



Three different techniques for administering analgesia during transrectal ultrasound-guided prostate biopsy: a comparative study

Volkan Izol, Bulent Soyupak, Gulsah Seydaoglu, I. Atilla Aridogan, Zuhtu Tansug

Department of Urology (VI, BS, IAA, ZT) and Biostatistics (GS), University of Cukurova, Faculty of Medicine, Adana, Turkey

ABSTRACT

Purpose: The efficacy of three different analgesic techniques during transrectal ultrasound (TRUS) guided prostate biopsy, including (i) periprostatic blockage (PPB), (ii) intrarectal gel instillation, and (iii) sedoanalgesia were compared.

Material and Methods: During a period of five months, 100 consecutive men were enrolled in this study. A 10-point linear visual analogue scale (VAS) was used to assess the pain scores during (VAS 1), immediately after (VAS 2) and one hour after (VAS 3) the needle biopsy procedure. The relationship between the level of pain, prostate volume, age and PSA was determined.

Results: There were no statistically significant differences between the four groups in terms of mean age and PSA values. The pain scores were significantly lower in sedoanalgesia and PPB groups ($p = 0.0001$). There was no statistically significant difference between the groups in terms of complications.

Conclusions: In this study, it was shown that patient comfort is better and it is possible to get decreased pain scores with PPB or sedoanalgesia. However, PPB is a preferable method in TRUS-guided prostate biopsy since it is much more practical in outpatient clinics.

ARTICLE INFO

Key words:

Prostate; neoplasms; biopsy

Int Braz J Urol. 2012; 38: 122-128

Submitted for publication:
April 28, 2011

Accepted after revision:
July 27, 2011

INTRODUCTION

Transrectal ultrasound (TRUS)-guided prostate biopsies have become widespread, and they are the most reliable method for the diagnosis of prostate cancer following the determination of abnormal prostate-specific antigen (PSA) levels and the routine use of PSA measurements in conjunction with a digital rectal examination (DRE). Today, debate continues about the need for analgesia and the technique used for administration (1-3). TRUS-guided prostate biopsy is a gold standard for diagnosing prostate cancer in patients at high risk of the disease (4,5). The

description provided by a sextant biopsy with TRUS guidance and the development of other biopsy techniques make this method crucial for histopathological diagnosis (3). Although TRUS-guided prostate biopsy is a common procedure, there is no standard guideline or protocol for the preparation of the patient.

There is pain and discomfort in patients undergoing this procedure when performed without using analgesia or anaesthesia. Consequently, patient-doctor compliance can be damaged, which could cause retrieval of an insufficient biopsy specimen from the incorrect location (2-4). The pain usually occurs during placement of the

probe into the anal canal, during the movement of the probe inside, and during retrieval of the biopsy by needle (1-5). An analgesic and anaesthetic protocol should be implemented to enhance the patient's adaptation to the procedure and to decrease their pain. There are several different approaches that can be used for this purpose, including a rectal gel with lidocaine or with lidocaine-prilocaine, a lidocaine suppository, a periprostatic nerve blockage, a pudendal block, nonsteroidal anti-inflammatory drugs, tramadol, propofol, midazolam and nitrous oxide with oxygen (6-8). There is no consensus on the selection of a method for use in the clinic. Criteria for this decision include patient tolerance to pain, existing pathologies (especially anorectal diseases), medical history, biopsy experience, socio-cultural level, and the patient's level of consciousness. In this prospective study, we compared the efficacy of three different analgesic techniques during TRUS-guided prostate biopsy, including (i) periprostatic blockage, (ii) intrarectal gel instillation, and (iii) sedoanalgesia.

MATERIALS AND METHODS

During a period of five months, 100 consecutive men were enrolled in this study and underwent TRUS-guided prostate biopsy at the Department of Urology, Faculty of Medicine, University of Cukurova after obtaining the necessary approvals from the local Ethics Committee. Informed consent was obtained from each patient after discussing the procedure in detail.

Biopsy patients were identified on the basis of an abnormal finding during the digital examination and/or elevated serum PSA levels higher than 2.5 ng/mL. Patient history as well as physical and laboratory examinations were evaluated and patients were randomised into four groups, each containing 25 individuals.

Analgesic methods

- a) In group one (the control group) biopsies were performed without any analgesia or anaesthesia protocol.
- b) In group two, after placing the TRUS probe, a periprostatic nerve block (PPB) in the sagittal

plane was performed by injection of 5 cc of 2% lidocaine with a 25-cm 18-gauge (G) spinal needle. The injection was made in the neurovascular bundle at the base of the prostate, between the prostate and seminal vesicles.

- c) In group three, ten minutes before the biopsy, 10 cc of 2% lidocaine gel was administered intrarectally.
- d) In group four, sedoanalgesia was used. Sedation was achieved by infusing 2 mg of midazolam intravenously, and 2 µg/kg of fentanyl was used for analgesia. All patients were monitored by an anesthesiologist during and after the procedure for possible complications in the operating room.

Exclusion criteria for this study included a history of transrectal prostate biopsy; a bleeding diathesis and/or anticoagulant treatment; active rectal malformations, such as haemorrhoids, anal fissures, strictures or other painful rectal conditions; acute prostatitis; paraplegia; a history of lidocaine allergies; concomitant use of analgesics and narcotic medications; and an inability to rate a visual analogue scale (VAS).

All patients received standard antibiotic prophylaxis with 500 mg of ciprofloxacin one day before and at least four days after the procedure. Bowel preparations were made with a fleet enema two hours before the biopsy. After the patient assumed the lithotomy position, a TRUS was performed using a 6.5-MHz transrectal probe, and the prostate was evaluated in both sagittal and transverse planes to calculate the volume. An 18-gauge, 25-cm automatic biopsy gun was used to obtain a standard of twelve core biopsies.

A 10-point linear visual analogue scale (VAS) was used to assess the pain scores during (VAS 1), immediately after (VAS 2) and one hour after (VAS 3) the needle biopsy procedure. Pain scores were measured via a simple ruler and recorded for analysis by a person other than the physician who performed the biopsy. The patients who underwent biopsy under sedoanalgesia completed the questionnaire after their drowsiness had been resolved. Additionally, the relationship between the level of pain, prostate volume, age and PSA was determined. After termination of the

procedure, all patients underwent follow-up for at least one hour for any complications and were then discharged.

STATISTICAL ANALYSIS

Each continuous variable was checked for normality. Because the data were not distributed normally, an appropriate non-parametric test was chosen. Ordinal data (VAS) were analysed using the Kruskal-Wallis test. Because the analysis of variance was significant, comparisons were applied using the Mann-Whitney U test. Data were analysed by the Friedman test for time-dependent groups. The Wilcoxon rank sum test was used to evaluate the differences between two groups. Bonferroni's correction was applied ($P < 0.05/n$; where n = number of comparisons) when multiple comparisons were made. The results are presented as mean \pm SD and median (min-max).

RESULTS

The mean ages of the subjects were not significantly different between study groups; 64.7 ± 10.5 for group 1, 63.4 ± 7.6 for group 2, 59.5 ± 12.1 for group 3 and 63.4 ± 8.6 for group 4 ($p = 0.293$). Mean patient PSA levels and prostate volume of the patients were similar, and there were no statistically significant differences between the groups (Table-1).

A statistically significant difference was determined when VAS 1, VAS 2 and VAS 3 were evaluated ($p = 0.001$). Although pain score levels during probe insertion and biopsy were significantly different between the control and PPB

groups ($p > 0.05$), we did not find a difference in comparison of post-procedural pain. Although decreases in VAS 1 and VAS 2 pain scores were statistically significant in the control and PPB groups, there was no significant difference in VAS 3. Three pain scores were significantly lower in the sedoanalgesia group than in the control group ($p = 0.0001$).

A decrease in all three pain scores was statistically significant when PPB was compared with the intrarectal gel group. In the sedoanalgesia group, a decrease in the three pain scores was statistically significant when compared with PPB and the intrarectal gel group ($p = 0.0001$).

Consequently, although acceptable pain scores were obtained in the PPB and sedoanalgesia groups, patients explicitly complained of pain in the control and intrarectal gel groups.

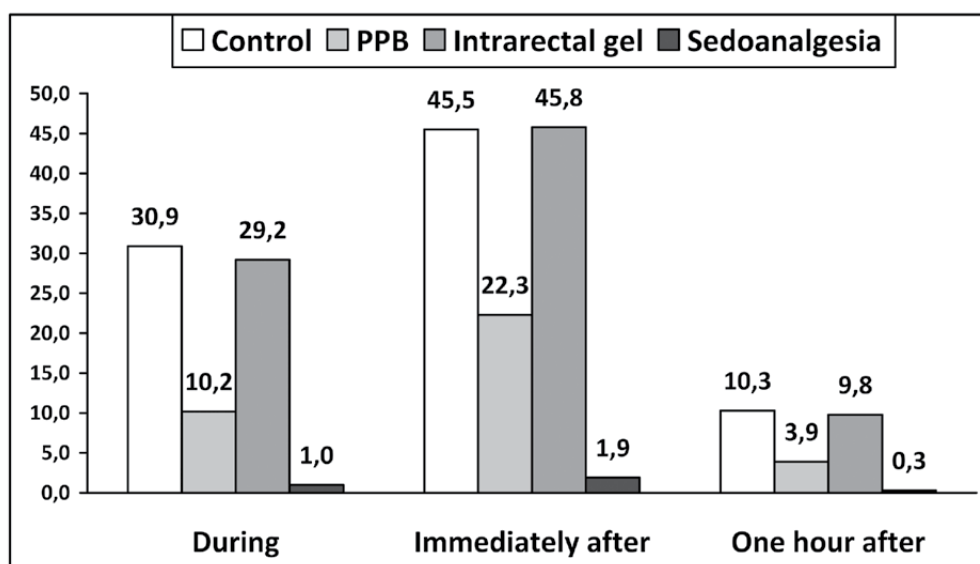
In groups 1, 2 and 3, 46.6% of the patients stated that they did not have pain one hour after the procedure, and the remaining patients had low or very low levels of pain. In the sedoanalgesia group, most of the patients experienced no pain, and two patients experienced very low pain (Figure-1). In Table-2, the distribution of VAS scores according to time and groups is shown.

The relationship between the level of patient pain and prostate volume, age, and PSA levels was analysed. It was determined that pain level decreased, whereas prostate volume increased, and this result was statistically significant. The relationship between age, PSA levels and pain scores was not statistically significant.

Prostate cancer was diagnosed in 33 patients who had undergone biopsy. There was no

Table 1 - Patients characteristics.

	Study Groups Mean \pm SD				p value
	Group 1 (Control)	Group 2 (Perip. blockage)	Group 3 (Intrarectal gel)	Group 4 (Sedoanalgesia)	
Serum PSA (ng/mL)	14.7 \pm 13.1	11.1 \pm 7.8	11.6 \pm 11.2	17.1 \pm 17.0	0.262
Prostate vol. (cc)	43.1 \pm 13.5	46.4 \pm 18.9	38.1 \pm 12.5	59.8 \pm 26.2	0.371

Figure 1 - Distribution of VAS pain scores along time according to groups.**Table 2 - Distribution of pain scores between groups and time.**

VAS	Study Groups Mean ± SD				p value [†]
	Group 1 (Control)	Group 2 (Perip. blockage)	Group 3 (Intrarectal gel)	Group 4 (Sedoanalgesia)	
VAS 1 (During biopsy)	30.9 ± 17.0	10.2 ± 13.2	29.2 ± 11.7	1.0 ± 2.7	0.0001
VAS 2 (just after the biopsy)	45.5 ± 20.7	22.3 ± 16.7	45.8 ± 16.8	1.9 ± 4.9	0.0001
VAS 3 (One hour later)	10.3 ± 13.4	3.9 ± 6.6	9.8 ± 12.1	0.3 ± 1.1	0.0001
p value*	0.0001	0.0001	0.0001	0.0001	

*p value comparison of VAS groups according to time (Friedman test)

†p value comparison of 4 groups (Kruskal Wallis test)

difference in the quality or quantity of fragments obtained during the biopsy between the groups. There was no statistically significant difference between the groups in terms of the incidence of diagnosed prostate cancer. Therefore, pain scores were compared between the 33 patients with

prostate cancer and the 67 patients without cancer. We found that pain scores were statistically lower in patients with prostate cancer (Table-3).

Rectal bleeding which was minimal was observed in 44% of the patients after the biopsy. There was no statistically significant difference

Table 3 - Distribution of pain scores according to the existence of prostate cancer.

	Prostate cancer Mean \pm SD		P [†] value
	Yes (n = 33)	No (n = 67)	
VAS 1 (During biopsy)	12.9 \pm 15.2	20.2 \pm 18.3	0.001
VAS 2 (Just after the biopsy)	22.9 \pm 24.03	31.8 \pm 23.8	0.001
VAS 3 (1 hour after the biopsy)	6.1 \pm 12.67	6.1 \pm 9.2	0.526
P value*	0.001	0.001	

* p value comparison of VAS groups according to time (Friedman test)

† p value comparison of 2 groups (Mann Whitney U test)

between the groups in terms of bleeding, volume and the number of the patients.

A short duration of hypotension was detected in a patient with a PPB, but the patient recovered from this condition in a short time. No complications were observed in the early period up to three weeks following the biopsy.

DISCUSSION

In this investigation, the effects of using an intrarectal gel with lidocaine, a commonly used periprostatic blockage, and a sedoanalgesia treatment were evaluated on their ability to reduce pain during prostate biopsy. In addition, the visual pain scale was used to determine the effects of anaesthesia and the degree of pain that a patient experienced.

Desgrandchamps and Chang have reported that intrarectal gel with lidocaine did not provide a statistically significant analgesic effect when compared with an ultrasonographic gel. In this study, patients who underwent the use of an intrarectal gel with 2% lidocaine were compared with a control group (9,10). Pain scores were higher in the control group; however, there were no statistically significant differences between the groups when all pain scores were compared. The postoperative course was uneventful.

Periprostatic nerve blockage (PPB) was initially defined by Nash et al. (11). The authors noted that pain scores were significantly lower in the patients who had a unilaterally prostatic nerve

blockage, compared with the pain scores of patients who did not. Recently, Soloway and Obek stated that anaesthesia and analgesia are necessary during biopsy, and they reported that pain was lower in all patients who underwent biopsy with a periprostatic nerve blockage. No complication was noted in all except one patient (12).

In our investigation, VAS 1 and VAS 2 pain scores in the periprostatic nerve blockage group were significantly lower than those in the control group. There was no statistically significant difference between the groups when VAS 3 was considered. In the PPB group, all three pain scores were significantly lower when compared with those of the other groups. Hypotension, which was treated in a short period of time, was observed in one patient for whom periprostatic blockage was performed. No other complication was detected. Minimal rectal bleeding was observed in approximately 50% of patients in all groups. However, there was no statistically significant difference between the groups in terms of bleeding and complications, as previously reported.

Periprostatic nerve blockage is a cost effective, easily performed and minimally invasive method with high success in patients. We recommend that periprostatic nerve blockage be routinely used before the procedure to improve patient comfort and increase the ease of the biopsy procedure. Alternatively, the application of an intrarectal gel may make the procedure easier without such a high cost. Obek et al. categorised patients

into four groups including a control group, a periprostatic blockage group, a periprostatic blockage with intrarectal gel group, and a tramadol (codein analogue) group (13). They showed that the group in which analgesia and anaesthesia were provided undertook the procedure far better than the control group, which received no treatment for pain. In addition, they reported that periprostatic blockage with intrarectal gel provided the best analgesia whereas tramadol and periprostatic blockage had similar effects. There were no severe complications that required hospitalization in any of the patients. Similarly, in several studies, it has been shown that the use of periprostatic blockage with an intrarectal gel is better than placebo (14-24).

Entonox, which is a gas anaesthetic material (50% NO and 50% O₂ mixture), is widely used in the UK during delivery, in minor procedures treating trauma, and in emergencies, because it provides short-term anaesthesia. The analgesic effect starts three minutes after application by inhalation and lasts until four minutes after termination. Masood et al. compared air inhalation with placebo in 110 patients who underwent a TRUS prostate biopsy and reported that entonox provided fast and effective pain control during biopsy, compared with two other groups (25). However, unlike patients who receive local anaesthesia, patients who receive entonox should be under active surveillance during and after biopsy, because they are unconscious under sedation. For this reason, although we have not evaluated the costs of the procedures, the cost of general anaesthesia is generally higher than that of local anaesthesia since it must be performed in the operating room.

Manikanda et al. assessed 235 patients who underwent treatment with entonox, periprostatic blockage or placebo along with a TRUS prostate biopsy, and they concluded that pain was significantly lower in the entonox and PPB groups, when compared with the placebo group. Both of these methods can be used safely in TRUS prostate biopsy applications (26). Peters et al. reported a significant decrease in discomfort when using IV-administered propofol, especially in repeated biopsies (27).

In our study, all the three patient pain scores in the sedoanalgesia group were found to be significantly lower when compared with those of

the other groups. After the procedure, no complication was observed, and patients were discharged after one hour. Although this method is effective, the need for a preoperative evaluation, the need for a close follow-up of the patient after the procedure, the risk of mortal complications (which are very rare) and the manpower lost associated with the procedure restrict the use of this method. However, it is potentially useful for patients who have a very low threshold for pain, need a saturation biopsy, have severe anorectal disease, or are allergic to local anaesthesia.

The goal of clinicians should be to reduce the pain and discomfort associated with TRUS-guided prostate biopsies. We found that patient-reported pain was higher in the control group and in the group in which an intrarectal gel was applied. Acceptable pain scores were reported in patients who received a periprostatic blockage or sedoanalgesia. Because sedoanalgesia is a complicated treatment due to relatively high costs and the need for comprehensive background and surveillance, it should only be used in special situations. We recommend the use of PPB in TRUS-guided prostate biopsies, because it is inexpensive, safe, easy to perform in outpatient clinics, and an effective anaesthetic method.

CONFLICT OF INTEREST

None declared.

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Correspondence address:

Dr. Volkan IZOL
Department of Urology
University of Cukurova, Faculty of Medicine
01330, Adana, Turkey
Fax: + 90 322 457-3072
E-mail: volkanizol@yahoo.com