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Role of Ketamine as an Adjuvant to Bupivacaine in C-Arm Guided Thoracic Paravertebral Block Analgesia for Modified Radical Mastectomy

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ABSTRACT

Background: Breast cancer is the most common type of cancer found in women and today represents a significant challenge to public health. Postoperative pain is the most distressing symptom experienced by the patient. Pain induces metabolic, hormonal and cardio-respiratory responses that affect the outcome of surgery.
Aim of the Work: The aim of this study was to evaluate the role of ketamine as an adjuvant to bupivacaine in c- arm guided thoracic paravertebral block analgesia for modified radical mastectomy. **Patients and Methods:** This study was carried out in Tanta University Hospitals in Surgery Department from April 2016 to October 2016 on sixty-two patients scheduled for elective modified radical mastectomy divided into two equal groups each contain 31 patients, group 1 received PVB with bupivacaine only under c arm and group 2 received PVB with bupivacaine and ketamine as pre emptive analgesia and watch what is the outcome. Written informed consent was taken from each patient. **Results:** This prospective randomized double blind study was carried out on 62 patients divided into two equal groups where group two showed statistically significant decrease in VAS , total amount of analgesic and delay in time of first analgesic requirement in comparison with group one and significant difference as regard hemodynamics and postoperative complication between two groups. **Conclusion:** We concluded that addition of ketamine to bupivacaine as an adjuvant in C-arm guided PVB appears to be more beneficial than the use of bupivacaine alone for postoperative analgesia in modified radical mastectomy surgery.
Keywords: Ketamine, Bupivacaine, Radical Mastectomy, C-Arm Guided Thoracic Paravertebral, Block Analgesia.

INTRODUCTION

Breast cancer is the most common type of cancer found in women and today represents a significant challenge to public health [(1)].

Several treatment decisions may be offered to women with breast cancer including surgery, radiotherapy, and endocrine and chemotherapy**.** Modified radical mastectomy (MRM) still represents a primary therapeutic strategy. It is an exceedingly common procedure with an increased incidence of acute and chronic pain [(2)].

Postoperative pain is the most distressing symptom experienced by the patient. Pain induces metabolic, hormonal and cardio-respiratory responses that affect the outcome of surgery [(3)].

The provision of intra and post-operative analgesia is an integral part of the anesthetic practice. It was found that pre-emptive analgesia has the potential to be more effective than a similar analgesic treatment initiated after surgery [(4)].

Metabolic stress response can be avoided if analgesia is provided thirty minutes prior to incision which stays well into postoperative period and saves the patients from the hazards of stress response. There is evidence that pain services affect morbidity and duration of hospital stay [(4, 5)].

Many pain services use co-analgesia based on four classes of analgesics, namely local anesthetics, opioids, non-steroidal anti-inflammatory drugs (NSAIDs), and acetaminophen (paracetamol) [(6)].

Thoracic paravertebral nerve block (TPVB) is a viable option to the classic multimodal analgesia in breast surgery as it enhances surgical anesthesia and postoperative analgesia.

This technique is associated with a superior control of the pain, a reduction in opioids consumption after surgery, a decrease in postoperative nausea and vomiting, and an overall decrease in length of hospital stay. So, it has been suggested as an ideal adjunct to general anesthesia for modified radical mastectomy [(7)]. While most trials of TPVB for breast surgery show benefit, their effect on postoperative pain intensity, opioid consumption, and prevention of chronic postsurgical pain varies due to use of different drugs [(8)].

Bupivacaine is the most often used local anesthetic for many blocks in adult. It provides analgesia which lasts for only 4-12 hours. Rescue analgesia is thus required when effect of block wears off [(9)].

Prolongation of local analgesia has been achieved by the addition of various additives like morphine, tramadol, fentanyl, ketamine, clonidine, dexmedetomidine and midazolam to prolong the postoperative analgesia. They were used in varying concentrations in different studies to achieve maximum benefit [(9)].

Ketamine is an N-methyl-D-aspartate receptor antagonist, with analgesia mediated by increased spinal inhibition of nociceptive

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transmission. Ketamine may reduce the dose requirement of local anesthetics and increasing its analgesic effect [10].

AIM OF THE WORK

The aim of this study was to evaluate the role of ketamine as an adjuvant to bupivacaine in c-arm guided thoracic paravertebral block analgesia for modified radical mastectomy.

PATIENTS AND METHODS

This study was carried out in Tanta University Hospitals in Surgery Department from April 2016 to October 2016 on sixty-two patients scheduled for elective modified radical mastectomy. Every patient received an explanation to purpose of the study and written informed consent was taken from each one. Research results used for scientific purposes and all data of patients were confidential with secret codes and private file for each patient. The study was prospective randomized double blinded and the data recorded by another anesthetist. **The study was approved by the Ethics Board of Tanta University.**

Inclusion criteria:

Sixty-two adult female patients, ASA physical status I &II scheduled to undergoing elective modified radical mastectomy.

Exclusion criteria

Patient refuse ,bleeding disorders ,allergy to amide-type local anesthetics ,infection at thoracic paravertebral injection site ,severe spinal deformity ,morbid obesity ,history of recent analgesic administration and uncontrolled concomitant medical condition.

The 62 patients were randomly assigned using sealed envelope into two equal groups, each group contained 31 patients.

Group I (n=31): Patients in this group received C-arm guided PVB by 20 ml plain bupivacaine (0. 25%) at dose of 0. 3 ml/kg about 15min before induction of anaesthesia after disinfection in the site of block.

Group II (n=31): Patients in this group received C-arm guided PVB by 20 ml mixture of plain bupivacaine (0. 25%) at dose of 0. 3 ml/kg and ketamine at dose of 0.5mg/kg about 15min before induction of anaesthesia at the level of T4 . The patient was turned to supine position on routine monitoring. Preoxygenation with 100% O_2 for 3-5 min. Induction of anaesthesia was carried out with Propofol IV (1.5mg/kg) till loss of the verbal response followed by cis-atracurium IV (0.15 mg/kg) to provide neuromuscular blockade, Fentanyl 2 ug/kg was administered. Lungs were ventilated for 3 minutes by tightly fitted face mask and intubation was performed with a cuffed endotracheal tube of appropriate size, tidal volume and respiratory rate were adjusted.

The anesthesia was maintained by 1.5% of isoflurane and oxygen which was adjusted. Additional doses of cis-atracurium (0.02 mg/kg) were given when needed. Fluid therapy included maintenance (4ml/kg/h for the first 0- 10 kg, 2ml/kg/h for the next 10-20 kg, 1ml/kg /h for each kg above 20 kg) plus deficit fluids (maintenance X fasting hours) and third space losses (4 ml/ kg/h) using ringer solutions in both groups.

At the end of the surgery closure of isoflurane and antagonizing the effect of muscle relaxant by neostigmine (0.05mg/kg) with atropine (0.01mg/kg) were given IV.

The patient was then transported to the post anesthesia care unit (PACU) with supplemental oxygen.

***The following data were recorded*:**

- Demographic data (age, weight and height)
- Duration of surgery
- Mean arterial blood pressure & Heart recorded at baseline (before induction of anesthesia) and every 30 min till the end of the surgery.
- Depth of anaesthesia by entropy was recorded at baseline (after induction of anesthesia) and every 30 min till the end of the surgery.
- Assessment of postoperative pain was done with visual analogue scale (VAS; 0=no pain and 10=worst possible pain) at 30 min post-operative and 2 hr. postoperative, 6 hr, 12hr, 18 and 24h postoperative.
- The first patient requirement for postoperative analgesics. Patient with pain score (VAS≥4) receive rescue analgesia (pethidine 1mg/kg).
- Total amount of analgesic requirements.
- Incidence of postoperative complications as nausea, vomiting (receiving metoclopramide amp) & hypotension (receiving I.V fluids).

Statistical analysis

Statistical presentation and analysis of the present study was conducted, using the mean, standard deviation and T test by SPSS V.16.

RESULTS

This prospective randomized double blind study was carried out in Tanta University Hospitals on 62 adult female patients (ASA physical status I/II) scheduled for elective modified radical mastectomy surgery.

Table (1): Comparison of VAS between GI and GII.

	Group I			Group II			T-test	
	Mean	±	SD	Mean	±	SD	t	P-value
After surgery	2.48	±	0.89	2.45	±	0.77	0.023	0.879
2 hrs	1.74	±	0.86	1.71	±	0.90	0.021	0.886
6 hrs	1.90	±	0.75	1.77	±	0.84	0.406	0.526
12 hrs	1.94	±	0.81	1.87	±	0.76	0.104	0.749
18 hrs	2.90	±	1.42	1.81	±	0.70	14.808	**0.001***
24 hrs	3.84	±	1.39	2.35	±	1.25	19.449	**0.001***

Table (2): Comparison of Mean arterial blood pressure (MABP) changes in the two studied groups

	Group I			Group II			T-test	
	Mean	±	SD	Mean	±	SD	t	P-value
Pre-induction	76.32	±	7.37	75.90	±	7.01	0.230	0.819
30 min	72.58	±	5.09	74.97	±	7.05	1.528	0.132
60 min	74.65	±	6.88	75.00	±	6.61	0.207	0.837
90 min	75.06	±	5.01	75.68	±	6.53	0.415	0.680
120 min	75.23	±	8.04	74.90	±	6.62	0.172	0.864

Table (3): Comparison of entropy values between GI and GII

	Group I			Group II			T-test	
	Mean	±	SD	Mean	±	SD	t	P-value
Baseline after induction	51.39	±	6.12	52.45	±	5.62	0.509	0.478
30 min	49.97	±	7.02	49.35	±	4.18	0.174	0.678
60 min	47.45	±	7.06	46.32	±	3.77	0.617	0.435
90 min	47.19	±	5.30	45.55	±	3.69	2.013	0.161
120 min	46.42	±	5.75	44.81	±	3.65	1.740	0.192

Table (4): Consumption of analgesic requirements per first 24 hours (Pethidine mg):

	Group I	Group II
Mean	63.87	14.84
SD	65.20	30.86
T test	14.322	
P value	<0.001**	

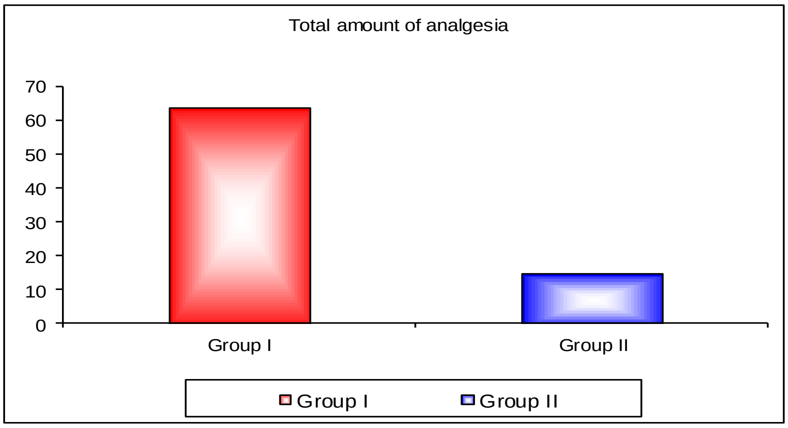

Figure (1): Consumption of analgesic requirements per first 24 hours (mg Pethidine)

DISCUSSION

Breast surgery is one of the most common forms of surgery conducted in hospitals, even relatively minor breast surgery can be associated with significant postoperative pain [11].

Poorly controlled postoperative pain has negative physiological and psychological consequences. Furthermore, effective acute pain control suppresses the surgical stress response and decreases the need for general anesthetics and opioids. Acute postoperative pain is an integral risk factor in the development of chronic post mastectomy pain. Regional anesthesia techniques have provided better quality of acute pain control and subsequently less chronic pain [12].

Modified radical mastectomy (MRM) still represents a primary therapeutic strategy. It is an exceedingly common procedure with an increased incidence of acute and chronic pain [13].

Thoracic paravertebral nerve block (TPVB) is a viable option to the classic multimodal analgesia in breast surgery as it enhances surgical anesthesia and postoperative analgesia. This technique is associated with a superior control of the pain, a reduction in opioids consumption after surgery, a decrease in postoperative nausea and vomiting, and an overall decrease in length of hospital stay. So, it has been suggested as an ideal adjunct to general anesthesia for modified radical mastectomy. While most trials of TPVB for breast surgery show benefit, their effect on postoperative pain intensity, opioid consumption, and prevention of chronic postsurgical pain varies due to use of different drugs [14].

In agreement with our result was ***Othman et al.*** [15] this study aimed to compare the analgesic efficacy and safety of modified Pecs block with ketamine plus bupivacaine versus bupivacaine in patients undergoing breast cancer surgery. A randomized, double-blind, prospective study on sixty patients aged 18 – 60 years scheduled for modified radical mastectomy were enrolled and randomly assigned into 2 groups (30 patients each):-Control group patients were given ultrasound-guided, Pecs block with 30 mL of 0.25% bupivacaine only. Ketamine group patients were given ultrasound-guided Pecs block with 30 mL of 0.25% bupivacaine plus ketamine hydrochloride (1 mg/kg). Patients were followed up for 48 hours postoperatively for vital signs, VAS score, first request of rescue analgesia and total morphine consumption. Ketamine plus bupivacaine in Pecs block compared to bupivacaine alone prolonged the mean time of first request of analgesia, reduced total morphine consumption and decreased VAS.

In contrast to our study, ***Soni et al.*** [16] a prospective randomized study comparing PVB versus epidural block on 60 patient scheduled for unilateral breast surgery. Patients were divided into two groups of 30 each, Group E (Thoracic epidural group), Group P (Thoracic paravertebral group), each who received 15ml of 0.5% ropivacaine either in the thoracic epidural region or thoracic paravertebral region. No patients had abnormal finding, such as hypotension and bradycardia throughout monitoring in paravertebral group. There was a significant decrease in HR and MABP in EP group compared with PVB group. This may be because of different drug and less volume of drug [16].

Also in agreement with our study that of **Fabricio *et al.*** [17] who compared between ketamine and morphine in epidural on 26 patient submitted to do mastectomy. The patients were divided into two equal group, group (k) received 12 ml ropivacaine and 50 mg ketamine and group (m) who received 12 ml ropivacaine and 2mg morphine. He found that blood pressure and heart rate of ketamine group were stable with no decrease.

The present study regarding of VAS in group II is in contrast with the study of ***Omar et al.*** [18] who prospectively randomized 60 ASA I–III women into three groups: group B (n= 20) who received PVB using 15 ml plain bupivacaine 0.5% (control group), group K (n= 21) who received ketamine (0.5 mg/ kg) added to bupivacaine 0.5%, and group T (n= 19) who received tramadol (1.5 mg/kg) added to bupivacaine 0.5%. They found that there was no statistically significant difference between the three groups regarding VAS, time of first analgesic consumption and total amount of analgesic requirement. There was no significance from adding ketamine to PVB in the mastectomy surgery, this may be due to less volume of drugs in their study.

As regard post operative complication there is no statistically significant difference between the two studied groups as both showed improve of the post-operative pain score and total analgesic consumption so decrease in incidence of PONV and hypotension. The study of ***Nai Liang et al.*** [19] is consistent with our study where they tested forty consecutive patients received either general anesthesia (GA group, n= 25) or GA plus ultrasound-guided PVB (GA PVB group, n = 15) for the surgery. Incidence of postoperative nausea and vomiting and doses of analgesics and narcotics given showed that there was decrease in PONV and complication in PVB group. Also in study of ***Anshu et al.*** [15] who compared among morphine, dexamedatomidine and ketamine in PVB during modified radical mastectomy on 120 patients. They found that there was no statistically significant difference between the groups except morphine group regarding PONV and other complication.

As regard depth of anaethesia we found that their statistically significant difference (decrease) in entropy in both group as compared to baseline values at (60, 90 and 120 min) and no significant difference between both groups as compared to each other.

In study of ***Hans et al.*** [20] who compared the effects of ketamine on Bispectral Index and spectral entropy under sevoflurane anaesthesia on twenty two female patients did gynecological surgeries received ketamine bolus 0.5 mg/ kg intravenous with general anaesthesia. They found increase in the values of entropy which is contradictory to our study. This may be related to methodological differences in ketamine administration or to the absence of surgical stimulation during some time of our recording.

CONCLUSION

We conclude that, the addition of ketamine to bupivacaine as an adjuvant in C-arm guided PVB appears to be more beneficial than the use of bupivacaine alone for postoperative analgesia in modified radical mastectomy surgery.

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