

# Comparing use of lidocaine periprostatic nerve block and diclofenac suppository alone for patients undergoing transrectal ultrasound guided prostate biopsy

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**Introduction** The objective of this study is to make a comparison between the effectiveness of the diclofenac suppository alone and periprostatic local anaesthesia infiltration alone to reduce the pain during a transrectal ultrasound-guided prostate biopsy procedure.

**Material and methods** Between January 2014 and December 2015, 100 patients from two centres who were scheduled for transrectal ultrasound guided prostate biopsy (TRUS Bx) were included in the study. Patients were divided into two groups; diclofenac suppository group (Group 1) and Lidocaine group (Group 2). After the prostate biopsy, patients were requested to fill out a visual analogue scale in order to evaluate their pain level during the procedure.

**Results** Since each group had been examined for VAS score, statistical differences were detected for VAS 0 and VAS 1. VAS 0 score was stated in 38 (71%) patients in Group 2, and in 25 (50%) patients in Group 1 ( $p = 0.040$ ). VAS 1 score was stated in 9 (17%) patients in group 2 and 19 (38%) patients in Group 1 ( $p = 0.030$ ).

**Conclusions** Although statistical difference was detected at lower VAS scores (0 and 1) in favor of the lidocaine group during transrectal ultrasound guided prostate biopsies, there was not a significant difference in higher ( $>2$ ) VAS scores; which was made with 100 mg of diclofenac suppository. Therefore, diclofenac suppository can be used as an alternative to periprostatic nerve block made with lidocaine.

**Key Words:** prostate ↔ biopsy ↔ transrectal ↔ diclofenac ↔ pain

## INTRODUCTION

Transrectal prostate biopsy is the existing diagnostic procedure for the identification of prostate cancer. In the beginning, this procedure was carried on with the transperineal method. Later, the transrectal method was preferred. In 1989, core biopsies having at least 10 pieces replaced the sextant biopsy concept: which was identified primarily by Hodge et al. [1]. Despite developing technology, pain control during prostate biopsy procedure is usually required.

The pain during the procedure originates from the movement of the transrectal ultrasound probe towards the prostate capsule and rectal wall, and from the tissues while the sample from the prostate is being removed. This procedure is generally performed in an outpatient clinic. To reduce the pain, different methods of anaesthesia are applied, varying from regional anaesthesia to systematic analgesia. Although every method has specific advantages, there is no consensus on which analgesia method is the best. However, there is a considerable number of patients

complaining about pain during the procedure. Despite the application of local anaesthesia, 65–90% of patients complain about varying degrees of discomfort, from uneasiness to intense pain [2]. It is reported that, pain during the prostate biopsy is derived from the needle stimulating sensory nerves in the prostate capsule and the parenchyma in the course of its insertion into the prostate capsule through the rectum [3].

The most common preferred anaesthetic methods are the utilization of intrarectal gel application or periprostatic local anaesthesia infiltration alone, or the combination of these two methods. In addition to these, suppository painkillers are also used separately or in combination with other methods. Nevertheless, there is no such study which compares the applications of periprostatic local anaesthesia and diclofenac suppository alone to reduce pain during prostate biopsy.

The aim of this study is to make a comparison between the effectiveness of the utilization of diclofenac suppository alone and periprostatic local anaesthesia infiltration to reduce pain during prostate biopsy procedure which is accompanied by transrectal ultrasound guidance.

## MATERIAL AND METHODS

Between January 2014–December 2015, due to PSA increase and/or abnormal rectal examination, 100 patients from two centres who were scheduled for transrectal ultrasound guided prostate biopsy (TRUSBx) were included in the study. Detailed medical history was collected from all patients and physical examinations were done. Patients who had abnormal rectal examination and PSA value higher than 2.5 ng/ml were included in the study. Patients were informed about the procedure and their written permission was taken. Patients who were allergic to lidocaine or non-steroidal anti-inflammatory drugs, who had a history of acute prostatitis, gastrointestinal ulcer or anorectal surgery, and those who had second TRUS biopsies because of their high or rising PSA, were excluded from the study. On the day before the prostate biopsy procedure, patients were started on 500 mg of ciprofloxacin orally twice a day for antibiotic prophylaxis, and it was continued for two more days after the procedure. A rectal enema was used one hour before the biopsy for rectal cleaning. Patients were divided in two groups, Group 1 (diclofenac suppository) and Group 2 (periprostatic lidocaine infiltration). Group 1 had a 100 mg Diclofenac suppository introduced one hour before the biopsy. Group 2 was given 10 cc of 1% Lidocaine with an 18 g Chiba needle

to both periprostatic areas in the lateral decubitus position, with the guidance of an ultrasound probe. One hour after the application of either drug, a 12 piece core biopsy, six specimens from each lobe, were taken from the base, apex and middle zones of the prostate using disposable prostate needles. After the prostate biopsy, patients were requested to fill the visual analogue scale to evaluate the pain level during the procedure. The visual analogue scale represents the severity of pain on a 10-cm line, with zero expressing no pain at all, and 10 being pain so severe that it cannot be withstood. All patients were asked to wait for at least two hours after the procedure, and were examined for any kind of acute complications. Patients without any complaints and who were urinating normally were sent home. In case of necessity, patients were recommended to use analgesic and anti-inflammatory drugs. All patients included in the study were invited back to the hospital two weeks after the procedure to discuss biopsy results and were simultaneously re-evaluated with regard to late complications, such as, hematospermia and persistent hematuria.

## Statistical analysis

The data was analysed with SPSS (Version 22.0, SPSS Inc., Chicago, IL, USA). Descriptive statistics with a normal distribution were presented as a mean  $\pm$  standard deviation; those with a non-normal distribution were presented as median; and ordinal variables were presented as number of cases and percentage (%). Normality distributions of the groups were evaluated with Shapiro-Wilk normality tests. To evaluate the homogeneity of variance, we used Levene's test. The significances of the difference between the two independent groups were evaluated by using an independent sample T-test in case of normally distributed data and Mann-Whitney U Test in case of data that was not normally distributed. We also used chi-square test to compare the proportion of visual analogue scale (VAS) scores. P value  $<0.05$  was considered statistically significant.

## RESULTS

103 patients, between the ages of 49 and 82, underwent transrectal ultrasound guided prostate biopsy. The average age was found  $64.14 \pm 6.7$  in the Diclofenac suppository group (Group 1) and  $64.98 \pm 7.6$  in the Lidocaine group (Group 2). There was no statistically significant difference between the two groups regarding age ( $p = 0.557 > 0.05$ ). The average PSA value was calculated as  $16.16 \pm 31.7$  for Group 1 and  $30.92 \pm 35$  for Group 2. Statistical dif-

ference regarding PSA values were detected between the two groups ( $p = 0.027 < 0.05$ ).

The average prostate volume was calculated as  $51.34 \pm 19.15$  for Group 1 and  $56.1 \pm 18.67$  for Group 2 ( $p = 0.081 > 0.05$ ). There is no significant difference regarding prostate volume between the two groups. Table 1. Descriptive statistics of Group 1 and Group 2

Since two groups had been examined in terms of VAS score, statistical difference was detected for VAS 0 and VAS 1. A VAS 0 value was stated by 38 (71%) patients in Group 2, and by 25 (50%) patients in Group 1 ( $p = 0.040$ ). A VAS score of 1 was stated by 9 (17%) patients in Group 2 and by 19 (38%) patients in Group 1 ( $p = 0.030$ ). When all patients were evaluated, the maximum VAS score identified was 5 (Tables 2 and 3).

## DISCUSSION

For prostate cancer diagnosis, the current standard method is taking a core biopsy from prostate tissue by transrectal ultrasound guidance. During this procedure, which can be very painful, many topical analgesics, such as lignocaine gel, glyceryl trinitrate and analgesia methods, such as an eutectic mixture of local anaesthetics (EMLA) cream, intravenous or inhalation anaesthesia, periprostatic nerve block, and oral or intrarectal analgesics are used [4, 5].

In a study made by Irani J et al., it is reported that 19% of patients are not willing to undergo a repeat biopsy in cases where no analgesia is applied [6].

Generally during a biopsy, a periprostatic nerve block is applied with local anaesthetic agents to control the pain. Also, intravenous sedation

**Table 1.** Descriptive statistics of Group 1 (diclofenac – D) and Group 2 (lidocaine – L)

Diclofenac-lidocaine	N (D/L)	Minimum (D/L)	Maximum (D/L)	Mean (D/L)	Std. Deviation (D/L)
Age	50 / 53	49 / 50	78 / 82	64.14 / 64.98	6.77 / 7.640
PSA	50 / 53	3.10 / 3.30	200.00 / 144.0	16.16 / 30.92	31.70 / 35.07
Prostate Volume	50 / 53	20 / 30	110 / 145	51.34 / 56.10	19.15 / 18.67

**Table 2.** Visual Analogue Scale Group Cross tabulation

		Group		p
		lidocaine	diclofenac	
0	Count	38	25	0.040*
	% within Group	71.7%	50.0%	
1	Count	9	19	0.030*
	% within Group	17.0%	38.0%	
2	Count	5	0	–
	% within Group	9.4%	0.0%	
3	Count	1	4	–
	% within Group	1.9%	8.0%	
5	Count	0	2	–
	% within Group	0.0%	4.0%	
Total	Count	53	50	–
	% within Group	100.0%	100.0%	

**Table 3.** Visual analogue scale for diclofenac (D) and lidocaine (L)

	Frequency (D/L)	Percent (D/L)	Valid Percent (D/L)	Cumulative Percent (D/L)
VAS 0	25/38	50.0/71.7	50.0/71.7	50.0/71.7
VAS 1	19/9	38.0/17.0	28.0/17.0	88.0/88.7
VAS 2	0/5	0/9.4	0/9.4	0/98.1
VAS 3	4/1	8.0/1.9	8.0/1.9	96.0/100.0
VAS 5	2/0	4.0/0	4.0/0	100.0/0
Total	50/53	100.0/100.0	100.0/100.0	

or diclofenac suppository in addition to a periprostatic nerve block is used, depending on the clinician's choice. The autonomic nerve fibres of the prostate originate from the inferior hypogastric plexus. The nerves innervating the prostate arrive to the prostatic tissue passing from the prostate capsule and outside of the Denonvillier's fascia. The prostatic capsule is surrounded with many nerve fibres and ganglions. This is named plexus prostaticus or plexus periprostaticus [7].

The pain felt during a prostate biopsy is due to the stimulation of the sensory nerves in the prostate capsule and the parenchyma caused by the movement of the needle passing through the rectal wall and penetrating the prostate capsule during the procedure [3].

All anaesthesia methods aimed at reducing the pain during prostate biopsy are based on desensitization of these nerve fibres. Therefore, because the prostate tissue includes a visceral nerve source, systematic anti-inflammatory drugs and various forms of diclofenac can be useful for these patients [8].

Although there is not a consensus on the amount of core that should be taken for diagnosis during a prostate biopsy, the most widely accepted view is to take at least eight core biopsies. Taking fewer cores may cause insufficient diagnosis and taking more may cause increase in the complication ratio after the procedure. In this study, we compared the effectiveness of using a diclofenac suppository alone and a periprostatic nerve block using lidocaine as a local anaesthetic agent, during transrectal ultrasound guided prostate biopsy.

Since diclofenac is a cyclooxygenase inhibitor, it can be used as a systemic or local agent. Oral suppository and injection forms are available. Analgesic, antipyretic and anti-inflammatory effects demonstrate themselves by inhibiting prostaglandin synthesis [9]. Peak concentrations are reached in about 30 to 60 minutes after the introduction of the diclofenac suppository in adults, but this could take longer with oral administration [9]. Therefore, utilization of the suppository form is more effective and convenient to prevent and eliminate the pain acutely. In our study, we applied the diclofenac suppository to our patients intrarectally one hour before the procedure. We did not encounter any problems during the application of the diclofenac suppository and there was no feedback reporting that the patients in the diclofenac suppository group did not want to use the drug.

During TRUS guided prostate biopsy, utilization of diclofenac suppository intrarectally in addition to a prostatic nerve block which is applied with local anaesthetic agents is evaluated in various studies.

Published studies on this issue show that this combination is reliable and effective in decreasing the pain during the prostate biopsy. There was no difference detected between the two groups regarding complications [8, 10].

In a study made by Adiyat et al., it was reported that diclofenac suppository or diclofenac patches could be used as complementary treatment [11]. Another study made by Ooi et al. states that this combination does not provide any specific reduction in pain nor it does improve the tolerability of the procedure [4].

In a study made by Batch T and Tauber R, in which the utilization of diclofenac suppository in addition to intrarectal lidocaine gel was compared to placebo, regarding their effectiveness to prevent pain, it was stated that the patients in the diclofenac suppository group showed lower pain scores than the ones in the placebo group [12].

In another study, in which patients were given a  $\pm 100$  mg diclofenac suppository in addition to 10 ml 2% lidocaine gel application one hour before the procedure, it was reported that the pain score was statistically lower than the patients in the control group who were given intrarectal glycerine ( $3.4 \pm 1.3$  versus  $5.9 \pm 1.7$   $p < 0.0001$ ). They also remarked that intrarectal diclofenac suppository application is a simple, safe and reliable method in reducing pain and developing patient tolerance during a transrectal prostate biopsy [13].

In a randomized study made by Haq et al., which compared diclofenac suppository and placebo during prostate biopsy, it was remarked that the diclofenac suppository, which had been applied one hour before the procedure, provided more relief as compared to the placebo and had a VAS score of 2.8 [14].

We also did not detect any difference regarding pain levels between the two groups. As it can be seen in the table, even the ratio of the patients having VAS scores of 3 or less in the group of periprostatic nerve block with lidocaine was 98.1%, while the ratio in the Diclofenac suppository group was 96%.

No differences regarding side effects such as hematuria, hematospermy and rectal bleeding were detected between the two groups. Three patients were catheterized due to globe vesical, which developed after the procedure. Two of these patients were in the diclofenac suppository group and the other was in the periprostatic nerve group. All three patients were discharged after conservative treatment. One patient, who received a periprostatic nerve block, had been hospitalized because of high fever. He recovered well after treatment. No life threatening infective complications were encountered.

After periprostatic nerve block, haemorrhagic and infectious complications rarely occur [15]. In a study made by Turgut et al., it was reported that the complication incidence related to local anaesthesia infiltration is 2% [16].

In a study made by Song et al., it was stated that patients had syncope with a ratio of 1% after the periprostatic nerve block [17]. Another study from Sen et al. reported that syncope developed in only one patient (1.6%) [15].

Although statistical differences were detected at lower VAS scores (0 and 1) in favor of the lidocaine group during transrectal ultrasound guided prostate biopsies, there was no significant difference in higher (>2) VAS scores between two groups. Therefore,

we are under the opinion that a diclofenac suppository can be used as an alternative to a periprostatic nerve block made with lidocaine.

## CONCLUSIONS

In transrectal ultrasound guided prostate biopsy, a 100 mg intrarectal diclofenac suppository showed similar analgesic effects as a periprostatic nerve block which with 10 cc of 1% lidocaine. Introduction of a 100 mg intrarectal diclofenac suppository was well tolerated by patients and no side effects of the drug were encountered.

## CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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