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Pain Relief during Transrectal Prostate Biopsy: Comparison between Oral Tramadol and Intrarectal Lidocaine Gel

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Original Research Article

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Abstract: The gold standard for diagnosis of prostate cancer is biopsy of the prostate gland. Though considered a minor procedure which is relatively safe, prostate biopsy has been reported to be painful. Due to the cheaper cost, relatively lesser discomfort in administration and comparable efficacy, non-infiltrative anaesthesia represents an attractive alternative to other invasive options. The aim of this study was to determine and compare the efficacy of intrarectal lidocaine gel with oral tramadol as non-invasive options in achieving pain relief during transrectal ultrasound-guided prostate biopsy. A total of 107 patients scheduled for transrectal prostate biopsy were randomly assigned to two groups. Group 1 received 100 mg of tramadol administered orally as well as intrarectal instillation of 20mls of KY jelly (placebo lidocaine gel) before the procedure. Group 2 received 100 mg of vitamin C (placebo tramadol) with intrarectal instillation of 20 mls of 2% lidocaine prior to the procedure. The severity of pain experienced during the procedure was assessed using the numerical rating score (NRS). The mean pain scores for the tramadol and lidocaine groups during ultrasound probe insertion were 3.1±2.2 and 3.9±2.1 respectively. The mean pain scores for both groups during biopsy needle insertion were 3.9 ± 2.3 and 4.2 ± 1.9 for the tramadol and lidocaine groups respectively. The differences in mean pain scores between the groups during ultrasound probe insertion was statistically significant (P = 0.004). Oral tramadol offers significantly better pain relief during rectal ultrasound probe insertion when compared with intrarectal lidocaine gel.
Keywords: Lidocaine; Tramadol, Prostate biopsy, Pain relief, Prostate cancer, Anaesthesia.

INTRODUCTION

Prostate cancer is the second most frequently diagnosed cancer in males with an incidence of 168.3/100,000 in black Americans [1]. Several studies have also reported an increasing incidence of the disease [2,3]. Cancer of the prostate rarely causes symptoms until it is advanced. Thus, suspicion of prostate cancer resulting in a recommendation for prostate biopsy is most often raised by abnormalities found on digital rectal examination or elevated prostate specific antigen levels [4].

The gold standard for diagnosis of prostate cancer is currently biopsy of the prostate gland as empirical treatment without tissue diagnosis is no longer acceptable. Prostate biopsy is a procedure in which small tissue samples are taken from the prostate gland to be tested for the presence of disease. This procedure may be done using the open technique or via the use of a needle. It may be performed through the rectal route, per urethram or through the perineum. However, the transrectal route for biopsy of the prostate has been the most widely used route of choice since the mid 1950s and ultrasound guidance of this route has been described as improving its diagnostic accuracy and yield [5, 6]. Current advocacy for PSA screening has resulted in a rise in the number of men being diagnosed with prostate cancer as well as the number of men undergoing biopsy of the prostate. An estimation of the annual prostate biopsy performed in the United States is one million, making it one of the most common office procedures performed by urologists [7]. With the call for performing biopsy of the prostate at lower PSA cut-offs as well as the increased need for repeat prostate biopsies in men with low-risk prostate cancer undergoing active surveillance protocols, there is likely going to be a rise in the number of prostate biopsies performed in the future [7].

Though considered a relatively safe procedure, it is beset with frequent minor complications such as haematuria, haematospermia, rectal bleeding, urinary tract infection and voiding symptoms in about half of

the patients, with pain as the most common complaint during and after the procedure [8, 9].

The physiological and psychological consequences of pain as well as benefits of their alleviation cannot be overemphasized. The adverse physiological consequences of pain could be endocrine, metabolic and even cardiovascular. These effects, especially the cardiovascular, are more devastating in the elderly who form majority of the population that would usually undergo prostate biopsy [10]. Judging from the aforementioned consequences, the benefit of alleviation of this pain or its possible elimination is highly desirable. In addition, adequate pain relief during transrectal biopsy of the prostate makes tissue retrieval easier and more accurate as patients would not jerk in response to pain. Its application would also greatly increase the acceptability of a repeat biopsy if the need arises.

Periprostatic nerve block (PPNB) though considered the standard anaesthesia for ultrasound guided transrectal prostate biopsy, constitutes a major, though often neglected, source of discomfort and pain during administration of the anaesthetic agent [11]. Non-infiltrative anesthesia therefore represents an attractive alternative to periprostatic infiltration. Oral tramadol and intrarectal lidocaine gel fall into this category of being noninfiltative [12,13]. Aside being attractively cheap when compared to periprostatic nerve block, some studies have even shown no difference in the comparative efficacy between these noninfilrative options and periprostatic nerve block in pain relief during TRUS guided biopsy [11,14].

This study aims to prospectively evaluate and compare the efficacy of intrarectal lidocaine gel and oral tramadol in achieving pain relief during transrectal ultrasound-guided prostate biopsy.

MATERIALS AND METHODS

This study was a hospital-based cross-sectional prospective study conducted at the Universityh of Uyo Teaching Hospital, Uyo. 107 were recruited in the study which spanned 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, and 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. Patients were placed following randomization into 2 groups. Group 1 received 100 mg of tramadol administered orally 1 hour before the transrectal biopsy as well as intrarectal instillation of 20mls of KY jellies (placebo lidocaine gel) 10 minutes before the procedure. Group 2 received 100 mg of vitamin C (placebo tramadol) 1 hour prior to the biopsy and intrarectal instillation of 20 mls of 2% lidocaine gel 10 minutes before the procedure. Both oral and rectal administrations were done by the radiologist and were double-blind both to the patient and researcher. All intrarectal instillation 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. Each patient underwent rectal wash out in the morning prior to the procedure and received prophylactic antibiotics (ciprofloxacin tablets 500mg) 1 hour before the biopsy, followed by a repeat dose 12 hours after.

Transrectal biopsy was carried out by the researcher using an 18G trucut biopsy needle loaded on a biopsy gun attached to and guided by a 7 MHz transrectal ultrasound probe with the patient in the left lateral position. Twelve (12) biopsy cores were taken (sextant with three lateral cores on each side). Subjects were required to grade pain felt during transrectal ultrasound probe insertion and pain felt during needle biopsy two minutes after the respective phases of the procedure using the 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). For test of significance we used Student's *t*-test for continuous variables and Chi square test for categorical variables with a confidence interval of 95%. Values <0.05 were considered statistically significant.

RESULTS

A total of 112 men were initially recruited for the study but 107 patients were eventually studied after exclusion of 5 men. Three men did not complete the prostate biopsy due to uncontrollable pain and 2 failed to show up for follow up. The age range of patients was from 40 to 86 years with mean age of 64.8 ± 8.2 years. The peak age group was in the age range 60-69 years and accounted for 46 patients (42.9%) of the entire study population (Figure 1). Cumulatively, 83 (77.6%) of the patients were above 60years of age (Table 1).

Table-1: Distribution of patients' age ranges amongst the study groups

Age (years)	Number of patients in Tramadol group (%)	Number of patients in Lidocaine group (%)	Total (%)
40 – 49	2 (3.6)	2 (3.8)	4 (3.7)
50 – 59	11 (20.0)	9 (17.3)	20 (18.7)
60 – 69	22 (40.0)	24 (46.2)	46 (43.0)
70 – 79	18 (32.8)	15 (28.9)	33 (30.9)
80 – 89	2 (3.6)	2(3.8)	4 (3.7)
Total	55	52	107(100)

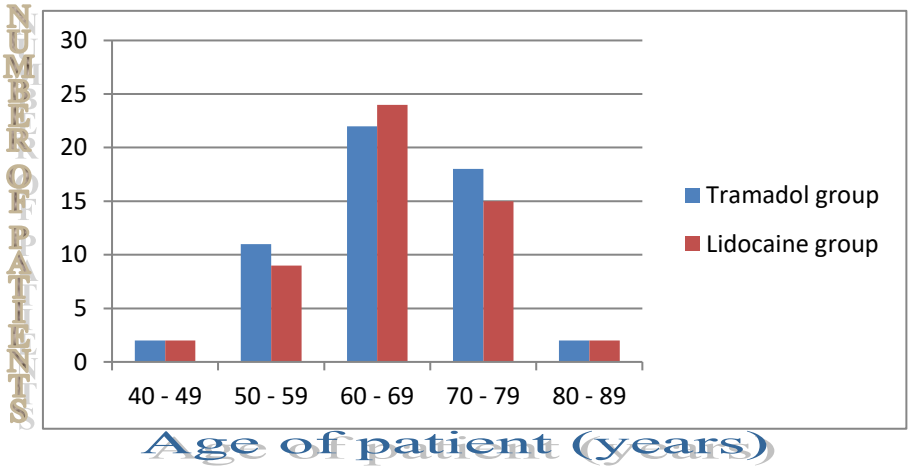

Fig-1: Distribution of patients with age ranges in decades

The mean ages were 64.7±10.3 and 65.9±8.0 in the Lidocaine and tramadol groups respectively which was not statistically significant (Table 2). The mean PSA of the study population was 39.4 ± 31.6 ng/ml. The mean PSA in the tramadol and lidocaine groups were 36.2 ± 30.8 ng/ml and 42.5 ± 32.4 ng/ml. The mean prostate volume in the study was 85.1 ± 51.0cm^3. The mean prostate volume in the lidocaine group was 88.5 ± 51.0cm^3 while that of the Tramadol group was 81.6 ± 46.4 cm^3 (Table 2).

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

Patient characteristics	Tramadol group Mean(+/- SD)	Lidocaine group Mean(+/- SD)	*P*- value
Age	64.7 (±10.3)	65.9 (±8.0)	0.511
Prostate volume	81.6 (±46.4)	88.5 (±51.0)	0.136
PSA level	36.2 (±30.8)	42.5 (±32.4)	0.288
PSA density	0.51 (±0.44)	0.54 (±0.42)	0.620

On assessment of pain severity using the numerical rating scale (NRS); during transrectal probe insertion, the tramadol group was found to have a mean score of 3.1 ± 2.2 whereas that of the lidocaine group was 3.9 ± 2.1(P = 0.004) (Figure 2). On biopsy needle insertion, the mean pain scores for the tramadol and lidocaine groups were 3.9 ± 2.3 and 4.2 ± 1.9 respectively (P = 0.366) (Figure 3)

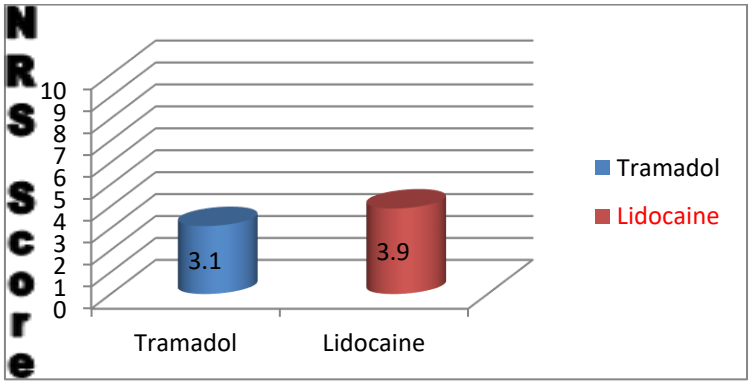

Fig-2: Mean NRS scores in both study groups during probe insertion

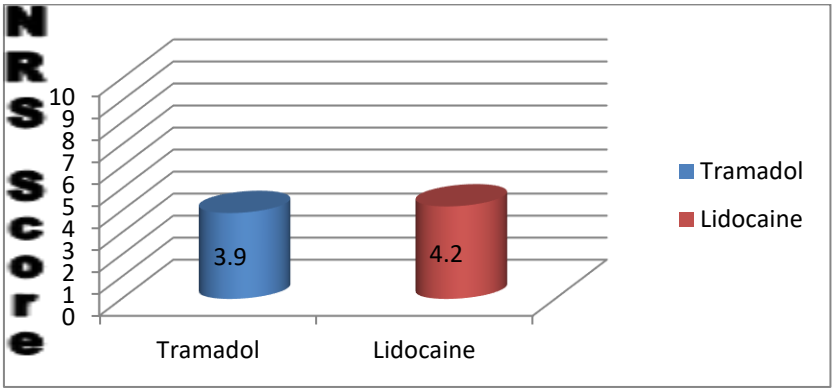

Fig-3: Mean NRS scores in both study groups during biopsy needle insertion

A higher percentage of patients in the tramadol group (66.2%) were found to be willing to accept a repeat biopsy compared with those in the lidocaine gel group (54.5%). This difference between the groups was found to be statistically significant (*P* = 0.038) (Figure 4).

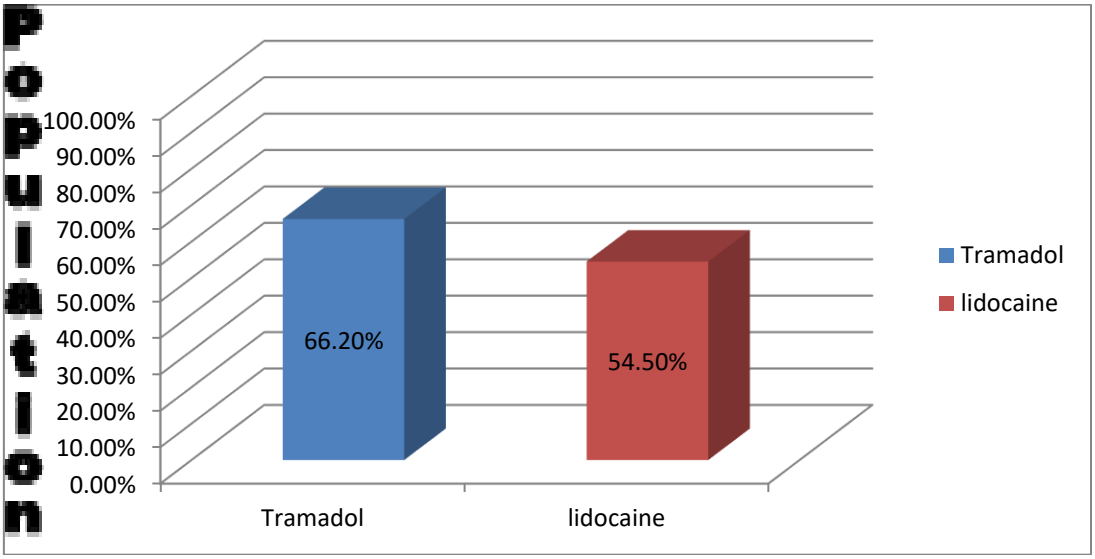

Fig-4: Willingness to accept repeat biopsy

DISCUSSION

Pain has remained an issue in relation with prostate biopsy. The lack of a consensus on the ideal form of pain relief further complicates this issue. Our study was aimed at providing some answers by comparing two non-infiltrative pain relief methods. The statistically insignificant differences in the patient characteristics of the two study groups underscore the similarity of the groups and therefore minimize bias in the subsequent comparison of our results.

Contrary to observations by Hirsh *et al*. [15] and Song *et al*. [16] that intrarectal lidocaine gel as a single agent played no role in pain relief during prostate biopsy, the mean pain score of patients in the lidocaine arm of this study indicated that it did offer some pain relief during the procedure. This difference in observation by Hirsh et *al*. [15] may be as a result of the relatively lower quantity of lidocaine in the gel which was 5 mls of 5% g *et*. The contrary observation made by Song *et al*. [16] could be as a result of their relatively smaller sample size of 30 patients. However, reports by Mallick [14] *et al.* that lidocaine gel is effective for pain relief during prostate biopsy, are in tandem with those of this study. The slightly higher mean pain scores in this study may be related to the higher sensitivity of NRS in pain scoring compared to VAS which was used in theirs and other studies [17,18].

The finding in this study regarding the effect of tramadol on pain during transrectal biopsy of the prostate is similar to that of Obek *et al*. [11] who compared three different methods of pain relief for transrectal biopsy and concluded that oral tramadol is effective in pain relief for prostate biopsy. When compared to periprostatic nerve block, which is regarded as the gold standard for pain relief during prostate biopsy, they found no difference in efficacy of pain relief offered by tramadol [11]. Nomi *et al*. [19] however had a contrasting view as their study reported tramadol to be ineffective in pain relief during transrectal biopsy. Their contrasting observation may

have been due to the rather shorter duration between administration of tramadol and inception of prostate biopsy of 30 minutes, as well as the inclusion of men who had just undergone haemorrhoidectomy.

This study demonstrated that oral tramadol was more effective in reducing pain associated with trans rectal ultrasound-guided prostate biopsy when compared with intra rectal lidocaine gel. This is depicted by the lower mean pain scores observed during both rectal probe insertion and trans rectal needle biopsy though the difference in the latter was not statistically significant. This finding is similar to the report of Vinco *et al.* [20] who observed that oral tramadol relieved pain significantly during Trans rectal probe insertion but not during needle biopsy when compared with intrarectal gel instillation. Though similar, the report of this study on the mean pain scores after biopsy was slightly lower than those reported by Vinco *et al*. [20]. This may be attributed to the relatively longer delay in scoring pain after the biopsy in their study which may have affected the memory of pain leading to underestimation of actual pain perceived. These lower pain scores may also be accounted for by their smaller study sample size of twenty eight patients, as well as the lower dose of both oral tramadol and intrarectal lidocaine gel administered during their study which was 50mg and 15mls of 2% gel respectively. Extensive literature search did not reveal similar studies comparing the efficacy of oral tramadol and intrarectal lidocaine gel.

The statistically significant difference between the proportion of patients in the tramadol and lidocaine arms of the study who agreed to undergo a repeat biopsy under the same conditions considering the level of pain perceived is also a reflection of the better pain relief effect of tramadol during the procedure. This advantage of tramadol could be due to its central action by interacting with the receptors in the limbic system and cortex where it acts on the affective components of discomfort and anxiety thereby diminishing the sensation of pain [21]. In addition, it interacts with the afferent system reducing spinothalamic pathway activity at its origin and postsynaptic ally inhibits neurons of the paleo spinothalamic pathway [21]. The insignificant difference in the average prostate volume of both groups also ruled out the effect of prostate volume, which is a known influencing factor [22] on the pain scores which further demonstrated the superior pain relief effect of oral tramadol when compared to lidocaine gel for Transrectal biopsy of the prostate.

CONCLUSION

In the performance of Transrectal ultrasound-guided prostate biopsy, oral tramadol and intrarectal lidocaine gel offer some pain relief during transrectal ultrasound-guided biopsy of the prostate. Oral tramadol offers significantly better pain relief during rectal ultrasound probe insertion when compared with intrarectal lidocaine gel. However, no significant difference in pain relief was found with the use of oral tramadol or intrarectal lidocaine gel during needle insertion in biopsy of the prostate.

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