



The Effect of Intrarectal Lidocaine Gel Instillation before Transrectal Ultrasound Guided Prostate Biopsy

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Purpose: To compare pain induced by a transrectal ultrasound (TRUS)-guided prostate biopsy in men between using local lidocaine gel or plain lubricant.

Materials and Methods: Between January and October of 2014, a total of 63 consecutive patients undergoing TRUS-guided prostate biopsy for elevated prostate-specific antigen (PSA) levels and/or a suspicious digital rectal examination were randomized to two groups: lidocaine group and control group. In the lidocaine group (n=31), patients received 20 ml of 2% lidocaine gel and betadine solution soaked gauze was administered via a transrectal route 10 minutes before the procedure. In the control group (n=32), 20 ml plain lubricant and betadine solution soaked gauze was administered under the same condition. After the biopsy procedure, patients were asked to rate their pain perception on a 10-point visual analog scale (VAS) score.

Results: There was no statistically significant difference with the mean patient age, PSA, prostate volume, biopsy duration time between lidocaine group and control group. The mean pain score and number of patients with VAS ≥ 5 in the lidocaine group (4.14 ± 2.0 , 10) were significantly lower than those in the control group (5.78 ± 2.3 , 19). In younger men (≤ 65 years), pain was reported significantly less in the lidocaine group than in the control group. Complication rates were not different between the two groups.

Conclusions: Intrarectal lidocaine gel is a simple, safe, and efficacious for reducing pain and discomfort during the TRUS-guided prostate biopsy procedure. It appears to have an enhanced effect, especially in younger than in older men.

Keywords: Biopsy; Anesthetics, local; Lidocaine; Pain; Prostate

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INTRODUCTION

Transrectal ultrasound (TRUS)-guided biopsy of the prostate is the standard procedure to diagnose prostate cancer. Although well tolerated by most men, some reviews have shown that between 65% and 90% of patients report discomfort during the procedure, and up to 30% of patients experience significant pain [1-3].

Local anesthetics are commonly used to perform TRUS-guided prostate biopsy [4-6]. Topical anesthesia with lidocaine gel in the rectum has been reported to have controversial results compared with the placebo [7,8] and, in some studies, topical anesthesia was reported to be inferior to periprostatic lidocaine injection [9,10]. The anesthetic gel, usually 10-20 ml of lidocaine (1-2%), is applied in the rectal ampulla 10-20 minutes before

introducing the TRUS probe and biopsy sampling. However, the best anesthetic method has not yet been decided. The sufficient anesthetic role of lidocaine gel was first announced by Ehrenstrom Reiz and Reiz [11]; they reported a meaningful reduction of pain during venous cannulation when lidocaine containing cream was applied, compared with the placebo. Several studies have identified the usefulness of topical anesthetics in percutaneous or surgical interventions of the skin, as well as surgical procedures of the buccal and genital mucosa [12,13]. Topical use of lidocaine-prilocaine cream, through the anus and anal canal, has also confirmed to be effective in patients with anal fissures [14]. It can be understood by various pain thresholds and recto-anal pathologies. A well-proven phenomenon of individual varying thresholds of pain somewhat complicates the evaluation of effectiveness of several attempts for taking local pain control. There have been a great number of studies that investigated the benefits of local anesthesia. While some of these studies reported favorable results with respect to the improvement of pain relief, others reported no observable benefits [15-18]. In our institution, intravenous sedation or lidocaine injection is not commonly carried out, nor do we apply intrarectal lidocaine gel due to a weak consensus on its effectiveness. Like other studies, we have investigated that patients tolerate the intervention well without anesthesia [15,16]. We underwent a prospective, simple randomized study on the efficacy and safety of local anesthesia by lidocaine gel in patients receiving TRUS-guided prostate biopsy.

MATERIALS AND METHODS

Our research was approved by the Institutional Review Board of National Police Hospital (IRB no. 116222-201409-HR-007-01). Between January and October of 2014, a total of 63 patients, who received TRUS-guided prostate biopsies due to elevated prostate specific antigen (PSA) and/or abnormal digital rectal examination, were included in this study. Patients with painful conditions of the prostate, anus, and rectum, such as prostatitis or prostatodynia, anal fissure or stricture, hemorrhoids, neurological conditions, and history of allergy to lidocaine were excluded. Patients taking any narcotic or analgesic medications were also excluded to minimize interruption of pain assessment. The 63 included patients were randomly assigned into two groups

using a random number generator. In lidocaine group (n=31), patients received 20 ml of 2% lidocaine gel and betadine solution soaked gauze through the transrectal route for 10 minutes before the biopsy. In the control group (n=32), subjects received 20 ml plain lubricant and betadine solution soaked gauze under the same conditions, respectively.

Informed consents were obtained from all subjects. Patients were unaware of which product was administered. As prophylactic antibiotics, a single dose of a fluoroquinolone and aminoglycoside were administered 30 minutes before biopsy. After that, oral fluoroquinolone was continued for five days.

Ultrasound of the prostate was performed with a measurement of its 3 dimensions during the 10-minute interim after instilling the lidocaine or placebo in the rectum and before the biopsy. In each group patients were placed in the lithotomy position and digital rectal examination was performed.

Prostate biopsy was performed under ultrasound guidance, using high-resolution (linear 6-16 MHz transducer) units (Aloka Prosound $\alpha 5$; Aloka, Tokyo, Japan) by one skilled urologist. Twelve biopsy cores were obtained from the prostate, including 3 from each lobe (apex, mid and base), using an automatic spring loaded biopsy gun and 18-gauge needle. The biopsy sites were lateral and far-lateral at a distance from the midline to minimize urethral injury. All patients were monitored for about 10 minutes after the biopsy. We defined the time duration as the time for ultrasound probing, and it was measured. Then, they were asked to score the pain and/or discomfort level experienced during the procedure via a 10-point linear visual analog scale (VAS) [19]. Pain perception was classified by utilizing

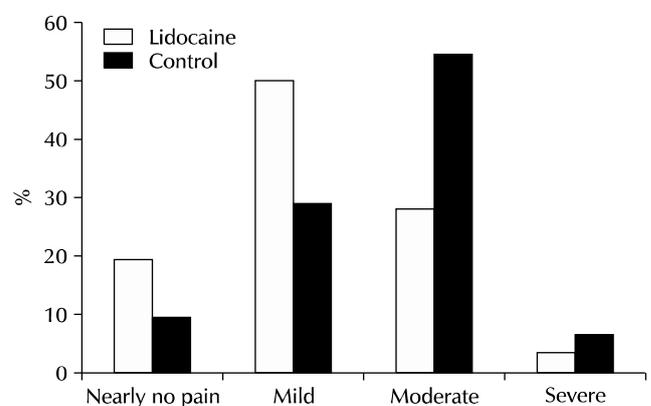


Fig. 1. Percent distribution of pain perception in the two groups.

a VAS score; nearly no pain (0-1), mild (2-4), moderate (5-7), and severe (8-10) pain (Fig. 1). The question was expressed in the same way in all cases to minimize any bias in the process of collecting data. All subjects were closely observed during and after the biopsy for potential complications. Patients were observed and questioned about the presence of hematuria, hematospermia, hematochezia, anal bleeding, vasovagal episodes, urinary tract symptoms, and fever at two weeks after the procedure. Categorical variables among the two groups were analyzed by chi-squared or Fisher exact test. T-test was used to compare continuous variables between the two groups. The variables were considered statistically significant when $p < 0.05$. Statistical analysis was done by using PASW Statistics ver. 18.0 (IBM Co., Armonk, NY, USA).

RESULTS

The mean patient age was 64.2 ± 9.4 and 66.03 ± 10.3 years, the mean PSA was 11.7 ± 2.6 and 12.5 ± 1.9 ng/ml, the mean prostate volume was 37.46 ± 13.7 and 48.50 ± 32.6 g, the mean biopsy duration time was 7.2 ± 3.1 and 7.0 ± 2.9 minutes, the number of detected prostate cancer was 8 (25.8%) and 10 (31.3%) in lidocaine and control group, respectively (Table 1). The mean age, total serum PSA, prostate volume, biopsy duration time, and pathologic findings were comparable between the two groups.

However, the mean VAS score was statistically lower in the lidocaine group than in the control group, and the number of patients with $VAS \geq 5$ was also smaller in the lidocaine group ($p < 0.01$, $p < 0.01$, respectively; Table 1).

Fig. 1 shows the distribution of pain perception in each group. A significant number (59.4%) of patients in the control group had pain during TRUS-guided prostate biopsy

Table 1. Variables comparison between the two groups

Variable	Lidocaine group (n=31)	Control group (n=32)	p-value
Mean age (y)	64.2 ± 9.4	66.03 ± 10.3	0.79
Mean total PSA (ng/ml)	11.7 ± 2.6	12.5 ± 1.9	0.82
Mean prostate volume (g)	37.46 ± 13.7	48.50 ± 32.6	0.69
Mean biopsy time (min)	7.2 ± 3.1	7.0 ± 2.9	0.67
No. with prostate cancer (%)	8 (25.8)	10 (31.3)	0.56
Mean VAS score	4.14 ± 2.0	5.78 ± 2.3	< 0.01
No. with VAS score ≥ 5 (%)	10 (32.3)	19 (59.4)	< 0.01

Values are presented as mean \pm standard deviation or number (%). PSA: prostate specific antigen, VAS: visual analog scale.

that was often understood as severe and bothersome with VAS score of 5 or greater on the ten-point scale. In contrast, the rate of patients with $VAS \geq 5$ in the lidocaine group was only 32.3%.

We stratified the results according to age, with a cut off of 65 years (median). In the younger population (≤ 65 years), a significantly lower VAS score was observed in the lidocaine group than in the control group (4.4 vs. 6.5, $p < 0.01$), and there was no difference in older (4.0 vs. 4.6, $p = 0.07$; Fig. 2). In the control group, the younger population answered significantly higher VAS score than the older population (6.5 vs. 4.6, $p = 0.01$).

Only minor and transient complications occurred in both groups. Complication rates were not different between the two groups (Table 2). All complications subsided within 4 weeks after the procedure.

DISCUSSION

TRUS-guided prostate biopsy has been a time-tested procedure with respect to the effectiveness and side effects

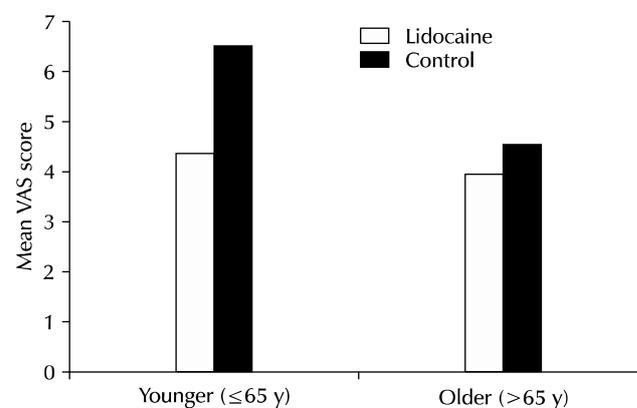


Fig. 2. Mean pain level in the lidocaine gel anesthetic group and control group in younger and older men during prostate biopsy. VAS: visual analog scale.

Table 2. Complications of the transrectal ultrasound guided biopsy between the two groups

	Lidocaine group (n=31)	Control group (n=32)	p-value
Hematuria	7 (22.6)	8 (25.0)	1.0
Hematospermia	5 (16.1)	3 (9.4)	0.82
Blood in the stool	9 (29.0)	8 (25.0)	0.91
Vasovagal episodes	1 (3.2)	0	1.0
Urinary tract infection	1 (3.2)	1 (3.1)	1.0
Fever	0	0	1.0

Values are presented as number (%).

[1-3]. Although well tolerated by most patients, it can cause a wide range of pain, from no pain to severe intolerable pain, as previously reported in the literature [2,3,20]. Pain associated with prostate biopsy is a result of the needle passing through the prostate capsule into the stroma. Conversely, there is little discomfort when the needle penetrates the rectal wall. Hollabaugh et al. [21,22] investigated the neuroanatomy of prostate for the fresh cadavers. They concluded that the nerve route to the prostate originated from the inferior hypogastric plexus in the position of the tip of the seminal vesicles, following the space between the prostate and rectum. These nerves lie on the inferior-lateral side of the prostate and produce main innervations to the prostate gland. In contrast, the anterior and superior-lateral aspect of the prostate has no meaningful neural input. Thus, it is believable that most proportion of pain is generated from direct needle stimulation with these nerves as it penetrates the prostate. Because the rectal wall has a good surface for drug absorption, it is a reasonable option for it to be used in delivering anesthetics to the adjacent nerves by instillation of lidocaine solutions directly into the rectum.

Intrarectal lidocaine gel has been the first local anesthetic method designed for the pain relief of transrectal biopsy. Researches on many kinds of techniques and medications have previously reported to minimize the pain. Because patients often feel pain by anal canal sensation during the biopsy, intrarectal local anesthesia is commonly used, which is highly absorbable through the rectal mucosa [7]. Lidocaine is the most common drug, both used alone or in combination with other molecules [23,24].

Unique techniques and/or agents have been proposed to minimize pain associated with TRUS-guided prostate biopsy, including local anesthetic gels, periprostatic nerve blockades, lidocaine suppositories, topical glyceryl trinitrate ointment, and topical and systemic non-steroidal anti-inflammatories. Intravenous sedation has also been considered; however, problems of higher cost and longer hospital stay reduce its further consideration. At this point, the pain reducing capability of these several anesthetic methods have not been verified universally. In addition, the periprostatic injection method must be underwent after introducing the ultrasound probe into the rectum in the absence of anesthetic, and a lot of patients complain that this discomfort is worse than that of the needle biopsy.

There have been several studies that evaluated the level of pain perception during a prostate biopsy in accordance with various pain evaluation scales. Our study also showed that the TRUS-guided prostate biopsy procedure was not negligible, painless experience in a significant percentage of patients, because more than half of the patients have experienced moderate to severe pain (VAS ≥ 5) in control group.

There have been some studies that also examined the level of pain perception without any anesthetic application. The majority of these studies showed that most patients did not experience moderate-to-intolerable pain during the procedure, even without anesthesia [15,18]. However, in other studies, periprostatic or intravenous anesthetic agents were used. Moreover, it remains to be controversial if a method other than lidocaine gel local anesthesia was used. Although there have been some studies that reported improved pain control using this method [16], there are other studies that claimed no improvement [15].

Our study shows that it can reduce pain during transrectal prostate biopsy with only lidocaine gel administration and bethadine soaking gauze in the rectum, which is very safe and can be protective from microorganisms. Other anesthetic methods can have a greater anesthetic effect; however, only an injection to the prostate or periprostate site is a very painful procedure. Thus, although patients may feel less discomfort during transrectal prostate biopsy, the overall satisfaction level to anesthesia may be low.

The level of pain perception, as a function of advancing age, was also addressed in a previous study, in which almost 80% of patients aged less than 60 years had a moderate-to-severe discomfort, and more than 80% of patients aged more than 70 years mostly had mild discomfort. Another study showed that younger men more often complain of higher overall pain than older men [25,26]. Previous reports showed that information from nociceptors of deep tissue are activated differently in the spinal cord than that from nociceptors of superficial tissue [27], with spinal input originated from deep tissue nociceptors being subject to stronger descending inhibitory control compared with the superficial nociceptors [28]. Finally, another study cited age-related decline in endogenous pain inhibition [29]. Our data also confirm such hypotheses; in the control group, younger men answered a higher VAS score than older men. The application of lidocaine gel significantly decreased

pain during the TRUS-guided prostate biopsy in men aged less than 65 years, but not in older men. Accordingly, we recommend this method especially to younger men, who may have high level of sensitivity.

CONCLUSIONS

Our results support that intrarectal lidocaine gel application is effective, safe, and simple to introduce satisfactory anesthesia before TRUS-guided prostate biopsy. It is more comfortable and better tolerated than plain lubricant application. The anesthetic effect seems to be more effective in younger men, and may reduce discomfort and pain during the TRUS-guided prostate biopsy procedure.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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