

Efficacy of Ketamine As an Adjuvant to Local Anesthetic in Modified Pectoral Block for Management of Postoperative Pain in Patients Undergoing Modified Radical Mastectomy

Manoj Kumar S¹, Ramanathan Rangasamy², S. Karthick³

¹Assistant Professor, Department of anesthesiology, Government Dharmapuri medical College

²Senior Resident, Department of Trauma care, Government Dharmapuri medical College

³Assistant Professor, (Trauma Care) Department of Anesthesiology, Government Dharmapuri Medical College, Dharmapuri

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Corresponding Author: Dr. Manoj Kumar S

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Abstract:

Background: Surgical resection of the primary breast tumor with axillary dissection is one of the main modalities of breast cancer treatment. The most common modality for anesthesia is general anesthesia with or without regional blocks. Regional blocks have been considered as one of the modalities for effective perioperative pain control. The addition of ketamine to epidural lidocaine or bupivacaine increases the duration of regional anesthesia and postoperative analgesia. Our study was meant to evaluate that adding ketamine as an adjuvant to bupivacaine, administered as a single injection in ultrasound guided Pectoral nerve block would enhance the quality of post-operative analgesia after modified radical mastectomy

Methodology: This is a prospective observational study, conducted in Government Dharmapuri medical college hospital, Dharmapuri after approval of the institutional ethical committee. Patients were given ultrasound guided, modified pecs block were included in control group. Patients were given ultrasound guided, modified pecs block with ketamine (1 mg/kg) were included in test group that is ketamine group.

Results: The mean duration of surgery in group 1 was 120 min +/- 40.58 min and in group 2 was 107 min +/- 31.64 min with a p value of 0.060, statistically not significant. Both the groups were comparable in the study. VAS was compared between 2 groups with chi square test at each hour at 8th hr-p value of 0.511, which is statistically not significant at 24 hrs p value of 0.605, statistically not significant mean value of vas score was lower in control group than ketamine group but statistically not significant. The mean time of request for rescue analgesic in group 1 (Control group) is 620 min (10hr 30 min) +/- 116.9 minutes and in group 2 (ketamine group) is 1091.5 min (18 hrs) +/- 106.91 min, with a p value of <0.001. There is statistical significance between 2 groups.

Conclusion: In conclusion, the addition of ketamine to modified Pecs block prolonged the time to first request of analgesia and reduced total opioid consumption without serious side effects in patients undergoing modified radical mastectomy.

Keywords: Ketamine, Pectoral Block, Adjuvant, Pain, VAS Score, Analgesia.

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Introduction

Breast cancer is the most common malignancies among women, accounting for 25%–32% of all female cancers in India [1]. Surgical resection of the primary tumor with axillary dissection is one of the main modalities of breast cancer treatment. The most common modality for anesthesia is general anesthesia with or without regional blocks. It has been reported that 40% of the females report moderate-to-severe pain in the immediate post-operative period after breast cancer surgery [2].

Acute post-surgical pain leads to delayed discharge from post-operative recovery area, impairs pulmonary and immune functions, increases risk of

thromboembolism, myocardial infarction and may lead to increased length of hospital stay [3]. It is also an important factor leading to the development of chronic persistent postoperative pain in almost half of the patients [4]. Hence, an effective perioperative pain management of patients undergoing breast surgery is essential.

Regional blocks have been considered as one of the modalities for effective perioperative pain control. They have an opioid-sparing effect, and allow early mobilization and early discharge from hospital. With the advent of ultrasound, newer interventions such as fascial plane blocks – pectoral nerve blocks

have been reported for perioperative analgesia in breast surgeries. The limited duration of analgesia provided by local anesthetics has warranted the use of various adjuvants, for example tramadol, dexamethasone epinephrine, clonidine or dexmedetomidine or ketamine aiming at synergistically enhancing the quality of analgesia.

Ketamine is a noncompetitive antagonist of the N-methyl-D aspartate receptor (NMDAR). It is used for premedication, sedation, induction, and maintenance of general anesthesia. Central, regional, and local anesthetic and analgesic properties have been reported for ketamine. Intravenous (IV) administration of low-dose ketamine decreases postoperative opioid use and improves analgesia. The addition of ketamine to epidural lidocaine or bupivacaine increases the duration of regional anesthesia and postoperative analgesia. It has been seen that perineuraxial use of 0.3-0.5% ketamine combined with local anesthetic in surgical wounds enhances analgesia by a peripheral mechanism [5]. Several studies have been performed to evaluate the effect of added ketamine to local anesthetics for nerve block and regional anesthesia.

Our study was meant to evaluate that adding ketamine as an adjuvant to bupivacaine, administered as a single injection in ultrasound guided Pectoral nerve block would enhance the quality of postoperative analgesia after modified radical mastectomy so that we can assess the analgesic efficacy of ketamine by noting the VAS Score, time for first rescue analgesia and total opioid consumption in 24 hrs following pecs block in modified radical mastectomy done in ca breast patients.

Material and Methods

This is a prospective observational study, conducted in Government Dharmapuri medical college hospital, Dharmapuri after approval of the institutional ethical committee. Total duration of study period was 1 year. A written informed consent was obtained from each patient after explaining the technique before inclusion in this study. We intended to recruit at least 30 per group. Total number of patients in our study was 60.

Patients were given ultrasound guided, modified pecs block with 30 ml of 0.25% bupivacaine hydrochloride divided into 10 ml injected between the 2 pectoral muscles on the interfascial plane, and 20 ml injected between the pectoralis minor and the serratus anterior muscles were included in control group. Patients were given ultrasound guided, modified pecs block with 30 ml of 0.25% bupivacaine hydrochloride, with ketamine (1 mg/kg) divided into 10 ml injected between the 2 pectoral muscles on the interfascial plane, and 20 ml injected between the pectoralis minor and the serratus anterior muscles were included in test group that is ketamine group.

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Patients of age 18 – 60 years, body weight of 50 – 90 kg, scheduled for modified radical mastectomy were included in our study. While patients with history of bleeding disorders or patients on anticoagulant therapy, refusal to participate, with known allergy to local anesthetic drugs, Psychiatric illness, and Opioid dependence were excluded

All patients were premedicated with 10 mg of oral diazepam on the night of surgery. On arrival to the operating room, an intravenous line was inserted in the contralateral upper limb to the side of surgery. Monitoring included electrocardiography (ECG), non-invasive blood pressure (NIBP), arterial oxygen saturation (Sao₂), and end-tidal carbon dioxide. Anesthesia was induced for all participating patients with 2 µg/kg fentanyl, 2 – 3 mg/kg propofol and 1.5 mg/kg lidocaine. Endotracheal intubation was facilitated by 2mg/kg suxamethonium

Skin incision was performed 15 minutes after the block was given. Anesthesia was maintained by 1 – 1.5 MAC sevoflurane in 50% oxygen/ nitrous mixture and 0.1mg/kg atracurium, respectively, at the end of surgery, a reversal of the muscle relaxant was done using neostigmine (0.04 mg/kg) and glycopyrolate (0.01 mg/kg).

After extubation, all patients were transferred to the post anesthesiacare unit (PACU). All patients were followed up and assessed at baseline and at different time intervals postoperatively for vital signs VAS score, the time for first request of rescue analgesia, and total opioid consumption in the 24 hours.

All patients were followed up and assessed at baseline, hourly for 24 hrs postoperatively for Vas score, the time for first request of rescue analgesia, total opioid consumption in the 24 hours.

Data were presented as number, percentage, mean, and standard deviation. Chi-square test was used to compare between qualitative variables. Mann-Whitney test was used to compare between 2 quantitative variables in case of non-parametric data. P-value considered statistically significant when $P < 0.05$.

Results and Analysis

In our study, totally 60 female patients undergoing modified radical mastectomy for ca breast were included, 30 patients in each group. Block was successful in all the patients enrolled in the study and all the enrolled patients completed the study.

In our study 11 patients were in age group of less than 40 years, 11 patients were between 40-50 yrs, 38 patients were more than 50 yrs. The mean age in group 1 is 52.9 yrs and in group 2 was 56.3 yrs with an p value of 0.210, which shows there is no statistical significance in both the groups so, the

age was comparable between both groups. The mean weight in group 1 was 59.1 kg \pm 6.7kg and in group 2 was 61.27kg \pm 7.69 kg, with a p value of 0.249, which was statistically not significant and both the groups were comparable.

The mean duration of surgery in group 1 was 120 min \pm 40.58 min and in group 2 was 107 min \pm 31.64 min with a p value of 0.060, statistically not significant. Both the groups were comparable in the study.

Table 1: Comparison of VAS score

	Group 1 (Control)			Group 2 (Ketamine)		
	0-3	4 to 6	7 to 10	0-4	4 to 6	7 to 10
30 min	30(100%)	0	0	30(100%)	0	0
1hr	30(100%)	0	0	30(100%)	0	0
2hr	30(100%)	0	0	30(100%)	0	0
4hr	30(100%)	0	0	30(100%)	0	0
8hr	27(90%)	3(10%)	0	30(100%)	0	0
12hr	15(50%)	15(50%)	0	30(100%)	0	0
24hr	1(3.3%)	29(96.6%)	0	3(10%)	27(90%)	0

VAS was compared between 2 groups with chi square test at each hour at 8th hr-p value of 0.511, which is statistically not significant at 24 hrs p value of 0.605, statistically not significant mean value of vas score was lower in control group than ketamine group but statistically not significant.

Table 2: Request of First Rescue Analgesia

Time For First Rescue Analgesia (in min)	Group 1	Group 2
Mean	620	1091.5
SD	116.9	106.91
p' value	< 0.001 Significant	

The mean time of request for rescue analgesic in group 1 (Control group) is 620 min (10hr 30 min) \pm 116.9 minutes and in group 2 (ketamine group) is 1091.5 min (18 hrs) \pm 106.91 min, with a p value of <0.001. There is statistical significance between 2 groups, Time for first request of analgesia prolonged in ketamine group when compared to control group.

Table 3: Total Opioid Consumption in 24 Hrs

Total Opioid Consumption	Group 1	Group 2
Mean	293.3	141.6
SD	59.79	32.39
P value	<0.001 significant	

The mean total opioid consumption in 24 hrs in group 1 is 293.3mg \pm 59.79 mg and in group 2 is 141.6mg \pm 32.39mg, with a p value <0.001. There is statistical significance between 2 groups, Total Opioid consumption is less in ketamine group when compared to control group.

Table 4: Side Effect

	Control Group	Percentage	Ketamine Group	Percentage	P value
Nausea	2	6.7%	3	10%	0.206
Vomiting	1	3.3%	2	6.7%	0.219
Chest pain	0	0	0	0	-
Hallucination	0	0	0	0	-
Delirium	0	0	0	0	-
Arrhythmias	0	0	0	0	-
Others	0	0	0	0	-

In our study 2 patients in control group had nausea and 3 patients in ketamine group had nausea. In our study one patient in control group and 2 patients in ketamine group had vomiting. No other significant side effect noted in both the group. No statistical significance in side effects between both the groups.

Discussion

Breast cancer is the most common cancer diagnosed and considered to be the most common in women worldwide. Several forms of regional techniques like local anesthetic infiltration, intercostal nerve block, epidural block, and paravertebral nerve block (PVB) have been used for management of pain after breast surgery.

In our study, ketamine added to bupivacaine in modified Pecs block prolonged the time to first request of analgesia and reduced the total amount of opioid consumption in comparison to bupivacaine alone. On the other hand, no significant difference in side effects was observed between the 2 groups.

Bashandy and Abbas [5] found that patients receiving Pecs block showed lower postoperative pain scores at all-time points (up to 24 hours) and significantly decreased opioid consumption for 12 hours in comparison to control group patients. Wahba and Kamal [6] found that Pecs block reduced postoperative morphine consumption in the first 24 hours and pain scores in the first 12 hours postoperatively following modified radical mastectomy in comparison to PVB.

This agrees with our findings, where the VAS values in both groups after receiving Pecs block were less than 3 for the whole follow-up period of 48 hours. However, in our study adding ketamine to local anesthetic in Pecs block increased the time to first request of analgesic requirement and reduced the total opioid consumption in comparison to plain Pecs block. Many studies have so far investigated the effect of adding local ketamine to local anesthetics.

Gantenbein et al [7] in a study conducted to address effects of ketamine on local bupivacaine activity found that ketamine increased the total anesthetic effect of bupivacaine. Dal et al [8] showed that local injection of ketamine in children undergoing adenotonsillectomy significantly reduced pain score, dose of rescue analgesia, and increased time interval to the first dose of opiate compared to the group receiving IV normal saline. Tverskoy et al [9] used local injection of 0.5 mg/kg ketamine after herniorrhaphy to reduce pain and showed that ketamine improved the quality of anesthesia and analgesia created by local anesthetics (0.5 % bupivacaine) used in these patients.

Lashgarinia et al [10] concluded that adding ketamine in a dose of 2mg/kg to lidocaine 5 mg/kg 1.5 % in ultrasound-guided brachial plexus block could decrease the postoperative pain and need for analgesia most probably due to the local anesthetic effect of ketamine at the level of surgical trauma. Further, Kazemeini et al [11] found that local wound injection with 50 mg of ketamine plus 2 mL of bupivacaine 0.5% provided superior postoperative analgesia compared to bupivacaine 0.5% alone following anal surgery. Abdel-Ghaffar et al [12] concluded that 30 mg epidural ketamine reduced post hysterectomy pain, prolonged the time to first analgesia request, and reduced postoperative epidural PCA consumption.

On the contrary, multiple studies have revealed negative results. 30 mg ketamine did not enhance

the onset time and duration of sensory and motor blockade when added to 30 mL of 0.5% ropivacaine for interscalene brachial plexus block [13]. The addition of 1 mg/kg ketamine to 0.1% ropivacaine infusion via the femoral nerve catheter after repairing an anterior cruciate ligament (ACL) injury/ tear could not improve postoperative pain control. [14]

Senel et al [15] compared the analgesic efficacy of 50 mg tramadol and 50 mg ketamine added to 40 mL 0.375% ropivacaine in axillary brachial plexus block and found that tramadol extended the onset and duration of the block and improved the quality of postoperative analgesia more than did ketamine.

The variable effects of ketamine probably come from the different ketamine concentrations used in different clinical trials. In addition, it has been observed that the effect of ketamine might be different when injected at the level of inflamed tissue compared with the normal tissue site. Ketamine has demonstrated an anti-inflammatory effect that significantly inhibits the early postoperative inflammatory response. It can act at different levels of inflammation, interacting with inflammatory cell recruitment, cytokine production, and inflammatory mediator regulation.

Our results strongly highlight the value of adding ketamine to local anesthetic in peripheral nerve block, especially in this relatively new technique of modified Pecs block, where postoperative analgesia lasted for a long period in the ketamine group.

Conclusion

In conclusion, the addition of ketamine to modified Pecs block prolonged the time to first request of analgesia and reduced total opioid consumption without serious side effects in patients undergoing modified radical mastectomy.

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