STUDY PROTOCOL

The study was a randomized clinical trial. It was carried out at the University College Hospital, Ibadan among male patients attending the clinics of the urological surgery division. A total of 80 patients were enrolled, with 40 subjects in each arm. A simple randomization technique was employed in the assignment of patients. This was achieved with a randomization schedule which was generated using an online computer software. Patients with bleeding disorders, acute prostatitis, and painful anal conditions were excluded.

Protocol for caudal block

For every patient assigned to the caudal block group, 160 mg of intravenous gentamicin was administered as pre-procedure antibiotic prophylaxis. Thereafter, the patient was positioned prone and the skin of the lower back was prepared with standard skin preparation solution, then 10ml of 2% lidocaine was injected with a 22G needle into the epidural space through the sacral hiatus. Inadvertent injection into a blood vessel was prevented by aspirating prior to injection and repositioning the needle if blood was aspirated into the syringe. The adequacy of the block was then assessed with a perineal needle prick and finding a lax anal sphincter when a rectal examination was done. Occasionally, a mild elongation of the penis was also observed. The patient was then repositioned in the left lateral decubitus position and after a 5- minute wait, the prostate biopsy was commenced.

Protocol for periprostatic nerve block

Each patient was placed in the left lateral position, and following the administration of intravenous antibiotic (gentamicin 160mg) prophylaxis, the transrectal ultrasound probe was inserted into the rectum. Under TRUS guidance, with a 22G 20cm-long spinal needle, 5ml of 1% lidocaine was infiltrated into the neurovascular bundle around the junction of the prostate and seminal vesicles bilaterally and on both sides of the prostatic apex to make a total of 20ml of 1% lidocaine infiltrated. Appropriate and adequate injection was confirmed by observing a hypoechoic wheal on the ultrasound screen as the anaesthetic agent was injected. Inadvertent intravascular injection was prevented by test aspiration prior to infiltration and adjusting the needle if blood was aspirated. After a 5- minute wait, the prostate biopsy was commenced.

Prostate biopsy protocol

Following a digital rectal examination, a 5.0–9.0 MHz transrectal ultrasound probe (SonoScape Medical Corp., Shenzhen, China) was inserted into the rectum, covered with a condom sheath and lubricated by ultrasound gel (Guang Dong University of Technology, China). The volume and echogenicity of the prostate gland was then assessed on the ultrasound machine. Following this, a twelve-core systematic prostate biopsy was performed using a reusable biopsy gun with an 18G core biopsy needle (Geotek Medical, Osb-Ankara, Turkey). At the end of the procedure digital pressure was placed, with a gauze pack, on the prostate via the rectum to control bleeding.

Pain assessment protocol

The pain scores of the participants were assessed with the 11-point numerical rating scale (NRS) at five different moments during the procedure: T1- when the caudal block or peri-prostatic block was administered; T2- when the TRUS probe was inserted; T3- during the prostate biopsy; T4- thirty minutes after the biopsy; and T5- the day after the biopsy (the participants were contacted on phone).

Data analysis

The data collected were analyzed with the IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp., Armonk, N.Y., USA). Parametric and non-parametric tests of significance (Chi Square, t-test and Mann-Whitney U test) were used in evaluating the differences between the groups. Statistical significance was defined for the study as $p < 0.05$.

APPENDIX C - INFORMED CONSENT FORM

IRB Research Approval number: UI/EC/17/0453 This approval will elapse on: 27/12/2018

Title: Transrectal ultrasound guided prostate biopsy: periprostatic block versus caudal block for analgesia

Researcher: This study is being conducted by Dr Oluwatobi Fasola of the Surgery Department, University College Hospital.

Sponsor of research: Self.

Purpose of research: The study will compare the efficacy of transrectal periprostatic nerve block and caudal block for analgesia in transrectal ultrasound guided prostate biopsy. It will assess the pain perception among participants of the study.

Procedure of research: A total of 80 participants will be recruited in this study; you will be assigned to either of two groups using a randomization schedule. In one group, you will be asked to lie on your chest and a local anaesthetic drug will be injected into the vertebral canal at the region of your lower back. Following which, you will be asked to sit up for a short while. You will then be asked to lie on your left side and fold up your lower limbs towards your chest. A rectal examination will be performed following which a transrectal ultrasound probe will inserted into your anus to scan the prostate and guide the biopsy needle for retrieving prostate tissue for histology. In the other group, you will be asked to lie on your left side and fold up your legs to your chest. A rectal examination will also be performed, thereafter a transrectal ultrasound probe will inserted into your anus to scan the prostate and guide a long needle which will be used in injecting local anaesthetic drug around nerves supplying the prostate. After this, a biopsy needle guided by the transrectal ultrasound probe will be used to retrieve prostate tissue for histology. For participants in both groups, at several times, you will be asked to

describe the pain and assess its severity by choosing a number from 0 to 10, 0 being no pain experienced and 10 signifying the worst pain ever experienced. In addition, prior to the procedure you will be given antibiotics to prevent an infection arising. A day after the procedure, you will be contacted on phone; to also do the same assessment described above, and ask about any potential complications.

Expected duration of participant's involvement: The study is expected to be carried out over a period of six months. However, your involvement in the research will last only up to 48 hours, either of both procedures for analgesia take about 10 to 20minutes, while the biopsy procedure lasts approximately between 30 minutes and one hour. You will be monitored for up to 2 hours after the procedure and thereafter asked to go home, if safe to do so.

Risk: The procedures for analgesia have uncommon side effects; caudal block has a rare risk of puncturing the spinal cord covering called the dura in the vertebral canal, with symptoms of nausea, vomiting, pain or tingling in arms and legs, hearing loss, ringing ears, dizziness. Should this happen, intravenous fluids will be administered and the dural puncture managed at no extra cost to the participant. With the other group, periprostatic nerve block could uncommonly be complicated with inadvertent injection of the local anaesthetic into a blood vessel with symptoms of metallic taste in the mouth, or tingling or numbness of the mouth, ringing in the ears, or heart failure. Should this happen, intravenous fluids will be administered and the patient treated promptly.

Costs entailed in joining the research: Your participation will not entail any additional costs over the regular hospital fees for the transrectal ultrasound guided prostate biopsy.

Benefits: There is no direct benefit to you for joining the research however, the findings of the study may benefit other patients by revealing which is of the procedures is a more effective method of alleviating pain for transrectal ultrasound guide prostate biopsy.

Confidentiality: All the information gathered in the course of this study will be given codes and the information cannot be linked to you in any way. Your name or other identifiers will not be in any report or publication from this study.

Voluntariness: Your participation in this study is entirely voluntary. If you choose not participate, your treatment in this hospital will not be affected.

Inducements: You will not be paid any fees for participating in this research.

Withdrawing from the research: You can choose to withdraw from the study at any time, and any information obtained about you will not be used. This will not affect your treatment in the hospital.

What happens to research participants when research is over: You will be informed on the outcome of the research through news bulletin or at follow-up clinic visits.

Statement of person obtaining informed consent: I have fully explained this research to…….. ……and have given sufficient information, including risk and benefits, to make an informed decision.

Date:_____ Signature _____ Name:

_____

Statement of person giving consent: I have read the description of the research and talked it over with my doctor to my satisfaction. I understand my participation is voluntary, and know enough about the purpose, method, risks and benefits of the research study to judge that I want to take part in it. I understand that I may freely stop being part of the study at any time. I have received a copy of this consent form to keep for myself.

DATE_____ SIGNATURE/THUMBPRINT_____

NAME_____

WITNESS SIGNATURE_____

WITNESS NAME_____

Contact information: This research has been approved by the Health Research Ethics Committee of the University of Ibadan and the Chairman of this Committee can be contacted at the Biode Building, Room T10, 2nd Floor, Institute of Advanced Medical Research and Training (IMRAT), College of Medicine, University College Hospital, Ibadan. E-mail: uiuchirc@yahoo.com. In addition, if you have any questions about your participation in this research, you can contact the principal investigator, Dr Oluwatobi Fasola in the Department of Surgery, UCH, Ibadan. E-mail: fasola.oluwatobi@yahoo.com

PLEASE KEEP A COPY OF THE SIGNED INFORMED CONSENT

RESULTS

5.1 Recruitment of participants

During the study period, a total of 80 subjects were recruited, 40 men were allocated randomly into each arm of the trial. The flow diagram for the recruitment is as follows:

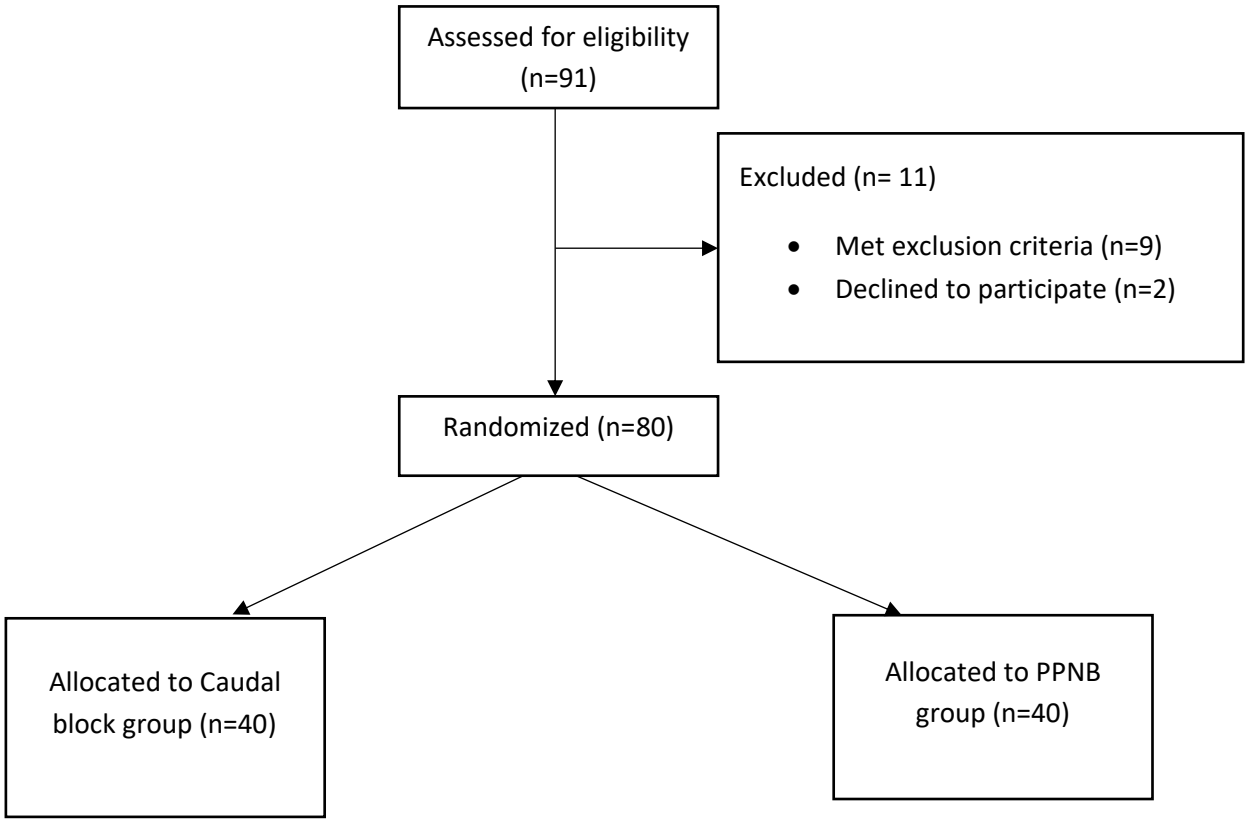

Figure V: Flow diagram showing how participants were recruited and allocated to the two intervention groups.

Group characteristics in terms of age, body mass index (BMI), prostate specific antigen (PSA), prostate size, DRE and TRUS findings, and previous caudal block or prostate biopsy

There were no statistically significant differences in the mean age, body mass index, pre-biopsy prostate specific antigen level, prostate size of the patients, DRE and TRUS findings in either group. There was also no significant difference in the proportion of men in both groups who had prior biopsy and caudal block. (Table 1)

Comparison of pain scores between groups

Table 2 shows the comparison of the mean pain scores between the two different groups. The mean pain score was highest at the moment of prostate biopsies for the CB group (3.1 ± 2.6) while it was highest at the moment of administering block for the PPNB group (3.1 ± 2.2). The difference in mean pain score was greatest at the moment of taking the prostate biopsies, with the men in the CB group experiencing a mean pain score that was 10% greater than the mean score of the PPNB group. However, this difference in mean pain score was not statistically significant. There was no statistically significant difference in the pain scores at any other moment of the procedure.

There was a slightly higher mean pain score at insertion of the TRUS probe in the PPNB group compared to the CB group, this was however not statistically significant. Figure I further shows that at the insertion of the TRUS probe, the pain scores for men in the PPNB group only ranged from 0 to 4 while it ranged from to 0 to 9 in the CB group. Also, the modal score was 0 for the CB group (30%), while it was 3 for the PPNB group (32.5%).

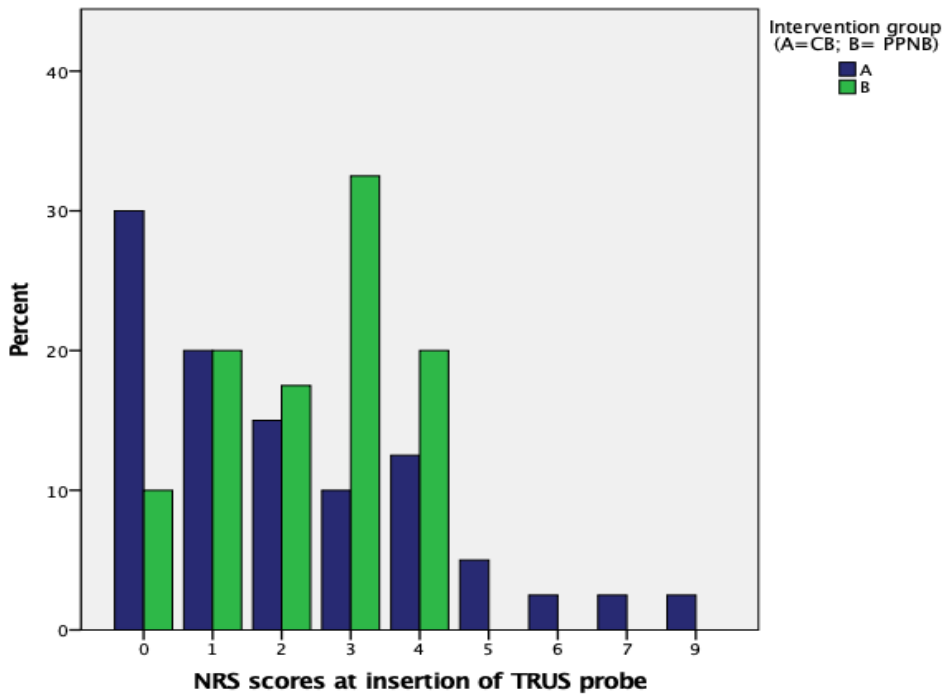

Figure I: Bar chart showing the percentages of men per reported NRS pain score for each intervention group the insertion of the TRUS probe. CB (Group A); PPNB (Group B)

Table 1: Comparison of mean ages, BMI, PSA, TRUS prostate volumes, prior procedures, and TRUS prostate findings between the group A and group B. (CB= caudal block; PPNB= periprostatic nerve block; BMI= body mass index; SD=standard deviation; PSA= prostate specific antigen; TRUS = Trans-rectal ultrasound)

	Group A (CB)	Group B (PPNB)	p value
	Mean ±SD	Mean ±SD	
Age (years)	69.2±8.7	68.5±6.4	0.67
BMI (kg/m^2)	24.9±4.7	27.0±5.1	0.06
	Median (IQR)	Median (IQR)	
PSA (ng/ml)	28.1 (16.8 – 98.4)	50.5 (17.2 – 211.9)	0.40
TRUS prostate size (cm^3)	60.2 (38.3 – 94.0)	57.8 (36.5 – 95.0)	0.98
	Number (%)	Number (%)	

Prior prostate biopsy?			
Yes	8 (20)	6 (15)	0.56
No	32 (80)	34 (85)	
Prior caudal block?			
Yes	8 (20)	7 (17.5)	0.73
No	32 (80)	33 (82.5)	
TRUS echogenicity?			
Homogeneous	13 (27.5)	11 (32.5)	0.63
Heterogeneous	27 (72.5)	29 (67.5)	

Table 2: Modal pain score at administration of block was 3 for both groups, while at insertion of probe, the modal scores were 0 and 3 for CB and PPNB respectively.

	Group A (CB) Mean ± SD	Group B (PPNB) Mean ± SD	Mean difference	p-value
At administration of block	2.9 ± 2.3	3.1 ± 2.2	-0.2	0.56
At insertion of TRUS probe	2.1 ± 2.2	2.3 ± 1.2	-0.2	0.18
At taking prostate biopsy	3.1 ± 2.6	2.8 ± 2.7	0.3	0.40
30 minutes post-procedure	1.4 ± 2.2	1.4 ± 1.7	0.0	0.48
1-day post-procedure	0.2 ± 0.4	0.3 ± 0.5	-0.1	0.32

Comparison of satisfaction with and willingness to repeat biopsy procedure and incidence of complications between groups

A higher proportion of the patients who had PPNB (72.5%) than those who had CB (65%) were satisfied with the method of block used. This was however not statistically significant. Furthermore, a similar proportion (42.5%) of men were willing to repeat the prostate biopsy procedure using the same method for blocking pain in both intervention groups. There was a low rate of complications in all the participants, with no significant difference between the groups (Table 3).

Table 3: Comparison of the proportion of patients who were satisfied with and who were willing to have repeat prostate biopsy using the same method of analgesia between the two groups, and the incidence of complications following prostate biopsy between groups

	Group A (CB) n=40 Number (%)	Group B (PPNB) n=40 Number (%)	p-value
Satisfaction with procedure			
Satisfied	26 (65%)	29(72.5%)	0.77
Indifferent	9 (22.5%)	7 (17.5%)	
Not satisfied	5 (12.5%)	4 (10%)	
Willingness to repeat biopsy with similar block			
Willing	17 (42.5%)	17 (42.5%)	0.96
Indifferent	13 (32.5%)	14 (35%)	
Not willing	10 (25%)	9 (22.5%)	
Hematuria?			
Yes	6 (15%)	6 (15%)	0.96
No	34 (85%)	34 (85%)	
Febrile reaction?			
Yes	1 (2.5%)	1(2.5%)	1.00
No	39 (97.5)	39 (97.5%)	
Urinary retention?			
Yes	2 (5%)	0 (0%)	0.15
No	38 (95%)	40 (100%)	