# Periprostatic Nerve Block vs. Intravenous Ibuprofen for Pain Management During Transrectal Prostate Biopsy Procedures: A Prospective Comparative Study

Ann. Ital. Chir., 2025: 1–7 https://doi.org/10.62713/aic.3938

Muharrem Baturu<sup>1</sup>, Elzem Sen<sup>2</sup>

AIM: This study aimed both to compare the efficacy of intravenous (IV) ibuprofen with periprostatic nerve block (PPNB) in pain control during prostate biopsy procedures and to investigate factors influencing pain scores.

METHODS: A total of 128 patients were prospectively enrolled between June and December 2023 and randomized into two groups: IV ibuprofen was Group 1 (n = 64) and PPNB was Group 2 (n = 64). Pain levels were assessed using a Visual Analog Scale (VAS) at various stages of the procedure. Demographic and clinical data, including age, prostate specific antigen (PSA) levels, prostate volume, body mass index (BMI), histopathology results, and Prostate Imaging-Reporting and Data System (PI-RADS) scores, were recorded and correlated among themselves.

RESULTS: The mean ages  $(64.68 \pm 5.87 \text{ vs } 63.33 \pm 7.26 \text{ years})$ , and median PSA level was  $[13.00 \ (8.04-41.68) \text{ ng/mL vs } 10.00 \ (6.73-23.80) \text{ ng/mL}]$  of Group 1 and 2 were as indicated, (p=0.267 and p=0.053), respectively). There were no statistically significant differences between the two groups in terms of prostate volume, BMI, PI-RADS score, and benign-malignant pathology on biopsy (p>0.05). The median VAS scores estimated during insertion of rectal probe  $[4 \ (2-5) \ \text{vs } 2 \ (0-3)]$ , prostate biopsy needle  $[3 \ (2-4) \ \text{vs } 0 \ (0-1)]$ , and overall median VAS scores  $[4 \ (3-4) \ \text{vs } 1 \ (0-2)]$  were lower in Group 2 than Group 1  $(p<0.001 \ \text{for all stages})$ . Correlation analyses revealed that PSA levels, and malignant pathology influenced the pain scores in Group 1 (p=0.230, p=0.024; r=0.268, p=0.032, respectively). Regression analysis demonstrated that PSA levels and malignant pathology affected the overall VAS scores in Group 1  $(p=0.024 \ \text{and } p=0.019, \text{ respectively})$ .

CONCLUSIONS: IV ibuprofen demonstrates promise as an easily applicable analgesic method for prostate biopsy, particularly for patients who are unwilling or unable to undergo PPNB. This study underscores the need for large-scale investigations to validate these findings.

CLINICAL TRIAL REGISTRATION: ClinicalTrials.gov with identifier (NCT06737939).

Keywords: prostate biopsy; IV ibuprofen; periprostatic nerve block; Visual Analog Scale

## Introduction

Prostate cancer was the fourth most commonly diagnosed cancer worldwide in 2020, with approximately 1.4 million new cases [1]. Radiological techniques including Multiparametric Magnetic Resonance Imaging (mpMRI) examinations and laboratory tests (prostate specific antigen (PSA), PSA velocity, and PSA density) are being used as auxiliary methods for the diagnosis of prostate cancer. However, prostate biopsy remains the gold standard technique for confirming the diagnosis [2].

Although biopsy procedures are generally well-tolerated by patients, up to 90% of them describe discomfort during the procedure [3]. While periprostatic nerve block

Submitted: 30 December 2024 Revised: 11 February 2025 Accepted: 17 February 2025 Published: 16 September 2025

Correspondence to: Elzem Sen, Department of Anesthesiology and Reanimation, School of Medicine, University of Gaziantep, 27310 Gaziantep, Turkey (e-mail: drelzemsen@gmail.com).

(PPNB) performed under lidocaine anesthesia provides the best pain control during local prostate biopsy procedures, it requires additional intervention and can still cause pain during nerve block [4]. For these reasons, alternative methods for periprostatic nerve block, such as intrarectal lidocaine application of intrarectal lidocaine, lidocaine-prilocaine, diclofenac sodium suppository applications, or their combination, have been tried. It has been found that while PPNB is effective in controlling pain, it cannot control pain during anesthetic infiltration for nerve block and manipulations of the rectal probe, suggesting that a combined approach may be more effective [5].

While a negative correlation with age and a positive correlation with biopsy core number and detection of malignant pathology have been shown in previous studies among factors affecting pain intensity, the effect of prostate volume and PSA level has been demonstrated to have a negligible impact on the severity of perceived pain [6,7]. While the existing literature has explored the effectiveness of various methods for pain control during prostate biopsy procedures, there are no prior studies investigating the use of in-

<sup>&</sup>lt;sup>1</sup>Department of Urology, School of Medicine, University of Gaziantep, 27310 Gaziantep, Turkey

<sup>&</sup>lt;sup>2</sup>Department of Anesthesiology and Reanimation, School of Medicine, University of Gaziantep, 27310 Gaziantep, Turkey

travenous (IV) ibuprofen in this context. Previous research on alternative analgesic methods has primarily focused on PPNB or other local applications [5]. This study presents the first prospective investigation evaluating the efficacy of IV ibuprofen compared to PPNB. In current study, we have aimed to compare the effect of IV ibuprofen and to investigate the factors influencing pain scores.

#### **Materials and Methods**

Between June 2023 and December 2023, 128 patients scheduled for prostate biopsy were included in the study following the acquisition of informed patient consent forms. Patients were enrolled prospectively after obtaining approval from the local ethics committee. This study was approved by the ethics committee of Gaziantep University (decision no: 2023/51) and was performed in accordance with the ethical standards laid down in the 2013 Declaration of Helsinki and its later amendments. All eligible par-ticipants signed an informed consent form. Informed con-sent was obtained from each study participant. Clinical Trial Registration: ClinicalTrials.gov with identifier (NCT06737939, https://clinicaltrials.gov/study/NCT 06737939?term=NCT06737939&rank=1).

The primary endpoint was to evaluate the pain-relieving effects of IV ibuprofen during transrectal ultrasound (TRUS)guided prostate biopsy procedures. The secondary endpoint was to identify factors influencing pain perception during the procedure.

## Patient Selection

Patients referred to us due to elevated PSA levels or evaluated in our clinic for lower urinary tract symptoms were included in our study. Prostate biopsies were planned for patients with PSA >4 ng/mL, abnormal findings such as prostate nodules or indurations palpated during digital rectal examination, or Prostate Imaging-Reporting and Data System (PI-RADS) score  $\geq 3$  on prostate mpMRI.

For pain control during prostate biopsy, the first group received IV ibuprofen 400 mg/100 mL, and the second group received PPNB with 10 mL of 2% lidocaine. Patients were randomized into two groups using a computer-generated randomization list to ensure unbiased group allocation. Allocation concealment was maintained by assigning group codes to participants, which were only revealed to the clinical team immediately before the intervention. While blinding was deemed unfeasible due to the inherent differences in the intervention techniques (IV ibuprofen infusion versus PPNB administration), efforts were made to minimize bias by standardizing outcome assessments and ensuring that pain evaluations were self-reported by the patients.

Age (years), body mass index (BMI), PI-RADS scores, prostate volumes (cc), PSA (ng/mL) levels, pathology results, and additional diseases of the patients were recorded. Patients were categorized based on the Charlson Comorbidity Index (CCI) scores for additional diseases [8].

Patients with renal failure, baseline creatinine level >1.8 mg/dL, a history of liver failure, use of antidepressants, bleeding diathesis, hemorrhoids and/or rectal fissures, and neurological diseases (such as dementia, Alzheimer's disease, epilepsy, paraplegia, etc.) and previous benign prostate biopsy results were excluded from the study.

#### Analgesia Administration Method

A 400 mg/100 mL solution of ibuprofen for IV infusion (Dorifen®, 4143074, Vem Pharmaceuticals Istanbul, Istanbul, Turkey) was administered intravenously over a 30minute period. After IV infusion was completed, we waited for 10 minutes to allow the analgesic to take effect before performing TRUS-guided prostate biopsy.

PPNB was performed bilaterally by injecting 10 mL of 2% lidocaine into the interface between the seminal vesicle and base of the prostate. Prostate biopsies were performed transrectally under ultrasound guidance 10 minutes after PPNB.

## Biopsy Technique

Following the explanation of the necessity of biopsy and its potential complications to patients, informed and voluntarily signed consent forms were obtained from them. One day before the prostate biopsy, patients were given gentamicin 3 mg/kg/day (Genta® 160 mg/2 mL, 2211006, Menarini Pharmaceuticals, Istanbul, Turkey), oral metronidazole 500 mg (Biteral® 500 mg, A112445, Deva Pharmaceuticals, Istanbul, Turkey) twice daily, and oral amoxicillinclavulanic acid (Augmentin-BID® 1000 mg, ELB0493, GlaxoSmithKline Pharmaceuticals, Istanbul, Turkey) antibiotic prophylaxis for 5 days [2,9]. Bowel preparation was performed with rectal enema two hours before the procedure. Patients were placed in the left lateral decubitus position, and after cleaning the rectal area with povidoneiodine solution, the prostate gland was evaluated longitudinally and sagittally with a 9 MHz transrectal probe (HS30, IS24544H1C00002X, Samsung®, Hongcheon-gun, Korea). Prostate volume was calculated using the ellipsoid formula, volume in ml:  $0.53 \times length \times height \times width$ of prostate measured during TRUS. TRUS-guided prostate biopsies were performed using an 18 gauge Tru-Cut biopsy needle. Before the procedure, all patients were requested to undergo prostate mpMRI. TRUS biopsy specimens were obtained from all the patients. A total of 12 cores were sampled, including systematic biopsy sample obtained from the peripheral zone, apex, mid, and base of the prostate, as well as cognitive targeted biopsies from areas described in mpMRI [10]. The patients were informed about the possibility of developing postprocedural complications such as urinary retention, hematuria, rectal bleeding, urosepsis, fever, and hemospermia.

#### Pain Assessment

A self-administered 10-point Visual Analog Scale (VAS) was used to assess pain levels at the beginning of the biopsy,

Table 1. Demographic and clinical data of groups.

	Group 1 Group 2		Test	
	n = 64	n = 64	icst	p
Age $^a$ (mean $\pm$ SD) (years)	$64.68 \pm 5.87$	$63.33 \pm 7.26$	1.156	0.267
PSA <sup>b</sup> (median) (IQR) (ng/mL)	13.00 (8.04-41.68)	(8.04–41.68) 10.00 (6.73–23.80)		0.053
Prostate_volume <sup><math>a</math></sup> (mean $\pm$ SD) (cc)	$64.73 \pm 24.28$	$69.55 \pm 22.26$	-1.169	0.245
$\mathrm{BMI}^a\ (\mathrm{mean} \pm \mathrm{SD})$	$27.97 \pm 5.04$	$28.05 \pm 5.10$	-0.029	0.977
PI-RADS <sup>b</sup> (median) (IQR)	3 (3–4)	3 (3–5)	0.119	0.906
CCI n (%)				
1	48 (75)	48 (75) 57 (89.1)		0.067
2	13 (20.3)	4 (6.3)	4 (6.3) 5.581	
3	3 (4.7)	3 (4.7) 3 (4.7)		
Pathology				
Benign n (%)	32 (50)	39 (60.9)	1.550	0.213
Malign n (%)	32 (50)	25 (39.1)		

a = Student *t*-test; b = Mann-Whitney U test.

Table 2. Comparison of VAS score according to groups.

	Group1	Group2	Test	p	Effect size	95% CI	
	n = 64	n = 64				Lower	Upper
Probe insertion <sup>a</sup> median (IQR)	4 (2–5)	2 (0-3)	-5.74	<0.001*	1.17	0.79	1.54
Probe needle insertion <sup>a</sup> median (IQR)	3 (2-4)	0 (0-1)	-9.55	< 0.001*	3.02	2.44	3.59
Overall <sup>a</sup> median (IQR)	4 (3-4)	1 (0-2)	-7.74	< 0.001*	1.96	1.54	2.39
Post procedural 2. hours <sup>a</sup> median (IQR)	2 (1–3)	1 (0-2)	-6.17	< 0.001*	1.31	0.98	1.64
Post procedural 1. day <sup>a</sup> median (IQR)	1 (1–2)	0 (0-1)	-5.191	< 0.001*	0.66	0.39	0.93

<sup>\*</sup>p < 0.05; a = Mann-Whitney U test.

during insertion of transrectal probe and then prostate biopsy needle, overall (the level of pain felt by the patient from the beginning to the end of the biopsy procedure was evaluated as overall), 2 hours and one day after the procedure. According to the scale, 0 indicated no pain, and 10 was defined as the most severe pain ever experienced. VAS scores below 3 were classified as mild, 3–6 as mild to moderate, and above 6 as moderate to severe pain [11].

#### Calculation of Sample Size

To determine the appropriate sample size, we utilized group means and standard deviations. The effect size (d) was set at 0.5 for comparing VAS scores between two groups. To achieve statistical significance with an alpha level of 0.05 and a power  $(1-\beta)$  of 0.80, the calculated sample size required 64 participants per group.

## Statistical Analysis

Data analysis was conducted using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). The normality of the variables was assessed using the Shapiro-Wilk test. Descriptive statistics, including mean and standard deviation for normal distributions and median with interquartile range (IQR) for non-normal distributions, were reported for numerical variables.

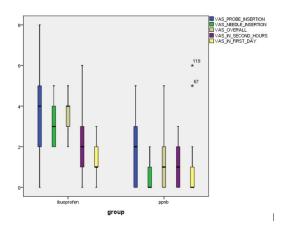


Fig. 1. Chartbox of VAS overall scores according to groups. VAS, Visual Analog Scale; PPNB, periprostatic nerve block. Figure produced with SPSS version 26 (IBM Corp., Armonk, NY, USA). \* indicates outlier values.

ables. Frequencies and percentages were reported for categorical variables. An independent samples *t* test was used to analyze differences between groups for measurements that followed a normal distribution, whereas the Mann-Whitney test was used for variables that did not meet the assump-

SD, standard deviation; n, number; PSA, prostate specific antigen; BMI, body mass index; PI-RADS, Prostate Imaging-Reporting and Data System; CCI, Charlson Comorbidity Index; cc, cubic centimeter; IQR, interquartile range.

SD, standard deviation; n, number; IQR, interquartile range; CI, confidence interval.

Table 3. Evaluation of associaton between VAS overall score and variables.

		Group 1	Group 2
		VAS overall	VAS overall
A a	r	-0.088	0.042
$Age^a$	p	0.490	0.743
$PSA^b$	r	0.230*	0.080
roa-	p	0.024	0.531
Prostate_volume <sup>a</sup>	r	0.043	-0.118
	p	0.737	0.353
$BMI^b$	r	0.025	0.077
BMI	p	0.845	0.547
Dath ala ava	r	0.268*	0.035
Pathology <sup>a</sup>	p	0.032	0.784
DI D A Dah	r	0.192	-0.166
PI-RADS <sup>b</sup>	p	0.128	0.191
CCIA	r	0.203	-0.068
$CCI^a$	p	0.108	0.593

\*p < 0.05; a = Pearson's correlation test; b = Spearman's rank corellation test.

PSA, prostat spesific antigen; BMI, body mass index; PI-RADS, Prostate Imaging-Reporting and Data System; CCI, Charlson Comorbidity Index.

tions of normality. Although non-parametric tests were applied to compare non-normally distributed data, Cohen's d effect sizes were calculated using group means and pooled standard deviations to provide standardized estimates of between-group differences. The relationship between categorical variables was analyzed using the chi-squared test or Fisher's exact test. For normally distributed variables, Pearson's correlation test was used to examine relationships, whereas Spearman's correlation test was employed for variables that did not meet the assumption of normality. The effect of variables on the overall VAS score was analyzed using linear regression model with a forward selection. p value < 0.05 was accepted as statistically significant.

# Results

## Demographic and Clinical Characteristics

Mean age of the patients in Groups 1 and 2 were 64.68  $\pm$ 5.87 years, and 63.33  $\pm$  7.26 years (t (1.156), respectively (p = 0.267). The median (range) PSA levels of Groups 1 and 2 were, 13.00 (8.04-41.68) ng/mL and 10.00 (6.73-23.80) ng/mL (z (1641), respectively (p = 0.053). There were no statistically significant differences in prostate volume, BMI, PI-RADS score, benign or malignant pathology detected on histopathological examination of prostate biopsy samples (p = 0.245, p = 0.977, p = 0.906, and p = 0.9060.213, respectively). CCI scores in Group 1 were classified as 75% CCI 1, 20.3% CCI 2, and 4.7% CCI 3, whereas in Group 2, they were classified as 89.1% CCI 1, 6.3% CCI 2, and 4.7% CCI 3 ( $\chi^2 = 5.581$ , p = 0.067) (Table 1).

#### Pain Scores Across Different Stages

Statistically significant differences were found between the VAS scores of groups at each of the five stages (during probe insertion, during prostate needle insertion, overall, 2 hours after the procedure, and one day after the procedure). The VAS scores were lower in the PPNB group (p <0.001 for all stages) (Table 2, Fig. 1). Effect sizes and 95% confidence intervals (CI) were calculated to better interpret the differences in VAS scores between the two groups. Cohen's d values indicated a large effect size for most stages, particularly during probe needle insertion (d = 3.02, 95% CI: 2.44–3.59) and overall scores (d = 1.96, 95% CI: 1.54– 2.39). Moderate effect sizes were observed in probe insertion (d = 1.17, 95% CI: 0.79–1.54) and in the second hour after the procedure (d = 1.31, 95% CI: 0.98-1.64), while a small to moderate effect was found on the first day postprocedure (d = 0.66, 95% CI: 0.39–0.93). These results suggest a clinically meaningful difference between the two analgesic methods (Table 2).

#### Correlation Analyses

The study investigated the relationship between the overall VAS score and multiple variables, such as age, PSA, prostate volume, BMI, pathology results, PI-RADS score, and CCI. Analysis of Group 1 revealed a weak positive correlation between the overall VAS score and both PSA level and malignant pathology (r = 0.230, p = 0.024; r = 0.268, p = 0.032, respectively). In contrast, Group 2 showed no significant associations between the overall VAS score and any of the examined variables (Table 3).

## Regression Analyses

A forward regression model was employed to examine the influence of age, PSA value, prostate volume, BMI, pathology results, PI-RADS score, and CCI score on the overall VAS score in Group 1. The analysis revealed that PSA and malignant pathology were significant factors, with beta coefficients of 0.283 (p = 0.024) and 0.186 (p = 0.019), respectively. The overall VAS score increased in Group 1, which was influenced by elevated PSA values and malignant pathology. The level of effect of PSA on the overall VAS score was 8.0% and that of the malignant pathology was 6.4% (Table 4).

## Complication Rates

When evaluating complication rates, treatment-requiring hematuria, rectal bleeding, and hemospermia were not observed in either group. Treatment-requiring fever and prostatitis were not observed in Group 1, but were observed in two patients in Group 2 (p = 0.496).

#### **Discussion**

In our study, PPNB and IV ibuprofen were used to control pain during prostate biopsy, and VAS scores were found to be lower in the PPNB group (p < 0.001 for all parameters)

Table 4. Evaluation the regression analyzes of VAS overall and variables in Group 1.

Depended variable	Independed variable	Beta	t	p	$\mathbb{R}^2$
VAS overall	PSA	0.283	2.319	0.024*	0.080
	malignant pathology	0.186	2.07	0.019*	0.064

<sup>\*</sup>p < 0.05 linear regression test.

(Table 2). Although PPNB is considered the most effective method for pain control during procedures like biopsies, various analgesic agents, such as ibuprofen, have been explored as alternatives due to the need for additional intervention when administering a nerve block. In current study, the ibuprofen group exhibited higher VAS scores than the PPNB group, with measurements of 3 (2–4) during the TRUS-guided prostate biopsy procedure and 4 (3–4) overall. Despite these higher scores, patients in the ibuprofen group experienced only mild, manageable discomfort [12,13]. When reviewing previous studies, no data on the use of IV ibuprofen in transrectal biopsy procedures were found. Our study supports the use of IV ibuprofen for tolerable pain control during prostate biopsy.

Prostate biopsy can be performed through transperineal or transrectal route. Due to lower post-biopsy infection rates, transperineal prostate biopsy is preferred, whereas transrectal biopsy is recommended in clinical condition where transperineal biopsy cannot be performed. With the use of prostate mpMRI, a combined application of targeted and systematic biopsies is recommended [14]. In current study, transrectal biopsy was chosen for the patients, and a combination of cognitive targeted and systematic biopsies was performed.

Ibuprofen, like other non-steroidal anti-inflammatory drugs (NSAIDs), exhibits its analgesic effects by inhibiting the arachidonic acid-cyclooxygenase (COX) pathway [15]. Ibuprofen has a higher COX-2 inhibition than COX-1, resulting in fewer gastrointestinal side effects, while its antiinflammatory effect is more dominant among NSAID types [15,16]. In rats, IV ibuprofen reaches its maximum dose in prostate tissue 2 hours after administration and continues to have an effect on prostate tissue for up to 6 hours [17]. It has been found that the use of ibuprofen 400 mg provides effective analgesia, while increasing the dose up to 800 mg does not augment the analgesic effect but only prolongs the duration of analgesia [18]. Studies indicate that IV ibuprofen 400 mg can be administered as a rapid IV infusion, which has been shown to decrease renal blood flow. However, to minimize adverse reactions at the injection site, and maintain renal blood flow, administer of the medication over a duration of at least 30 minutes [19,20]. It is recommended to administer it over a period not less than 30 minutes to minimize injection site-related adverse reactions. Researches have suggests that the median onset of analgesic effect occurs approximately 32 minutes after administration of the medication at 30-minute IV infusion rates [20]. In current study, IV ibuprofen (400 mg/100 mL) was administered over a 30-minute period. After the infusion was finished, a 10-minute waiting period was implemented to allow the pain medication to become effective before proceeding with the biopsy procedure.

Pain during biopsy occurs during the insertion of the ultrasound probe into the rectum due to mechanical pressure on the unrelaxed anal sphincter and when the biopsy needle punctures the rectum and prostate capsule [21]. PPNB is the most effective method to alleviate pain, and studies have been conducted on intrarectal applications of alternative analgesics such as lidocaine, ketorolac, and diclofenac [22–24]. In a meta-analysis by Kim et al. [25], which included 14 prospective studies, pain scores were evaluated in patients undergoing prostate biopsy with TRUS guided intrarectal application of local anesthetic agents. Lidocaineprilocaine cream was used in 3, diclofenac sodium suppositories in 2, and lidocaine cream and lidocaine with PPNB in 9 studies. The study concluded that the VAS score in favor of PPNB was -1.373 (95% confidence interval -1.876 to -0.863) [25].

In a study examining the effect of systemic NSAID use on pain during TRUS-guided prostate biopsy, pain scores evaluated on a scale of 0 (no pain)-10 (severe pain) mean VAS scores of 2.24  $\pm$  1.63 in the PPNB group, 3.7  $\pm$  2.36 in the intramuscular diclofenac group, and  $5.10 \pm 3.14$  in the control group without analgesics [26]. The PPNB group of patients reported significantly lower intensity pain compared to both groups (p = 0.002 and p = 0.001, respectively); without any difference in the intensity of perceived pain between the diclofenac and control groups (p = 0.120) [26]. In a comparative study of oral 50 mg rofecoxib versus placebo applied during TRUS-guided prostate biopsy procedures, median VAS scores were similar in both groups (p = 0.3139) [27]. No adverse effects related to systemic NSAID use were reported in either study. In current study, the overall median VAS scores were 1 (0-2) in the PPNB and 4 (3-4) in the IV ibuprofen group. Similar to other studies using systemic NSAIDs, mild pain occurred in patients receiving IV ibuprofen during biopsy in present study. None of the patients experienced treatment-requiring side effects.

Pain during prostate biopsy is associated with various factors. Previous prostate biopsy, age, prostate volume and anorectal angle, type of enema used, and the number of biopsy cores obtained have been identified as factors influencing pain intensity felt during prostate biopsy [28,29]. Cebeci and Ozkan [28] demonstrated that malignant pathology results and more than 12 biopsy cores had a negative impact on pain. In a study by Han and Lee [29], an inverse correlation was found between perceived pain and the parameters of age, bowel preparation with enema, pre-

procedural analgesic application. Extended biopsies have also been found to increase pain severity. Since we routinely performed 12-core biopsies, the effect of the core number on pain could not be evaluated. Upon analyzing the groups separately, significant positive correlations emerged between PSA level, malignant pathology, and the overall VAS score (p < 0.05) in Group 1. In contrast, similar correlation were not observed in Group 2.

In the current study, PPNB application during TRUS guided prostate biopsy was more effective in achieving pain management than IV ibuprofen use (p < 0.001). However, in the IV ibuprofen group, the overall median VAS score was 4 (3-4), and it was 3 (2-4) during the puncture of the rectum and prostate by the biopsy needle. The observation of mild VAS scores with the use of IV ibuprofen, which has not been applied in any previous study, and the absence of any complications during TRUS-guided prostate biopsy demonstrated the feasibility of IV ibuprofen as an analgesic in our study.

In this study, while a statistically significant correlation was observed between PSA levels and VAS scores in Group 1, the correlation coefficient was relatively weak (r = 0.230, p= 0.024). This highlights the distinction between statistical significance and clinical relevance. While the correlation indicates a potential relationship, the strength of the association may not be sufficient to imply meaningful clinical implications. It is possible that other unmeasured factors, such as individual pain thresholds or psychological components, may play a more substantial role in influencing pain perception. Future studies should aim to explore these variables further to better understand the factors contributing to pain during prostate biopsy.

Although the study acknowledges its limitations, such as the absence of an analgesic-free control group, the inability to conduct a blinded trial due to differing administration techniques, and reliance on a subjective pain assessment scale, these factors may influence the interpretation of our findings. For example, the lack of a control group prevents a comprehensive comparison to standard care or no intervention, which could have provided additional context for the efficacy of IV ibuprofen. Similarly, the subjective nature of the VAS scores introduces potential bias, as pain perception can vary significantly between individuals. These limitations should be taken into account when considering the clinical applicability of IV ibuprofen as an alternative analgesic. Future studies incorporating objective measures of pain and a broader range of control conditions could help validate and refine these findings.

## **Conclusions**

Our study revealed that adequate pain management can be achieved during transrectal prostate biopsy procedures performed with the aid of ultrasound guidance by administering IV ibuprofen. In patients who do not desire or cannot tolerate PPNB, the use of IV ibuprofen can be shown as

an alternative, easily applicable analgesic method in office urology. Larger-scale comprehensive studies are required to confirm the findings of the present study.

## Availability of Data and Materials

The data are freely available upon reasonable request from the corresponding author.

## **Author Contributions**

MB and ES designed the research study. MB and ES performed the research. MB analyzed the data. ES drafted this manuscript. Both authors contributed to important editorial changes in the manuscript. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

# **Ethics Approval and Consent to Participate**

This study was approved by the ethics committee of Gaziantep University (decision no: 2023/51) and was performed in accordance with the ethical standards laid down in the 2013 Declaration of Helsinki and its later amendments. All eligible participants signed an informed consent form. Informed con-sent was obtained from each study participant.

## Acknowledgment

Not applicable.

## **Funding**

This research received no external funding.

#### **Conflict of Interest**

The authors declare no conflict of interest.

#### References

- [1] Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a Cancer Journal for Clinicians. 2024; 74: 229-263. https: //doi.org/10.3322/caac.21834.
- [2] Mottet N, van den Bergh RCN, Briers E, Van den Broeck T, Cumberbatch MG, De Santis M, et al. EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer-2020 Update. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent. European Urology. 2021; 79: 243-262. https://doi.org/10.1016/j.eururo.2020.09.
- [3] Nguyen CT, Gao T, Hernandez AV, Jones JS. Can residents perform transrectal ultrasound-guided prostate biopsy with patient comfort comparable to biopsy performed by attending staff urologists? Prostate Cancer and Prostatic Diseases. 2010; 13: 52-57. https: //doi.org/10.1038/pcan.2009.36.
- [4] Giannarini G, Autorino R, Valent F, Mogorovich A, Manassero F, De Maria M, et al. Combination of perianal-intrarectal lidocaineprilocaine cream and periprostatic nerve block for pain control during transrectal ultrasound guided prostate biopsy: a randomized, controlled trial. The Journal of Urology. 2009; 181: 585-585-91; discussion 591-3. https://doi.org/10.1016/j.juro.2008.10.002.

- [5] Wang J, Wang L, Du Y, He D, Chen X, Li L, et al. Addition of intrarectal local analgesia to periprostatic nerve block improves pain control for transrectal ultrasonography-guided prostate biopsy: a systematic review and meta-analysis. International Journal of Urology: Official Journal of the Japanese Urological Association. 2015; 22: 62–68. https://doi.org/10.1111/iju.12595.
- [6] Sonmez G, Tombul ST, Demirtas T, Demirtas A. Risk factors associated with pain in fusion prostate biopsy. Prostate International. 2020; 8: 185–189. https://doi.org/10.1016/j.prnil.2020.05.004.
- [7] Bastide C, Lechevallier E, Eghazarian C, Ortega JC, Coulange C. Tolerance of pain during transrectal ultrasound-guided biopsy of the prostate: risk factors. Prostate Cancer and Prostatic Diseases. 2003; 6: 239–241. https://doi.org/10.1038/sj.pcan.4500664.
- [8] Charlson ME, Sax FL, MacKenzie CR, Fields SD, Braham RL, Douglas RG, Jr. Assessing illness severity: does clinical judgment work? Journal of Chronic Diseases. 1986; 39: 439–452. https://doi.org/10.1016/0021-9681(86)90111-6.
- [9] Hadjipavlou M, Eragat M, Kenny C, Pantelidou M, Mulhem W, Wood C, et al. Effect of Augmented Antimicrobial Prophylaxis and Rectal Swab Culture-guided Targeted Prophylaxis on the Risk of Sepsis Following Transrectal Prostate Biopsy. European Urology Focus. 2020; 6: 95–101. https://doi.org/10.1016/j.euf.2018.06.016.
- [10] Lim LY, Tan GH, Zainuddin ZM, Fam XI, Goh EH, Syaris OS, et al. Prospective evaluation of using multiparametric magnetic resonance imaging in cognitive fusion prostate biopsy compared to the standard systematic 12-core biopsy in the detection of prostate cancer. Urology Annals. 2020; 12: 276–282. https://doi.org/10.4103/UA.UA\_98\_19.
- [11] Campbell WI, Lewis S. Visual analogue measurement of pain. The Ulster Medical Journal. 1990; 59: 149–154.
- [12] Mazdak H, Abtahi AM, Momeni F, Izadpanahi MH. A comparison of pain control and complications using three different ways of anesthesia in patients undergoing transrectal ultrasound-guided prostate biopsy. Journal of Research in Medical Sciences: the Official Journal of Isfahan University of Medical Sciences. 2018; 23: 17. https://doi.org/10.4103/jrms.JRMS\_639\_17.
- [13] Adamakis I, Mitropoulos D, Haritopoulos K, Alamanis C, Stravodimos K, Giannopoulos A. Pain during transrectal ultrasonography guided prostate biopsy: a randomized prospective trial comparing periprostatic infiltration with lidocaine with the intrarectal instillation of lidocaine-prilocain cream. World Journal of Urology. 2004; 22: 281–284. https://doi.org/10.1007/s00345-003-0386-4.
- [14] Drost FJH, Osses DF, Nieboer D, Steyerberg EW, Bangma CH, Roobol MJ, et al. Prostate MRI, with or without MRI-targeted biopsy, and systematic biopsy for detecting prostate cancer. The Cochrane Database of Systematic Reviews. 2019; 4: CD012663. https://doi.org/10.1002/14651858.CD012663.pub2.
- [15] Vane JR, Botting RM. Mechanism of action of nonsteroidal antiinflammatory drugs. The American Journal of Medicine. 1998; 104: 2S-2S-8S; discussion 21S-22S. https://doi.org/10.1016/ s0002-9343(97)00203-9.
- [16] Ratliff TL. Aspirin, ibuprofen, and other non-steroidal anti-inflammatory drugs in cancer prevention: a critical review of non-selective COX-2 blockade (review). The Journal of Urology. 2005; 174: 787–788. https://doi.org/10.1016/s0022-5347(01)68393-9.
- [17] Yellepeddi VK, Radhakrishnan J, Radhakrishnan R. Penetration and pharmacokinetics of non-steroidal anti-inflammatory drugs in rat prostate tissue. The Prostate. 2018; 78: 80–85. https://doi.org/10. 1002/pros.23447.
- [18] Lyngstad G, Skjelbred P, Swanson DM, Skoglund LA. Analgesic effect of oral ibuprofen 400, 600, and 800 mg; paracetamol 500 and 1000 mg; and paracetamol 1000 mg plus 60 mg codeine in acute postoperative pain: a single-dose, randomized, placebo-

- controlled, and double-blind study. European Journal of Clinical Pharmacology. 2021; 77: 1843–1852. https://doi.org/10.1007/s00228-021-03231-9.
- [19] Shen Y, Nan F, Li M, Liang M, Wang Y, Chen Z, et al. Pharmacokinetic Properties of Intravenous Ibuprofen in Healthy Chinese Volunteers. Clinical Drug Investigation. 2016; 36: 1051–1058. https://doi.org/10.1007/s40261-016-0453-4.
- [20] Bookstaver PB, Miller AD, Rudisill CN, Norris LB. Intravenous ibuprofen: the first injectable product for the treatment of pain and fever. Journal of Pain Research. 2010; 3: 67–79. https://doi.org/10. 2147/jpr.s6993.
- [21] Nazir B. Pain during transrectal ultrasound-guided prostate biopsy and the role of periprostatic nerve block: what radiologists should know. Korean Journal of Radiology. 2014; 15: 543–553. https://doi. org/10.3348/kjr.2014.15.5.543.
- [22] Senturk AB, Yaytokgil M, Ekici M, Sari S, Demir E, Çakiroglu B. Comparing use of lidocaine periprostatic nerve block and diclofenac suppository alone for patients undergoing transrectal ultrasound guided prostate biopsy. Central European Journal of Urology. 2018; 71: 38–42. https://doi.org/10.5173/ceju.2017.1381.
- [23] Bolat D, Degirmenci T, Gunlusoy B, Aydin E, Aydogdu O, Ceylan Y. A Novel Pain Alternative for Patients with Anorectal Pathologies: The Comparison of Transperineal Prostatic Blockage Technique with Periprostatic Nerve Blockage and Rectal Gel Technique in Initial Transrectal Ultrasound-Guided Prostate Biopsy A Prospective, Randomized Trial. Urologia Internationalis. 2016; 97: 416–420. https://doi.org/10.1159/000448337.
- [24] Cormio L, Pagliarulo V, Lorusso F, Selvaggio O, Perrone A, Sanguedolce F, et al. Combined perianal-intrarectal (PI) lidocaine-prilocaine (LP) cream and lidocaine-ketorolac gel provide better pain relief than combined PI LP cream and periprostatic nerve block during transrectal prostate biopsy. BJU International. 2012; 109: 1776–1780. https://doi.org/10.1111/j.1464-410X.2011.10622.x.
- [25] Kim DK, Lee JY, Jung JH, Hah YS, Koo KC, Lee KS, et al. What is the most effective local anesthesia for transrectal ultrasonographyguided biopsy of the prostate? A systematic review and network meta-analysis of 47 randomized clinical trials. Scientific Reports. 2019; 9: 4901. https://doi.org/10.1038/s41598-019-41412-w.
- [26] Bhomi KK, Lim HH, Consigliere DT, Tiong HY. Control of pain during transrectal ultrasound-guided prostate biopsy: a prospective study comparing two methods. Urologia Internationalis. 2007; 79: 332–335. https://doi.org/10.1159/000109719.
- [27] Moinzadeh A, Mourtzinos A, Triaca V, Hamawy KJ. A randomized double-blind prospective study evaluating patient tolerance of transrectal ultrasound-guided biopsy of the prostate using prebiopsy rofecoxib. Urology. 2003; 62: 1054–1057. https://doi.org/10.1016/s0090-4295(03)00788-x.
- [28] Cebeci OÖ, Ozkan A. An evaluation of factors affecting pain during transrectal ultrasonographic prostate biopsy: a real-life scenario in a retrospective cohort study. PeerJ. 2021; 9: e12144. https://doi.org/ 10.7717/peerj.12144.
- [29] Han KS, Lee KH, Korean Urologic Oncology Society Prostate Cancer Study Group. Factors influencing pain during transrectal ultrasonography-guided prostate biopsy. Prostate Cancer and Prostatic Diseases. 2008; 11: 139–142. https://doi.org/10.1038/sj.pcan. 4501004.

© 2025 The Author(s).

