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

[Author's unedited version]

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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 with TRUS Bx decision 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 groups has been examined for VAS score, statistical differences was 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 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.

INTRODUCTION

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Transrectal prostate biopsy is the existing diagnostic procedure for the identification of prostate cancer. In the beginning this procedure was carried on with transperineal method. Later on transrectal method was preferred. In 1989, core biopsies having at least 10 pieces replace the sextant biopsy concept: which was identified primarily by Hodge et al. [1]. Despite developing technology, it is usually required to make a pain control during prostate biopsy procedure. The pain during the procedure originate from the movement of the transrectal ultrasound probe towards the prostate capsule and rectal wall and also from tissues while they are removing from the prostate. This procedure is generally performed at outpatient clinic. In order to reduce the pain, different methods of anaesthesia are applied varying from local regional anaesthesia to systematic analgesia. Although every method has specific advantages, there is no consensus on which analgesia method is best . However, there is a considerable number of patients complaining about pain during 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 derives 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 and periprostatic local anaesthesia infiltration alone or 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, as a result of PSA increase and/or abnormal rectal examination, 100 patients from two centres with the TRUS Bx decision were included in the study. Detailed medical history was collected from all patients and their physical examinations were done. Patients who had abnormal rectal examination and PSA value higher than 2.5 ng/ml were included into the study. Patients were informed about the procedure and their written permission was taken. Patients who were allergic to lidocaine or non-steroidal antiinflammatory drugs, who had a history of acute prostatitis, gastrointestinal ulcer and anorectal surgery and 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 started to take 500 mg of ciprofloxacin orally twice a day for antibiotic prophylaxis and it was continued for two more days after the procedure. 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 was orally intrarectally applied 100 mg of Diclofenac suppository one hour before the biopsy procedure. Group 2 was applied 10 cc 1% of Lidocaine with 18 g. Chiba needle to both periprostatic areas in the lateral decubitus position, with the guidance of ultrasound probe . One hour after the application of both two drugs, 12 pieces of core biopsy, six from each lobe, were taken from basic, apex and middle zones of prostate by using disposable prostate needles. After the prostate biopsy, patients were requested

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to fill the visual analogue scale in order to evaluate the pain level during the procedure. Visual analogue scale shows the patient points to the severity of his or her pain on a 10-cm line, that zero expresses no pain at all, and the other hand, 10 is so severe that they cannot withstand. All patients were asked to wait at least for 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 to the hospital after two weeks from the procedure in order to evaluate about biopsy results and they were also re-evaluated simultaneously with regard of late complications such as hematospermy and persistent hematuria.

Statistical analysis

Data were analysed with SPSS (Version 22.0, SPSS Inc., Chicago, IL, USA). Descriptive statistics with a normal distribution were presented as 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 independent samples T-test in case of normally distributed data and Mann-Whitney U Test in case of data were not normally distributed. Also we used chi-square test to compare the proportion of visual analogue scale (VAS). P value <0.05 was considered statistically significant.

RESULTS

103 patients, between ages 49 and 82, were applied transrectal ultrasound guided prostate biopsy. The average age was found 64.14 ± 6.7 in Diclofenac suppository group (Group 1) and 64.98 ± 7.6 in Lidocaine group (Group 2). There was not any difference determined statistically between two groups regarding age ($p = 0.557 > 0.05$).

The average PSA value was calculated as 16.16 ± 31.7 for Group 1 and 30.92 ± 35 for Group 2. Statistical difference regarding PSA values were detected between two groups ($p = 0.027 < 0.05$).

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

Table 1. Descriptive statistics of Group 1 and Group 2

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

Table 2. VAS Group Cross tabulation

Table 3. VAS for Diclofenac and Lidocaine

DISCUSSION

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For prostate cancer diagnosis, the current standard method is taking core biopsy from prostate tissue with 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 eutectic mixture of local anaesthetics (EMLA) cream, intravenous or inhalation anaesthesia, periprostatic nerve block and oral or intrarectal analgesics are researched [4, 5].

In a study made by Irani J et al., it is reported that 19% of patients are not willing to a repeating biopsy procedure in case not any analgesia is applied [6].

Generally during biopsy procedure periprostatic nerve block is applied with local anaesthetic agents to control the pain. Also intravenous sedation or diclofenac suppository in addition to periprostatic nerve block is used depending on the clinician's choice. The autonomic nerve fibres of prostate are originated from inferior hypogastric plexus. The nerves innervating the prostate arrive to the prostate tissue passing from prostate capsule and outside of the Denonvillier's fascia. Prostatic capsule is surrounded with many nerve fibres and ganglions. This is named as plexus prostaticus or plexus periprostaticus [7].

The pain felt during prostate biopsy procedure 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 rectal wall and penetrating the prostate capsule during prostate biopsy procedure [3].

All anaesthesia methods aiming to reduce the pain during prostate biopsy are based on desensitization of these nerve fibres. Therefore, because the prostate tissue includes 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 during prostate biopsy for diagnosis, 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 complication ratio after the procedure. In this study, we compared the effectiveness of using diclofenac suppository alone and periprostatic nerve block formed by using lidocaine as local anaesthetic agent, during transrectal ultrasound guided prostate biopsy.

Since diclofenac is a cyclooxygenase inhibitory, 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]. The duration of diclofenac suppository to the maximum concentration is from 30 to 60 minutes in adults, but this could take longer with oral administration [9]. Therefore, utilization of suppository form is more effective and convenient to prevent and eliminate the pain acutely. In our study, we applied diclofenac suppository to our patients intrarectally one hour before the prostate biopsy procedure. We haven't encountered any problems during application of diclofenac suppository and there was not any 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 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 procedure. There was not any difference detected between the two groups regarding complications [8, 10].

As a result of a study made by Adiyat et al., it was reported that diclofenac suppository or diclofenac patches could be used as complementary treatment [11]. Also in a study made by

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Ooi et. al. states that this combination does not provide any specific reduce in pain clinically nor it does not improve the tolerability of the procedure [4].

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

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

In a randomized study made by Haq et al., which was comparing 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 compared to the placebo and there was 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 on 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%, besides this ratio in Diclofenac suppository group was 96%.

Not any kind of differences regarding side effects such as hematuria, hematospermy and rectal bleeding were detected between the two groups. Three patients were catheterized because of globe vesicale which was developed after the procedure. Two of these patients were in diclofenac suppository group and the other was in periprostatic nerve group. All three patients were discharged after the conservative treatment. One patient who was applied periprostatic nerve block had been hospitalized because of high fever. He recovered well after treatment. Not any kind of life threatening infective complications were encountered.

After periprostatic nerve block, haemorrhagic and infectious complications could rarely occur [15]. In a study made by Turget et al., it was reported that, the complication incidence is 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 [1]. Also a study from Sen et al. reported that syncope was developed only in one patient (1.6%) [15].

Although statistical differences were detected at lower VAS scores (0 and 1) in favor of lidocaine group during transrectal ultrasound guided prostate biopsies, there was not a significant difference in higher (>2) VAS scores between two groups. Therefore, we have the opinion that diclofenac suppository can be used as an alternative to periprostatic nerve block made with lidocaine.

CONCLUSIONS

In transrectal ultrasound guided prostate biopsy, 100 mg of intrarectal diclofenac suppository showed similar analgesic effects to the periprostatic nerve block which is made by 10 cc 1% lidocaine. Application of 100 mg. of intrarectal diclofenac suppository was well tolerated by patients and any side effect of the drug was not encountered.

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Conflicts of interest

The authors declare no conflicts of interest.

Table 1. Descriptive statistics of group 1 (Diclofenac) and group 2 (lidocaine)

| 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. VAS Group Cross tabulation

| | | Group | | p |
|-------|----------------|----------|------------|--------|
| | | lidocain | 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 | 0.325 |
| | % 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. VAS for diclofenac and lidocain

| | 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 | |

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