Original Article

Comparison of heated topical intrarectal anesthesia and periprostatic nerve block in transrectal ultrasound-guided prostate biopsy in Chaophrayayommarat Hospital: a prospective randomized trial

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Abstract

Objective: To compare efficacy between heated intrarectal local anesthesia (HIRLA) and periprostatic nerve block (PNB) with respect to pain reduction during transrectal ultrasound-guided prostate biopsy (TRUS-Bx).

Materials and Methods: A prospective randomized trial including 60 participants scheduled for TRUS-Bx from July to December 2024. Participants were assigned to a group using heated intrarectal local anesthesia with 10 ml 40 °C 2% lidocaine gel (n=30) or PNB (n=30). Primary outcome was the level of pain as measured by pain score using a visual analog scale (VAS) during TRUS-Bx. The secondary outcome was complications which occurred during and after the procedure.

Results: The level of pain in the HIRLA group was greater in comparison to PNB (4.03±1.85 versus 2.57±1.68; p=0.002). No differences in complications were observed between the two groups.

Conclusion: PNB provides more effective pain reduction in comparison to HIRLA during TRUS-Bx.

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Introduction

Prostate cancer is one of the most common cancers in men, ranking fourth among all cancers in males. According to the Thai Cancer Registry data from the National Cancer Institute, approximately 3,700 new cases of prostate cancer are reported each year, with an incidence rate of 7.7 cases per 100,000 population. The Bureau of Strategy and Planning in the Ministry of Public Health has reported that each year approximately 1,700 people die from prostate cancer. Early detection, whether through screening for prostate-specific antigen (PSA) or other methods, can significantly improve outcomes. A digital rectal examination by a doctor involves the insertion of a finger into the rectum to feel for any abnormalities of the prostate. Early detection of the disease allows for prompt treatment, leading to better treatment outcomes and increased chance of survival from the disease.[1]

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Currently, transrectal prostate biopsy guided by ultrasound (Ultrasound-guided transrectal prostate biopsy; TRUS-Bx) remains the standard method for the diagnosis of prostate cancer.[2] The systematic biopsy was first introduced by Hodge in 1989, and involved six punctures. Later, Eichler and colleagues conducted a systematic review and found that 12 punctures significantly increased the rate of detection of prostate cancer without adding complications. This has led to the widespread adoption of this biopsy method, and is now included in the treatment guidelines published by the European Association of Urology (EAU). Although there are recommendations to perform magnetic resonance imaging (MRI) before TRUS-Bx to increase the rate of cancer detection1, these recommendations may be difficult to implement in Thailand due to limitations of the healthcare budget, a problem experienced in many other countries. Additionally, interpretation of a prostate MRI requires a radiologist who has received specialist training.

TRUS-Bx often causes pain or discomfort during the procedure, and various forms of analgesics are available. The most commonly used method is a local anesthetic due to its convenience, speed, cost, and the feasibility to be applied by the surgeon. These include intrarectal local anesthesia (IRLA), periprostatic nerve block (PNB), intraprostatic local anesthesia (IPLA), and pelvic plexus block (PPB).[3] Intravenous sedation (IVS) and spinal anesthesia (SA) can also be used.[4] The most widely used methods in practice are IRLA and PNB since they are simple and quick to perform. However, some studies indicate that the use of local anesthesia may not reduce pain during TRUS-Bx.[5-8] Subsequently, meta-analyses have revealed that the use of local anesthetics can reduce pain during TRUS-Bx.[3,9] Several studies have found that IRLA provides more effective pain relief than regular lubricants[10,11], while IRLA is less effective than PNB.[3,9,12] According to some studies, application of the two IRLA creams together reduces pain to the same extent as applying IRLA plus PNB, while others have found no difference between IRLA and PNB.[13,14] The main disadvantage associated with the use of PNB is the pain caused by the needle which is used to apply anesthesia around the nerve group near the prostate.[13-15]

The application of heat in combination with topical anesthetics has been shown to improve pain relief[16,17], pointing to a mechanism by which heat facilitates the faster and more efficient penetration of the medication into the epidermal layers. One study found that heated IRLA (Heated IRLA; HIRLA) is a more effective method of pain relief method regular IRLA.[18] Jang and colleagues compared HIRLA with PNB and found that HIRLA was no less effective than PNB.[19,20] However, research studying the efficacy of local anesthetics is still limited in Thailand in comparison to other countries. The primary objective of this study was to compare the efficacy of HIRLA with PNB in patients undergoing prostate interventions. The secondary objective was to compare post-procedural complications following prostate biopsy between the two methods.

Materials and Methods

A prospective randomized trial was performed from July to December 2024 with a 1:1 allocation ratio. The sample size was calculated based on the study by Ding et al[21] Eligibility criteria were: men aged 50 years and above with PSA≥4.0 ng/ml and/or abnormal finding on digital rectal examination. Exclusion criteria included: bleeding disorders, use of antiplatelet/anticoagulant 7 days prior to the study, use of analgesics 2 days prior to the study, no prior antibiotic prophylaxis, comorbidities including inflammatory bowel disease, anal stricture, anal fissure, hemorrhoid, colorectal cancer, urinary tract infection, prostatitis, and cognitive impairment. The study protocol was reviewed and approved by the Ethics Committee Chaophrayayommarat Hospital (YM025/2567), and written informed consent was obtained from all participants. Data was collected in the operating theater and the outpatient clinic in Chaophrayayommarat Hospital. Age, comorbidities, PSA level, and prostate size were recorded as demographic data. After having obtained informed consent and data, participants were randomly assigned to the HIRLA group and PNB group using computer-generated software.

Biopsy protocol

A prophylactic antibiotic (ciprofloxacin 500 mg), along with a cleansing enema, was started on the day of the procedure. Participants were placed in the dorsal lithotomy position. The HIRLA group received 10 ml 2% lidocaine gel, which was heated to 40°c in a temperature-controlled cabinet (Warmer solution model WS-01, Iso tech

instrument (Thailand) co. ltd.), and applied inside the anal canal 5 minutes prior to TRUS-Bx. The PNB group received 10 mL of 1%lidocaine 5 minutes prior to TRUS-Bx by injecting 5 mL on each side of the junction between the prostate and seminal vesicle where the neurovascular bundle is located. After local anesthesia was applied, an ultrasound probe (Toshiba Xario SSA-660 A, Schmidt Biomedtech (Thailand) Ltd.) was inserted transrectally and a standard 12-core prostate biopsy was performed. Pain score was evaluated using a visual analog scale (VAS) ranging from 0 (no pain) to 10 (worst pain ever experienced). The VAS board was positioned at the eye level of the participant to allow self-evaluation. The team member who recorded the pain score of the participant was blinded from the method of anesthesia used. The participant was then transferred to the recovery room, vital signs were monitored for 30 minutes and the patient was checked for signs of lidocaine toxicity.[22-24] The patient was discharged home if vital signs were stable and was directed to continue with the prophylactic dose antibiotic for 3 days. After 1 week, the patient was seen at the outpatient clinic for to discuss the pathology results and as a regular follow-up. Other members of the research team documented any problems, including significant hematuria, defined as gross hematuria lasting more than 48 hours, urinary tract infection, hematospermia, and severe rectal bleeding. Pathology results were recorded by the urologist performing TRUS-Bx.

Outcome measurement

The primary outcome was measured from the pain scores recorded during TRUS-Bx. The secondary outcome was the recording of any significant complications which were noted after the procedure. The margin of difference in VAS score was defined as 1 based on a previous randomized controlled trial.[21] Continuous variables are presented as mean and standard deviation and analyzed using either a Mann-Whitney U test or an unpaired t-test. For the categorical variables, the data are presented as number and percentage, the chi-square test or Fisher exact test were implemented. Analysis of the primary outcome was assessed using a two-sided 95% confidence interval (CI) of the mean difference. Additionally, the 95% CI for the mean difference in VAS score was estimated. Two-sided p-values for the superiority test were used for evaluation of the secondary outcome. Statistical software SPSS version 15 was used to evaluate the data by documenting age, prostate size, PSA value, pathological results, and pre-existing conditions in the data entry form, with a $p < 0.05$ considered statistically significant.

Results

Between July and December 2024, 85 patients underwent a prostate biopsy at Chaophrayayommarat Hospital, 60 of whom fulfilled the selection criteria of the study. Figure 1 shows a flow diagram of the study. Demographic data of all participants

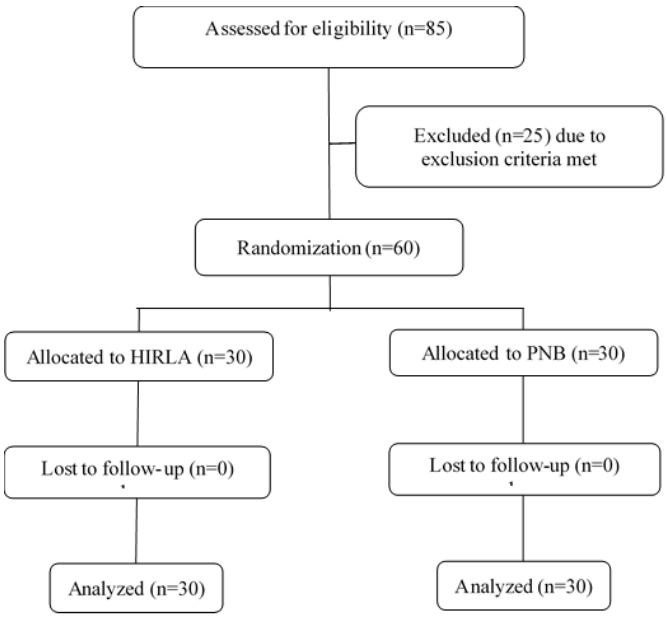

Figure 1. Flow diagram of the study according to consolidated standard of reporting trials (CONSORT)

is presented in Table 1 and shows no significant differences between two groups. Mean pain score during TRUS-Bx was 4.03 in the HIRLA group and 2.57 in the PNB group; the difference was 1.47 with a 95% CI of 0.56 to 2.38 (p = 0.002) as shown in Table 2.

Regarding post-biopsy complications, no statistically significant differences were observed between the two groups, as shown in Table 3. Overall complication rate was 13.3% in both groups. Urinary tract infections were reported in 6.7% of patients in both groups. Significant hematuria was observed in 6.7% of patients in the HIRLA group and 3.3% in the PNB group. Hematospermia persisting for more than 48 hours was recorded in 3.3% of patients in the PNB group, whereas no cases were reported in the HIRLA group. No severe rectal bleeding occurred in either group. No severe adverse events or lidocaine toxicity were noted in either group.

Discussion

TRUS-Bx is a widely performed procedure, yet pain management remains a crucial consideration.[2] While PNB has traditionally been regarded as the gold standard for local anesthesia[3,9,12,21,25], and there are studies that have demonstrated that IRLA and PNB may alleviate pain equally[14,20], HIRLA has been proposed as a potential alternative due to its ease of use.[18,19] However, the findings of this study demonstrate that PNB provides significantly more effective pain relief than HIRLA.

Jung et al introduced the use of HIRLA, showing that it demonstrated improved analgesic efficacy in comparison to standard IRLA.[18] Sub-

Table 1. Characteristic data of the patients

	HIRLA (n=30)	PNB (n=30)	P-value
Age (years) mean ± SD	69.47 ± 8.74	69.67±6.4	0.92
Comorbidities			
- Diabetes melliutus n (%)	6 (20.0)	7 (23.3)	0.754
- Hypertension n (%)	8 (26.7)	11 (36.7)	0.405
- Chronic kidney disease n (%)	3 (10.0)	3 (10.0)	1.000
Cancer present on pathologic result n (%)	10 (33.3)	9 (30.0)	0.781
Prostate volume (ml) median (IQR)	38.5 (22, 67)	42.5 (26, 56)	0.988
PSA level (ng/ml) median (IQR)	10.6 (7.8, 33)	12.4 (5.8, 39)	0.706

SD = standard deviation, PSA = prostate specific antigen, HIRLA = heated intrarectal local anesthesia, PNB = periprostatic nerve block, IQR = interquartile range

Table 2. Mean pain score between two groups

	HIRLA (n=30)	PNB (n=30)	Treatment difference (95%CI)	P-value
Pain score mean ± SD	4.03±1.85	2.57±1.68	1.47 (0.56, 2.38)	0.002*

SD = standard deviation = HIRLA = heated intrarectal lidocaine gel, PNB = periprostatic nerve block, CI = confidence interval

Table 3. Characteristic data of the patients

	HIRLA (n=30)	PNB (n=30)	P-value
Complications n (%)	4 (13.3)	4 (13.3)	1
Significant hematuria	2 (6.7)	1 (3.3)	1
Severe rectal bleeding	0 (0.0)	0 (0.0)	1
Hematospermia	0 (0.0)	1 (3.3)	1
Urinary tract infection	2 (6.7)	2 (6.7)	1

SD = standard deviation, PSA = prostate specific antigen, HIRLA = heated intrarectal local anesthesia, PNB = periprostatic nerve block, IQR = interquartile range

sequently, Jang et al reported that HIRLA was non-inferior to PNB in terms of pain control during TRUS-Bx[19], suggesting that HIRLA could be a viable alternative to PNB, especially considering its simpler technique and fewer procedural requirements.

In contrast, the present study found that PNB provided significantly more effective analgesia than HIRLA, with patients in the PNB group reporting predominantly mild pain levels, whereas those in the HIRLA group reported moderate pain levels. The mean difference in pain scores between the two groups was 1.47. Several factors may explain this discrepancy. First, the methodology differed in terms of drug dosage and timing. In this study, HIRLA was administered using 10 mL of lidocaine gel retained for 5 minutes, while Jang and Jung used 20 ml retained for 10 minutes.[18,19] It is plausible that a higher volume and longer retention time enhance mucosal absorption and analgesic depth, which could explain the lower mean pain scores reported in their studies (3.44 and 3.2) compared to ours (4.03).

Additionally, the concentration and volume of lidocaine used in PNB differed across studies. In our study, 10 ml of 1% lidocaine was used, whereas Jang et al utilized 5 ml of 2% lidocaine. Although the total amount of active drug (100 mg) was equivalent, a larger volume of a lower-concentration solution may provide broader periprostatic tissue coverage and facilitate a more effective nerve blockade. This might explain the lower mean pain score observed in our PNB group (2.57) in comparison to Jang's study (3.14).[19]

From a cost-effectiveness perspective, PNB may require more resources and operator expertise, whereas HIRLA is easier to administer and may offer logistical advantages in high-volume settings. However, the trade-off in analgesic efficacy, as shown in our study, should be carefully considered when selecting the appropriate method.

In terms of safety, both PNB and HIRLA were well tolerated. No patients developed severe allergic reactions to any local anesthetics. The overall complication rate, including urinary tract infection, hematuria, rectal bleeding, and hematospermia lasting more than 48 hours, was 13%. This is in alignment with previously reported complication rates and reinforces the safety of TRUS-Bx with local anesthesia.

This study has several limitations. First, the study was conducted at a single institution, potentially introducing selection bias. Second, the pain assessment was performed during the procedure without long-term follow-up to assess delayed pain or other discomfort. Third, the study did not include plain unheated intrarectal lidocaine gel, which could potentially demonstrate the efficacy of heating the lidocaine gel. Finally, variations in operator technique and individual pain thresholds could have influenced the results. Future multicenter studies with larger sample sizes and extended follow-up periods are needed to confirm the findings of this study.

Conclusions

PNB is superior to HIRLA in reducing pain during TRUS-Bx and has an equivalent safety profile. While HIRLA may be considered when PNB is unavailable, PNB remains the preferred local anesthesia technique for optimizing patient comfort during TRUS-Bx.

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Conflict of Interest

The authors declare no conflict of interest

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