Original Article

Comparison of ropivacaine alone versus dexmedetomidine or ketamine as an adjuvant for pectoral type II nerve blocks in patients undergoing mastectomy – A randomized controlled trial

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Abstract

Background and Aims: This study evaluates the analgesic efficacy of ketamine and dexmedetomidine as an adjuvant with ropivacaine 0.2% in pectoral nerve type II block (PECS-II) in modified radical mastectomy. The primary outcome of the study was the time to first rescue analgesia postoperatively. The secondary outcomes were intraoperative and postoperative opioid consumption and postoperative pain on the numerical rating scale.

Material and Methods: Seventy-five adult female patients who underwent a modified radical mastectomy participated in this prospective, randomized, double-blinded clinical trial. The patients received 30 ml of 0.2% ropivacaine with or without adjuvants by the ultrasound-guided PECS-II block. Group R (n = 25) received ropivacaine 0.2% without adjuvants. Group RD (n = 25) and group RK (n = 25) received dexmedetomidine 1μg/kg and ketamine 1 mg/kg, respectively, along with ropivacaine 0.2%.

Results: Duration of analgesia determined by time to first rescue analgesia was longer in group RD (18.42 ± 02.15 h) compared to group RK (15.91 ± 03.21 h) and group R (14.64 ± 02.85 h), which was statistically significant (P < 0.001). Fentanyl consumption in the first 48 h after surgery was significantly less in the dexmedetomidine group compared to other groups.

Conclusion: We conclude that dexmedetomidine with 0.2% ropivacaine in the PECS-II block provides better postoperative analgesia and has less sedative effects than ketamine with 0.2% ropivacaine.

Keywords: Dexmedetomidine, ketamine, mastectomy, patient-controlled analgesia, postoperative pain, ropivacaine

Introduction

Breast cancer surgery has been associated with moderate to severe postoperative pain, which needs to be managed with large doses of opioid.[1,2] Pain in the postoperative period can impair the lung function and the immune system, increase the risk of thromboembolism and myocardial infarction, and cause impairment of gastrointestinal and renal systems, all of which can lead to prolonged hospital stay.[3] Regional anesthesia techniques that usually supplement general anesthesia for mastectomy surgeries provide better acute pain control.[4] The interfascial plane block, like erector spinae block, serratus anterior plane block, and pectoral nerve block, has been used for perioperative analgesia in breast surgery. In pectoral nerve type II block (PECS-II), the local anesthetic is deposited in the plane between the pectoralis major muscle and the pectoralis minor muscle and above the serratus anterior muscle

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at the level of the third rib. The PEC-II block with general anesthesia reduces the perioperative opioid consumption and postoperative nausea and vomiting in patients undergoing breast surgery.[5] For breast cancer surgery, a PECS-II block is less invasive than the paravertebral block and provides analgesic efficacy superior to systemic analgesia alone and comparable to a thoracic paravertebral block.[6] This study was conceived as it compares the combination of a relatively cardiostable local anesthetic agent, ropivacaine, with two drugs as adjuvants with opposing cardiovascular effects, that is, ketamine and dexmedetomidine. The study aimed to determine whether adjuvant ketamine or dexmedetomidine, when combined with ropivacaine in PECS-II block, would provide improved analgesic efficacy in mastectomy patients. The primary outcome of the study was the time to first rescue analgesia postoperatively. The secondary outcomes were intraoperative and postoperative opioid consumption, postoperative pain on the numerical rating scale (NRS), and sedation on the Ramsay sedation score (RSS).

Material and Methods

This prospective, randomized, double-blinded clinical trial was carried out between March 2020 and May 2021 after receiving approval from the ethics committee. This study was registered with the Clinical Trials Registry-India before the recruitment of participants. The procedures were carried out in accordance with the Helsinki Declaration of 1975, as amended in 2013. Informed written consent was obtained from all the patients. Seventy-five female patients with American Society of Anesthesiologists (ASA) physical grades I and II who were planned for modified radical mastectomy (MRM) were included in the study. Patients with underlying severe cardiopulmonary compromise (ASA III), morbid obesity body mass index >35 kg/m^2, chest wall infiltration, pregnancy, lactation, dementia, and patients already on prescribed oral opioid analgesics/psychotropic agents were excluded from the study.

General anesthesia was induced by using intravenous (IV) fentanyl 2 μg/kg, IV propofol 2 mg/kg, and IV vecuronium 0.1 mg/kg for providing neuromuscular blockade. The airway was managed using a supraglottic airway device (I-gel size based on patient's weight), and anesthesia was then maintained with oxygen in air (1:1), isoflurane to maintain a minimum alveolar concentration of 0.8–1.0 and intermittent doses of vecuronium. Ultrasound-guided PECS-II block was performed after induction of general anesthesia by a trained anesthesiologist (who had performed more than 50 ultrasound-guided pectoral nerve blocks previously) using a high-frequency linear probe (6–13 MHz) after taking all aseptic precautions. Patients were randomized into three groups by the computer-generated technique. Simple block randomization was done using a computer-generated random number table with a block size of five. Sequence was generated by an independent person not involved in the study.

Allocation concealment was done using a sealed opaque envelope method. The envelopes were arranged sequentially as per their randomization. After enrollment, the envelopes were opened on the morning of the surgery by an independent person, and patients were assigned into groups as per the sequence number. The individual who prepared the drug was not the same as the person who conducted the block. Double blinding was ensured in the study as the patient, the investigator who performed the block, and the outcome assessor were blinded to the group assigned.

In group R, only ropivacaine 0.2% was given. Group RD received additional dexmedetomidine 1 μg/kg body weight, and in Group RK, ketamine 1 mg/kg body weight was added to ropivacaine 0.2%. An independent anesthesiologist loaded all the study drugs in the syringe, and the block performer and the outcome assessor were unaware of the group allocation. All patients were given 10 ml of the drug combination in the interfascial plane between the pectoralis major and the pectoralis minor and 20 ml of drug volume in the interfascial plane between the pectoralis minor and the serratus anterior muscle based upon their group allocation.

The vitals including heart rate, blood pressure, and oxygen saturation (SpO_2) were recorded every 5 min till 30 min, then every 15 min till the end of surgery, and postoperatively at 1, 2, 4, 6, 12, and 24 h. IV paracetamol 15 mg/kg was given to all the patients before skin incision.

Anesthesia was maintained with sevoflurane in a 1:1 mixture of oxygen, air, and sevoflurane with a minimum alveolar concentration of 0.8–1. If there was an increase in heart rate or blood pressure of 20% from the baseline, 0.5 μg/kg of fentanyl was given IV and noted. At the end of surgery, the muscle relaxant was reversed using neostigmine (0.04 mg/kg) and glycopyrrolate (0.01 mg/kg). All the patients were shifted to the post-anesthesia care unit (PACU). Postoperative analgesia was controlled using a patient-controlled analgesia pump (CADD-Legacy® PCA Pump Model 6300) with IV fentanyl at a dose of 0.25 μg/kg as the demand dose with a lockout interval of 20 min and IV paracetamol 15 mg/kg every 6 h. Side effects like hypotension, bradycardia, hypoxemia, postoperative nausea and vomiting, hallucinations, and pneumothorax were noted.

In PACU, analgesic efficacy was noted using NRS on rest and at movement. The time for first rescue analgesia and total

intraoperative and postoperative fentanyl consumption (in μg) were noted. The postoperative pain was assessed by NRS at rest and on movement at 1, 2, 4, 6, 12, 18, 24, and 48 h. Postoperative sedation was assessed using RSS for up to 6 h.

The sample size was calculated using data from a study by Kaur *et al.*,[7] in which the mean time to first analgesic requirement after PECS block with ropivacaine 0.25% was 469.6 ± 81.5 min. Assuming an expected increase of 15% in the duration of analgesia by adding adjuvants, the sample size was calculated to be 14 patients in each arm, taking a power of 80% with 95% confidence interval and two-tailed alpha errors of 0.05. Considering 10% dropouts and errors in assumptions, 25 patients were included in each group.

All the data entry and analyses were done by using Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) version 19 for Windows. Continuous data were expressed as mean ± standard deviation and median with interquartile range (IQR). The Chi-square test or the Fisher's exact test was used to compare qualitative data. Parametric and nonparametric quantitative data were compared using the Student's *t*-test and the Mann–Whitney test, respectively. The Wilcoxon signed-rank test was used to compare quantitative factors between the baseline and each subsequent period in each group. Comparison of means between the groups was done using analysis of variance. *Post hoc* analysis using Tukey's test or Kruskal–Wallis H test was used for intergroup comparisons. *P*-value < 0.05 was taken as statistically significant. Median and IQR of time to rescue medication are described, and Kaplan–Meier survival curves generated with equality of survivor functions between the groups are compared with a log-ranktest.

Results

In this study, 95 patients were assessed for all eligibility criteria, of which 20 patients were excluded and 75 patients with breast cancer scheduled for MRM were enrolled. Final analysis was then done on 25 patients in each group. The Consolidated Standards of Reporting Trials (CONSORT) flowchart is shown in Figure 1.

In all three groups, the demographic data were equal ($P > 0.05$) [Table 1]. Duration of analgesia

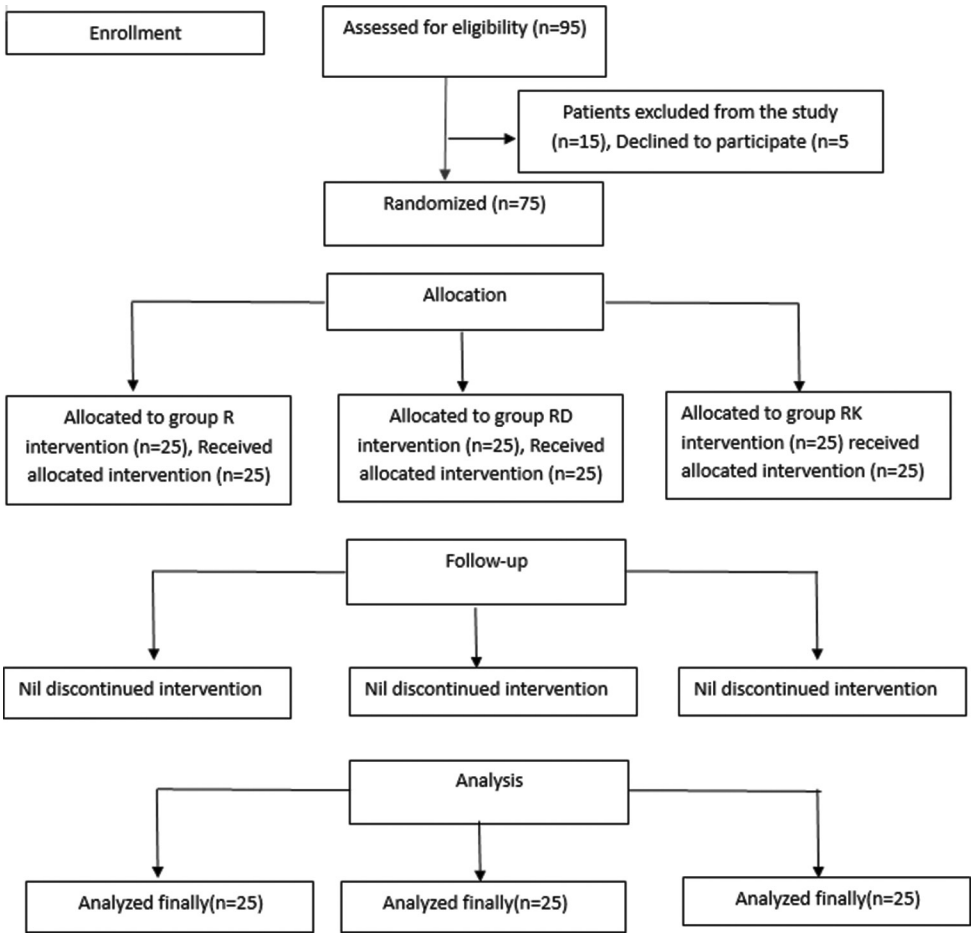

Figure 1: CONSORT diagram

determined by time to first rescue analgesia was longer in group RD (18.42 ± 02.15) compared to groups RK (15.91 ± 03.21) and R (14.64 ± 02.85) and was statistically significant ($P < 0.001$) [Table 2].

The Kaplan–Meier survival curves [Figure 2] for the three groups showed that the time to first analgesic request was longer in patients receiving adjuvant dexmedetomidine (median 18 h, IQR 18–20 h) compared to those receiving plain ropivacaine (median 14 h, IQR 13–15 h) and adjuvant ketamine (median 13 h, IQR 13–13.5 h) (P-value 0.001 by log-rank test for equality in survivor function).

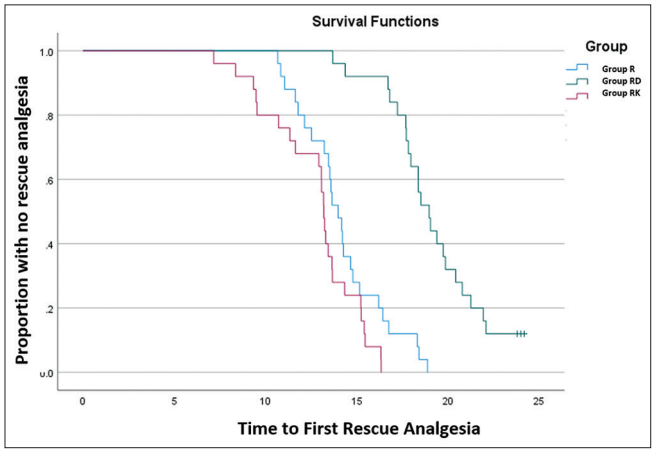

Figure 2: Kaplan–Meier survival curves for the three groups

Table 1: Demographic and clinical data

Parameters	Group R (n=25)	Group RD (n=25)	Group RK (n=25)
Age (years), mean±SD	48.25±05.68	47.81±06.21	47.81±06.21
Height (cm), mean±SD	159.20±4.32	160.39±5.90	159.54±6.32
Weight (kg), mean±SD	75.53±7.60	76.24±9.04	75.65±5.98
BMI, mean±SD	26.34±3.93	25.32±2.92	24.65±4.65
ASA classification			
ASA I	12 (48.00%)	14 (56.00%)	10 (40.00%)
ASA II	13 (52.00%)	11 (44.00%)	15 (60.00%)
Site of surgery			
Right MRM	12 (48.00%)	10 (40.00%)	11 (44.00%)
Left MRM	13 (52.00%)	15 (60.00%)	14 (56.00%)
Duration of surgery (hours)	02.64±0.72	02.79±0.76	02.52±0.67

ASA=American Society of Anesthesiologists, BMI=body mass index, MRM=modified radical mastectomy, SD=standard deviation

The postoperative fentanyl consumption was similar in group R (93.00 ± 34.24) to that of group RK (84.00 ± 32.17) and significantly less in group RD (51.00 ± 23.36) with $P < 0.001$ [Table 2]. Postoperative fentanyl consumption was similar in group R and group RK [Table 2]. NRS at rest was significantly low at all time points in group RD compared to the other two groups ($P < 0.05$) [Table 3]. NRS on movement was also significantly lower in group RD than in groups RK and R [Table 4]. None of the patients in either group required intraoperative fentanyl.

Patients in group RK had higher level of sedation score compared to other two groups ($P < 0.001$) [Table 5].

Discussion

The study shows that use of dexmedetomidine as an adjuvant to local anesthetics in PECS-II block prolongs the time to initial rescue analgesia and reduces overall postoperative opioid consumption without causing side effects. Breast cancer is the most common cancer in women around the world. For postoperative analgesia after breast surgery, a variety of regional procedures have been utilized, including epidural block, paravertebral block, local anesthetic infiltration, and intercostal nerve blocks.[8] The PECS-II is a superficial nerve block associated with fewer complications than the epidural and paravertebral blocks. It blocks the pectoral, the intercostobrachial, the ventral rami of third to sixth intercostal, and the long thoracic nerves.

Bhavani *et al.*[9] used the PECS-II block in 20 patients undergoing MRM. All the patients had good analgesia up to 8 h after the block. Kaur *et al.*[7] also found that ropivacaine increases duration of analgesia up to about 8 h in PECS-II block. Deng *et al.*[10] conducted a study in which three ropivacaine concentrations of 0.2%, 0.3%, and 0.4% were used in PECS-II block patients undergoing mastectomy and found the time for first pain was up to 20 h. In our study, the

Table 2: First request of rescue analgesia and postoperative analgesic consumption

Variables	Group R (mean±SD)	Group RD (mean±SD)	Group RK (mean±SD)	95% CI	P	P (post hoc analysis)
First request of analgesia (hours)	14.64±02.85	18.42±02.15	15.91±03.21	14.53–16.28	0.001*	0.001* (group R vs. group RD) 0.332 (group R vs. group RK) 0.006* (group RD vs. group RK)
Postoperative fentanyl requirement (μg)	93.00±34.24	51.00±23.36	84.00±32.17	67.95–84.05	0.001*	0.001* (group R vs. group RD) 0.548 (group R vs. group RK) 0.001* (group RD vs. group RK)

*Intergroup comparison among all three groups based on the first request of rescue analgesia (hours) and postoperative fentanyl consumption (μg) showed it to be statistically significant; group RD was comparatively better than other two groups. *P<0.05 is significant. CI=confidence interval, SD=standard deviation*

Table 3: Postoperative NRS at rest

Time (hours)	Group R	Group RD	Group RK	*P*
Postoperative pain (NRS at rest)		Median (IQR)		
1 h	0.99 (0.81–1.22)	0.72 (0.50–0.90)	1.55 (1.41–1.73)	0.001*
2 h	1.14 (0.83–1.38)	0.95 (0.77–1.04)	2.12 (1.79–2.35)	0.001*
4 h	1.45 (1.08–1.58)	1.14 (1.02–1.43)	2.83 (2.55–3.02)	0.001*
6 h	1.94 (1.80–2.21)	1.72 (1.57–1.82)	3.07 (2.84–3.22)	0.001*
12 h	2.95 (2.89–3.07)	2.14 (2.04–2.28)	3.95 (3.83–4.09)	0.001*
18 h	2.20 (2.07–2.42)	1.57 (1.31–1.69)	2.87 (2.67–3.04)	0.001*
24 h	2.08 (1.92–2.34)	1.25 (1.09–1.58)	2.89 (2.68–2.95)	0.001*
48 h	2.08 (1.85–2.14)	1.42 (1.06–1.59)	2.66 (2.47–2.79)	0.001*

*The NRS scores at rest were significantly lower in RD group at all time intervals compared to RK group and the difference was statistically significant. *P<0.05 is statistically significant. IQR=interquartile range, NRS=numerical rating scale*

Table 4: Postoperative NRS on movement

Time (hours)	Group R	Group RD	Group RK	*P*
Postoperative pain (NRS at movement)		Median (IQR)		
1 h	2.73 (2.34–3.11)	2.43 (1.70–2.93)	2.79 (2.42–3.42)	0.264
2 h	2.65 (2.05–3.51)	2.31 (1.92–2.76)	3.51 (2.88–3.81)	0.001*
4 h	3.28 (2.29–3.98)	2.42 (2.15–2.78)	4.32 (3.47–4.57)	0.001*
6 h	2.44 (2.22–2.85)	2.32 (1.70–2.72)	4.18 (3.63–5.19)	0.001*
12 h	2.73 (2.12–3.25)	2.76 (2.18–3.06)	3.94 (3.56–4.14)	0.001*
18 h	2.42 (2.03–3.12)	2.37 (2.13–2.82)	3.39 (3.15–3.59)	0.001*
24 h	2.58 (2.23–2.97)	2.35 (1.91–2.83)	2.71 (2.26–3.00)	0.073
48 h	2.57 (2.16–2.93)	2.43 (1.89–2.64)	2.81 (2.37–3.03)	0.225

*The NRS scores at movement were significantly lower in RD group at all time intervals compared to RK group, except at 24 h, where the difference was statistically significant. *P<0.05 is statistically significant. IQR=interquartile range, NRS=numerical rating scale*

Table 5: Sedation score (mean±SD) in the studied groups

Time interval in hours	Sedation score, median (IQR)			*P*	Post hoc analysis
	Group R	Group RD	Group RK		*P*
0	2.03 (1.66–2.30)	2.52 (2.32–3.04)	2.85 (2.49–3.38)	0.001*	0.001 (R vs. RD) 0.001 (R vs. RK) 0.068 (RD vs. RK)
1	1.92 (1.57–2.41)	2.65 (2.29–2.79)	2.82 (2.68–3.17)	0.001*	0.001 (R vs. RD) 0.001 (R vs. RK) 0.134 (RD vs. RK)
2	1.77 (1.57–2.09)	1.90 (1.77–2.07)	3.02 (2.38–3.39)	0.001*	0.271 (R vs. RD) 0.001 (R vs. RK) 0.001 (RD vs. RK)
3	1.87 (1.55–2.13)	1.99 (1.81–2.17)	2.73 (2.50–3.07)	0.001*	0.210 (R vs. RD) 0.001 (R vs. RK) 0.001 (RD vs. RK)
4	1.81 (1.48–2.13)	1.87 (1.65–2.23)	3.05 (2.71–3.48)	0.001*	0.314 (R vs. RD) 0.001 (R vs. RK) 0.001 (RD vs. RK)
5	2.04 (1.67–2.26)	1.94 (1.73–2.26)	2.90 (2.33–3.32)	0.001*	0.880 (R vs. RD) 0.001 (R vs. RK) 0.001 (RD vs. RK)
6	1.87 (1.73–2.23)	2.03 (1.84–2.25)	2.94 (2.73–3.16)	0.001*	0.359 (R vs. RD) 0.001 (R vs. RK) 0.001 (RD vs. RK)

*Intergroup comparison between different groups was done using ANOVA and an inference on sedation score at an individual hour among all three groups was done; The sedation scores were higher and significant in group RK as compared to group R during 0–6 h (P<0.001). *P<0.05 is statistically significant. ANOVA=analysis of variance, IQR=interquartile range, SD=standard deviation*

duration of analgesia was up to 14 h with ropivacaine alone and up to 18 h when dexmedetomidine was added. Hefni *et al.*[11] found that adding ketamine and dexmedetomidine to bupivacaine in PECS-II block increased the time to first analgesic request [(16.7 ± 4.5 h) and (21.6 ± 1.6 h) in both groups respectively vs (11.5 ± 1.2 h)] compared to patients

who received bupivacaine alone. However, our results were similar to those of Manzoor *et al.*[15] who also used bupivacaine 0.25% in the PEC II block and found bupivacaine to be effective for up to 12 h. A meta-analysis of 1565 patients who received primarily PECS-II block compared to no block found that it moderately reduced pain at rest.[12] There are few studies on the efficacy of adjuvants used with ropivacaine in PECS-II blocks for postoperative analgesia following MRM. Dexmedetomidine is used as an adjuvant to ropivacaine in PECS-II blocks to lengthen the duration between requests for analgesics and decrease the overall intake of opioids.

A study carried out by Bakr *et al.*[13] showed that patients who received PECS-II block with local anesthetics and adjuvants (bupivacaine plus dexmedetomidine 1 μg/kg) had reduced postoperative pain levels up to 24 h in comparison to the control group and considerably lower opioid usage for 12 h. In several studies, PECS block with bupivacaine has been found to offer postoperative analgesia lasting more than 12 h.[14,15] In our study, the duration of postoperative analgesia was longer when dexmedetomidine was added as an adjuvant compared to ropivacaine alone (18.42 ± 02.15 h vs. 14.64 ± 02.85 h). Survival analysis also showed significantly longer postoperative analgesia in the group using dexmedetomidine as an adjuvant compared to R and RK groups. The duration of analgesia in the R and RK groups was nearly similar. The postoperative fentanyl requirement was also less with dexmedetomidine (51.00 ± 23.36 μg vs. 93.00 ± 34.24 μg). Dexmedetomidine delivers analgesic activity via central action by inhibiting substance *P* release in the nociceptive pathway at the dorsal root neuron and by activating alpha-2 receptors in locus coeruleus in the midbrain.[16] The peripheral action of this alpha-2 agonist to produce analgesia is mediated by decreasing the release of norepinephrine.[17] Dexmedetomidine has also been used as an adjuvant for direct infiltration and intra-articular administration with local anesthesia.[18]

Othman *et al.*[19] found that adding ketamine as an adjuvant to bupivacaine reduced the need for postoperative morphine and the pain scores for up to 24 h in a PECS-II block. In our study, there was no statistically significant difference in postoperative fentanyl requirement (84.00 ± 32.17 μg [group RK] vs. 93.00 ± 34.24 μg [group R]) and duration of postoperative analgesia (15.91 ± 03.21 h [group RK] vs. 14.64 ± 02.85 h [group R]) when ketamine was added as an adjuvant.

The mean NRS at rest and on movement was statistically nonsignificant compared to that on ropivacaine alone. Our criterion was to give rescue analgesia when NRS reached 4, despite a slightly higher NRS with the RK group. Since the exact analgesic dose of ketamine for nerve blocks is yet unknown, we used 1 mg/kg in this group. Compared to other groups, our patients in this trial reported mild drowsiness that lasted for up to 6 h. However, psychologic agitation, hallucinations, confusion, and delirium were not noted in the patients.

Bashandy and Abbas[20] found that patients who received a PECS block had lower postoperative pain scores and a significant decrease in opioid use over 12 h compared to patients in the control group at all times (up to 24 h).

In a study by Wahba and Kamal[21] comparing the analgesic effects of PECS block versus Paravertebral block (PVB) following MRM, it was found that less morphine was consumed in the first 24 h and pain score was reduced in the first 12 postoperative hours. We also found that NRS at rest and NRS while moving were statistically significant for up to 48 and 18 h, respectively.

Ketamine has been shown to improve or extend pain relief when used as a local anesthetic adjunct in peripheral and neuraxial anesthesia.[22,23] Both the central and peripheral N-methyl-D-aspartate (NMDA) receptors could have been inhibited, which would explain these findings. By interacting with inflammatory cell recruitment, reduced cytokine generation, and regulation of inflammatory mediators, ketamine's anti-inflammatory characteristics lessen the postoperative inflammatory response.[24,25]

In this study, we found that adding dexmedetomidine to ropivacaine in the PECS-II block prolongs the duration of analgesia, reduces the need for opioids, and causes less sedation in the postoperative period compared to other groups. Based on our study, it is recommended to use dexmedetomidine as an adjuvant to ropivacaine in interfascial plane blocks like PECS-II block. In future studies, we recommend using a larger sample size, additional adjuvants, and a long-term follow-up period to further determine the efficacy of adjuvants in PECS-II block on chronic post-mastectomy pain. Our study limitations includes its inability to evaluate the effect of PECS-II block on postsurgical chronic pain, metastasis, and breast cancer recurrence.

Conclusion

The use of dexmedetomidine as an adjuvant to local anesthetics in PECS-II block prolongs the time to initial rescue analgesia and reduces overall postoperative opioid consumption without causing side effects.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Khan JS, Ladha KS, Abdallah F, Clarke H. Treating persistent pain after breast cancer surgery. Drugs 2020;80:23-31.
2. Habib AS, Kertai MD, Cooter M, Greenup RA, Hwang S. Risk factors for severe acute pain and persistent pain after surgery for breast cancer: A prospective observational study. Reg Anesth Pain Med 2019;44:192-9.
3. The Lancet. Best practice in managing postoperative pain. Lancet 2019;393:1478.
4. Sherwin A, Buggy DJ. Anaesthesia for breast surgery. BJA Educ 2018;18:342-8.
5. Khemka R, Chakrborty A, Agrawal S, Ahmed R. Is COMBIPECS the answer to perioperative analgesia for breast surgery? A double blinded randomized controlled trial. Indian J Anaesth 2019;63:530-6.
6. Versyck B, van Geffen GJ, Chin KJ. Analgesic efficacy of the Pecs II block: A systematic review and meta-analysis. Anaesthesia 2019;74:663-73.
7. Kaur H, Arora P, Singh G, Singh A, Aggarwal S, Kumar M. Dexmedetomidine as an adjunctive analgesic to ropivacaine in pectoral nerve block in oncological breast surgery: A randomized double-blind prospective study. J Anaesthesiol Clin Pharmacol 2017;33:457-61.
8. Mehrotra R, Yadav K. Breast cancer in India: Present scenario and the challenges ahead. World J Clin Oncol 2022;13:209-18.
9. Bhavani V, Dhanger S, Gupta N, Joseph RI, Pandian S. Comparison of the efficacy of ultrasound-guided pectoral versus erector spinae plane blocks for postoperative analgesia in patients undergoing modified radical mastectomy: A randomised controlled trial. J Clin Diagn Res 2022;1:16.
10. Deng W, Fu D, He L. Evaluation of pectoral nerve block in modified radical mastectomy: Comparison of three concentrations of ropivacaine. Clin Interv Aging 2020;15:937-44.
11. Hefni AF, Eldeek AM, Ismael SA, Shaban AR. Comparing effect of adding ketamine versus dexmedetomidine to bupivacaine in Pecs-II block on postoperative pain control in patients undergoing breast surgery. Clin J Pain 2022;38:568-74.
12. Meißner M, Austenfeld E, Kranke P, Zahn PK, Pogatzki-Zahn EM, Meyer-Frießem CH, *et al*. Pectoral nerve blocks for breast surgery: A meta-analysis. Eur J Anaesthesiol 2021;38:383-93.
13. Bakr MA, Mohamed SA, Mohamad MF, Mohamed MA, El Sherif FA, Mosad E, *et al*. Effect of dexmedetomidine added to modifiedpectoral block on postoperative pain and stressresponse in patient undergoing modified radical mastectomy. Pain Physician 2018;21:87–96.
14. Kumar S, Goel D, Sharma SK, Ahmad S, Dwivedi P, Deo N, Rani R. A randomised controlled study of the post-operative analgesic efficacy of ultrasound-guided pectoral nerve block in the first 24 h after modified radical mastectomy. Indian J Anaesth 2018;62:436-42.
15. Manzoor S, Taneja R, Sood N, Puri A, Kadayaprath G. Comparative study to assess the quality of analgesia of bupivacaine and bupivacaine with dexmedetomidine in ultrasound-guided pectoral nerve block type I and II in breast surgeries. J Anaesthesiol Clin Pharmacol 2018;34:227-31.
16. Zhao Y, He J, Yu N, Jia C, Wang S. Mechanisms of dexmedetomidine in neuropathic pain. Front Neurosci 2020;14:330.
17. Gilsbach, R. and Hein, L. Are the pharmacology and physiology of $\alpha_2$adrenoceptors determined by α_2-heteroreceptors and autoreceptors respectively?. British Journal of Pharmacology. 2012; 165: 90-102.
18. Parida S, Theerth KA. Dexmedetomidine: A drug for all seasons?. Indian J Anaesth 2021;65:789.
19. Othman AH, Abd El- Rahman AH, Adel El Sherif F. Effect of ketamine added to bupivacaine in Pecs Block. Pain Physcian 2016;19:485-94.
20. Bashandy GMN, Abbas DN. Pectoral nerves I and II blocks in multimodal analgesia for breast cancer surgery: A randomized clinical trial. Reg Anesth Pain Med 2015;40:68–74.
21. Wahba SS, Kamal SM. Thoracic paravertebral block versus pectoral nerve block for analgesia after breast surgery. Egypt J Anaesth 2014;30:129–35.
22. Israel JE, St Pierre S, Ellis E, Hanukaai JS, Noor N, Varrassi G, *et al*. Ketamine for the treatment of chronic pain: A comprehensive review. Health Psychol Res 2021;9:25535.
23. Shehabi Y, Serpa Neto A, Howe BD, Bellomo R, Arabi YM, Bailey M, *et al*. Early sedation with dexmedetomidine in ventilated critically ill patients and heterogeneity of treatment effect in the SPICE III randomised controlled trial. Intensive Care Med 2021;47:455-66.
24. Wilcox MR, Nigam A, Glasgow NG, Narangoda C, Phillips MB, Patel DS, *et al*. Inhibition of NMDA receptors through a membrane-to-channel path. Nat Commun 2022;13:4114.
25. Zhang W, Ross PJ, Ellis J, Salter MW. Targeting NMDA receptors in neuropsychiatric disorders by drug screening on human neurons derived from pluripotent stem cells. Transl Psychiatry 2022;12:243.