



## Effect of analgesia in in pectoral nerve block among ropivacaine and dexmedetomidine for breast cancer surgery

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### Abstract

**Aims and objective:** The study was done to compare the effect of dexmedetomidine as an adjuvant to ropivacaine versus ropivacaine alone in ultrasound guided pec block in breast cancer surgeries.

**Material and Methods:** The hospital based randomized comparative interventional study included sixty ASA physical status I and II patients undergoing elective breast cancer surgery and were divided into two groups of 30 each. Group A received 30 ml of ropivacaine 0.25% for pec block. Group B received 30 ml of ropivacaine 0.25% with 1 µg/kg of dexmedetomidine for pec block. The parameters observed include: Time for requirement of first rescue analgesia (duration of analgesia), total analgesic consumption, haemodynamic parameters (HR, SBP, DBP, MBP) and Spo2 and side effect/complications if any.

**Results:** Duration of analgesic, NRS score, total analgesic consumption, total sedation score were showed statistically significant results. The mean baseline systolic blood pressure, diastolic blood pressure and mean arterial pressure were comparable in both the groups

**Conclusion:** The addition of 1 µg/kg dexmedetomidine to ropivacaine in Pecs block is associated with a significantly prolonged duration of postoperative analgesia and decreased postoperative analgesic (opioid) requirement as compared to ropivacaine alone.

**Keywords:** dexmedetomidine, adjuvant, ropivacaine, ropivacaine

### Introduction

Pain is a distressing feeling caused by intense or damaging stimulus. It is a major symptom and can interfere with quality of life and general functioning. Pain is the conscious experience of sensorial information and a feeling of unpleasantness that manifests as a result of nociception. The taxonomy committee of International Association for the Study of Pain (IASP) defines pain as "An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage" [1]. Inadequate pain control, apart from being inhuman, may result in increased morbidity or mortality. Effective management of postoperative pain relieves suffering and leads to earlier mobilization, fewer pulmonary and cardiac complications, a reduced risk of deep vein thrombosis, faster recovery with less likelihood of development of neuropathic pain, reduced cost of care and increased patient satisfaction [2].

Breast surgeries are one of some commonly performed procedures and patient experience varying degree of pain peri-operatively. Targeting pain preoperatively prevents sensitization of nociceptors, decreases perioperative analgesic requirement and development of chronic pain syndrome [3]. The management of perioperative pain has been opioids. However, opioids are associated with significant risk and adverse effects such as pruritus, constipation, nausea, vomiting, urinary retention, over sedation, respiratory depression.

Regional anaesthesia is the administration of local anaesthetic agents and adjuvants to specific anatomic areas, resulting in a combination of motor and sensory blockade.

These advantages, such as improved postoperative pain relief, decreased postoperative opioid requirement, and reduced recovery time, have led to widespread acceptance of a variety of regional nerve blocks. Several practical and theoretical aspects of regional nerve blocks must be considered to optimize the beneficial effects and minimize the risk of complications [4].

Regional anaesthesia for breast cancer surgery could be either intercostal block/thoracic paravertebral block/thoracic epidural injection / Pecs block. Intercostal nerve block has been used for minor surgeries, the block alone cannot guarantee adequate anaesthesia for surgical incision of entire breast, higher rate of local anaesthesia toxicity compared with paravertebral block and thoracic epidural. Routine postoperative chest radiographs showed an incidence of non-symptomatic pneumothorax of 0.42% [5]. Paravertebral block is associated with complications like subdural or epidural injection [6]. Intravascular injection through lumbar vessels, venacava, aorta is possible. Pleural puncture and pneumothorax have occurred with frequencies of 1.1% and 0.5% respectively [7].

### Block 1(Pectoral Nerve 1 Block)

It is an interfascial plane block where local anaesthetic is deposited in between pectoralis major muscle and pectoralis minor muscle [8].

### PECS Block 2(Pectoral Nerve 2 Block)

It is an interfascial plan block where local anaesthetic is deposited between pectoralis minor and serratus anterior muscle at the third rib. These novel technique attempt to

block the pectoral, intercostobrachial, intercostal III,IV,V,VI, and long thoracic nerve [8].

Ropivacaine is an aminoamide local anesthetic that blocks the peripheral afferents acting on voltage dependent sodium channels. It is less cardiac and central nervous system (CNS) toxic than other long acting local anesthetics like bupivacaine.

Local anaesthetics have a limited duration of action. For denser blocks, faster onset and prolonging the duration of analgesia various adjuvants have been added to local anaesthetic solution to achieve these while minimizing systemic adverse effects along with a reduction in total dose of local anaesthetic used. Adjuvants like epinephrine [9], sodium bicarbonate [10], dexamethasone [11], midazolam [12], ketamine [13], tramadol [14], morphine [15], buprenorphine [16], fentanyl [17], alfentanil [18], sufentanil [19], butorphanol [20], naloxone [21], ketorolac [22], verapamil [23], neostigmine [24], adenosine [25], magnesium [26], clonidine [27] and dexmedetomidine [28] etc. have been injected concomitantly with local anaesthetic solution in various regional block to achieve quick, dense, and prolonged block, but the results are either inconclusive or associated with side effect.

The present study was planned to evaluate whether the addition of dexmedetomidine, alpha-2 agonist, as an adjuvant to ropivacaine helps to achieve a significant longer pain relief or not when compared to ropivacaine alone<sup>3</sup> in pecs block for breast cancer surgeries.

## Materials and Methods

The study was conducted in the department of anaesthesia (General surgery OT), SMS medical college, Jaipur, Rajasthan after obtaining permission from institutional ethical committee, review board and written informed consent from patient.

A hospital based randomised double blinded prospective and interventional study after approval of plan from institutional ethics committee till the completion of sample size among Patients undergoing breast cancer surgery.

The sample size required was 30 eligible patients in both groups at 95% confidence and 80% power to verify the expected minimum difference of 171.6 +/- 81.5 minutes in time duration for requirement of first rescue analgesia. This sample size was adequate for all other study variable.

## Randomisation

60 Eligible breast cancer surgery patient were randomly allocated in 2 groups using computerized random number table.

## Blinding

The Anaesthetist who would give pectoral block was different. All the observation recorded by different anaesthetist.

## Eligibility Criteria

### Inclusion criteria

- Age group between 18 to 60 years.
- ASA Grade I and II.
- Patient undergoing breast cancer surgery.

### Exclusion criteria

- Patient refusal.
- Deranged coagulation profile.
- Infection at injection site.

- History of opioid use or addiction.
- Obesity with BMI  $\geq 35$  Kg/m<sup>2</sup>.
- Pregnancy.

Pre anaesthetic check-up was done a day before the surgery that included a complete history of patient including any known drug allergy. General and systemic examination, local examination of supraclavicular area was done. Pulse rate, blood pressure, respiratory rate height and weight of the patients were recorded. The procedure to be carried out was explained to the patients. All the patients were kept nil per oral as per the fasting guidelines.

Informed consent was obtained for performance of block after completely explaining about the study protocol and the procedure.

The patients were randomly allocated in to one of the two groups by 'computerized random number table'.

## Study drugs

Inj. Ropivacaine 0.25%

Inj. Dexmedetomidine

- **Study Group:** The study was conducted in two groups of patients. Each group consisted of 30 patients (n=30/group).
- **Group A:** given USG-guided pecs block with 30ml of ropivacaine 0.25%.
- **Group B:** given USG-guided pecs block with 30ml of ropivacaine 0.25% and dexmedetomidine 1  $\mu$ /kg.

## Total duration of analgesia

Time taken from USG-guided pecs given to patient's first demand of rescue analgesia (On NRS 3)

**Sedation:** postoperative sedation level will be measured by using Ramsay sedation score.

## Analysis of Data

Statistical analysis was performed with the SPSS (Statistical Package for the Social Science), version 21 for Windows statistical software package (SPSS inc., Chicago, IL, USA). Categorical data were compared in two groups and the difference in the proportion was inferred by Pearson's Chi-square test. Numerical data were compared in two groups and differences in means were inferred by student t-test. For significance  $p < 0.05$  was considered as significant for both types of data.

## Results and Observations

We recruited 30 patients per group. There were no drop outs.

**Group A** patients (n=30) received 30 ml of ropivacaine 0.25% for pec block.

**Group B** patients (n=30) received 30 ml of ropivacaine 0.25% + 1  $\mu$ g/kg dexmedetomidine for pec block.

Mean age was in group A is 47.4 and in group B it was 46.57. Mean weight was in group A is 59.4 and in group B it was 59.47. In group A Out of 30, 24 patients had ASA grade I and 6 patients had ASA grade II. In group B, 25 patients had ASA grade I and 5 patients had ASA grade II.

Within intra-operative, the mean heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were comparable in both the groups only at 20 minutes time intervals. Mean saturation was showed statistically non-significant results.

Within post-operative, the mean heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were comparable in both the groups only at Extubation and 2

hrs time intervals. Mean saturation was showed statistically non-significant results.

**Table 1:** Numerical Rating Scale

	Group A		Group B		P value
	Mean	SD	Mean	SD	
At Extubation	1.00	0	0.93	0.25	0.155 (NS)
1 hrs	1.00	0	0.90	0.31	0.077 (NS)
2 hrs	1.00	0	0.93	0.25	0.155 (NS)
3 hrs	1.00	0	0.97	0.18	0.321 (NS)
4 hrs	1.00	0	0.97	0.18	0.321 (NS)
5 hrs	1.70	0.75	1.60	0.50	0.545 (NS)
6 hrs	2.90	0.55	1.63	0.49	p<0.001 (S)
7 hrs	2.67	0.61	1.73	0.45	p<0.001 (S)
8 hrs	2.57	0.63	1.77	0.43	p<0.001 (S)
9 hrs	2.60	0.62	2.17	0.70	0.013 (S)
10 hrs	2.93	0.64	2.47	0.51	0.002 (S)
11 hrs	2.77	0.63	2.40	0.50	0.014 (S)
12 hrs	2.50	0.57	2.37	0.49	0.336 (NS)
18 hrs	2.57	0.63	2.80	0.55	0.130 (NS)
24 hrs	2.83	0.70	2.73	0.52	0.532 (NS)

Table 4 shows comparison of mean NRS between the groups which is statistically significant at 6 hours upto 11 hours (p<0.05) while not significant from 12 hours to 24 hours (p >0.05). Group B showed less NRS score upto 11 hour as compared to group A.

**Table 2:** Mean Sedation score

	Group A		Group B		P value
	Mean	SD	Mean	SD	
0 hrs	2.10	0.61	2.80	0.41	p<0.001 (S)
1 hrs	2.03	0.56	2.57	0.50	0.0002 (S)
2 hrs (NS)	1.87	0.35	1.93	0.25	0.619 (NS)
6 hrs (NS)	1.87	0.35	1.93	0.25	0.619 (NS)
12 hrs (NS)	1.87	0.35	1.93	0.25	0.619 (NS)
18 hrs (NS)	1.87	0.35	1.93	0.25	0.619 (NS)
24 hrs (NS)	1.87	0.35	1.93	0.25	0.619 (NS)

TABLE shows comparison of mean sedation score between the groups which is statistically significant upto 1 hour (p<0.05). Group B showed more sedation as compared to group A.

**Table 3:** time for requirement of first rescue analgesia (minutes)

Group A		Group B		P value
Mean	SD	Mean	SD	
447.67	43.07	677.67	32.74	p<0.001 (S)

The mean time for requirement of first rescue analgesia in Group A was 447.67 ± 43.04 minutes and in Group B was 677.67 ± 32.74 minutes. This difference was found to be statistically significant (p<0.05).

**Table 4:** Total Analgesic (Fentanyl) Consumption(µg)

Group A		Group B		P value
Mean	SD	Mean	SD	
341.97	75.74	206.03	50.18	p<0.001 (S)

The mean total analgesic consumption in Group A was 341.97 ± 75.74 microgram and in Group B was 206.03 ± 50.18 microgram. This difference was found to be statistically significant. (p<0.05). Group A required more analgesia as compared to group B.

**Discussion**

Thoracic epidural and paravertebral blocks (PVB) became The gold standard techniques to achieve pain relief after breast surgery [29, 30]. However, both techniques may be associated with serious complications such as pneumothorax, total spinal anaesthesia, inadvertent intravascular injection.

As an alternative for these techniques, Blanco *et al.* designed a novel series of blocks: Pecs I and Pecs II [31]. The administration of Pecs block requires skill to use ultrasonography.

The groups were evenly matched with respect to the above demographic variables. This helped us to judge the clinical significance of our study as the distribution, metabolism, excretion and action of drugs are undoubtedly varied in different age groups. Therefore, clinically insignificant variation simply helped to alleviate these confounding factors.

**Duration of analgesia and NRS score**

In our study, in Group B, the duration of analgesia was 677.67 ± 32.74 minutes and in the Group A it was 447.67 ± 43.04 minutes. This difference was found to be statistically significant (p value-<0.001). At 0 and 12 hours, Group A and Group B showed statistically significant. At 6 and 11 hours, Group A and Group B showed statistically significant.

Similar results were observed in the studies conducted by Kaur H *et al.* [3], A statistically highly significant increase in total duration of analgesia (in minutes) was recorded in Group RD (ropivacaine and dexmedetomidine) as compared to Group R (ropivacaine only) (469.6 ± 81.5 in Group RD and 298.2 ± 42.3 in Group R) (P = 0.000).VAS Score was statistically significant lower in group RD from 4 hour as compared to group R in pecs block for breast cancer surgery Bansal P. *et al.* [32] showed that addition of dexmedetomidine to ropivacaine for TAP block in patients undergoing C-section resulted in a longer mean time to initial reporting of significant postoperative pain (6.6 vs. 5.03 h; P = 0.01) and time to initial rescue analgesia (7.8 vs. 6.47 h; P = 0.03) when compared with ropivacaine alone.

Kathuria S *et al.* [33], showed that in supraclavicular brachial plexus block addition of dexmedetomidine as adjuvant to 0.5% ropivacaine shortens the sensory and motor block onset time, prolongs both sensory and motor block duration. It also significantly delays the first demand for analgesia supplementation, decreases 24 h analgesic consumption and is not associated with any major side-effect.

Gupta R. *et al.* [34] showed that duration of analgesia (time for requirement of first rescue analgesic) was significantly prolonged in group D (3 ml of 0.75% isobaric ropivacaine + 5 µg dexmedetomidine in 0.5 ml of normal saline) (478.4±20.9 minutes) as compared to group R (3 ml of 0.75% isobaric ropivacaine + 0.5 ml normal saline) (241.67±21.67 minutes) in spinal anaesthesia for lower limb surgery. The maximum visual analogue scale score for pain was less in group D (4.4±1.4) as compared to group R (6.8±2.2).

These similar studies prove that addition of dexmedetomidine to ropivacaine enhances quality of block in terms of increased duration of analgesia and decreased NRS score.

Dexmedetomidine has more selective affinity for alpha-2 receptor (α2: α1) (1620: 1), which permits its application in relatively high doses for sedation and analgesia without unwanted vascular effects from activation of α1 receptors.

The mechanism by which  $\alpha_2$  adrenoreceptor agonist produces analgesia is likely to be multifactorial. Peripherally,  $\alpha_2$ -adrenoreceptor agonist produce analgesia by reducing release of norepinephrine and causing  $\alpha_2$  receptor-independent inhibitory effect on nerve action potentials [35]. Centrally,  $\alpha_2$  adrenoreceptor agonists produce analgesia by inhibition of substance P release in the nociceptive pathway at the level of the dorsal root neuron and by activation of  $\alpha_2$  adrenoreceptor in locus coeruleus [36]. The greater analgesic effect seen with dexmedetomidine has been attributed to its greater  $\alpha_2$  selectivity.

### Total Analgesic Consumption

In our study, in Group A, mean total analgesic consumption in 24 hour in form of fentanyl ( $\mu\text{g}$ ) was higher and in Group B was lower which showed statistically significant. ( $p$  value- $<0.05$ ).

Similar results were observed in the studies conducted by Kaur H *et al*, total postoperative morphine consumption in mg was statistically significantly lower in Group RD (ropivacaine and dexmedetomidine) as compared to Group R (ropivacaine) ( $14.8 \pm 2.4$  in Group RD and  $21.6 \pm 3.1$  in Group R) ( $P = 0.000$ ).

Luan H *et al*.<sup>37</sup> showed that US-guided TAP block with ropivacaine and dexmedetomidine (Group-RD) reduced overall patient-controlled analgesia (PCA) in patients undergoing abdominal hysterectomy when compared with ropivacaine alone (Group-R). 24h total sufentanil consumption and frequency of PCA pressed were also higher in Group R ( $63.9 \pm 10.0$  vs  $51.8 \pm 9.1$ ,  $8.3 \pm 1.7$  vs  $5.4 \pm 1.6$ ) ( $P < 0.05$ ).

### Sedation Score

Sedation score observed in our study showed that more number of patients had sedation score of 3, i.e., patient asleep but arousable to loud/repeated verbal stimulation on arrival to Post anaesthesia care unit (PACU) at 1 h in Group B as compared to Group A ( $p$  value- $<0.005$ ), however sedation score was comparable after that ( $P = 0.619$  at 2 hr and 0.619 at 24 hr).

Similar results were observed in study of Kaur H *et al*, Group-RD had significantly higher sedation score on arrival to PACU as compared to Group R. A total of 17 patients in group RD had sedation score of 3 as compared to only 1 patient in group R.

These results favour the addition of dexmedetomidine to ropivacaine in view of sedation as there is no undue sedation in dexmedetomidine group as side effect.

### Effect on Vital Parameters

The mean baseline heart rate was  $94.63 \pm 14.17$  beats/minute in the group A and  $92.87 \pm 17.17$  beats/minute in the group B. It was comparable in both the groups. Statistically significant decrease in heart rate was seen 20 minutes following the administration of block in group B but no active clinical intervention was required.

Similar findings were seen in studies done by Kaur M *et al*. This could be explained by the fact that  $\alpha_2$  agonists enhance baroreceptor sensitivity and presynaptically mediated inhibition of norepinephrine release at the neuroeffector junction or by the vagomimetic effect [38].

The mean baseline systolic blood pressure, diastolic blood pressure and mean arterial pressure were comparable in both the groups. Statistically significant change was observed after

20 minutes of administration of block till 2 hour post-operatively in group B. However, fall in blood pressure was easily managed by intravenous fluid and no drug therapy was required.

Similar findings were seen in studies done by Kaur M *et al*. Dexmedetomidine act by stimulating  $\alpha_2$  receptors in the vasomotor centre in the brainstem, which decreases peripheral vascular resistance, thereby lowering blood pressure. This binding of the drugs to the receptors decreases the presynaptic calcium levels, thus inhibiting the release of norepinephrine. The net effect is a decrease in the sympathetic tone, resulting in a decrease in blood pressure [39].

Thus Group-B showed better and stable haemodynamic parameters. The patients in both the groups had an uneventful course without any major complications. Hypotension and bradycardia that occurred did not require any drug treatment.

### Conclusion

From our study, we conclude that the addition of  $1\mu\text{g}/\text{kg}$  dexmedetomidine to ropivacaine in Pecs block is associated with a significantly prolonged duration of postoperative analgesia and decreased postoperative analgesic (opioid) requirement as compared to ropivacaine alone. Thus Pecs block is very effective technique to provide post-operative analgesia in breast cancer surgery patients and adding dexmedetomidine to local anesthetic further enhances its efficacy.

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