Novel Approach for Pain Control in Patients Undergoing Prostate Biopsy: Iliohypogastric Nerve Block with or without Topical Application of Prilocaine-Lidocaine: A Randomized Controlled Trial

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Purpose: To investigate the efficacy of a novel anesthetic technique called iliohypogastric nerve block (INB) for pain control in patients undergoing prostate biopsy.

Materials and Methods: A total of 59 consecutive patients who underwent transrectal ultrasound guided prostates biopsies were included in the study. Patients were randomized into four groups: (1) control, no method of anesthesia was administered, (2) intrarectal prilocaine-lidocaine cream application, (3) INB and (4) INB + intrarectal prilocaine-lidocaine cream application (combined group). Patients were asked to use a scale of 0-10 in a Visual Analogue Scale (VAS) questionnaire about pain during probe insertion (VAS 1) and prostate biopsy (VAS 2).

Results: The mean VAS 1 and VAS 2 scores were 0.7 and 4.9 for controls, 0.5 and 1.8 for INB, 0.5 and 2.6 for the intrarectal cream group, and 0.4 and 1.8 for the combined group. The mean VAS 1 scores were not different between groups. However, the mean VAS 2 scores were significantly lower in INB, prilocaine-lidocaine cream and combined groups compared to the control group ($P < .001$). In addition, the INB group had significantly lower VAS 2 scores compared to the cream application group ($P = .03$). On the other hand, there was no difference between the INB and combined groups ($P = .8$).

Conclusion: Any form of anesthesia was superior to none. However, INB alone seemed to be superior to prilocaine-lidocaine cream application in patients undergoing prostate biopsy. Addition of prilocaine-lidocaine cream application to INB may not provide better analgesia.

Keywords: anesthetics; local; administration; lidocaine; pain management; methods; prostate treatment; outcome.

INTRODUCTION

Prostate biopsy is considered to be an invasive procedure and is likely painful, requiring some form of anesthesia.[1] Transrectal probe insertion and multiple punctures of the anterior rectal wall, periprostatic soft tissue and prostate capsule may cause the pain. The gold standard for the best pain control during prostate biopsy is to use periprostatic infiltration of lidocaine.[2-10] However, the periprostatic injection itself may cause pain and makes the entire biopsy procedure more uncomfortable.[11] It has been shown that preventive topical anesthesia combined with periprostatic infiltration is successful in achieving more complete pain control during the biopsy procedure. Previously, it was shown that a lidocaine-prilocaine mixture as a topical anesthetic had a pain control advantage versus placebo when the prostate capsule was punctured.[12] The efficacy of topical prilocaine-lidocaine cream was reported by other authors as well.[13-15] During the last decade, the use of ultrasound-guided regional anesthesia has increased, and developments in ultrasound technology have enabled direct visualization of peripheral nerves.[16] A technique for ultrasound-guided iliohypogastric nerve block (INB) has been described in adults.[16-18] In pediatric patients, ultrasound-guided blocks have been associated with a higher success rate and a lower volume of local anesthetic needed, compared with conventional landmark based techniques.[19,20] It has been shown that the use of INB for patients undergoing herniorrhaphy resulted in a shorter time-to-home readiness, quicker oral intake post-surgery, and no need for recovery room care.[21] In light of these findings, primary outcome of the study was to investigate the efficacy of a novel anesthesia technique called INB and the secondary outcome was to determine whether application of local anesthetics enhance the pain relief in patients undergoing prostate biopsy.

MATERIALS AND METHODS

Patients and Study Design

After obtaining approval from the local ethics committee, a total of 59 consecutive patients who underwent transrectal ultrasound guided biopsies were included in this single blind randomized prospective study. All participants were informed and written consents were taken. The random allocation procedure was determined by opening a sequentially numbered envelope, thereby determining whether the patients should receive[1] no

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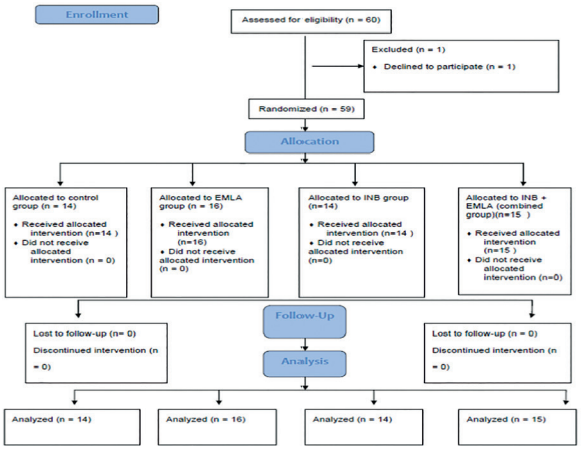

Figure 1. CONSORT flow diagram for patients who were brought into trial.

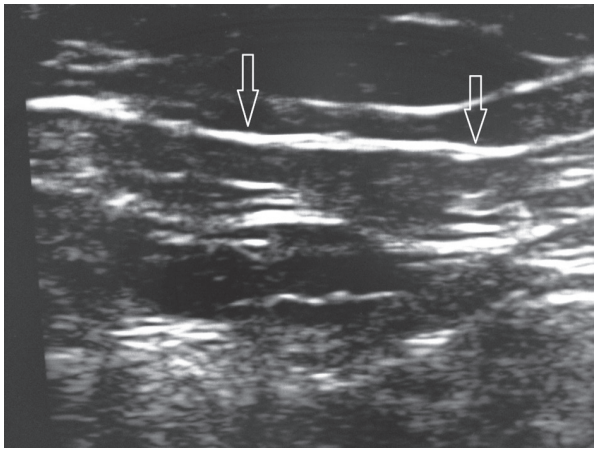

Figure 2. The application of ultrasound-guided iliohypogastric nerve block.

method of anesthesia,[2] intrarectal prilocaine-lidocaine cream (EMLA®, AstraZeneca Inc, Macclesfield, Cheshire UK) application,[3] INB or[4] INB + intrarectal prilocaine-lidocaine cream application (combined group). This random sequence was generated by computer, and the investigator was unaware of the sequence. CONSORT flow diagram of the trial is shown in **Figure 1**. Physician performing prostate biopsy and evaluating VAS scores, was blind to the patient's group assignment.

Iliohypogastric Nerve Block (INB)

Once the target nerves had been identified in a cross-sectional view, the following measurements were made: distance from the anterior superior iliac spine to the ilioinguinal nerve, distance between the ilioinguinal and iliohypogastric nerves, depth of the ilioinguinal and iliohypogastric nerves relative to the skin and distance from the ilioinguinal nerve to the peritoneum. Following aseptic preparation of both the puncture site and the ultrasonographic probe, the nerve block was performed using an insulated 22-gauge 40-mm needle with a facette tip needle and an injection line. Initially, the anterior superior iliac spine was palpated and a mark made 2 cm medial and 2 cm superior from it (**Figure 2**). The needle was then visualized by ultrasound (**Figure 3**). A loss of resistance was appreciated as the needle passed through the muscle to lie between the muscle and the internal oblique. After the initial loss of resistance and negative needle aspiration of blood, the needle was placed in an optimal position relative to the nerves, and a single injection of lidocaine 0.2% was administered under real-time ultrasound control until both nerves were surrounded by the local anesthetic. The needle was then inserted further to encounter another resistance, which was the internal oblique muscle. A further loss of resistance was appreciated once the needle passed through the internal oblique to lie between it and the transversus abdominis muscle. After the second loss of resistance, another 2 mL of local anesthetic was administered. The needle was then withdrawn to the skin and redirected at a 45-degree angle medially to again pierce the external and then the internal oblique muscles (**Figure 4**). After each loss of resistance, 10 mL of local anesthetic was again administered. The needle was then returned to the skin and inserted 45 degrees laterally, and the procedure repeated. Thus, a total of 20 mL of local anesthetic was placed in a fan-like distribution between the external and internal oblique and the internal oblique and transversus abdominis muscles. Note: In patients with little abdominal wall musculature, the internal oblique muscle may be too thin to appreciate a loss of resistance as it is penetrated. To prevent entering the abdomen after piercing the external oblique muscle, the author limits further abdominal wall penetration without loss of resistance to 1.5 cm. Lower abdominal skin or inguinal region is checked for the maintenance of anesthesia.

Pain Score

Patients were asked to use a scale of 0-10 to complete a Visual Analogue Scale (VAS) questionnaire about pain during probe insertion (VAS 1) and prostate biopsy (VAS 2) (**Figure 5**).

Prostate Biopsy Procedure

Table 1. Demographic and clinical characteristics of study groups.

Variables	Group 1	Group 2	Group 3	Group 4	*P* Value
Patients number	14	16	14	15	
Age, years, mean ± SD	60.2 ± 5.6	60.5 ± 5.2	63.3 ± 11.7	65.0 ± 5.7	.100
Prostate volume, mL mean ± SD	41.5 ± 10.2	49.1 ± 6.6	50.5 ± 24.6	49.9 ± 8.3	.100
Serum PSA, (ng/mL) mean ± SD	8.2 ± 3.5	8.2 ± 1.9	13.0 ± 15.7	8.5 ± 3.4	.700
VAS 1	0.7 ± 0.5	0.5 ± 0.5	0.5 ± 0.6	0.4 ± 0.5	.300
VAS 2	4.9 ± 0.7	2.6 ± 1.0	1.8 ± 0.5	1.9 ± 0.4	< .001

Abbreviations: PSA, prostate specific antigen; VAS, visual analogue scale, SD, standard deviation.

Table 2. Ordinal regression results of effective factors for estimating the values of VAS 1 and VAS 2.

Variables		Score	Estimate		SE	*P* Value	95% Confidence Interval	
							Lower	Upper
VAS 1	Prostate volume		0.005	0.020	.809		-0.034	0.043
	Age		-0.028	0.038	.453		-0.103	0.046
	BMI		-0.293	0.133	.028		-0.555	-0.032
	Group	0	0		.	.	.	.
		1	-1.250	0.782		.110	-2.783	0.282
		2	-1.091	0.812		.179	-2.682	0.500
		3	-0.753	0.792		.342	-2.305	0.799
VAS 2	Prostate Volume		0.035	0.021	.099		-0.007	0.076
	Age		-0.068		0.040	.089	-0.146	0.010
	BMI		-0.106		0.126	.401	-0.353	0.141
	Group	0	0		.	.	.	.
		1	-5.265		1.296	< .001	-7.805	-2.725
		2	-7.405		1.468	< .001	-10.282	-4.529
		3	-7.107		1.463	< .001	-9.975	-4.238

Abbreviations: BMI, body mass index; VAS, visual analogue scale, SE, standard error.

Included in the study were 59 consecutive patients with concerning elevated prostate-specific antigen (PSA) values or suspicious digital rectal exam (DRE) results, and/or who underwent transrectal ultrasound (TRUS)-guided needle biopsy of the prostate. Exclusion criteria included lidocaine allergy, hemostasis disorders, anticoagulant therapy, prediagnostic unbearable pain, chronic pelvic pain syndrome, or anorectal pathologies. Prophylaxis was carried out by oral administration of ciprofloxacin 500 mg twice a day, starting the evening before sampling until 3 days after the procedure. For bowel cleaning, fleet-enema was self-administered on the morning of the biopsy. Biopsies were performed in left lateral decubitus position; an 18G Tru-cut core needle biopsy gun was used. For all patients, 12 core biopsy samples were taken. Two prostate cores were randomly obtained from each peripheral side, and from the apical margin or basement (**Figure 6**).

Statistical Analysis

Power analysis of the study showed that a total 57 patients were needed to gain 80% power when alpha error was set at 0.05, beta error at 0.20 and effect size at 0.50. Groups were controlled in terms of conformity to normal distribution by graphical check and Shapiro-Wilk test. The groups were distributed normally and mean and SD parameters were used. ANOVA with Bonferroni correction was used for comparison of four independent groups, respectively. Analysis of Pearson correlation was performed to examine the correlation between parameters and VAS scores may be effective. Ordinal regression analysis was performed in order to determine parameters that could be effective in predicting VAS scores. *P* value of < .05 was taken as of significant. The Statistical Package for the Social Science (SPSS Inc, Chicago, Illinois, USA) version 15.0 was used for statistical analysis.

Table 3. Complications seen after prostate biopsy.

Variables	Group 1	Group 2	Group 3	Group 4
Gross hematuria	1	1	1	1
Rectal bleeding	5	2	2	3
Dysuria	-	1	1	1
Gross hematuria + High fever	2	1	1	-
Rectal bleeding + Hematuria	-	-	-	1
Total	8	5	5	6

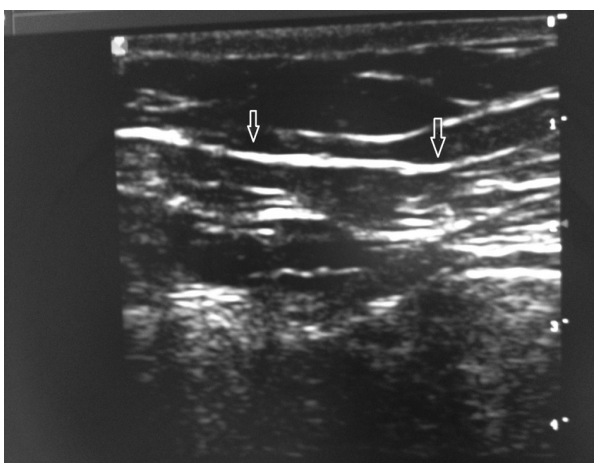

Figure 3. Iliohypogastric nerve block application shown by in a patient.

Figure 4. Needle insertion of ultrasound-guided iliohypogastric nerve block.

RESULTS

The median age of the 59 men was 62.0 (range 47-87) years. The median prostate volume and PSA levels were 47.8 (range 20-103) mL and 9.4 (range 3.6-60.3) ng/mL, respectively. The mean VAS 1 and VAS 2 scores were 0.7 and 4.9 for controls, 0.5 and 1.8 for INB, 0.5 and 2.6 for the intrarectal cream group, and 0.4 and 1.9 for the combined group. Characteristics of patients are shown in **Table 1**. The mean VAS 1 scores were not different between groups. However, the mean VAS 2 scores were significantly lower in INB, prilocaine-lidocaine cream and combined groups compared to the control group ($P < .001$). In addition, the INB group had significantly lower VAS 2 scores compared to the cream application group ($P = .03$). On the other hand, there was no difference between the INB and combined groups ($P = .8$). Age and prostate volume were not correlated with VAS 1 and VAS 2 scores ($P > .05$). Regression results on the effective factors to estimate the values of VAS 1 and VAS are shown in **Table 2**. Ordinal regression analysis showed that increasing body mass index (BMI) decreased VAS 1 scores significantly ($P = .028$). There was no significant effect in predicting VAS 1 scores by including other parameters ($P > .05$). Among all the groups and the control group, prediction of VAS 1 scores was found to be significantly no different from using other methods ($P > .05$). No significant differences were detected in VAS1 score between INB and the combined method and EMLA ($P = .412$ and $P = .774$, respectively), or between INB and the combined method ($P = .649$). When VAS 2 values were examined, compared with the control group, the combined method was 7.1 times decreased, the INB group 7.4 times decreased and the EMLA group 5.4 times decreased ($P < .001$). Between INB and the combined method and EMLA, a significant difference was detected in terms of predicting VAS 2 scores ($P = 0.039$ and $P = .016$, respectively). Compared to the EMLA group there was 1.9 times the combined method in pain scores, which were reduced 2.2-fold in the INB group. Comparing the INB and the combined group in terms of estimating VAS 2 scores, no significant differences were detected ($P = .798$). A detailed summary of complications after prostate biopsy are presented in **Table 3**. No complication was detected during INB application.

DISCUSSION

It is intuitive that a potentially painful procedure such as prostate biopsy should require some form of anesthesia. Recently, the superiority of combined local lidocaine-prilocaine for intrarectal anesthesia in controlling pain during all phases of the biopsy procedure has been demonstrated.[22] Several studies have shown that topical prilocaine-lidocaine application was more efficient than placebo[12] and the formulation of this synergistic mixture yields a higher concentration (approximately 80%) of active substance, compared with the commonly used lidocaine gel, which yields approximately 20%.[23] This property leads to a better penetration of the drug and better anesthetic effect. It has been shown that preventive topical anesthesia combined with periprostatic infiltration is successful in achieving more complete pain control during the entire prostate biopsy procedure.[24] INB is also widely used for postoperative pain relief because it is free of many side effects, such as motor block of the lower limbs and urinary retention. Indications for INB include anesthesia for any somatic procedure involving the lower abdominal wall/inguinal region such as inguinal herniorrhaphy[18,21] and for analgesia after surgical procedures using a Pfannenstiel incision as for cesarean section[16] and abdominal hysterectomy.[25] These blocks do not provide visceral anesthesia and thus cannot be used as the sole anesthetic for procedures

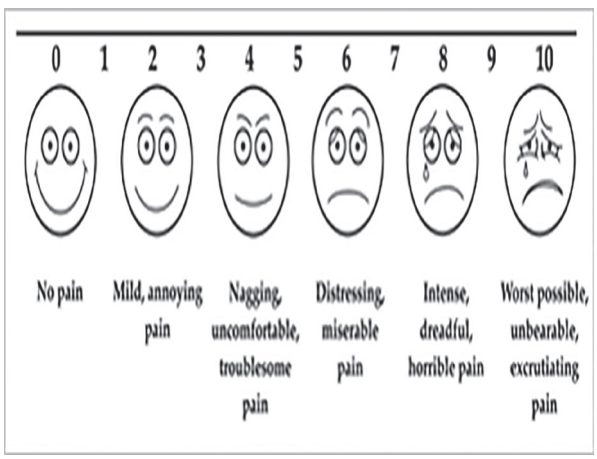

Figure 5. Visual Analogue Scale score questionnaire.

Figure 6. Transrectal prostate biopsy after iliohypogastric nerve block application.

such as lower intra-abdominal surgery. When used for inguinal herniorrhaphy, the sac (containing peritoneum) must be infiltrated with local anesthetic by the surgeon to complete anesthesia for the procedure. There are no specific contraindications for these blocks apart from the generic contraindications for performance of any regional block, such as infection at the procedure site, allergy to local anesthetics, indeterminate neuropathy and so on. INB has several advantages and limited complications because since the block is limited to the lower abdominal wall and inguinal region, any hemodynamic changes would be unusual. As with other blocks, the patient is advised to protect the anesthetized area from trauma. Although periprostatic nerve blockade is a commonly used method for this purpose, the equally painful process of fibrosis is a disadvantage of repeated injection. During TRUS-guided prostate biopsies, sedation is also performed. For this purpose Entonox (50% nitrous oxide in 50% oxygen), intravenous propofol, and intravenous ketorolac have been used. Usually, rapid-acting and rapidly failing anesthetic agents are used in outpatient cases, but they cannot be applied to all patients. In our patients, no complications such as bleeding, hematoma, or micturition-defecation disorder were seen. Significant numbers of studies have been done to develop an efficient program for local anesthesia during prostate biopsy to date. However, this is the first article that evaluated the efficacy of INB for pain control in patients undergoing prostate biopsy in the English literature. According to our results, both INB with or without topical anesthesia and use of topical anesthesia alone were effective for pain control when compared to the control group. However, addition of topical anesthesia to INB did not provide better analgesia. On the other hand, the main limitation of our study was the small patient population. Moreover, VAS is not a precise and reproducible tool, but currently there is no better way than VAS to compare anesthetic effects during prostate biopsy. To increase the reliability of VAS scores, the same operator questioned the patients to obviate interobserver variability for reliable results. The other limitation of the study was, this study was not double blinded. The patients were aware of the anesthetic method that they will receive, so the results may be influenced by this awareness.

CONCLUSION

In conclusion, INB may be an easily applicable and minimally invasive method with effective pain control for patients undergoing prostate biopsy. Addition of topical anesthesia may not have benefit for pain relief. Subsequent prospective, double-blind, randomized studies in a larger number of patients are required to support our results.

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CONFLICT OF INTEREST

None declared.

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