have evaluated the role of rectal preparation in preventing infective problems following prostate biopsy (6, 16, 17). A randomized control study showed that mechanical bowel preparation before rectal surgery can significantly decrease infectious complications (17) while a retrospective study demonstrated that the number of biopsy cores and the use of an enema had a significant association with infection, prompting the recommendation of enema before prostate biopsy to minimize the risk of infectious complications (16).

Studies have also been conducted into novel forms of rectal decontamination and report that povidone-iodine administration can significantly reduce postbiopsy infection (6, 18, 19). A further systematic review found that a povidone-iodine enema can significantly reduce the risk of bacteremia and bacteriuria (5). A randomized control study comparing antimicrobial and standard lubricants demonstrated that the antimicrobial option significantly decreased bacterial colonization; however did not reduced quinolone resistance bacterial growth and also reported that there was significant difference between groups in terms of fever and readmission rate (20).

Further to these results, our study suggests that a second rectal administration could decrease infectious complications. The advantages of such preparation methods are that they are easy to administer, have low costs, and the effect of their administration is regardless of microbial antibiotic resistance patterns. In diabetic patients, hyperglycemic-related impairment of the immune response may increase the risk of infectious complications, hence only including those with regulated glycemic levels, and our study demonstrates that a second enema reduces infection in patients with diabetes mellitus. We therefore suggest that an additional prebiopsy enema could be beneficial in other patients who are prone to infectious complications.

There are some limitations of our study. First, routine rectal cultures were not taken. Although studies have shown that this plays a preventative role for infective complications because of targeted prophylaxis, guidelines do not yet recommend it as routine practice (21, 22). Second, the biopsies were performed by several staff, and so exposure time could vary. That said, all procedures were performed by experienced residents following standard protocols. Last, the study was retrospective in nature and based on a single center meaning that those with bacterial resistance may change during the period in question. We nevertheless also observed that there was no difference in bacteria-related complications during the study period.

Conclusion

Infectious complications remain a problematic outcome of TRUS-bx. Older age and the presence of diabetes mellitus are independent risk factors for UTI following prostate biopsy. A second rectal enema before the biopsy procedure may have a protective effect on any subsequent infectious complications.

Acknowledgement:

None

Funding:

The authors declared that there is no funding received for this study

Conflict of Interest:

The authors declared that there is no conflict of interest.

Reference:

1. Lindert KA, Kabalin JN, Terris MK. Bacteremia and bacteriuria after transrectal ultrasound guided prostate biopsy. *J Urol*. 2000;164(1):76-80.
2. Shandera KC, Thibault GP, Deshon GE, Jr. Variability in patient preparation for prostate biopsy among American urologists. *Urology*. 1998;52(4):644-6.
3. Wagenlehner FM, van Oostrum E, Tenke P, Tandogdu Z, Çek M, Grabe M, 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(3):521-7.
4. Carignan A, Roussy JF, Lapointe V, Valiquette L, Sabbagh R, Pépin J. Increasing risk of infectious complications after transrectal ultrasound-guided prostate biopsies: time to reassess antimicrobial prophylaxis? *Eur Urol*. 2012;62(3):453-9.

5. Pu C, Bai Y, Yuan H, Li J, Tang Y, Wang J, et al. Reducing the risk of infection for transrectal prostate biopsy with povidone-iodine: a systematic review and meta-analysis. *Int Urol Nephrol*. 2014;46(9):1691-8.
6. Abughosh Z, Margolick J, Goldenberg SL, Taylor SA, Afshar K, Bell R, et al. A prospective randomized trial of povidone-iodine prophylactic cleansing of the rectum before transrectal ultrasound guided prostate biopsy. *J Urol*. 2013;189(4):1326-31.
7. Carey JM, Korman HJ. Transrectal ultrasound guided biopsy of the prostate. Do enemas decrease clinically significant complications? *J Urol*. 2001;166(1):82-5.
8. Vallancien G, Prapotnich D, Veillon B, Brisset JM, Andre-Bougaran J. Systematic prostatic biopsies in 100 men with no suspicion of cancer on digital rectal examination. *J Urol*. 1991;146(5):1308-12.
9. Itani KM, Wilson SE, Awad SS, Jensen EH, Finn TS, Abramson MA. Polyethylene glycol versus sodium phosphate mechanical bowel preparation in elective colorectal surgery. *Am J Surg*. 2007;193(2):190-4.
10. Liss MA, Ehdaie B, Loeb S, Meng MV, Raman JD, Spears V, et al. An Update of the American Urological Association White Paper on the Prevention and Treatment of the More Common Complications Related to Prostate Biopsy. *J Urol*. 2017;198(2):329-34.
11. 6. Glycemic Targets: Standards of Medical Care in Diabetes-2021. *Diabetes Care*. 2021;44(Suppl 1):S73-s84.
12. Cecconi M, Evans L, Levy M, Rhodes A. Sepsis and septic shock. *Lancet*. 2018;392(10141):75-87.
13. Wei TC, Lin TP, Chang YH, Chen TJ, Lin AT, Chen KK. Transrectal ultrasound-guided prostate biopsy in Taiwan: A nationwide database study. *J Chin Med Assoc*. 2015;78(11):662-5.
14. Berry B, Parry MG, Sujenthiran A, Nossiter J, Cowling TE, Aggarwal A, et al. Comparison of complications after transrectal and transperineal prostate biopsy: a national population-based study. *BJU Int*. 2020;126(1):97-103.
15. Roberts MJ, Bennett HY, Harris PN, Holmes M, Grummet J, Naber K, et al. Prostate Biopsy-related Infection: A Systematic Review of Risk Factors, Prevention Strategies, and Management Approaches. *Urology*. 2017;104:11-21.
16. Jeon SS, Woo SH, Hyun JH, Choi HY, Chai SE. Bisacodyl rectal preparation can decrease infectious complications of transrectal ultrasound-guided prostate biopsy. *Urology*. 2003;62(3):461-6.
17. Bretagnol F, Panis Y, Rullier E, Rouanet P, Berdah S, Dousset B, et al. Rectal cancer surgery with or without bowel preparation: The French GRECCAR III multicenter single-blinded randomized trial. *Ann Surg*. 2010;252(5):863-8.
18. Ryu JW, Jung SI, Ahn JH, Hwang EC, Yu HS, Kang TW, et al. Povidone-iodine rectal cleansing and targeted antimicrobial prophylaxis using rectal swab cultures in men undergoing transrectal ultrasound-guided prostate biopsy are associated with reduced incidence of postoperative infectious complications. *Int Urol Nephrol*. 2016;48(11):1763-70.
19. Allen JL, Lehman K, Dewan K, Kirimanjeswara G, Raman JD. Procedural povidone iodine rectal preparation reduces bacteriuria and bacteremia following prostate needle biopsy. *Can J Urol*. 2017;24(4):8883-9.
20. Salomon G, Saul J, Prues S, Schneider M, Budäus L, Tilki D, et al. Antimicrobial lubricant reduces rectal bacteria at transrectal prostate biopsy: results from a prospective randomized trial. *World J Urol*. 2018;36(6):871-6.
21. Buck B, Fumo D, Arora K, Jain S, Sindhwani P. Ciprofloxacin-Resistant Bacteria on Pre-Prostate Biopsy Rectal Swab Culture: A Northwest Ohio Study. *Surg Infect (Larchmt)*. 2018;19(6):614-7.
22. Taylor AK, Zembower TR, Nadler RB, Scheetz MH, Cashy JP, Bowen D, 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(4):1275-9.

Hosted file

Table 1.docx available at <https://authorea.com/users/369958/articles/538442-a-novel-enema-method-can-prevent-infectious-complications-of-transrectal-ultrasound-guided-prostate-biopsy-a-single-center-experience>

Hosted file

Table 2.docx available at <https://authorea.com/users/369958/articles/538442-a-novel-enema-method-can-prevent-infectious-complications-of-transrectal-ultrasound-guided-prostate-biopsy-a-single-center-experience>

Hosted file

Table 3.docx available at <https://authorea.com/users/369958/articles/538442-a-novel-enema-method-can-prevent-infectious-complications-of-transrectal-ultrasound-guided-prostate-biopsy-a-single-center-experience>

Hosted file

Table 4.docx available at <https://authorea.com/users/369958/articles/538442-a-novel-enema-method-can-prevent-infectious-complications-of-transrectal-ultrasound-guided-prostate-biopsy-a-single-center-experience>