Topical Anaesthesia for Pain Relief During High Dose Rate Brachytherapy for Carcinoma of the Cervix

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ABSTRACT

Purpose: To determine the clinical efficacy of a local anaesthetic spray of 10% xylocaine in reducing pain and discomfort in patients undergoing high dose rate (HDR) brachytherapy. **Patients and Method:** Ninety two consenting patients diagnosed with cervical cancer and planned for HDR as part of their treatment were enrolled for the study. Each patient had three sessions of brachytherapy following the standard procedures. In the first session all the patients had brachytherapy in the usual manner with conscious Sedation with parenteral diazepam and pentazocine. For the second and third sessions, they had treatment sessions using conscious sedation and 10% xylocaine spray and a control session using conscious sedation and a placebo spray with 0.9% normal saline (NS) respectively. Visual Analogue Scale (VAS) was used in assessing pain during each of the procedure. **Results:** Only 80 patients completed the study. Their age ranged from 28-70 years with a median age of 54 years. The pre-treatment VAS median scores in the treatment and the control sessions were similar at 0.275 and 0.200. However, the post-procedure median VAS scores were increased to 6.3 in the control group and 3.2 in the xylocaine-treated group ($P < 0.0001$). The haemodynamic status including the blood pressure (BP) and pulse rates (PR) were similar pre and post procedure in both groups. **Conclusion:** Topical xylocaine spray is efficacious in reducing pain and discomfort in HDR Brachytherapy without any appreciable adverse effect.

Key words: High dose rate brachytherapy, pain, xylocaine spray

Introduction

High Dose Rate (HDR) brachytherapy is an important modality in the treatment of women with carcinoma of the uterine cervix.[1] This entails the insertion of radioactive sources into applicators that have been previously inserted into the uterine cavity and the paracervical recesses in the vagina. The placement of the applicators requires precision in other to ensure even distribution of the radiation dose within the uterus, the cervix, vagina, the parametrium and the pelvis. This procedure usually requires patient's cooperation and immobilization which can only be achieved when patient is comfortable and relatively free from pain. In an uncomfortable patient, insertion may not be properly done and this may result in poor distribution of dose and complications arising from giving too much radiation dose to the rectum and the bladder and inadequate dose to the tumour itself.

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Conscious sedation using parenteral pentazocine and diazepam is used in our centre for this procedure but it has been observed that many patients appear uncomfortable during the procedure due to pain despite the conscious sedation. This is not surprising considering previous studies have also shown that this is a moderately painful procedure as it has been observed that patients experience some pain and discomfort during the procedure.[2]

Finding more effective means of controlling pain during the procedure is therefore necessary. This study is conducted to assess the efficacy of topical anaesthetic agent (10% xylocaine) in improving pain control in patients undergoing brachytherapy.

Objectives

Our main aim was to determine the clinical efficacy of a local anaesthetic spray of 10% xylocaine in reducing pain and discomfort in patients undergoing brachytherapy and to

also assess its effects on hemodynamic responses like blood pressure (BP) and pulse rate (PR).

Patients and Methods

The study was carried out in Radiotherapy Department of the University College Hospital, Ibadan. Ethical approval was obtained from the UCH/UI Institutional Review Board.

Sample size determination for two proportions in a clinical trial with a quantitative outcome

$$N = \frac{(Z_{1-\alpha/2} + Z_{1-\beta})^2 [P_1(100-P_1) + P_2(100-P_2)}{(P_1 - P_2)}$$

P_1 = Proportion who experienced 20% reduction in moderate pain in a previous study on pattern of pain and distress during HDR Brachytherapy procedure.[1]

P_2 = Projection is that intervention should bring about a 40% reduction

Z_α = Alpha error, for a two tailed test 95% with confidence interval (p = 0.05) is 1.96

Z_β = Beta error which for 80% power (20% beta error) is 0.84

$K = (Z1\text{-}a/2 + Z1\text{-}b)^2$ (using p = 0.05 and 80% power) = 7.9 (from statistical table)

Was the method used to calculate the sample size.

Ninety-two consenting patients were eventually enrolled for the study. Simple randomization method was used to allot patients into two groups as they presented. Each patient had three sessions of brachytherapy following the standard procedures [Table 1].

In the first session all the patients had brachytherapy in the usual manner. They had conscious Sedation with parenteral Diazepam and Pentazocine.

For the second and third sessions, they had treatment sessions using conscious sedation and 10% xylocaine spray and a control session using conscious sedation and a placebo spray with 0.9% normal saline (NS) respectively Patients acted as their own control to avoid bias such as getting patients with the same stage and same threshold for pain. The placebo was placed in a xylocaine spray container (bottle similar to 10% xylocaine bottle and both were covered) so as to maintain the patients' blinding as to which spray was being used.

The procedure was carried out with HDR remote after loader brachytherapy unit (Gynesource®) using Co-60 radionuclide as the source. All Patients underwent three brachytherapy sessions. Treatment was given once a week in a dedicated brachytherapy room. The procedure is an aseptic one. The patients were placed in lithotomy position and uterus sounded to determine its length and hence tandem size. The topical anaesthesia using 200 mg (20 puffs) of 10% xylocaine spray was sprayed liberally on the cervix and vagina.

Within 1–5 minutes appropriate applicators were placed into the uterine cavity and vagina of the patient and this was screwed properly. Barium soaked gauze was used to pack the vagina to displace the bladder and rectum away from excess radiation dose as well as securing desired positioning of the applicators and a rectal marker was inserted into the rectum for identification.

Visual Analogue Scale (VAS) was used to assess pain in all the patients. It was a conscious sedation procedure. Patients were awake but calm. E ach patient's pain was assessed before and after each of the brachytherapy sessions. The procedure, including pain assessment scoring was explained to the patients before the procedure. Only patients who gave informed consent were included in the study.

The PR and BP was again recorded 5 minutes after the procedure and this was documented for the treatment and control sessions accordingly to evaluate the physiological responses. Intranasal oxygen, intravenous fluids, hydrocortisone was made available in case of anticipated side effect such as symptoms of an allergic reaction which include: shortness of breath, wheezing or difficulty breathing, swelling of the face, lips tongue or other parts of the body, rash, itching or, hives on the skin.

NB: Treatment group were those that received xylocaine and control group those that received the placebo.

Results

Ninety-two respondents participated in this study. However, only 80 patients completed the three sessions. The rest completed either one or two sessions only and were then dropped from the study.

The age range of the respondents was between 28-70 yrs with a median age of 54 yrs as shown in Figure 1.

Table 1: Methodology

First session	Second session (treatment session)	Third session (control Session)
VAS scoring	VAS scoring	VAS scoring
Pulse	Pulse	Pulse
Blood pressure	Blood pressure	Blood pressure
Conscious sedation	Conscious sedation	Conscious sedation
Procedure	20 puffs of xylocaine spray	20 puffs of placebo spray
VAS scoring	Procedure	Procedure
Pulse	VAS scoring	VAS scoring
Blood pressure	Pulse	Pulse
	Blood pressure	Blood pressure

VAS – Visual analogue scale

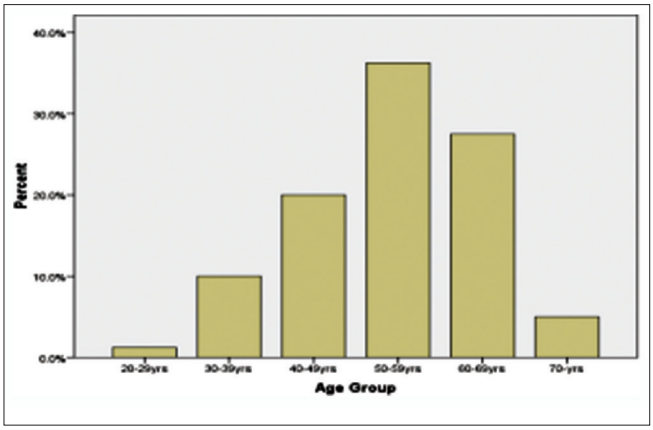

Figure 1: Age distribution

Half (50%) of the participants were of the Yoruba ethnic tribe closely followed by the Ibos (28.8%). Other tribal groupings in Nigeria accounted for the rest.

Sixty eight (85%) of the respondents were married, 10 (12.5%) were widows, 1 (1.2%) was single, and another 1 (1.2%) was divorced. Fifty two (65%) were grand multiparous women. Fifty nine (73.8%) of the patients presented with advanced stage diseases (2b–4a) while sixty seven (83.8%) had squamous cell carcinoma as the histological type.

The result of the VAS used to score pain during the procedure is shown below Table 2.

The mean pain scores by the VAS at the treatment and control sessions were 3.72 + 2.07 standard error of mean 0.231 and 6.34 + 2.26 standard error of mean 0.253 respectively.

A paired *t*-test analysis of the pain VAS scores after HDR brachytherapy in the cross-over treatment and control groups showed a Mean of 2.613 + 1.579 standard error of mean was 0.177 with a 95% confidence interval which lied between 2.964 and 2.261. This was found to be statistically significant at $P < 0.0001$. There was a strong correlation of 0.737 in the VAS scores between the treatment and control groups.

Table 2 shows the VAS values graded for the treatment and control groups; more patients in the control group, seventy (87.5%) had moderate to severe pain post treatment compared to 41 (51.3%) in the treatment group [Table 3].

Table 3: Pain score (VAS) values graded as mild, moderate and severe pain (VAS 0 = No pain, 1-3 = mild pain, 4-6 = moderate pain, and 7–10 = severe pain)

The pre-procedure median VAS score was similar in the two sessions at 0.275 and 0.200. However, the median VAS Score post-treatment showed a striking disparity in the two sessions at 6.3 (in the placebo session) and 3.2 (in the xylocaine session). This difference was found to be statistically significant with $P < 0.0001$.

Table 2: RAW pain score, VAS values: Treatment and control sessions

Visual analog score	Treatment (*n*=80) *N* (%)		Control (*n*=80) *N* (%)	
	Pre-insertion	Post-insertion	Pre-insertion	Post-insertion
0	62 (77.5)	4 (5.0)	63 (78.8)	1 (1.2)
1	17 (21.2)	5 (6.2)	14 (17.5)	0 (0)
2	0 (0)	19 (23.8)	1 (1.2)	3 (3.8)
3	0 (0)	9 (11.2)	0 (0)	6 (7.5)
4	0 (0)	16 (20.0)	0 (0)	10 (12.5)
5	1 (1.2)	11 (13.8)	0 (0)	6 (7.5)
6	0 (0)	7 (8.8)	0 (0)	12 (15.0)
7	0 (0)	6 (7.5)	0 (0)	12 (15.0)
8	0 (0)	2 (2.5)	0 (0)	19 (23.8)
9	0 (0)	1 (1.2)	0 (0)	5 (6.2)
10	0 (0)	0 (0)	0 (0)	6 (7.5)
Total	80 (100)	80 (100)	80 (100)	80 (100)

VAS – Visual analogue scale

Table 3: Pain score (VAS) values graded as mild, moderate and severe pain (VAS 0=No pain, 1-3=mild pain, 4-6=moderate pain, and 7-10=severe pain)

Grade of pain (VAS)	Treatment *N* (%)		Control *N* (%)	
	Pre-insertion	Post-insertion	Pre-insertion	Post-insertion
No pain	62 (77.5)	4 (5.0)	63 (78.8)	1 (1.2)
Mild	17 (21.2)	35 (43.8)	17 (21.2)	9 (11.2)
Moderate	1 (1.2)	31 (38.8)	0 (0)	30 (37.5)
Severe	0 (0)	10 (12.5)	0 (0)	40 (50.0)
Total	80 (100)	80 (100)	80 (100)	80 (100)

VAS – Visual analogue scale

The mean PR for treatment and control sessions before and after the procedure were similar at 85.58 and 84.16; 85.81 and 85.00 respectively.

The mean systolic blood pressure for the treatment and control sessions before and after the procedure was 126.23 and 124.54; 125.93 and 125.3 respectively.

The mean diastolic blood pressure for the treatment and control sessions before and after the procedure was 82.18 and 81.47; 81.75 and 81.83 respectively as shown below [Table 4].

The differences in the changes of the PR and BP before and after the procedure in both sessions were not statistically significant.

We did not record any significant adverse reaction during the procedures.

Discussion

Pain is an unpleasant sensory and emotional experience

Table 4: Pulse and blood pressure

	Treatment session		Control session	
	Before	After	Before	After
Mean pulse rate B/M	85.58	84.16	85.81	85.00
Mean systolic blood pressure mmHg	126.23	124.54	125.93	125.30
Mean diastolic blood pressure mmHg	82.18	81.47	81.75	81.83

associated with actual or potential tissue damage, or described in terms of such damage.[3]

A person's self-report is the most reliable measure of pain. Pain assessment by health care professionals tends to underestimate its severity.[4] A definition of pain widely employed that emphasized its subjective nature and the importance of believing patient reports was introduced by Margo McCaffery in 1968. McCaffery said that pain should be seen as "whatever the experiencing person says it is, existing whenever he says it does".[5]

HDR brachytherapy like most gynaecological procedures including hysteroscopy, hysterosalpingography (HSG), sonohysterography, endometrial ablation etc., are increasingly performed in an outpatient setting and the primary reason for failure to complete these procedures is pain.

Ahmed *et al*., compared the effectiveness and safety of different types of pharmacological intervention for pain relief in office gynaecological procedures and found a benefit for the use of local anaesthetics for outpatient hysteroscopy and hysterosalpingo-contrastsonography. They suggested that local anaesthetics should be considered when performing hysteroscopy in postmenopausal women to reduce pain and ultimately the failure rate.[6]

Outpatient HDR brachytherapy has become increasingly common in the treatment of women with cervical cancer and this procedure has also been associated with pain.

Kwekkeboom *et al*., explored women's experiences of pain and distress over a series of five HDR brachytherapy procedures given for cervical cancer.[7] The majority of women reported worst pain in the mild to moderate range and similar ratings of worst distress across the series of procedures. The most physically uncomfortable aspect of treatment was removal of the instruments after the procedure, when sedatives had worn off, a subset of women reported having recalled pain from previous procedures, despite the use of conscious sedation medications.

Kwekkebom *et al*., concluded that for most patients, HDR brachytherapy delivered with conscious sedation is well-tolerated with only mild pain and distress. However, a number of patients may experience more significant symptoms and may require additional medical and psychosocial support.[7] These findings are similar to findings in this study where in spite of conscious sedation with intravenous sedatives and analgesics, patient still reported considerable pain which only improved with the use of topical anaesthetic.

In the study we analysed results of 80 patients who completed the three sessions of HDR Brachytherapy.

Our findings concerning the age range of the patients and the staging of their diseases were similar to findings by other workers in the region. The age-group with the highest frequency was 50-59 years and this accounted 36.26% of patients.The mean age was 54 years + 10 years and this is similar to a findings by Abdus-slam *et al*., where the patients' age in their series ranged between 29 and 85 years with a mean age of 55 years.[8] Uzoigwe *et al*., also found that cervical cancer was commonest between the ages of 50-69 years in their study.[9]

Majority of the patients 59 (73.8%) presented with advanced disease which correlates with findings in other studies where patients with cancer of the cervix presented commonly in advanced stage 2b and above.[10,11] However, in this study stage 2b was the commonest stage of presentation with 41.2% which is in contrast to some of the studies earlier referred to where stage 3b is the commonest stage. We believe that this is likely to be due to the fact that patients with advanced disease are usually not suitable for brachytherapy.

Table 3 shows the VAS scores when graded as no pain, mild, moderate and severe pain, 31 (38.8%) and 30 (37.5%) in the treatment and control groups respectively had moderate pain, but an appreciable difference was noted in the severe pain column where during the treatment group 10 (12.5%) had severe pain post procedure as compared to the control group were 40 (50%) had severe pain. The mean VAS at the treatment (those that had 10% xylocaine spray) and control (those that had placebo) sessions which were 3.72 and 6.34 with standard deviation of 2.07 and 2.26 respectively. A paired *t*-test analysis of the pain VAS scores was found to be statistically significant at $P = 0.0001$.

There was also a strong correlation of 0.737 in the VAS scores between the treatment and control groups. This corroborates findings by Hui-Chun Chen *et al*., who also evaluated the clinical efficacy of local vaginal lidocaine application for pain relief during HDR intracavitary brachytherapy for patients with cervical cancer among Chinese patients and found that the mean VAS values recorded during the treatment sessions and control sessions were 49.9±- 24.1 versus 60.1 ± 24.8, respectively. The value of VAS in the treatment session was significantly lower than that of the control session[12] Mikhail *et al*., also compared

the effectiveness of cocaine spray (10%, 4 ml) with a placebo in 50 patients undergoing laser vaporization of the cervix for cervical intraepithelial neoplasia and found that there was a significant reduction in pain as assessed by a VAS and a verbal rating scale.[13]

In another study by CP Chan and FL Lau, lidocaine spray was found to significantly reduce patient's discomfort, and also reduced the procedure's difficulty, duration and number of insertions attempts during NG tube insertion.[14]

A major barrier to the use of this method in addressing the pain and discomfort felt by patient undergoing brachytherapy might be the fear of side effects and disruptions of hemodynamic status. However, as indicated in our findings, there was neither documented evidence of disruptions of hemodynamic status nor any major side effects.

There was no significant change in the physiological responses as shown from the pulse, systolic and diastolic BP and this is similar to the study by Hui-Chun Chen *et al*., where they found that lidocaine solution did not induce significant changes in systolic BP and heart rate during the course of HDR brachytherapy.[12] One can therefore conclude that this procedure is quite safe and could help reduce pain and discomfort in the course of HDR brachytherapy.

Conclusion

Local vaginal anaesthesia with 10% xylocaine spray can decrease the degree of pain during HDR intracavitary brachytherapy with no expected major side effects. It is therefore recommended for additional pain relief during HDR intracavitary brachytherapy in addition to conscious sedation.

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