

Comparison of Efficacy of Intravenous Tramadol and Bupivacaine Irrigation through Surgical Drains after Modified Radical Mastectomy in patients with Carcinoma Breast

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ABSTRACT

Background: Severe postsurgical pain continues to be hard to manage in patients who experience breast cancer surgery. Badly managed pain can lead to meager patient satisfaction, prolonged hospital stay, and increased risk of complication by analgesics, and may be a reason in the development of long-lasting pain.

Aim: To compare the efficacy of Intravenous Tramadol and Bupivacaine irrigation through surgical drains after Modified Radical Mastectomy in patients with carcinoma breast.

Methods: This was a randomized controlled trial conducted in the Department of Anesthesia, Mayo Hospital Lahore. Total 70 female patients aged 18-70 years undergoing radical mastectomy for CA breast diagnosed on histopathology were selected. Patients were divided into two groups A and B through simple random sampling technique. Group A received intravenous Tramadol. Group B received Bupivacaine through surgical drains.

Results: At 0, 2, 4 and 6 hour postoperatively no significant difference was seen in severity of pain in both treatment groups. In Group-A at 0, 2, 4 and 6 hour postoperatively, 68.8%, 71.4%, 57.1% and 60% respectively had reported no pain while in Group-B at 0, 2, 4 and 6 hour postoperatively, 48.6%, 65.7%, 45.7% and 54.3% patients had reported no pain. Complaints of Nausea, vomiting, sedation, urinary retention was higher in patients in Tramadol Group as compared to Bupivacaine Group.

Conclusion: Results of this study demonstrated that bupivacaine administered through surgical drain was equally effective as intravenous tramadol for controlling postoperative mastectomy pain with less side effects.

Keyword: Breast Cancer, Acute Pain, Analgesia, Tramadol, Bupivacaine, Radical Mastectomy, Nausea, Vomiting, Sedation, Urinary retention, Hypotension

INTRODUCTION

WHO defined pain as "Pain is an unpleasant sensory and emotional expression associated with actual tissue damage or described in terms of such damage¹. There are different types of pain like visceral pain, somatic pain, acute pain, chronic pain, persistent pain, post-operative pain etc²

Breast cancer is one of the most common malignancies, badly affecting about 11% of our women in Pakistan. It has psychological impacts³. In comparison to India and Iran, the breast cancer incidence in Pakistan is 2.5 times higher, which is calculated as 34.6% of female cancer⁴.

Post mastectomy pain is acute superficial pain characterized by dull, burning and aching sensation exacerbated by movement of shoulder girdle(5) which can be treated with different types analgesics like NSAIDs, narcotics, local anesthetics^{5,7}.

NSAIDs and narcotics can be used to treat post-mastectomy pain in immediate post-operative period⁶. Both groups are very effective in relieving post-mastectomy pain but these drugs are not without side-effects⁶. NSAIDs cause gastritis, gastric ulcer, interstitial nephritis, renal failure in diabetics and increased bleeding tendency. Narcotics causes drug dependence, addiction, drug tolerance, nausea, vomiting constipation, urinary retention, respiratory depression and pruritis⁷.

Tramadol is a mu opioid receptor-agonist, nor epinephrine and serotonin reuptake inhibitor¹. Tramadol has been found a better pain reliever but it can develop other complications like vomiting, nausea and urinary retention etc⁸.

Local anesthetics can be used in various modes for relieving pain e.g., infiltration, nerve blocks, caudal, epidural block, shower of LA through drains placed in wound^{6,7}. The advantage of local anesthetics over other modalities is that there are no systemic side effects provided maximum dosage of local anesthetics is not used^{6,7}, provides analgesia for longer duration and decreased need of IV analgesics⁶.

Studies have showed that both tramadol and bupivacaine groups had equally good pain relief with equal mean pain relief at rest and movements (36.4% vs. 52.1%, $p > 0.05$)⁹. Tramadol group had significantly more nausea as compare to Bupivacaine (63.6% vs. 21.7% $p < 0.007$)⁹. Although in Tramadol group higher incidence of vomiting (68.2% vs. 39.1%), urinary retention (31.8% vs. 17.4%), Sedation (5% vs. 0%) when compared with Bupivacaine were seen, but this was not significant statistically (p -value > 0.05)⁹. Another study has also showed that both tramadol and bupivacaine groups had equally good pain relief with equal mean pain relief at rest and movements (35% vs. 40%, $p > 0.05$)⁷.

Tramadol group had significantly more nausea as compare to Bupivacaine (75% vs. 25% $p < 0.007$) and vomiting (75% vs. 25%, $p < 0.05$) and Sedation (0% vs. 25%). Although in Tramadol group higher incidence of urinary retention (10% vs. 0%), when compared with Bupivacaine were seen, but this was not significant statistically (p -value > 0.05)⁷.

The rationale of this study is that previous studies showed conflicting results comparing the efficacy of bupivacaine and tramadol. Also these are the studies with small sample size. This prompted us to conduct this study in our set up.

MATERIALS AND METHODS

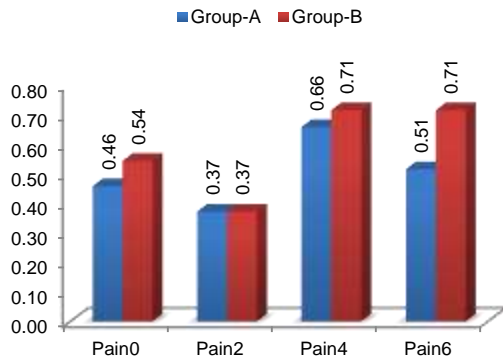
This randomized controlled trial was conducted in the Department of Anesthesia, Mayo Hospital Lahore. A total of 70 patients (35 in each group) were included in this study. The sample size was calculated using 90% power of study, 1% level of significance and taking expected percentage of nausea i.e. 63.6% with tramadol vs. 21.7% with bupivacaine. Females of age 18-70 years (ASA I and II) undergoing modified radical mastectomy for Carcinoma of breast diagnosed on histopathology were included in the study. Patients having pregnancy, allergic to local anesthetics, Regularly consuming analgesics, having Liver disease, patient with Coronary artery disease, were not included in the study.

Data Collection Procedure: Mayo hospital ethical committee and institutional review board KEMU approved the synopsis. Pre-operative assessment was done a day before surgery. 70 patients coming to surgical departments for MRM, meeting our criteria,

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Figure-1: Pain score in Treatment groups at 0, 2nd, 4th and 6th hour postoperatively

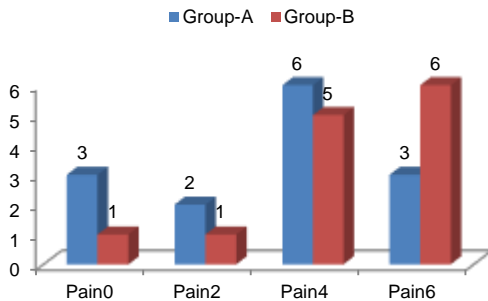


Study Group	0-Hour		2-Hours		4-Hours		6-Hours	
	A	B	A	B	A	B	A	B
Mean±SD	0.45±0.81	0.54±0.56	0.37±0.68	0.37±0.54	0.65±0.90	0.71±0.78	0.51±0.74	0.71±0.95
Minimum	0	0	0	0	0	0	0	0
Maximum	3	2	3	2	3	3	3	3

Group-A: Intravenous Tramadol (0.5mg.kg⁻¹)

Group-B: Bupivacaine

Figure-2: Rescue Analgesia in Treatment groups at 0, 2nd, 4th and 6th hour postoperatively



Study Group	0-Hour		2-Hours		4-Hours		6-Hours	
	A	B	A	B	A	B	A	B
Rescue Analgesia (no. of patients)	3(9%)	1(3%)	2(6%)	1(3%)	6(17%)	5(14%)	3(9%)	6(17%)
p-value	0.304		0.742		0.285		0.742	
p-value	0.304		0.555		0.742		0.285	

Dose of Rescue Analgesia: Ketorolac 30mg IV

Group-A: Intravenous Tramadol (0.5mg.kg⁻¹)

Group-B: Bupivacaine

Table-4: Nausea in Treatment Groups at different time Intervals

Nausea	0-Hour		2-Hours		4-Hours		6-Hours	
	A	B	A	B	A	B	A	B
Yes	19(54.3%)	8(22.9%)	7(20%)	7(20%)	4(11.4%)	6(17.1%)	4(11.4%)	3(8.6%)
No	16(45.7%)	27(77.1%)	28(80%)	28(80%)	31(88.6%)	29(82.9%)	31(88.6%)	32(91.4%)
Total	35	35	35	35	35	35	35	35
p-value	0.007		-		0.495		0.690	

Group-A: Intravenous Tramadol (0.5mg.kg⁻¹)

Group-B: Bupivacaine

Table-5: Vomiting in Treatment Groups at different time Intervals

Vomiting	0-Hour		2-Hours		4-Hours		6-Hours	
	A	B	A	B	A	B	A	B
Yes	9(25.7%)	6(17.1%)	4(11.4%)	2(5.7%)	4(11.4%)	4(11.4%)	1(2.9%)	1(2.9%)
No	26(74.3%)	29(82.9%)	31(88.6%)	33(94.3%)	31(88.6%)	31(88.6%)	34(97.1%)	34(97.1%)
Total	35	35	35	35	35	35	35	35
p-value	0.382		0.393		-		-	

Group-A: Intravenous Tramadol (0.5mg.kg⁻¹)

Group-B: Bupivacaine

Table-6: Sedation in Treatment Groups at different time Intervals

Sedation	0-Hour		2-Hours		4-Hours		6-Hours	
	A	B	A	B	A	B	A	B
Yes	10(28.6%)	4(11.4%)	5(14.3%)	3(8.6%)	2(5.7%)	1(2.9%)	1(2.9%)	0(0%)
No	25(71.4%)	31(88.6%)	30(85.7%)	32(91.4%)	33(94.3%)	34(97.1%)	34(97.1%)	35(100%)
Total	35	35	35	35	35	35	35	35
p-value	0.073		0.452		0.555		0.314	

Group-A: Intravenous Tramadol (0.5mg.kg⁻¹)

Group-B: Bupivacaine

Table-7: Urinary Retention in Treatment Groups at different time Intervals

	0-Hour		2-Hours		4-Hours		6-Hours	
	A	B	A	B	A	B	A	B
Yes	5(14.3%)	1(2.9%)	3(8.6%)	0(0%)	3(8.6%)	0(0%)	2(5.7%)	0(0%)
No	30(85.7%)	34(97.1%)	32(91.4%)	35(100%)	32(91.4%)	35(100%)	33(94.3%)	35(100%)
Total	35	35	35	35	35	35	35	35
p-value	0.088		0.077		0.077		0.151	

Group-A: Intravenous Tramadol (0.5mg.kg⁻¹)

Group-B: Bupivacaine

Table-8: Hypotension in Treatment Groups at different time Intervals

Hypotension	0-Hour		2-Hours		4-Hours		6-Hours	
	A	B	A	B	A	B	A	B
Yes	4(11.4%)	3(8.6%)	1(2.9%)	6(17.1%)	2(5.7%)	3(8.6%)	0(0%)	1(2.9%)
No	31(88.6%)	32(91.4%)	34(97.1%)	29(82.9%)	33(94.3%)	32(91.4%)	35(100%)	34(97.1%)
Total	35	35	35	35	35	35	35	35
p-value	0.690		0.046		0.643		0.314	

Group-A: Intravenous Tramadol (0.5mg.kg⁻¹)

Group-B: Bupivacaine

DISCUSSION

Incidence of pain after mastectomy is 25–60%¹. It is a neuropathic postsurgical pain which may last for more than 3 months¹. Post-Mastectomy Pain Syndrome can occur immediately or after numerous months and can continue for many years². The said syndrome has a significant adverse effect on life of the patient³. The use of local anesthetics for wound instillation and wound infiltration are gaining popularity over intravenous and intramuscular use of opioids and NSAIDs and intramuscular use of local anesthetic¹⁰. Wound irrigation with local anesthetics through surgical drains is a newer concept^{8,11}. Wound perfusion with local anesthetics through drains or catheters has been described after cholecystectomy, splenectomy, abdominal hysterectomy and cardiac surgery.

In our study a total of 70 patients were included and randomly divided into two groups. Patients in Group-A were given IV Tramadol and the patients in Group-B were given Bupivacaine through surgical drain. Results of this study demonstrate that no significant difference was seen for pain control in both treatment groups. i.e. Frequency of severe pain at 0,2,4,6 hour in Group-A patients was 5.7%, 2.9%, 5.7% and 2.9% respectively and in Group-B it was 0%, 0%, 2.9% and 8.6% respectively. In our study frequency of nausea, vomiting, sedation and urinary retention was higher in patients who were given tramadol as compared to bupivacaine. However frequency of hypotension was higher from 2-6 hours follow up in bupivacaine Group.

An Indian study also showed similar findings regarding no significant difference in pain control for Intravenous Tramadol and Bupivacaine (Irrigation through surgical Drains) in patients undergoing radical breast surgery. His study showed significant higher nausea (75% vs. 25% p < 0.007), vomiting (75% vs. 25%, p<0.05) and sedation (0% vs. 25%) in Tramadol group as compared to Bupivacaine. Although in Tramadol group higher incidence of urinary retention (10% vs. 0%), when compared with Bupivacaine were seen, but this was not significant statistically (p-value > 0.05)⁷. The same trend was seen in this study but no significant difference was seen for these variables in both treatment groups at 0,2,4 and 6th hour post operatively⁶.

Jacek Zielinski in his study compared bupivacaine Infiltration of incision site with placebo to see the post-operative acute pain control. His findings showed significantly lower pain scores at 4th and 12th hour after the surgery among patients who were given bupivacaine⁷.

The results of study by Anjum S Khan-Joad is in agreement with our results. They also reported no significant difference in pain score for bupivacaine and tramadol groups for both pain at rest and pain at movement.⁽⁸⁾ The results of complications observed by them were consistent with our study. They reported higher frequency of nausea (63.6% vs. 21.7%), vomiting (68.2% vs. 39.1%) urinary retention (31.8% vs. 17.4%) and sedation (4.5% vs. 0%) in the Tramadol group⁸.

Tugsan Egemen Bilgin studied the effect of wound infiltration with bupivacaine and IM diclofenac administration on PCA in

patients who underwent radical retropubic prostatectomy. As per his findings wound infiltration with bupivacaine during surgical closure combined with IM diclofenac administration may reduce tramadol consumption within 24 hours in patients who underwent radical retropubic prostatectomy under general anesthesia. Pain scores were considerably lower and decreased antiemetic and analgesic requirement in group who received wound infiltration with bupivacaine and intramuscular Diclofenac¹².

Nirmala Jonnavithula in her study, found that patients who were given 0.25% bupivacaine through surgical drains, experienced less pain as compared with patients who were given saline, and the control group¹³. This finding support the result of our study as bupivacaine when used through surgical drain produces effective analgesia and pain control and reduced requirement of rescue analgesia.

Legeby et al. reported that after breast reconstruction surgery, three hourly injection of levobupivacaine at site of incision along with oral paracetamol, and morphine given by Patient Control Analgesia improved pain relief at rest and during mobilization compared with placebo¹⁴.

Leonard Lu and Neil A studied the use of indwelling catheters for the continuous infiltration of local anesthetic (bupivacaine) in 74 successive breast reduction and 74 successive tissue expander breast reconstruction patients. Pain was recorded on a verbal response scale of 0 to 10, while in the recovery room was significantly less in the pain pump group than in the comparison group (p < 0.01), as were cumulative amounts of pain medications (p < 0.01). There were no statistically significant differences in the number of complications or in the rate of nausea or vomiting¹⁵.

Ian Campbell and his team members examined the effect of wound infiltration of bupivacaine (0.25%) for post-operative pain, analgesic use and complications in patients who underwent breast lump excision, wide local excision and mastectomy with or without axillary surgery. Analysis revealed that the group who received local anesthetic needed less opioids than the group who did not receive local anesthetics. There were no significant differences in post-operative pain scores or complications¹⁶.

Moshe Fayman reported no significant difference in analgesia effects achieved in bupivacaine infiltration and ropivacaine infiltration in patients who underwent bilateral breast surgery¹⁷.

But in a study by Fredman et al. it was seen that after major abdominal surgery repeated wound instillation of 0.25% bupivacaine solution via an electronic patient-controlled analgesia (PCA) device and a double-catheter system did not decrease postoperative pain or opioid requirements¹⁸.

H TalBot in his prospective double-blind, randomized, placebo-controlled trial used bupivacaine irrigation through the axillary wound drain 4-hourly for 24 h postoperatively in patients who underwent modified Patey mastectomy. These results were in accordance with our study as morphine requirements or pain scores between the two groups had no significant difference, nor

were there differences in anti-emetic or supplemental analgesic consumption¹¹.

In a study by Kristensen et al. in which catheters were placed between muscle layer and peritoneum, bolus injections of bupivacaine 15ml of a 2.5mg/ml solution did not decrease pain or analgesic requirement after abdominal hysterectomy performed through a Pfannenstiel incision¹⁹. These were inconsistent with our study results reason being difference in surgical procedure.

Instead of intensive efforts for pain management, the postsurgical pain results in poor consequences. With multimodal analgesia, the postsurgical pain can be better controlled. Local anesthetics are important constituents of multimodal analgesia owing to their ability to inhibit pain transmission and their relative tolerability on appropriate administration. The major disadvantage of using traditional local anesthetics in the postsurgical setting is the need of continuous infusions via infusion control devices due to their relatively short duration of action. Complication rates are high because of the use of catheters and infusion control devices.

There are certain limitations in our study. Firstly long term follow up of the patients pain was not evaluated. Secondly, our study utilized only single doses of bupivacaine and tramadol rather using infusion and continuous infiltration. Thirdly, we compare two different modalities rather comparing drug effects at different strength of same drug.

Further studies are needed to assess the long term effect of our multimodal approach after breast surgery. There should be a study to measure dose versus response relationship for either drug

CONCLUSION

Results of this study demonstrated that bupivacaine administered through surgical drain was equally effective as that of intravenous tramadol for controlling postoperative mastectomy pain with less side effects.

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