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Original article

The Role of Histopathological Outcome on Pain of Transrectal Ultrasound Guided Prostate Biopsy: A Randomised trial

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Abstract

Introduction: Transrectal ultrasound guided prostate biopsy is the gold standard for diagnosis of carcinoma of the prostate. The pain of prostate biopsy is of immense challenge. Many factors have been ascribed to it. Identifying such risk factors will assist in mitigating the pain associated with this procedure. This study therefore aims to assess the role of histopathological outcome on pain of TRUS guided prostate biopsy. ***Methods:*** The study was a prospective randomized study carried out in University of Benin Teaching Hospital over a 1year period between 2017 and 2018. Consecutive patients who met indications for biopsy were randomized into Group A: intrarectal xylocaine gel group and Group B: periprostatic block group. Pain was assessed during probe insertion, biopsy and one hour post biopsy using an 11-point visual analogue scale. Association between mean pain scores and histological diagnosis in both groups was assessed using the independent t- test, association between use of intrarectal xylocain gel, periprostatic block was done using the independent t-test. Level of significance set at $p < 0.05$. ***Results:*** There was no statistically significant difference in mean pain score during probe insertion, biopsy and post biopsy (p=0.3888), (p=0.089) and (p=0.584) respectively between benign and malignant histological diagnosis for Group A, while there was also no statistically significant difference in mean pain score during probe insertion, biopsy and post biopsy (p=0.266), (p=0.506) and (p=0.522) respectively between benign and malignant histological diagnosis in Group B. Cancer detection rate for Group A and Group B was 64.3% and 59.1% respectively, which was not statistically significant p=0.662. ***Conclusions:*** The study demonstrated that pain of TRUS guided prostate biopsy is not influenced by histopathological outcome irrespective of mode of anaesthesia. Cancer detection rate was also not influenced by choice of anaesthesia during TRUS guided prostate biopsy.

Keywords: ***Anaesthesia, Carcinoma of the prostate, Histopathological outcome, Pain, Periprostatic, Prostate biopsy, Transrectal ultrasound, Xylocaine***

Introduction

The second leading cause of cancer among men worldwide is carcinoma of the prostate [CAP] [1]. Transrectal ultrasound (TRUS) guided prostate biopsy is the gold standard for diagnosis of carcinoma of the prostate (CaP) [2]. Studies have revealed that without anesthesia, 65%-90% of patients reported discomfort and 30% reported significant pain [3,4]. Therefore, the pain experienced by the patient during prostate biopsy poses significant challenges both for patients and clinicians performing the biopsy procedure [5].

There are established factors that influenced experience of severe pain during TRUS guided prostate biopsy; age, [6] prostate volume, [7] number of biopsy core samples, [8] sampling site [9] and pre biopsy anxiety which occurs in 67% of patients resulting in exaggerated pain perception [10-12], have all been reported as significant predictors of pain. The intensity of pain felt during prostate biopsy maybe ascribed to activities performed prior to biopsy which include digital rectal examination, insertion of ultrasound probe in TRUS-guided prostate biopsy or insertion of needles in to the rectum during peri-prostatic block [13]. Apex of the prostate is the most painful site during biopsy, [14] due to a predominantly somatic nerve supply to the anorectal mucosa below the dentate line, the apex of the prostate has other peculiar features, it is entirely composed of peripheral zone and its sampling is critical as it is the common conduit for cancer spread [13]. It is also the most common site for missed cancers on TRUS guided prostate biopsy as the sampling of this site is often avoided due to anticipated intense pain [4,15]. It is possible if measures are adopted to prevent pain during sampling of this sites may increase the cancer detection rate.

Controversies exist as to the relationship between pain and histopathology of biopsy specimen. Temiz et al [16] proposed a relationship between pain experienced by patients and histopathological outcome, which was attributed to the inability to adequately manipulate probe effectively to sampling sites where cancers are more likely to occur such as apical and far lateral regions. Recent studies by Bolat et al, [17] has controverted this finding by establishing that there is no significant relationship between histopathology results and pain intensity, also corroborating this finding was a study by Sonmez et al, [7]. The inconsistencies regarding pain of prostate biopsy in the literature has necessitated the need for further exhaustive research on factors predicting pain of prostate biopsy.

This study aims to establish if any relationship exists between pain of TRUS-guided prostate biopsy and histopathological outcome of biopsy specimen.

Patients and Methods

Design, setting, period and population of the study: This is a prospective randomized study carried out over one year between 2017 and 2018. It involved consecutive patients presenting at the outpatient urology clinic of University of Benin Teaching Hospital Edo State. Forty-five patients were each randomized into two groups. ***Group A:*** Intra-rectal xylocaine gel group (I-X) and ***Group B:*** Peri-prostatic block group (P-P). It was a double-blind study; both the researchers and patients were blinded to the groups and measurement of outcome measures.

Inclusion and exclusion criteria: Inclusion criteria included patients with elevated prostate specific antigen (PSA) level greater than 4ng/ml and/ abnormal digital rectal examination. Exclusion criteria included patients with painful anorectal conditions, bleeding diathesis, strictures and allergy to local anesthetic.

Methods: Apical infiltration of 10mls of 1% xylocaine (5mls on each side) was carried out under Trans-rectal ultrasound guidance using a 7-inch, 22-gauge spinal needle for Group A. Group B patients had 10mls of intra-rectal instillation of xylocaine gel before insertion of ultrasound probe.

Prostate volume was measured before commencement of needle biopsy.

Pain during insertion of probe and capsular penetration was assessed using an 11-point visual analogue scale (0= no pain; 10= most severe pain). Pain after an hour post biopsy was also recorded before discharge. Patients were followed up in out -patient clinic for 1 month to assess for complications.

Data collection and statistical analysis: Data was collected using a researcher administered proforma and analysed using statistical package for social sciences (SPSS) version 21.0. Continuous variables were expressed as means while categorical variable were expressed in frequency. Test of association was done using student t-test. Level of significance was set at $p < 0.05$.

Ethical approval was obtained from the University of Benin Ethics and research committee. Written informed consent was also obtained from patients who participated in this study.

Results

The mean (SD) age of the study population is 68.6 ± 9.2 years. A higher proportion of patients in both Xylocaine (44.4%) and Peri-prostatic (40.0%) study group were in the 60 to 69 years age range.

Table 1: Age of study population

Variable	Frequency (%)			
	Xylocaine (n=45)	**P-P block (n=45)**	**Test statistic**	**p-value**
Age group				
40-49	2 (4.4)	1 (2.2)	Fishers' exact = 5.337	0.251
50-59	5 (11.1)	1 (2.2)		
60-69	20 (44.4)	18 (40.0)		
70-79	15 (33.3)	17 (37.8)		
≥80	3 (6.7)	8 (17.8)		
Mean (sd) age	66.5 ± 8.7 (years)	70.8 ± 9.3 (years)	t=-2.270	**0.026**

Table 2: Pain score and histological diagnosis within xylocaine group

Variable	Histopathology of specimen			
	Benign Mean ± SD	**Malignant Mean ± SD**	**t statistic**	**p value**
Pain score during probe insertion	2.7 ± 1.9	3.2 ± 2.0	-0.874	0.388
Pain score during biopsy	5.5 ± 2.1	6.6 ± 1.7	-1.745	0.089
Pain score post biopsy	2.1 ± 1.6	2.4 ± 1.8	-0.552	0.584

There was no statistically significant difference in the mean pain score during probe insertion between patients with benign and malignant histological diagnosis in the Xylocaine anaesthesia group (p=0.388).
There was no statistically significant difference in the mean pain score during biopsy between patients with benign and malignant histological diagnosis in the Xylocaine anaesthesia group (p=0.089).
There was no statistically significant difference in the mean pain score post biopsy insertion between patients with benign and malignant histological diagnosis in the Xylocaine anaesthesia group (p=0.584).

Table 3: Pain score and histological diagnosis within p-p block group

Variable	Prostate Histology			
	Benign Mean ± SD	**Malignant Mean ± SD**	**t statistic**	**p-value**
Pain score during probe insertion	3.3 ± 1.6	2.7 ± 1.8	1.127	0.266
Pain score during biopsy	3.3 ± 1.7	2.9 ± 1.9	0.671	0.506
Pain score post biopsy	1.3 ± 0.8	1.1 ± 0.8	0.646	0.522

There was no statistically significant difference in the mean pain score during probe insertion between patients with benign and malignant histological diagnosis in the P-P block anaesthesia group (p=0.266).
There was no statistically significant difference in the mean pain score during biopsy between patients with benign and malignant histological diagnosis in the P-P block anaesthesia group (p=0.506).
There was no statistically significant difference in the mean pain score post biopsy between patients with benign and malignant histological diagnosis in the P-P block anaesthesia group (p=0.522).

Table 4: Histologic findings among study groups

	Frequency (%)		Test statistic	p-value
Histologic diagnosis	**Xylocaine (n=42*)**	**P-P block (n=44*)**		
Benign	15 (35.7)	18 (40.9)	$\chi 2 = 0.245$	0.662
Malignant	27 (64.3)	26 (59.1)		

*Results obtained for this number in sample

There was no statistically significant difference in proportions regarding the histological diagnosis between the Xylocaine and P-P study groups (p=0.662).

Table 5: Clinical characteristics of study population

Variable	Frequency (%)			
	Xylocaine (n=45)	**P-P block (n=45)**	**Test statistic**	**p-value**
Presenting symptoms				
LUTS	44 (97.8)	45 (100.0)	Fishers exact=1.011	1.000
LUTS + ED	1 (2.2)	0 (0.0)		
Median (range) duration of symptoms	36.0 (1, 410) months	24.0 (3, 468) months		0.735*
Indication for biopsy				
Abnormal DRE	5 (11.1)	8 (17.8)	$\chi 2 = 1.329$	0.520
Elevated PSA	10 (22.2)	12 (26.6)		
Both	30 (66.7)	25 (55.6)		
Mean ± sd QOL	4.27 ± 1.08	4.46 ± 1.10	t = -0.655	0.515
*Mann-Whitney test				

Lower Urinary Tract Symptoms (LUTS) were the most common clinical feature among both Xylocaine (97.8%) and P-P block (100.0%) study groups. The median (range) duration of symptoms was 36.0 (1-410) months in the Xylocaine group and 24.0 (3-468) months in the P-P block study group. This difference was not statistically significant. Thirty (66.7%) patients in Xylocaine group and 25 (55.6%) in P-P block group were referred for biopsy based on both elevated PSA results and abnormal digital rectal examination findings (p=0.515). Mean Quality of Life scores (QOL) of patients were higher among patients in the P-P block group (4.46±1.10) compared to Xylocaine group (4.27±1.08). This was however not statistically significant (p=0.515).

Discussion

Diverse opinion have been held by various researchers regarding relationship between pain of TRUS guided prostate biopsy and histopathology of biopsy specimen, this is in a bid to assess the potential risk factors associated with pain during TRUS guided prostate biopsy. In this study there was no statistically significant difference in mean pain score during probe insertion between patients with benign and malignant histopathological diagnosis in both intra rectal xylocaine gel group (p= 0.388) and the peri-prostatic block group (p=0.266), similarly it was also observed that mean pain score on the visual analogue scale during biopsy between patients with benign and malignant histopathology was insignificant for both intra rectal xylocaine group and peri-prostatic block group. The study also evaluated pain score post biopsy for patients with benign and malignant histopathological diagnosis, findings also revealed no statistically significant difference in mean pain scores using either xylocaine gel instillation or carrying out apical peri-prostatic block.

Findings in this study were corroborated by Bolat et al, [17] who reported that there is no significant relationship between histopathology results and pain intensity. In a more recent study by Sonmez et al, [7] in which preoperative prostate imaging- reporting and data system (PI-RADS) scores and histopathology were evaluated, no relationship was established with pain experienced during prostate biopsy. In contrast Temiz et al, [16] reported a relationship between pain experienced by patients and the histopathology of biopsy specimen. They adduced inability to manipulate probe effectively to biopsy region of the prostate where cancer is likely to occur such as apical and far lateral region as reasons why more pain is felt [16], as a corollary, this could be ascribed to the competence of the personel who carried out this biopsy. In another study, Rempega et al [18] established that the apex of the prostate is extremely pain sensitive part of the prostate due to predominance of somatic nerves in the area below the dentate lines, this area coincides with region where cancers are most likely to occur [16] hence maybe responsible for the deduction that there is a correlation between histopathological outcome and pain of prostate biopsy.

Furthermore, Demir et al [19] also investigated the correlation between pain control method and pathological diagnosis. Findings in their study revealed anaesthesia type influences pain felt during prostate biopsy in relation to the histopathological diagnosis. They reported significant pain during biopsy in the group of patients that had intra rectal lidocaine gel instillation for chronic prostatitis, however this could not be assessed in our study as there was no histopathological report of chronic prostatitis.

It is noteworthy to state that the visual analogue score for benign and malignant histopathology during probe insertion, biopsy and post biopsy was lower with peri-prostatic block compared to the use of intra rectal xylocaine gel in this study, even though statistical significance was not tested, this supports findings in previous studies [20,21] that demonstrated superiority of peri-prostatic block over use of xylocaine gel instillation.

Cancer detection rate in both intra-rectal xylocaine gel group and peri-prostatic block group was 64.3% and 59.1% respectively, the difference was not statistically significant (p=0.662). This finding is at variance with the study by Temiz et al [16] who reported improved cancer detection rate with peri-prostatic block compared to intra-rectal lidocaine gel instillation.

Conclusion

This study has clearly demonstrated that pain of prostate biopsy is not influenced by histopathological outcome, irrespective of whether intrarectal xylocaine gel instillation or periprostatic block was administered during biopsy. Cancer detection rate is also not determined by choice of anaesthesia following results of this study. Overall, superiority of periprostatic block over intra-rectal xylocaine gel instillation is not in doubt.

Declarations

Ethics approval and consent to participate

Ethical approval was sought and obtained from University of Benin Teaching Hospital Ethics and Research Committee. Written informed consent was also obtained from patients who participated in this study. Participation of human research subjects conformed to institutional review board guidelines, applicable laws, and the World Medical Association Declaration of Helsinki.

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Conflict of Interest

No conflict of interest has been declared by the authors.

Availability of data and materials

Datasets generated and /or analysed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

EO and EVE made substantial contributions to the conception and design of this work.
EO and EVE also contributed immensely to the acquisition, analysis and interpretation of data.
EO and EVE were involved in drafting the work and substantively revised it.
EO and EVE have approved the submitted version and to have agreed both to personally accountable for the authors own contributions and to ensure that questions related to the accuracy or integrity of any part of the work.

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