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Comparison of Dexamethasone and Magnesium Sulphate with Plain Bupivacaine in Pectoral Nerve Block for Postoperative Analgesia: A Randomised Double Blind Controlled Trial

Nisha Sharma[1], Sonali Kaushal[2], Surinder Singh[3], Shweta Mahajan[4]

[1]Senior Resident, Department of Anaesthesiology, Dr. Radhakrishnan Medical College, Hamirpur, Himachal Pradesh 177001, India. [2]Assistant professor, [3]Professor, [4]Assosiate Professor, Department of Anaesthesiology, Indira Gandhi Medical College, Shimla, Himachal Pradesh 171001, India.

Abstract

Background and Aims: Patients undergoing breast cancer surgeries face significant postoperative pain. We aimed to compare the analgesic efficacy of plain bupivacaine and plain bupivacaine with magnesium sulphate and dexamethasone in pectoral nerve block (PECS). *Methods:* Sixty ASA status I and II female patients between age 18 to 60 years scheduled for unilateral modified radical mastectomy (MRM) under general anaesthesia, were enrolled in this prospective randomised double blind controlled study. All patients received USG guided PECS block. Patients in group C were given a total of 30 cc 0.25% bupivacaine while group D received total of 30 cc 0.25% bupivacaine with 4 mg dexamethasone and group M received 150 mg of magnesium sulphate with 0.25% of bupivacaine 30cc in total. General anaesthesia was administered in a standardised manner to all three groups before giving block. The various parameters observed included duration of analgesia, VAS score, number of rescue analgesics required and any adverse effects. The primary outcome was to compare total duration of analgesia between the three groups. *Results:* The mean duration of analgesia was 778.95 ± 94.735 min (13 hrs) in group D, 519.90 ± 66.607 min (9.3 hrs) in group M and 384.30 ± 49.558 min (6.4 hrs) in group C. At 12 and 24 hrs, VAS scores were significantly lower in group D as compared to group M and group C ($p > 0.001$). The difference in VAS scores between group M and group C at 12 and 24 hrs was not statistically significant. At 48 hrs VAS scores among the three groups were comparable. *Conclusion:* In the postoperative period, the use of dexamethasone and magnesium sulphate as adjuncts to bupivacaine in PECS block results in lower VAS scores, decreased demands for rescue analgesia and prolonged duration of analgesia. The use of these adjuvants provides better patient satisfaction without causing any noticeable side effects.

Keywords: Analgesia, Pectoral Nerve Block, Modified Radical Mastectomy, Dexamethasone, Magnesium Sulphate

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Introduction

Modified radical mastectomy for breast cancer treatment is associated with a significant postoperative pain. Hence achieving adequate postoperative analgesia is very important as acute post-operative pain is not only debilitating but is an important risk factor for the development of persistent chronic pain after breast surgery.[1]

Breast surgery is generally performed under general anaesthesia with regional anaesthetic techniques like thoracic epidural and paravertebral blocks for post-operative analgesia. These techniques may be

Corresponding Author: Sonali Kaushal, Assistant Professor Department of Anaesthesiology, Indira Gandhi Medical College, Shimla, Himachal Pradesh 171001, India.
E-mail: : sonalikaushal33@gmail.com
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associated with complications like pneumothorax, vascular puncture, nerve damage etc. [2]However these complications have widely been overcome with advent of USG. Another USG guided block pectoral nerve block (PECS) has been introduced for MRM which provides better safety profile and comparable pain relief. PECS block is an interfacial plane block where local anaesthetic is deposited into the plane between the pectoralis major muscle and the pectoralis minor muscle (PECS I block) blocking lateral and medial pectoral nerves and between pectoralis minor and serratus anterior muscle (PECS II block) blocking the intercostobrachial, intercostals III, IV, V, and VI; and long thoracic nerves.[3,4] Adjuvants like dexamethasone, dexmedetomidine, adenosine and magnesium have been used in PECS block to prolong the analgesic effect of block.[5-8] However, no comparative study till date is available comparing dexamethasone and magnesium sulphate. Therefore in view of providing safe, long and effective postoperative analgesia along with patient comfort we planned to conduct a study comparing analgesic efficacy of dexamethasone and magnesium sulphate as adjuvants to bupivacaine in ultrasound guided pectoral nerve block for modified radical mastectomy.

Materials and Methods

After obtaining approval from our Institutional Ethical Committee, 60 patients belonging to the ASA physical status I-II undergoing modified radical mastectomy (MRM) with axillary dissection over a period of 24 months were selected for the study.

Sample size was calculated using pain scores as the primary variable. Literature review revealed an average difference of 10 mm on VAS of 10 cm with standard deviation of 10 mm. Assuming a standard deviation of 10 mm, the minimum needed sample size to detect a difference of 10 mm on the VAS of 10 cm, with alpha error of 0.05 and power of study 80% was 54. Thus, each group required at least 18 patients. Hence, a total of 60 patients were enrolled to compensate for any probable block failures and dropouts.

All patients were explained the purpose of the study along with the procedure and thereafter written, informed consent was obtained from all the patients. Exclusion criteria included history of allergy to local anaesthetics, bleeding disorder or receiving anticoagulants, pregnancy, infection at the block site, BMI >35kg/m^2 and patients refusal. The patients were randomly allocated by a computer-generated random number table to three groups of 20 each: Group C (receiving PECS block with 30 cc of 0.25% bupivacaine), Group D (receiving PECS block with 0.25% bupivacaine with dexamethasone 4mg, total volume 30cc) and Group M (receiving PECS block with bupivacaine 0.25% and magnesium sulphate 150 mg, total volume given 30cc) of 20 patients each. Allocation concealment was ensured by having the random group assignment enclosed in a sealed opaque envelope. The sealed envelope was opened by an anaesthesiologist not involved in the study. The observer who collected the peri-operative data as well as the patient was masked to the technique of analgesia and the drug used.

During the pre-anaesthetic visit, patients were explained about the study purpose, advantages and risks of procedure and instructed to demand analgesia as per requirement. Patients were educated about the 10 cm visual analogue scale (VAS) during the pre-operative assessment. All the patients were kept nil orally for 8 hours before surgery, and pre-medication with oral alprazolam 0.5 mg and oral ranitidine 150 mg was given night before surgery.

All patients received midazolam 1–2 mg before induction of anaesthesia and monitored with fiveleads ECG, pulse oximetry, non-invasive bloodpressure and capnography. General anaesthesia was induced with fentanyl 2 μg/kg, Propofol 1.5–2 mg/kgand endotracheal intubation was facilitated withatracurium 0.5 mg/kg. Anaesthesia was maintained with isoflurane and O_2/NO_2 mixture with a fractionof 33% inspired oxygen.

After induction, USG guided PECS block was performed with patient in supine position and placing ipsilateral upper limb in abduction position using a linear US probe of high frequency (6-13 MHz, Sonosite). The USG probe was placed at infra-clavicular region after skin sterilization and moved laterally to locate the axillary artery and axillary vein directly above first rib where pectoralis minor and pectoralis major muscles were identified at this US window. A 22G spinal needle was inserted in plane with US probe to the fascial plane between pectoralis muscles and 10ml of total drug was injected after negative aspiration according to the groups allocated.

Then US probe was moved towards axilla till serratus anterior muscle was identified above second, third and fourth ribs and then the needle was reinserted into fascial plane between pectoralis minor and serratus anterior and 20 ml of the remaining drug was injected after negative aspiration according to the groups allocated.

Throughout the surgery, non-invasive mean arterial blood pressure, heart rate and oxygen saturation was monitored continuously and recorded every 5 minutes till completion of the procedure. Intraoperatively fentanyl 1µg/kg I.V. in bolus doses was given to the patients whenever the mean arterial pressure (MAP) or heart rate exceeded 20% above the preoperative value. Diclofenac sodium 75 mg I.V. was also administered before incision. Ondansetron 0.1mg/kg was given for antiemesis. After completion of surgery neuromuscular blockade was reversed with I.V. neostigmine 50µg/kg and glycopyrrolate 10µg/kg.

After recovery from anaesthesia, patients were shifted to Post anaesthesia care unit (PACU). postop pain assessement was done at 0 min (on being shifted to recovery), 15 min, 30 min , 45 min and 60 min in PACU and at 2hrs, 4hrs, 6hrs, 12hrs, 24hrs, 36hrs and 48hrs postoperatively in ward by VAS score. Whenever the VAS score was > 4 rescue analgesic was given with I.V. diclofenac 75 mg, supplemented with I.V. tramadol 50 mg. Amount of doses of diclofenac and tramadol were recorded.

The level of postoperative nausea and vomiting (PONV) was assessed with the Numerical Rating Scale (NRS 0-4; 0- no nausea, 1- nausea, 2- retching, 3-vomiting, 4- severe vomiting (4-5 episodes). Injection metoclopramide 10 mg I.V. was given whenever PONV NRS score was greater than two. Patient satisfaction for post-operative analgesia wasrecorded according to satisfaction score: Poor = 0; Fair = 1; Good = 2; Excellent = 3. Any untoward side effects or complications related to procedureand local anaesthetic were recorded.

Statistical analysis was performed using SPSS software version 20. The one-sample Kolmogorov–Smirnov test was employed to determine whether data sets differed from a normal distribution. Normally distributed data were analysed using a repeat-measures general linear model analysis of variance for time-related variables, whereas non-normally distributed data were analysed using Kruskal-Wallis test. $p < 0.05$ was considered statistically significant.

Results

The total number of patients enrolled during the study period was 60 in three groups being 20 in each group. Group C (30 cc of 0.25% bupivacaine), Group D (30cc of 0.25% bupivacaine with 4mg of dexamethasone) and Group M (30 cc of 0.25% bupivacaine with 150 mg of magnesium sulphate) were comparable to each other with respect to age, weight and duration of surgery (Table 1). Mean duration of analgesia, that is, duration to first analgesic requirement was found to be significantly prolonged in Group D {778.95 ± 94.735 min (13hrs)} compared to Group M {519.90 ± 66.607 min (9.3 hrs)} and Group C {384.30 ± 49.558 min (6.4 hrs)}(P < 0.001) (Table 2).

Mean VAS scores were significantly lower in group D than group M at 2, 4, 6, 12 and 24 h while values were lower in group M as compared to group C at 0, 2, 4 and 6 hrs (Tables 3) (Fig. 1).

The mean number of doses of I.V. Diclofenac/Tramadol required were maximum in group C (3.20 ± 0.616) followed by group M (2.50 ± 0.688) and least in group D (1.90 ± 0.641) and the difference was found to be statistically significant between the groups (Table 4).

No complications such as vascular puncture, hypotension, pleural puncture or pneumothorax were observed in any of the groups.

Table 1. Demographic Profile

Parameter	Group D Mean ± SD	Group M Mean ± SD	Group C Mean ± SD	*p* value
Age (Yrs.)	50.35 ± 9.505	50.75 ± 7.656	50.20 ± 9.070	0.979
Weight (kg)	54.13 ± 5.620	53.95 ± 7.037	58.50 ± 9.655	0.105
Duration of Surgery (min)	90.80 ± 17.961	86.30 ± 15.597	86.70 ± 16.633	0.645

p-value: >0.05 not significant, <0.05 significant, <0.001 highly significant

Table 2. Duration of Analgesia

Group D Mean ± SD (min)	Group M Mean ± SD (min)	Group C Mean ± SD (min)	*p* value intergroup		
			D vs M	M vs. C	D vs C
778.95 ± 94.735	519.90 ± 66.607	384.30 ± 49.558	<0.000*	<0.000*	<0.000*

* Highly significant

Table 3: Postoperative VAS Scores

Time Interval	Group D	Group M	Group C	*p* value		
				D vs M	M vs C	D vs C
0 min	0	0	0			
15min	0	0	0.15 ± 0.366	1	0.73	0.73
30min	0	0.05 ± 0.224	0.45 ± 0.510	0.876	<0.000*	<0.000*
45min	0	0.40 ± 0.503	1.30 ± .470	.007	<0.000*	<0.000*
60min	0	1.15 ± 0.48	1.65 ± 0.489	<0.000*	<0.000*	<0.000*
2 hrs	0.65 ± 0.489	2.05 ± 0.510	3.25 ± 0.639	<0.000*	<0.000*	<0.000*
4 hrs	1.60 ± 0.503	2.95 ± 0.510	4.30 ± 0.571	<0.000*	<0.000*	<0.000*
6 hrs	2.40 ± 0.503	3.70 ± 0.470	5.05 ± 0.605	<0.000*	<0.000*	<0.000*
12 hrs	3.25 ± 0.550	4.10 ± 0.852	4.45 ± 0.510	<0.000*	0.218	<0.000*
24 hrs	2.85 ± 0.671	3.45 ± 0.605	3.70 ± 0.470	0.006	0.377	<0.000*
36 hrs	2.15 ± 0.671	2.05 ± 0.605	2.50 ± 0.607	0.870	0.069	0.192
48 hrs	0.65 ± 0.587	0.60 ± 0.578	0.65 ± 0.671	1	0 .965	1

* Highly significant

Table 4: Total Doses of Rescue Analgesic (I.v. Diclofenac / I.v. Tramadol)

Group D Mean ± SD	Group M Mean ± SD	Group C Mean ± SD	*p* value	*p* value inter group		
				D vs M	M vs. C	D vs C
1.90 ± 0.641	2.50 ± 0.688	3.20 ± 0.616	<0.000*	0.014	0.003	<0.000*

* Highly significant

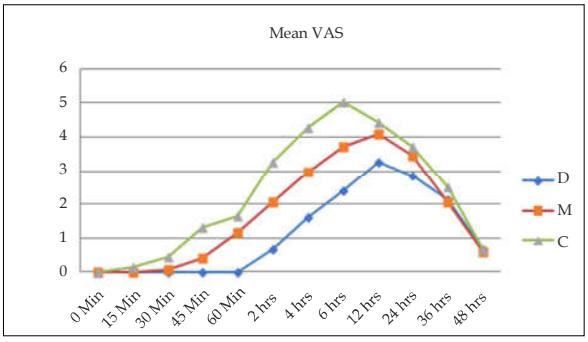

Fig. 1: Comparison of Mean Vas Scores

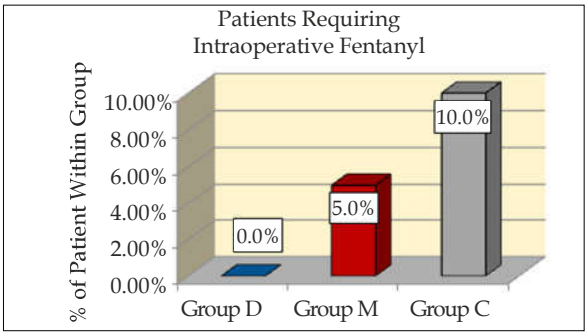

Fig. 2: Percentage Of Patients Requiring Intraoperative Fentanyl (Single Dose)

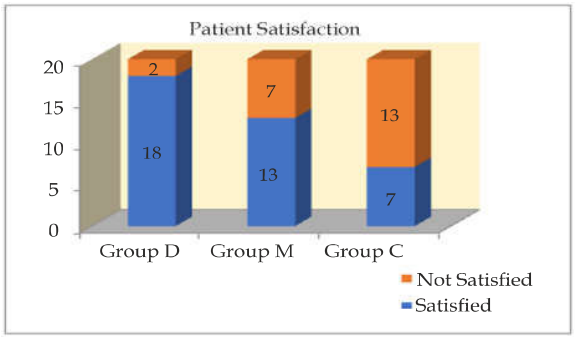

Fig 3: Patient Satisfaction Score (p = 0.001)

Discussion

In recent years, there has been increasing interest on a novel, less invasive nerve block, the pectoral nerve (PECS) block. Compared with general anaesthesia (GA) alone, PECS block when combined with GA are more advantageous in reducing intraoperative opioid consumption, postoperative opioid consumption, postoperative early pain, incidence of PONV, and the need for postoperative rescue analgesia.[9,10] Postoperative pain can reduce the quality of life of patients.[11] Controlling postoperative pain can help patients participate actively in postoperative rehabilitation and improve short-term and long-term recovery after surgery. Various studies have demonstrated that early postoperative pain (0–6 hours) is significantly reduced in patients administered PECS block combined with GA as compared with those administered GA alone, but this difference gradually disappeared in the late postoperative period (24 hours), hence advocating the role of

adding adjuvants in PECS block.[3,4,9,10] Though there are reports on use of adjuvants in various other peripheral nerve blocks, there is little systematic research on the comparison of efficacy and tolerability of the addition of adjunctive analgesic agents in PECS block.[12-15] Therefore, the objective of our randomized controlled study was to evaluate the clinical effectiveness and tolerability of dexamethasone and magnesium in combination with bupivacaine in PECS block analgesia after breast surgery.

In this randomised double blind controlled trial, we compared dexamethasone with magnesium sulphate as an adjuvant with bupivacaine in PECS block and found that duration of analgesia was maximum in dexamethasone group {778.95 ± 94.735 min (12.9 hours)} followed by magnesium {519.90 ± 66 min (8.6 hours)} then the bupivacaine group alone {384.30 ± 49.558 min (6.4 hours)}. In addition, we found that VAS scores were significantly lesser in dexamethasone and magnesium group compared to plain bupivacaine group.[5,6]

With regard to total duration of analgesia, most of the authors have claimed a mean duration of analgesia as 4–6 h with plain bupivacaine in PECS block and our study also shows similar results.[2-4] Similarly the mean duration of analgesia in group M in our present study was comparable to study by Ahmed et al, however it was significantly shorter than Group D.

Dexamethasone yields analgesia by three mechanisms. Firstly, it blocks transmission of nociceptive myelinated c fibers and suppressing ectopic neuronal discharge. Secondly, dexamethasone also inhibits the action of phospholipase A and alters the function of potassium channels in the excitable cells via glucocorticoid receptors and lastly, by its local vasoconstrictive effect. Choi et al. (2014) in a meta-analysis of literature of brachial plexus blocks found that dexamethasone in doses of 2mg, 4mg and 8mg was associated with prolonged duration of anaesthesia with no side effects in upper limb surgeries.[16] Hence, we selected dose of 4 mg as 2 mg was having less analgesic effect while 8 mg has similar effect as 4 mg.

Magnesium sulphate blocks the effects of excitatory amino acids (e.g., glutamate, aspartate) on NMDA receptors and contributes to central sensitization. It is proved that the addition of magnesium sulphate to local anaesthetic for neuraxial anaesthesia improves the quality of analgesia and prolongs the duration of anaesthesia.[38] In our study we selected a dose of 150 mg of magnesium sulphate at par with studies by Goyal P et al., Gunduz et al. and Mukherjee K et al., as these authors did not reported any side effects with a dose of 150 mg of magnesium sulphate and found that 150 mg of magnesium sulphate produced significantly increased duration of analgesia compared to 100 mg of magnesium sulphate in axillary plexus block for forearm and hand surgery.[17-19]

Intraoperative pain relief was adequate with PECS block in our three groups as assessed on the basis of heart rate and mean arterial pressure. One patient (5%) in group M and two patients (10%) in group C required only one dose of intraoperative fentanyl in the beginning of surgery which may have been due to delayed onset of block. Bashandy and Abbas reported PECS block patients consumed 50% less intraoperative fentanyl as compared to general anaesthesia without block.[10] Similarly, Wahba et al reported that intraoperative fentanyl consumption was significantly lower in PECS group [105 (95–110) μg] compared with PVB group [127.5 (110–145) μg].[19] Our study showed similar results where the intraoperative fentanyl requirement (Fig. 2) between the three groups was not statistically significant ($p = 0.349$).

Regarding the number of rescue analgesics in PECS block, maximum number of demand boluses were observed between 4 and 24 h with plain bupivacaine in studies, while our study shows maximum demands between 6 and 12 h. This discrepancy may be due the fact that block was given before giving GA in study done by Blanco while we gave block after GA.[3] The bupivacaine group required rescue analgesic after 4 hrs, magnesium group demanded rescue analgesic after 8 hrs postoperatively while dexamethasone group required analgesic after 12 hrs indicating shorter pain-free period and more requirement of postoperative analgesia in the bupivacaine group. Therefore, use of magnesium and dexamethasone in block has a beneficial effect in reducing the number of systemic analgesic requirement.

In our study, the addition of Magnesium sulphate to bupivacaine in a dose of 150 mg and dexamethasone in dose of 4 mg have led to lower VAS pain scores, prolongation of analgesia and lesser requirement of postoperative rescue analgesia. Our results are comparable to other studies in the use of dexamethasone and magnesium sulphate in significantly reducing the post-operative VAS in peripheral nerve blocks. In our study, the nausea vomiting score was comparable in all three groups and was insignificant. Statistically

significant difference was also found in terms of satisfaction score being better in magnesium and dexamethasone group (Fig. 3).

Conclusion

PECS block is an effective technique in reducing post-operative pain in patients undergoing modified radical mastectomy. Our data support the specific action of adjuvants to local anaesthetic such as magnesium and dexamethasone on peripheral nerves leading to decreased pain scores resulting in decreased postoperative analgesic requirement. Dexamethasone has advantages over Magnesium sulphate regarding longer duration of the block and lesser rescue analgesic requirement. Further studies should be carried out to investigate the possibility of using PECS with dexamethasone as sole anaesthetic technique for breast surgery.

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