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Efficacy of intrarectal lidocaine gel in pain relief during transrectal prostate biopsy

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Abstract: Prostate biopsy is the gold standard for tissue diagnosis of prostate cancer. A significant proportion of men undergoing transrectal ultrasound (TRUS) guided prostate biopsy report pain during the procedure thereby underscoring the need for some pain relief. The aims of this study were to determine the effect of intrarectal lidocaine gel in improving pain relief during ultrasound-guided transrectal biopsy. This was a prospective study of 108 patients scheduled for transrectal prostate biopsy in our hospital over a 16 month period. Patients were randomly assigned to receive 100mg of oral tramadol and 20ml of intrarectal 2% lidocaine gel 10 minutes before the procedure (lidocaine group) or 100mg of oral tramadol and 20ml of intrarectal KY jelly(placebo) 10 minutes before the procedure (placebo group). Pain severity was assessed at 2 minutes after both phases of the procedure using the numerical rating score (NRS). The mean pain scores for the lidocaine and placebo groups during ultrasound probe insertion where 3.4±2.1 and 4.1±1.8 respectively. The mean pain scores for both groups during biopsy needle insertion were 5.2 ± 2.0 and 6.4 ± 1.9 for the lidocaine and placebo groups respectively. The differences in mean pain scores during ultrasound probe insertion as well as during biopsy needle insertion were statistically significant (P = 0.036 and 0.002 respectively). 43 patients (78.2%) in the lidocaine group gave consent for a possible repeat biopsy under the same conditions as against 31 patients (58.5%) in the placebo group (P 0.026). Results of our study show that intrarectal lidocaine gel is effective in improving pain relief during both phases of transrectal ultrasound-guided biopsy of the prostate.
Keywords: Lidocaine, Prostate, Biopsy, Pain relief, Prostate cancer

INTRODUCTION

Prostate cancer is an important cause of morbidity and mortality worldwide [1]. It is the most common cancer detected in Nigerian men with an incidence of 62-127/100,000 [2,3]. According to the American Cancer Society, prostate cancer is least common in Asian men and most common in black American men with figures for Caucasians in between [4]. Although serum prostate specific antigen (PSA) testing, digital rectal examinations and transrectal ultrasound scan help identify men at risk for prostate cancer, the gold standard for tissue diagnosis is currently biopsy of the prostate. It has been estimated that as many as a million biopsies of the prostate are performed in the United States each year making it one of the most common office procedures for urologists [5]

Prostate biopsy though considered a minor and safe procedure, is beset with pain as the most common complaint during and after the procedure [6]. Despite various documented attempts at providing pain relief, no consensus on optimum analgesia during the procedure has been reached [7, 8]. In recent years, the tendency has been to increase the number of cores obtained during prostate biopsy, with the aim of increasing the diagnostic yield of the technique. An increase in the number of cores implies greater patient discomfort [9]. There has also been an increase in patients requiring repeat prostate biopsies due to suspected false negative biopsies on initial testing, suspicious pathology or active surveillance [10]. This equally translates to greater discomfort as well as reluctance to undergo a repeat biopsy thereby underscoring the need for adequate anaesthesia during this procedure.

Considering the physical and psychological trauma associated with pain, the need for adequate pain relief cannot be overemphasized thereby necessitating an assessment of relatively cheap, safe and non-infiltrating means of alleviating this complaint. Lidocaine gel as a pain relief agent is considered to be safe, easy to handle and relatively inexpensive. Studies have revealed that this type of anaesthetic is effective in controlling pain associated with rectal probe insertion and manipulation [11] though there is scanty information on its efficacy in controlling pain felt on needle penetration of the prostate gland.

This study aimed at prospectively evaluating the role of intra rectal lidocaine gel in improving pain relief during transrectal ultrasound-guided prostate biopsy using the numerical rating scale (NRS) which has been shown to be superior to other self-report assessments of pain intensity such as the visual analogue scale (VAS) and verbal rating scale (VRS) [12].

MATERIALS AND METHODS

The study was a hospital-based cross-sectional prospective study carried out at the University of uyo teaching hospital, Uyo, Nigeria. It spanned 16 month between 1st March 2014 and 30th June 2015. The ethical approval for the study was obtained from the hospital's Ethics Committee and written informed consent was obtained from the patients. The subject selection was by purposive criterion sampling method. Included in the study were all new patients aged 40 years and above with lower urinary tract symptoms attending the urology clinic with elevated PSA >4ng/ml and/or digital rectal examination findings suggestive of cancer of the prostate who did not possess exclusion criteria and voluntarily gave their consent to take part in the study. Exclusion criteria included Patients with painful anorectal conditions, neurological conditions, acute prostatitis, metastatic cancer of the prostate as well as patients on analgesics for other reasons. The WINPED computer software was used for random subject allocation into the two study groups.

After explanation of the aims of the study and obtaining written consent from the patient, demographic and clinical information were collected from each patient by the investigator using an interviewer-administered questionnaire. Patients were placed following randomization into either of two groups. Group 1 (lidocaine group) had 100 mg of tramadol administered orally 1 hour before and then 20 mls of 2% lidocaine gel administered per rectum10 minutes before transrectal ultrasound probe insertion, while group 2 (placebo group) had 100 mg of tramadol administered orally 1 hour before as well as 20 mls of placebo (KY jelly) administered per rectum 10 minutes before transrectal ultrasound probe insertion. These administrations were double-blind (both to the subject and investigator). All subjects underwent soap-water enema in the morning of the procedure as well as received prophylactic antibiotics (200mg of ciprofloxacin and 500mg of metronidazole) intravenously, 1 hour before the biopsy, followed by 500mg of ciprofloxacin and 400mg of metronidazole orally 12 hours after. All intrarectal instillations were done with the patients in the left lateral position. Subsequent to the intrarectal instillation of the gel, the gloved right index finger of the researcher was used to smear it over the prostate gland to maximize surface area covered by the gel and also re-determine the characteristics of the prostate gland.

Transrectal biopsy was carried out using an 18G trucut biopsy needle on a loaded biopsy gun attached to and guided by a 7 MHz transrectal ultrasound probe, with the subject in the left lateral position. Ten (10) biopsy cores were taken from both lobes (sextant with two lateral cores on each side). Subjects were required to grade pain felt during transrectal probe insertion and pain felt during needle biopsy 2 minutes after these respective phases of the procedure using the 10-point numerical rating scale, NRS. The question concerning grading of pain was phrased in the same manner in all cases to minimize bias during data collection.

Data derived were entered into Microsoft Excel spreadsheet and analyzed using the statistical package for social sciences (SPSS, version 20).

RESULTS

This study was carried out over a period of 16 months. A total of 112 men were recruited for the study but 108 patients were studied after exclusion of 4 men. 3 men did not complete the prostate biopsy due to uncontrollable pain and 1 failed to show up for follow up. The results and findings of the men studied are shown in the following tables and figures.

The age range of patients was from 40 to 88 years with mean age of 65.3 ± 9.2 years. The peak age group was in the age range 60-69 years and accounted for 44 patients (40.7%) of the entire study population. Cumulatively, 82 (75.9%) of the patients were above 60years of age (Table 1).

Table-1: Distribution of patients with age ranges in decades

Age (years)	Number of patients in lidocaine group (%)	Number of patients in placebo group(%)	Total (%)
40 – 49	3 (5.4)	2 (3.8)	5 (4.6)
50 – 59	11 (20.0)	10 (18.9)	21 (19.4)
60 – 69	23 (41.8)	21 (39.6)	44 (40.7)
70 – 79	14 (25.5)	19 (35.8)	33 (30.6)
80 – 90	4 (7.3)	1(1.9)	5 (4.6)
Total	55	53	108

The mean ages were 64.7±10.3 and 65.9±8.0 in the Lidocaine and placebo groups respectively which was not statistically significant (table 2). The distribution of PSA in the 2 study groups showed no significant statistical difference with the lidocaine and placebo groups having mean PSA of 35.0 ± 29.4 ng/ml

and 40.3 ± 31.4 ng/ml respectively (Table 2). Prostate volume on ultrasound ranged from 22cm^3 to 246cm^3 with mean prostate size at 83.2 ± 49.4cm^3. Mean prostate size in the placebo group was 89.6 ± 54.0cm^3 while that of the lidocaine group was 77.0 ± 44.1 cm^3 and there was no significant difference in prostate size between the two groups of patients (Table 2).

Table-2: Distribution of patient characteristics between the study groups

Patient characteristics	Lidocaine group Mean(+/- SD	Placebo group Mean(+/- SD)	p- value
Age	64.7 (±10.3)	65.9 (±8.0)	0.511
Prostate volume	77.0 (±44.1)	89.6 (±54.0)	0.189
PSA level	35.0 (±29.4)	40.3 (±31.4)	0.368
PSA density	0.52 (±0.49)	0.55 (±0.45)	0.730

Using the numerical rating scale, NRS, the mean pain score during transrectal probe insertion in the lidocaine group was 3.4 ± 2.1 whereas the value for the placebo group was 4.1 ±1.8. This difference in mean pain score was statistically significant (Figure 1). A statistically significant difference was also observed between the mean pain scores of the two groups during biopsy needle insertion. The mean pain scores for both groups during biopsy needle insertion were 5.2 ± 2.0 and 6.4 ± 1.9 for the lidocaine and placebo groups respectively (Figure 2). In the lidocaine group, 78.2% of patients (43) gave consent for a possible repeat biopsy under the same conditions as against 31 patients (58.5%) in the placebo group (Figure 3).

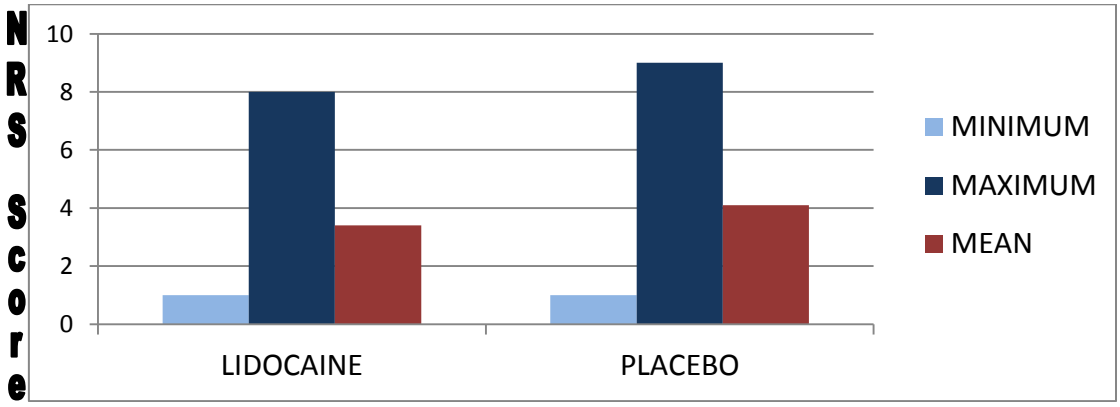

Fig-1: NRS scores in both study groups during probe insertion
p* = 0.036

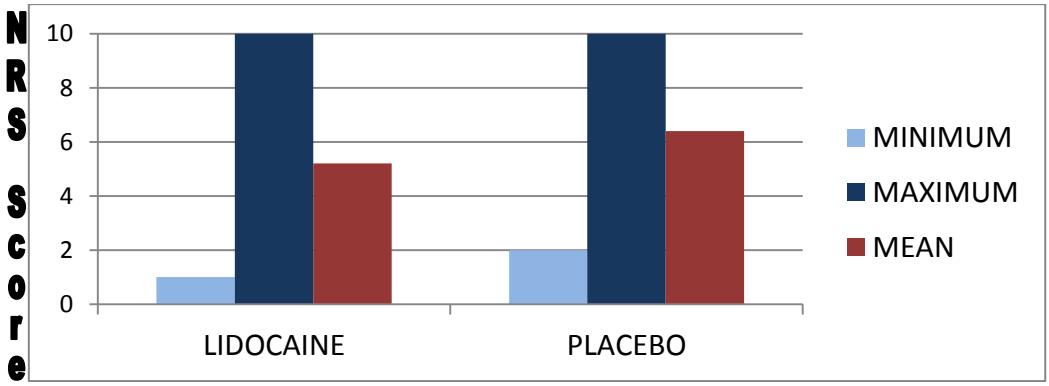

Fig-2: NRS scores in both study groups during needle insertion
p* = 0.002

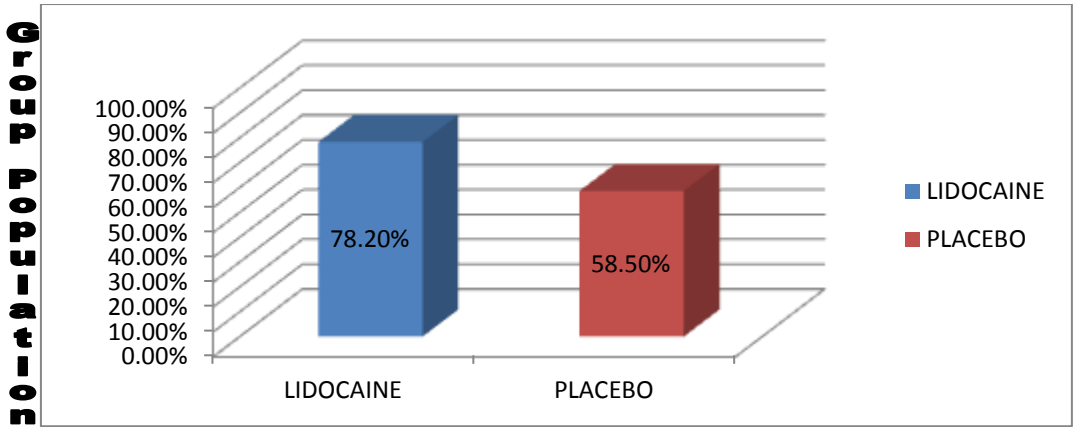

Fig-3: Willingness to accept repeat biopsy.
p* = 0.026

DISCUSSION

Transrectal ultrasound guided prostate biopsy as an essential mordality for the diagnosis of prostate cancer is considered a minor procedure. Despite its simplicity, the procedure is associated with some level of patient discomfort and morbidity.

Pain associated with the prostate predominantly arises in the prostatic capsule or stroma. These are structures richly innervated with autonomic fibres. Innervation of the prostate is derived from the caudal roots of S2 to S5 and also from the sympathetic chain via the presacral and hypogastric neural plexuses. These neural plexuses are located just above the seminal vesicles and from this point, provide fibers that run in a plane between the prostate and the rectum alongside the prostatic vascular pedicles. These nerves are located inferior and laterally to the prostate and represent its main nervous supply. On the other hand, the anterior and supero-lateral surfaces do not appear to have significant innervations. Pain fibres from the prostate travel through postero-lateral fibres to the inferior hypogastric plexus, entering the spinal cord at S2 to S5 levels [13].Pain during prostate biopsy is generated by direct contact between these nerves and the needle as it passes through the prostate as well as during transrectal probe insertion during transrectal ultrasound-guided biopsies due to mechanical stretching of the anal canal distal to the dentate line, which is full of sensory fibres [14].

Several studies have shown conflicting results concerning patients' tolerance to pain during transrectal ultrasound-guided prostate biopsy. Irani and colleagues [15] reported a mean visual analogue scale (VAS) evaluation of pain score of 3, with only 5% of patients having a score of 5 or more and inferred that prostate biopsy is a mildly uncomfortable procedure. However, Crundwell and co-workers [16] reported that 24% Of the 104 men studied found the procedure moderately to extremely painful and concluded that the procedure is a painful experience which is similar to Elabbady's report[17] that 31% of patients studied required intravenous sedation to complete the procedure effectively. Ukoli *et al* reported that none of the screened patients in their study done in rural Nigeria agreed to undergo a prostate biopsy despite adequate counselling, citing fear of possible pain following the procedure as one of the reasons [18].

Various forms of analgesia, including oral tramadol[19] intrarectal lidocaine gel [20] lidocaine nerve blockade[21] caudal block[22] nitrous oxide inhalation (entonox) [23] sedation and even general anaesthesia using propofol [24] have been reported to effectively decrease patient pain and discomfort during TRUS-guided prostate biopsy. Nonetheless, there is no consensus on optimum analgesia during the procedure.

Lidocaine gel, apart from being the most widely used lubricating agent during prostate biopsy, also offers anaesthetic benefit [20]. Lidocaine was synthesized by Lofgren and Lundqvist in Sweden in 1943 and introduced into clinical practice in 1947 [25]. Lidocaine alters signal conduction in neurons by blocking the fast voltage gated sodium (Na^+) channels in the neuronal cell membrane that are responsible for signal propagation. With sufficient blockage the membrane of the postsynaptic neuron will not depolarize and will thus fail to transmit an action potential[26]. This creates the anaesthetic effect by not merely preventing pain signals from propagating to the brain but by stopping them before they begin. The efficacy profile of lidocaine as a local anaesthetic is characterized by a rapid onset of action and intermediate duration of efficacy thereby making lidocaine suitable for infiltration and surface anaesthesia[27]. Penetration of lidocaine gel through the rectal mucosa has been experimentally confirmed[28], a local effect on the pain fibres along the neurovascular bundle of the prostate and that of the sensory innervations of the rectal mucosa have been proposed as the mechanisms for the reduction in pain caused by biopsy and probe manipulation respectively[14].

In our study, the mean age of patients in this study was 65.3 ± 9.2 years. This is similar to the mean age of 66.4 years reported by Obi *et al*. [22] as well as a similar study by Shittu *et al*[29] that documented a mean age of 63.6 years. Most of the patients in our study (40.7%) where in their seventh decade with 75.9% cumulatively accounting for patients over the age of 60 years. This further demonstrates the fact that prostate biopsy is mostly performed on the elderly.

This study demonstrated the efficacy of lidocaine in improving pain relief during transrectal prostate biopsy by demonstrating a statistically significant difference in pain level between the lidocaine and placebo groups during both transrectal ultrasound probe and biopsy needle insertion using Numerical rating score (NRS) pain scale. This finding is corroborated by that of Issa *et al*. [30] who studied 50 men and demonstrated the effectiveness of intrarectal lidocaine gel in delivering effective anaesthesia during needle biopsy of the prostate. However, this contradicts the findings of Desgrandchamps *et al*. [31] and Autunnes *et al*. [32] who found a slight reduction in pain which was not statistically significant and concluded that lidocaine exerts minimal effect on patient's tolerance to transrectal needle biopsy of the prostate. This conclusion may have arisen as a result of the use of the verbal rating score (VRS) by the latter studies, which lumped up patients' responses and affected the derivation of a statistically significant difference in the studies. Although the finding of this study is in tandem with that of Issa *et al*. [30], the higher pain score recorded in this study compared to those in the corresponding groups in their study may be attributed to the higher accuracy of NRS compared to VAS in assessing pain which may result in higher pain scores[12]. The significantly greater proportion of patients in the lidocaine group consenting to a possible repeat prostate biopsy as compared to the placebo group, may be a further reflection of the anaesthetic effect of intrarectal lidocaine gel.

CONCLUSION

Transrectal ultrasound-guided prostate biopsy, which is the gold standard in the diagnosis of prostate cancer, is associated with pain. The need for effective and preferably non-invasive pain relief during this procedure cannot be over-emphasized. Intrarectal lidocaine gel was found to be efficacious in improving pain relief during transrectal ultrasound probe insertion as well as during needle insertion in transrectal ultrasound-guided biopsy of the prostate. Intrarectal lidocaine gel, which is relatively inexpensive and readily available, can be routinely utilized in improving pain relief during this procedure.

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