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Effectiveness of 5% Lidocaine Patch in Post Mastectomy Cancer Pain – A Randomized Controlled Trial

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Abstract

Background: The control of cancer pain still is a significant problem in patients undergoing major oncological surgical procedures. The use of high dose opioids has resulted in multiple side effects. The present study was carried out to analyze the effectiveness of a 5% lidocaine patch in patients with cancer pain undergoing mastectomy.

Methods: This was a prospective randomized control trial. Sixty patients were included in the study. Group A patients have 5% lidocaine patch applied, and in Group B, a placebo patch was used. Demographic profile, the severity of pain score, and opioid requirement, at the beginning and conclusion of the treatment, patients' impression, drug-related side effects all were noted.

Results: 60 patients took part in the study, with fourteen days mean follow up. The Mean Verbal Numerical Scale (VNS) score was 3.5 in Group A and 6.76 in Group B at Day 1(P=0.00), and VNS Score was 4.06 in Group A and 7.3 in Group B at Day 5(P=0.00). At days 10 and 14, both the groups had no statistically significant difference in pain score. The opioid requirement in group A was significantly less, the average being 636.67 mg and in Group B being 2123.34 mg.

Conclusions: 5 % lidocaine patch was found to be useful for short period management of neuropathic pain along with allodynia derived from a painful scar. But its long term usefulness is yet to be validated.

Keywords: Cancer Pain; Lidocaine; Nociceptors; Mastectomy; Neuralgia; Allodynia; Pain Assessment; Opioid.

Introduction

Cancer patients commonly experience pain ranging from 30% in the early stages to 90% at advanced stages.[1] Treatment of such pain remains a challenge. Cancer pain results from multiple interactions between the central and peripheral nervous system, cancer cells, and the immune system.[2,3] Local immune cells, along with cancer cells, secrete a range of substances that stimulate the pain receptors/nociceptors. Neuropathic pain is an area that is often ignored in patients undergoing cancer treatment as well as post-treatment when the patient is on follow up.

In a multicentre international survey, neuropathic mechanisms were seen in 40% of the patients with cancer pain.[4] On using the Edmonton Staging System in palliative care services, 17% incidence of neuropathic pain was seen in cancer patients.[5] This type of pain is described by the character of burning pain, hyperalgesia, and paroxysmal pain.

Post-mastectomy pain syndrome (PMPS) is a condition with a chronic pain that is neuropathic in nature and occurs following surgery.

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The neuropathic pain brings in many complex challenges for the treating physician, and also, in addition to the family and caregivers, the patients undergo anxiety, distress, and frustration. The treatment options at present include opioids, tramadol, and other drugs, blocks, stimulators, and intrathecal catheters.[6] Opioids have been widely used in cancer pain, and despite constipation and respiratory problems, it also has issues like addiction. Tricyclic antidepressants and anticonvulsants have been used for neuropathic pain as first-line drugs.[7,8] Since the early 1990s, opioids have been successfully used for neuropathic pain and has established itself as an option for moderate-to-severe cancer pain.[9,10]

Management of neuropathic pain remains a challenge for cancer patients who have been exposed to multiple drugs.[11] To date, there are very few studies carried out to focus on other newer options to deal with post-mastectomy neuropathic pain, in spite of it being an area of concern.

5% lidocaine plaster (LP5) is recommended for localized neuropathic pain, but evidence in postsurgery neuropathic pain is missing. Thus, in the present study, we compared the efficacy of lidocaine 5% patches with a placebo patch in post-mastectomy patients.

Material and Methods

The study was conducted in the tertiary care center in Pain and Palliative care OPD and Ward by the Department of Anesthesia. The Good Clinical Practice standards and the ethical principles, according to the Helsinki Declaration, were followed. Our study followed the CONSORT recommendations. After approval from the Institutional Ethical Committee, 68 patients of breast cancer post-mastectomy were included in the study. Informed written consent was taken from all patients included in the study. A sample size of 46 patients was required for this placebo-controlled parallel-design study. With a 20% drop out rate, a total of 56 cases were sufficient to close the study; however, 68 subjects were enrolled.

Patients were randomized into two groups using a computer-generated random number sequence. One being test group, Group A, which received 5% lidocaine patch and the other control Group B which received a placebo patch. Informed written consent was taken from all the participants.

Inclusion criteria included females ranging from the age of 18 to 65 yrs with mastectomy and visited the outpatient department with complaints of pain. The patient had undergone mastectomy for early and advanced stages of breast cancer by a surgeon who had comparable surgical skills. To be included in the study, the patient should have been on one analgesic, such as paracetamol at therapeutic dose before the addition of the patch, and the pain score had to be > 4/10 on the Verbal Numerical Score (VNS). The patients with advanced breast cancer and ASA grade 3 and 4 were excluded from the study. 5% lidocaine patch was used in Group A, and a placebo patch in Group B. Maximum of 3 patches was allowed to be used by the patients at the scar site for 12 hours each day. The painful scar was found to be the main cause of pain in these patients. The patients were followed up in day one that is the next day after patch application, on day 5, day ten and day 14.

The primary objective was to study the short term efficacy of a 5% lidocaine patch for cancer pain. Patients' perception of the treatment and adverse effects of 5% lidocaine patch evaluation was the secondary objective. Demographic data, variable relating to the severity of the pain using Numerical Verbal Score (VNS), the concomitant opioid requirement in both groups, i.e., breakthrough pain, patients' subjective perception, and treatment-related side effects were all recorded. The patient perception was assessed with a simple question and answer like "Have you noticed any improvement in the pain since the treatment with the patch?" with the response categories of "none," "mild," or "significant." VNS was used to assess the severity of pain by giving score "0" for no pain at all and score "10" for worst imaginable pain. Opioid dose modification was allowed, but a dose of co-analgesics had to be the same.

Statistical Analysis was done using Stata 11.1 software and t-test and chi-square test. Mean and Standard deviation was calculated for quantitative variables, and the percentage was used for categorical variables.

Results

There were 68 patients willing to participate in the study. Out of these, four were excluded in the initial phase as two patients did not meet inclusion criteria, while two did not give consent. The rest (n = 64) were randomized and allocated to the two different intervention groups (Groups A and B), with proper allocation concealment in place (n = 32 each). The interventions were applied to the cases and followed up. In group A, two patients were lost to follow up, so n=30. However, in group

B, one patient was excluded from the study due to the need for hospitalization, and one was lost to follow n=30. Thus, a total of 60 patients were analyzed (n = 30 in each group). Details have been summarized in the CONSORT flow diagram (Fig. 1). The average age of the patients in both groups was similar and statistically, not significant. Even the ASA grade was similar and non-significant. This ensures that randomization had been done correctly, and there is no selection bias. The Mean Verbal Numerical Scale (VNS) score was 3.5 in Group A and 6.76 in Group B at Day 1(P=0.00), and VNS Score was 4.06 in Group A and 7.3 in Group B at Day 5(P=0.00). At days 10 and 14, the pain scores were almost comparable average being 7.3 and 8.06, respectively, in Group A and 7.6 and 8.1, respectively, in Group B (Table 1). The opioid requirement in group A was significantly less, average daily tramadol requirement being 636.67 mg Group B being 2123.34 mg. 63.66 % of patients were satisfied with the therapy in Group A (Table 2). Patients did not report any local site adverse effect or any systemic misadventure.

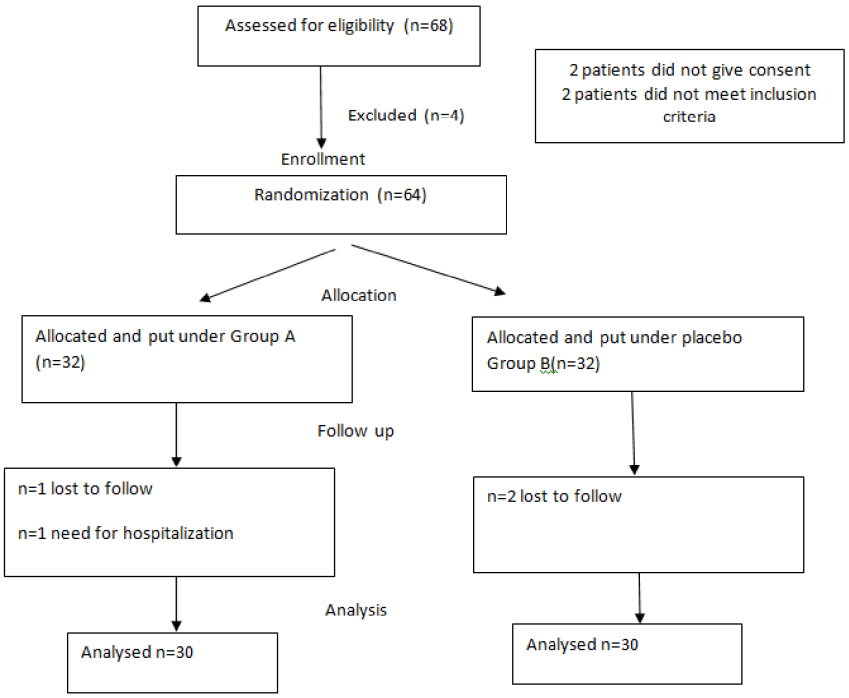

Fig. 1: Consort Flow Chart.

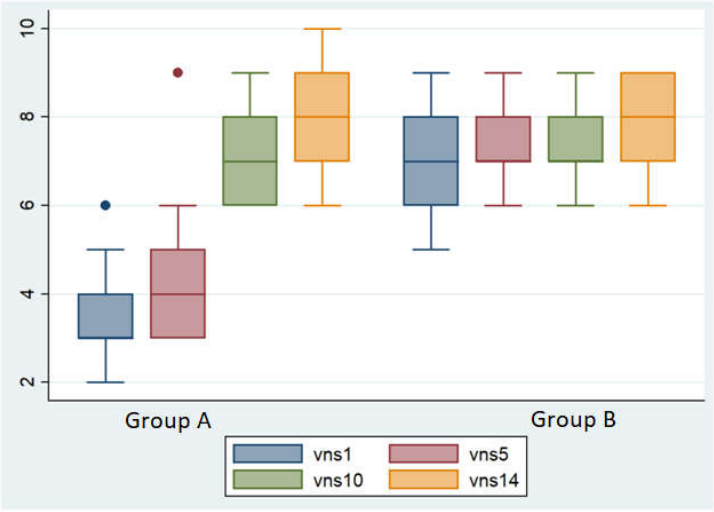

Fig. 2: Graph Box showing VNS in both Groups.

Table 1: Mean VNS in both Groups.

	Group A	Group B	P Value
VNS at day 1	3.5	6.76	0.0000
VNS at day 5	4.06	7.3	0.0000
VNS at day 10	7.3	7.6	0.1240
VNS at day 14	8.06	8.1	0.4473

Table 2: Mean Opioid Requirement and Patient Satisfaction.

	Group A	Group B	P Value
Tramadol requirement	636.67 mg	2123.34 mg	0.0000
Patient satisfaction	63.66 %	38.5 %	0.0000

Discussion

To date, there are not many randomized trials showing the efficacy of 5% lidocaine patch for these painful scars. 5% lidocaine patch showed short term effectiveness in this study for neuropathic cancer pain, derived from the painful scar. In patients with allodynia, the mechanism of symptomatic relief with lidocaine patch has not been understood. Lidocaine acts by blocking the abnormally functioning sodium channels in nociceptors of the skin, thus decreasing the ectopic discharges.

The result of our study is similar to the nonrandomized study by Cristina Garzón-Rodríguez et al.[12] Only three patients required an interventional anesthetic technique during the follow-up period in their study. The authors stressed the role of the selection of patients having neuropathic pain, which should be well localized, superficial, and have allodynia or hyperalgesia occurring from both painful scars. We studied patients who had neuropathic pain secondary to post-mastectomy. Ours was a randomized placebo-controlled trial, which clearly showed improvement in pain score by application of a 5 % lidocaine patch.

Julia Ann Fleming et al.[13] also conducted a retrospective study for the role of lidocaine patch in neuropathic pain. No analgesic effect or benefit was seen in 45% of the patients. The potent benefit was seen in 35% of patients with persistent postsurgical pain.

The VNS was used to assess the severity of pain, but no scale was used for the Analysis of emotional stress, quality of sleep, and interference with daily activity. This is one limitation of the study.

Optimum duration of treatment with patch also lacks consensus. Fleming et al. proposed the use of the patch for at least ten days before labeling it as nonbeneficial.[13] Cheville et al. used the patch for four weeks but did not find its usefulness in the reduction of pain intensity.[14]

The safety of the patch was taken into account for the study. Levels in the blood are minimal when three patches are used for 12 hours a day. Only 1/10th of the concentration required in cardiac arrhythmias for lidocaine is reached.[15] As reported in various studies,[11-14] the withdrawal of patients from our study could not be attributed to any adverse events due to the use of the drug.

Conclusion

To conclude, we can say that a 5% lidocaine patch is helpful for short term pain, but for a longer duration, its role is still to be validated. Further trials are required for its role in long term management of neuropathic pain in cancer patients.

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