North Clin Istanb 2025;12(4):419–424
doi: 10.14744/nci.2024.79577

Original Article UROLOGY

Comparison of two analgesia applied to periprostatic nerve blockage during transrectal ultrasound guided prostate biopsy

Halil Cagri Aybal,[1] Taha Numan Yikilmaz,[2] Halil Basar[3]

[1]Department of Urology, Polatli Duatepe State Hospital, Ankara, Turkiye

[2]Department of Urology, Egekent Private Hospital, Denizli, Turkiye

[3]Department of Urology, University of Health Sciences, Abdurrahman Yurtaslan Oncology Training and Research Hospital, Ankara, Turkiye

ABSTRACT

OBJECTIVE: A combination of local anesthetic treatments provides better pain alleviation than periprostatic nerve block (PPNB) alone during a prostate biopsy procedure. The primary objective of this study was to compare Visual Analog Scale (VAS) pain levels during transrectal ultrasound (TRUS)- guided prostate biopsy whilst the use of prilocaine-lidocaine cream, diclofenac suppository, or PPNB only in a prospective, randomized study.

METHODS: This study included 162 patients who had TRUS-guided prostate biopsies performed at the Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Center within a 6 month period, from April to October 2017. Three groups of patients were randomly assigned: group 1 underwent PPNB plus prilocaine-lidocaine cream, group 2 received diclofenac suppository along with PPNB, and group 3 underwent PPNB alone. The VAS was used to measure the degree of pain: VAS 1 was used to record the pain at the time the ultrasound probe was inserted, VAS 2 was used to document the pain during PPNB, and VAS 3 was used to record the pain during needle biopsy. Following the biopsy, any complications or negative consequences were recorded.

RESULTS: Mean age or serum prostate specific antigen (PSA) levels were similar between the three groups. The VAS 1, VAS 2, and VAS 3 pain scores showed statistically significant difference among the three groups (p=0.001). Between groups 1 and 2, there was a statistically significant difference in VAS 1 pain scores (p=0.01). There was no statistically difference in VAS 2 and VAS 3 pain scores between the groups 1 and 2 (p=0.08 and p=0.23, respectively). Patients between the groups 3 and other groups had significantly difference in VAS pain scores (p<0.05).

CONCLUSION: In this study, we highlight that when applied as an adjuvant to PPNB, either 5% prilocaine-lidocaine cream or a 100 mg diclofenac suppository reduced pain levels relative to PPNB alone. When compared to a 100 mg diclofenac suppository, prilocaine-lidocaine cream significantly reduces pain during the insertion and manipulation of the ultrasound probe.

Keywords: Analgesia; anesthesia; biopsy; prostate.

Cite this article as: *Aybal HC, Yikilmaz TN, Basar H. Comparison of two analgesia applied to periprostatic nerve blockage during transrectal ultrasound guided prostate biopsy. North Clin Istanb 2025;12(4):419–424.*

Prostate cancer (PCa) is the second largest cause of cancer-related mortality worldwide, making up 15% of all cancer cases [1]. Patients with PCa have been diagnosed with great success using the raised serum prostate-specific antigen (PSA) level and abnormal digital rectal examination (DRE) findings [2].

The study has been reported in abstract form at the 5th International Hippocrates Congress on Medical and Health Sciences (18–19 December 2020).

Received: June 01, 2024 *Accepted:* July 07, 2024 *Online:* August 08, 2025

Correspondence: Halil Cagri AYBAL, MD. Polatli Duatepe Devlet Hastanesi, Uroloji Klinigi, Ankara, Turkiye.
Tel: +90 505 717 20 05 e-mail: halilcagri@gmail.com

Istanbul Provincial Directorate of Health - Available online at www.northclinist.com

Prostate biopsy is the gold standard diagnostic method for obtaining the histopathological diagnosis [3]. Ultrasound (US)-guided transrectal or transperineal biopsy is the two main procedures used to the diagnose of PCa. Local analgesia with PPNB is the well-known technique in analgesia before prostate biopsy [4]. PPNB reduces the pain and discomfort associated with the prostate biopsy. However, the ultrasonography probe's insertion and the needle's movement during infiltration of local anesthetic (ILA) can both be uncomfortable [5]. Numerous studies have demonstrated that the administration of intrarectal local analgesia reduces discomfort during prostate biopsies [6, 7].

In a prospective, randomized trial, the main goal of this research was to assess the Visual Analog Scale (VAS) pain scores during TRUS-guided prostate biopsy while utilizing prilocaine-lidocaine cream, diclofenac suppository, or PPNB alone.

Highlight key points

- During transrectal US-guided prostate biopsy, administration of diclofenac suppository or prilocaine-lidocaine cream in addition to PPNB provides better analgesia than PPNB alone.
- Prilocaine-lidocaine cream is more effective analgesia than diclofenac suppository during US probe insertion and manipulation.

MATERIALS AND METHODS

Study Design

A randomized, prospectively controlled study design was used to compare the pain level during a TRUS-guided prostate biopsy. This study included 162 patients who had TRUS-guided prostate biopsies performed at the Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Center within a 6-month period, from April to October 2017. The Dr. Abdurrahman Yurtaslan Ankara Onkoloji Training and Education Hospital Center ethical committee approved the study protocol (No. 2017-03/01). All patients signed an informed consent form. The study was conducted in accordance with the guidelines of the Declaration of Helsinki.

Population Selection

Inclusion criteria were adult males aged 40 and over, PSA levels higher than 4 ng/mL, or solid nodules on digital rectal examination (DRE). Exclusion criteria were known sensitivity to lidocaine, prilocaine, or diclofenac; hemorrhagic diathesis; anticoagulant use; undiagnosed pain; chronic pain syndrome; and anorectal disease.

Study Protocol

Patients referred to transrectal ultrasound guided prostate biopsy (TRUS-PB) based on the inclusion criteria as well as those referred for repeat biopsies as have been enrolled. The treatment of patients taking anticoagulants has been consulted with the relevant clinics. Those who took aspirin discontinued five days before the biopsy; coumadin, clopidogrel, and other drugs were discontinued one week ago. All patients had a negative urine culture prior to the procedure. To reduce the risk of urinary infection and sepsis, all patients without a history of drug allergy were prophylactically started with ciprofloxacin 500 mg S: 2x1 one day before the biopsy and maintained for one week afterward. A fleet enema was administered half an hour before the biopsy to purify the bowels. After infection prophylaxis, group 1 received a 5 g concentration of 5% prilocaine/lidocaine cream and waited 30 minutes; whereas group 2 received a 100 mg diclofenac suppository and waited one hour. Group 3 was determined as patients who underwent PPNB only. Age, serum PSA levels, DRE findings, prostate size at TRUS, presence of diabetes mellitus (DM), and hypertension (HT) were recorded after ILA was performed.

Prostate Biopsy

Participants were placed in the left lateral decubitus position, and transrectal ultrasound was performed using an ultrasound scanner (Sonoscape SSI5500BW) with a 3-15 MHz/ R 8 mm endorectal biplane transducer. The prostate has been scanned in both the axial and sagittal planes for evidence of abnormalities. Prostate volume was measured. Subsequently, ILA was performed in all groups by injecting 5 ml of 2% lidocaine hydrochloride lateral to the junction between the base of the prostate and the seminal vesicle using a 25 cm 18-gauge spinal needle. After 5 minutes, the prostate biopsy was conducted. All patients had six core samples obtained from each lobe, for a total of 12 core samples per participant. All specimens were obtained utilizing an automated biopsy gun (Geotek Alfa-Gun) and a 25-cm, 18-gauge tru-cut biopsy needle.

Table 1. Comparison of groups' demographic datas

	Group 1 (n=54)	Group 2 (n=54)	Group 3 (n=54)	p
Age*	63.36±6.28	66.04±7.58	67.41±7.99	0.06
PSA (ng/mL)**	6.56±4.67	6.67±5.47	7.55±7.46	0.99
Prostat volume (mL)**	40±17.48	45±32.32	46.5±23.96	0.57
Diabetes mellitus (%)	22.2	13	14.8	0.39
Hypertension (%)	25.9	29.6	29.6	0.88

PSA: Prostate Specific Antigen; *: Statistically analyzed with One Way ANOVA test; **: Analyzed with Kruskal. Wallis test, others analyzed with Pearson Chi- Square test.

Table 2. Comparison of groups' Pain VAS scores

	Group 1 (n=54)	Group 2 (n=54)	Group 3 (n=54)	p
Insertion of probe (VAS 1)	4 (3.75)	5 (5)	6 (2)	**0.001**
PPNB (VAS 2)	2 (1.75)	3 (2.75)	5 (2)	**0.001**
Biopsy sampling (VAS 3)	2 (1)	2 (2)	3 (2)	**0.001**

PPNB: Periprostatic nerve block, VAS: Visual Analog Scale. Statistically analyzed with Kruskal Wallis test.

Pain Assessment and Complications

Pain was assessed using a 10-point VAS (VAS, 0=no pain, 10=severe pain) at three points: VAS 1 pain related to the probe insertion and manipulation, VAS 2 pain related to ILA, and VAS 3 pain related to prostate sampling. The performing urologist briefed patients about the various stages of the procedure. Pain was recorded following each stage. Three hours and one week after the biopsy, patients were assessed for possible complications. Complications such as hematospermia, hematuria, rectal bleeding, acute urinary retention (AUR), dysuria, and fever were documented.

Statistical Analysis

IBM Statistical Package for the Social Sciences (SPSS) version 23 was utilized for the analysis. A One-way analysis of variance (ANOVA) was used to compare patient characteristics. Kruskal – Wallis test was conducted to assess differences in pain scores; a non-parametric Mann–Whitney U test or parametric Student t-test were used to determine the comparison of binary groups. Pearson Chi-square or Fisher's Exact test to evaluate the categorical datas. Statistical significance was indicated by p-values less than 0.05.

RESULTS

Demographic Data

There were no significant differences in age (p=0.06), PSA levels (p=0.99), prostate volume (p=0.57), presence of DM (p=0.39), or HT (p=0.88) between the groups. The clinical values of the participants are shown in Table 1.

Pain Scores

Significant differences in VAS scores among all research groups are observed (p=0.001). Table 2 displays clinical values of the VAS scores. The pain scores of the groups are examined separately. A statistically significant difference was found between Group 1 and Group 2 in the VAS 1 score (p=0.01). There was no statistically significant difference in the VAS 2 and VAS 3 scores between Group 1 and Group 2 (p=0.08 and p=0.23, respectively). A significant difference in VAS scores was found between groups 1 and 3 (p=0.001). Significant differences in VAS 1, 2, and 3 scores were found between groups 2 and 3 (p=0.014, p=0.005, and p=0.008, respectively). Table 3 shows the clinical values of VAS scores between the groups.

Table 3. Comparison of pain VAS scores between the groups

	Group 1 & 2 p-value	Group 1 & 3 p-value	Group 2 & 3 p-value
Insertion of probe (VAS 1)	**0.01**	**0.001**	**0.014**
PPNB (VAS 2)	0.08	**0.001**	**0.005**
Biopsy sampling (VAS 3)	0.23	**0.001**	**0.008**

PPNB: Periprostatic nerve block; VAS: Visual Analog Scale. Statistically analyzed with Kruskal Wallis test. P<0.016 value were considered statistically significant.

Table 4. Comparison of complications

	Group 1 (n=54)	Group 2 (n=54)	Group 3 (n=54)	p
Fever (%)	1 (1.9)	0 (0)	0 (0)	0.36
Hematospermia (%)	18 (33.3)	21 (38.9)	18 (33.3)	0.78
Hematuria (%)	15 (27.8)	20 (37)	17 (31.5)	0.58
Rectal bleeding (%)	6 (11.1)	8 (14.8)	7 (13)	0.84
Acute urinary retention (%)	1 (1.9)	2 (3.7)	4 (7.4)	0.35
Dysuria (%)	3 (5.6)	3 (5.6)	4 (7.4)	0.89

Statistically analyzed with Pearson Chi-Square test.

Complications

Fever was seen in only one patient in Group 1. Other complications were seen in all of the groups. Table 4 shows that there were no significant differences in the complication incidence between groups (p>0.05).

DISCUSSION

In this study, when compared to a control group of patients who administered PPNB alone, the intrarectally applied 5% prilocaine lidocaine cream or 100 mg diclofenac suppository considerably reduced the severity of pain. This pain was assessed by VAS at the time placement and movement of the US probe, during PPNB, and at prostate sampling. It was demonstrated that 5% prilocaine-lidocaine cream significantly reduced pain during US probe placement and movement compared to 100 mg diclofenac suppositories; however, no significant difference was observed during PPNB and prostate sampling.

Previous studies demonstrated pain during prostate biopsy is associated with three factors: the insertion and manipulation of the US probe in the rectum, the core-biopsy needle puncture to the periprostatic nerve area and to multiple prostate gland tissues. Prostatic pain can originate from the inferior rectal nerve or capsule of the prostate gland. Pelvic plexus fibers go to the prostate with cavernous nerves. The inferior rectal nerve, located above the prostate apex, is a pain sensitive area [8, 9].

Nash et al. [10] reported that the PPNB technique was effective in providing anesthesia for prostate biopsy. This technique provides blocking the neurovascular bundles, having no effect on the dentate line or the anal sphincter. Previous studies have demonstrated that prilocaine–lidocaine cream when applied before PPNB, is superior to the application of PPNB alone in terms of reducing the level of pain, during ultrasound probe placement, ILA application, and biopsy taking [4]. Moreover, in another study, pain was lower during probe placement and biopsy application in patients treated with prilocaine lidocaine cream, during ILA application did not show any significant difference [6]. In this study, the use of 5% prilocaine lidocaine cream showed a significant difference compared to the PPNB alone group during US probe placement, ILA, and prostate biopsy sampling.

The analgesic function of diclofenac has been reported in previous studies using a suppository form. Diclofenac,

a non-steroid anti-inflammatory drug (NSAID), acts by inhibiting prostaglandin synthesis. Prostaglandins, along with leukotrienes and cytokines, cause edema and pain sensations in the rectal mucosa. Diclofenac acts by decreasing the effects of local mediators on pain responses both locally and systemically [11]. The analgesic function of diclofenac demonstrated that there was a significant difference in pain relief in the 100 mg diclofenac suppository group only one hour after prostate biopsy [11, 12]. Interestingly, in this study, there was a significant difference in pain level during US probe placement, ILA, and prostate biopsy in the diclofenac group compared to the PPNB only group.

Although diclofenac suppository has systemic and local effects, prilocain-lidocaine cream has a local effect by inhibiting neurovascular innervation in the rectal mucosa. The pain relief function of prilocaine-lidocaine cream was found to be significantly higher than that of the diclofenac suppository group during ultrasound probe insertion in the study of Valdez-Flores, while no significant difference was observed related to the prostate sampling [7]. In this study, the VAS pain scale was compared during PPNB in addition to probe placement and prostate sampling, no significant difference was observed.

In the current study, complication rates were recorded;post-biopsy complication rates were similar to previously reported results [13, 14]. Hematospermia, hematuria, and rectal bleeding were the most frequent complications that did not need treatment. No significant differences were observed between the groups (Table 4).

Despite the use of the PI-RADSv2 scoring system by magnetic resonance imaging (MRI), all patients do not have a PIRADS score greater than three. Patients with PSA-density >0.20 ng/mL/mL and a PI-RADS score of 3 have elevated prostate cancer risk; targeted and systematic biopsies are required [15, 16].

The limitations of this study are that PSA density was not calculated and did not include targeted biopsy. MRI-targeted prostate biopsy is commonly performed, and further prospective studies can be conducted on its use for analgesia.

Conclusion

In conclusion, this study emphasizes that the application of 100 mg diclofenac suppository or 5% prilocaine-lidocaine cream as an adjunct administration to PPNB decreased the amount of pain when compared to PPNB alone. The efficiency increased when diclofenac suppository was applied one hour ago and prilocaine-lidocaine cream 30 minutes ago before US probe insertion. Moreover, prilocaine-lidocaine cream provides significant pain reduction at the placement and movement of the US probe when compared with a 100 mg diclofenac suppository.

Ethics Committee Approval: The University of Health Sciences, Dr. Abdurrahman Yurtaslan Oncology Training and Research Hospital Ethics Committee granted approval for this study (date: 09.03.2017, number: 2017-03/01).

Informed Consent: Written informed consent was obtained from the participants and their parents.

Conflict of Interest: The authors declared that they have no conflict of interest.

Financial Disclosure: The authors declared that no support was received from any person or institution for the study.

Use of AI for Writing Assistance: Not declared.

Authorship Contributions: Concept – HCA, TNY; Design – HCA; Supervision – TNY; Data Collection and processing – HCA, TNY; Analysis and interpretation – HCA; Literature search – HCA; Writing – HCA, HB; Critical review – TNY, HB.

Peer-review: Externally peer-reviewed.

REFERENCES

1. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer 2010;127:2893-917. [Crossref]
2. Xue J, Qin Z, Cai H, Zhang C, Li X, Xu W, et al. Comparison between transrectal and transperineal prostate biopsy for detection of prostate cancer: a meta-analysis and trial sequential analysis. Oncotarget 2017;8:23322-36. [Crossref]
3. Thomson A, Li M, Grummet J, Sengupta S. Transperineal prostate biopsy: a review of technique. Transl Androl Urol 2020;9:3009-17. [Crossref]
4. Giannarini G, Autorino R, Valent F, Mogorovich A, Manassero F, De Maria M, et al. Combination of perianal-intrarectal lidocaine-prilocaine cream and periprostatic nerve block for pain control during transrectal ultrasound guided prostate biopsy: a randomized, controlled trial. J Urol 2009;181:585-91; discussion 591-3. [Crossref]
5. Berger AP, Frauscher F, Halpern EJ, Spranger R, Steiner H, Bartsch G, et al. Periprostatic administration of local anesthesia during transrectal ultrasound-guided biopsy of the prostate: a randomized, double-blind, placebo-controlled study. Urology 2003;61:585-8. [Crossref]
6. Raber M, Scattoni V, Roscigno M, Deho F, Briganti A, Salonia A, et al. Topical prilocaine-lidocaine cream combined with peripheral nerve block improves pain control in prostatic biopsy: results from a prospective randomized trial. Eur Urol 2008;53:967-73. [Crossref]
7. Valdez-Flores RA, Campos-Salcedo JG, Torres-Gomez JJ, Sedano-Lozano A, Pares-Hipolito J, Shelton LM, et al. Prospective comparison among three intrarectal anesthetic treatments combined with periprostatic nerve block during transrectal ultrasonography-guided prostate biopsy. World J Urol 2018;36:193-9. [Crossref]
8. Issa MM, Ritenour C, Greenberger M, Hollabaugh R Jr, Steiner M. The prostate anesthetic block for outpatient prostate surgery. World J Urol 1998;16:378-83. [Crossref]

9. Tanagho EA, Schmidt RA, de Araujo CG. Urinary striated sphincter: what is its nerve supply? Urology 1982;20:415-7. [Crossref]
10. Nash PA, Bruce JE, Indudhara R, Shinohara K. Transrectal ultrasound guided prostatic nerve blockade eases systematic needle biopsy of the prostate. J Urol 1996;155:607-9. [Crossref]
11. Haq A, Patel HR, Habib MR, Donaldson PJ, Parry JR. Diclofenac suppository analgesia for transrectal ultrasound guided biopsies of the prostate: a double-blind, randomized controlled trial. J Urol 2004;171:1489-91. [Crossref]
12. Ooi WL, Hawks C, Tan AH, Hayne D. A randomised controlled trial comparing use of lignocaine periprostatic nerve block alone and combined with diclofenac suppository for patients undergoing transrectal ultrasound (TRUS)-guided prostate biopsy. BJU Int 2014;114(Suppl 1):45-9. [Crossref]
13. Pinsky PF, Parnes HL, Andriole G. Mortality and complications after prostate biopsy in the Prostate, Lung, Colorectal and Ovarian Cancer Screening (PLCO) trial. BJU Int 2014;113:254-9. [Crossref]
14. Raaijmakers R, Kirkels WJ, Roobol MJ, Wildhagen MF, Schrder FH. Complication rates and risk factors of 5802 transrectal ultrasound-guided sextant biopsies of the prostate within a population-based screening program. Urology 2002;60:826-30. [Crossref]
15. Schoots IG, Padhani AR. Risk-adapted biopsy decision based on prostate magnetic resonance imaging and prostate-specific antigen density for enhanced biopsy avoidance in first prostate cancer diagnostic evaluation. BJU Int 2021;127:175-8. [Crossref]
16. Weinreb JC, Barentsz JO, Choyke PL, Cornud F, Haider MA, Macura KJ, et al. PI-RADS Prostate Imaging - Reporting and Data System: 2015, Version 2. Eur Urol 2016;69:16-40. [Crossref]