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Combination of ultrasound-guided pectoral nerve block I and serratus anterior plane block for attenuation of surgical stress response during modified radical mastectomy: A prospective interventional randomized controlled trial

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ABSTRACT

Background: General anesthesia with multimodal analgesia is the standard anesthetic management during modified radical mastectomy. In this study, a combined ultrasound-guided pectoral nerve block (PECS I) and serratus anterior plane (SAP) block were used for surgical stress response attenuation and post-operative analgesia. **Aims and Objectives:** This study aimed to compare the efficacy of combined PECS I and SAP block to intravenous (IV) multimodal analgesia in attenuating surgical stress response and post-operative analgesia in patients who underwent modified radical mastectomy with axillary clearance. The primary objective was to estimate the intraoperative fentanyl requirement to reduce autonomic response due to surgical stimulus. The intraoperative vitals, post-operative numeric rating scale pain score, post-operative analgesic use in the recovery room, and incidence of post-operative nausea vomiting were the secondary objectives. **Materials and Methods:** Thirty-six consenting patients were randomized into two groups. After induction of general anesthesia, Group B patients received ultrasound-guided PECS I and SAP block whereas Group C patients received IV analgesics only. Intraoperative fentanyl dosage to keep the systolic blood pressure (SBP) and heart rate (HR) within 20% of baseline were noted in the both groups. Intraoperative vitals, post-operative pain score, analgesic requirement, and incidence of post-operative nausea, and vomiting were also recorded in the both groups. **Results:** Surgical stress response attenuation was achieved with a lower dosage of fentanyl in Group B compared to Group C (intraoperative fentanyl [mean ± SD], 116.11 ± 25.70 µg vs. 134.44 ± 20.07 µg, P = 0.023). Compared to Group C, intraoperative reduction in SBP and HR was higher in Group B (SBP reduction [mean ± SD], 24.03 ± 12.5 mm of Hg vs. 15.2 ± 13.05 mm of Hg, P = 0.045 and HR reduction [mean ± SD], 18.61 ± 6.6 beats/min vs. 10.73 ± 10.03 beats/min, P = 0.009, respectively). The apparently higher pain scores in the control group were statistically insignificant. **Conclusion:** A combined PECS I and SAP block attenuates intraoperative autonomic stress response due to the surgical stimulus with significantly less opioid requirement.

Key words: Breast cancer; Modified radical mastectomy; Regional anesthesia

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INTRODUCTION

Modified radical mastectomy is a commonly performed breast cancer surgery where the removal of the whole breast and pectoralis major fascia along with complete axillary clearance is performed.[1,2] The mode of anesthesia administered during this procedure is general anesthesia along with a multimodal form of analgesia. The efficacy of fascial plane blocks such as pectoral nerve block (PECS),[3-5] serratus anterior plane (SAP) block,[6,7] and erector spine plane block has been proven in previous studies.[8,9] Regional blocks as an adjunct to multimodal analgesia have been proven to attenuate the autonomic response to surgical stimulation and thus reduce opioid requirements in patients undergoing modified radical mastectomy. PECS I blocks the pectoral nerves which supply the pectoral muscles including the fascia covering the pectoralis major muscle.[10,11] During the SAP block, local anesthetic is deposited either superficial or deep to the serratus anterior muscle and causes dermatomal paresthesia of the anterolateral chest wall from T2-T9.[12] Hence, the combined PECS I and SAP block can be effective in reducing the surgical stress response during modified radical mastectomy.

Aims and objectives

The aim of the study was to assess the efficacy of a combined PECS I and SAP block as compared to an intravenous (IV) multimodal analgesic regime in attenuating surgical stress response and post-operative analgesia in cases posted for a post-chemotherapy modified radical mastectomy with complete axillary clearance. The primary objective was to estimate the intraoperative fentanyl requirement to reduce autonomic response due to surgical stimulus. The intraoperative vitals, post-operative numeric rating scale (NRS) pain score, post-operative analgesic use in the recovery room, and incidence of post-operative nausea vomiting (PONV) were the secondary objectives.

MATERIALS AND METHODS

After obtaining approval (Project approval no OIEC/11000607/2023/00005 dated June 07, 2023) from the Institutional Ethics Committee (IEC Mahamana Pandit Madan Mohan Malaviya Cancer Centre and Homi Bhabha Cancer Hospital, DCGI Reg. Number: ECR/1501/Inst/UP/2021) this prospective interventional single-blinded randomized controlled trial was registered with the Clinical Trial Registry of India (CTRI/2023/06/054125 Registered on: June 19, 2023 https://ctri.nic.in/Clinicaltrials/login.php).

Inclusion criteria

The study was conducted on 36 American Society of Anesthesiologists (ASA) I-II female patients between 18 and 65 years who underwent post-chemotherapy unilateral modified radical mastectomy with complete axillary clearance at Mahamana Pandit Madan Mohan Malaviya Cancer Centre and Homi Bhabha Cancer Hospital.

Exclusion criteria

The exclusion criteria were patient refusal and patient unable to give valid consent, patient undergoing supraclavicular lymph node dissection, pregnant patients, known hypersensitivity to local anesthetics, infection at the site of injection, and history of chronic analgesic use.

After obtaining written informed consent, the patients were recruited between the time periods from March 24th, 2023 to May 30th, 2023. The study complied with the principles of the Helsinki Declaration 2013 and good clinical practices were followed. Consenting patients were randomized into two groups with the help of a computer-generated randomization chart – the block group (Group B) and the control group (Group C). Baseline vitals were noted in the pre-operative holding area.

A similar anesthesia protocol was followed for each patient. Inside the operating room after securing the IV access standard ASA monitors were attached. General anesthesia was induced using fentanyl 2 μg/kg, propofol 2 mg/kg, and atracurium 0.5 mg/kg IV. The airway was secured using I-gel™ (Intersurgical Ltd, Wokingham, UK). Post-induction all patients received dexamethasone 6 mg IV. Anesthesia was maintained using sevoflurane, 50% nitrous oxide in oxygen, and 0.1 mg/kg boluses of atracurium. Patients were ventilated to maintain normocapnia. The minimum alveolar concentration (MAC) was maintained within the range of 0.8–1.3 to ensure adequate depth of anesthesia. Intraoperative vitals and MAC were noted at 3 min intervals. IV fentanyl 0.5 μg/kg was administered if systolic blood pressure (SBP) and heart rate (HR) increased to ≥20% of the basal values.

For patients enrolled in Group B, the blocks were provided after induction of general anesthesia. The patient's position was supine with the arm abducted at 90°. After skin preparation with 2.5% chlorhexidine in alcohol, to identify the targeted planes, a high-frequency (6–11 MHz) linear array ultrasound transducer (M7 Premium™, Mindray) was used. For PECS I, the transducer was placed medial to the coracoid process in a parasagittal orientation. In the deltopectoral groove, the axillary vessels were identified above the second rib. The probe was further moved inferiorly and laterally until the third rib was encountered. The fascial plane between the pectoralis major and pectoralis minor was identified at

the level of the third rib. A 20G echogenic needle was inserted from the cephalad end to reach the fascial plane. After negative aspiration, 10 mL of 0.25% bupivacaine was administered. SAP block transducer was placed on the midaxillary line at the nipple level. The fifth and sixth ribs were identified with the pleura sliding underneath. The serratus anterior muscle lies immediately over the ribs. The needle was inserted from the anterior aspect towards the posterior direction. After negative aspiration, 25 mL of 0.25% bupivacaine was injected deep to the serratus anterior muscle.

Patients in Group C did not receive any block and received only IV analgesics.

All patients received paracetamol 1 g and tramadol 100 mg IV prior to surgical incision. Before reversal, all patients received ondansetron 6 mg IV. Once the procedure was over patients were shifted to the recovery room where the NRS scores were noted at 0, 30, 60, 90, and 120 min. Any analgesic requirement (in the form of IV diclofenac sodium 75 mg IV or fentanyl 0.5 μg/kg bolus) during this time period and incidence of PONV were noted. Metoclopramide 10 mg IV was administered if found necessary. Patients were shifted to the ward after 2 h with a routine analgesic prescription.

The sample size was calculated using the online sample size calculator of OpenEpi (Open Source Epidemiologic Statistics for Public Health).[13] In a similar study conducted by Wang et al.,[14] it has been found that in patients who were administered a combination of PECS I and SAP block, intraoperative IV morphine equivalent consumption (mg) was significantly lower than the patients who did not receive any block ([mean±SD] 18.10±4.76 and 21.22±4.17, respectively). Morphine equivalents are optimal for opioid utilization studies as they facilitate both interpretation and comparison between opioids across geographical locations. Morphine equivalent is expressed as milligrams of morphine and is used to standardize the opioid dosage across different drugs and studies.[15] Hence, we utilized the difference in morphine equivalents reported by the study for the sample size calculation.[14] Considering a 95% confidence interval, power of 85%, and ratio of sample size as 1,16 patients were required in each group. An attrition rate of 10% made the sample size 18 patients for each group.

All analyses were done using R Statistical Software version 4.3.0 (April 21, 2023). To test the normal distribution of the continuous data, the Shapiro–Wilk test was used. Comparison between the two groups was done using the Wilcoxon rank-sum test (non-normally distributed continuous data and ordinal data) or a two-tailed Student's t-test (normally distributed continuous data). The Chi-square test was used to assess the categorical data. A $P<0.05$ was considered statistically significant for all comparisons between the groups.

RESULTS

Forty-one patients were assessed for eligibility among whom four patients were fulfilling the exclusion criteria and one patient refused to participate. Hence, 36 patients were recruited for the study. All of them complied with the study protocol and the data were put up for final analysis (Figure 1). Demographic parameters were similar in both groups. The baseline diastolic and mean blood pressure of Group B patients were higher and found to be statistically significant. However, those values were clinically insignificant (Table 1).

The intraoperative fentanyl requirement and perioperative fentanyl requirement (total fentanyl received intraoperatively and during the 2 h stay in the recovery room) were significantly lesser in patients who received a combination of PECS I and SAP block (intraoperative fentanyl [mean±SD] 116.11±25.70 vs. 134.44±20.07, P=0.023 and perioperative fentanyl [median, interquartile range] 120, 102.5–145 vs. 150, 132.5–173.75, P=0.009) (Figure 2).

Attenuation of stress response due to the surgical stimulus was achieved with a significantly lower dosage of IV fentanyl and equivalent anesthetic depth (MAC were similar in both groups) in Group B patients. The intraoperative vitals were well controlled with a decrease in blood pressure and HR. Compared to Group C, intraoperative reduction in SBP and HR was significantly higher in Group B (Table 2).

Table 1: Demographic parameters and patient characteristics

Variables	Group B (n=18)	Group C (n=18)	P-value
Age (years)	45.89±6.82	45.61±11.62	0.931
Weight (kg)	58.44±12.34	63.17±8.77	0.196
BMI (kg/m^2)	25.75±5.22	27.29±3.55	0.309
ASA status % (I/II)	22.2/77.8	5.6/94.4	0.148
Baseline SBP (mm of Hg)	133.94±10.99	127.67±12.61	0.120
Baseline DBP (mm of Hg)	83.72±5.20	78.44±8.48	0.032
Baseline MBP (mm of Hg)	101.09±6.26	95.00±8.94	0.024
Baseline HR (beats/min)	92.22±9.94	87.67±10.04	0.180

Values are in mean±SD and percentage (%) of patients. ASA: American society of anesthesiologists, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MBP: Mean blood pressure, HR: Heart rate, BMI: Body mass index

Table 2: Intraoperative hemodynamic parameters

Intraoperative change in vitals	Group B (n=18)	Group C (n=18)	P-value
Intraoperative reduction of SBP from baseline (mm of Hg)	24.03±12.5	15.2±13.05	0.045
Intraoperative reduction of DBP from baseline (mm of Hg)	8.10 (4.42–18.32)	6.06 (3.59–11.99)	0.355
Intraoperative reduction of MBP from baseline (mm of Hg)	16.7±9.63	12.15±9.9	0.171
Intraoperative reduction of HR from baseline (beats/min)	18.61±6.6	10.73±10.03	0.009

Values are in mean±SD and median with interquartile range. SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MBP: Mean blood pressure, HR: Heart rate

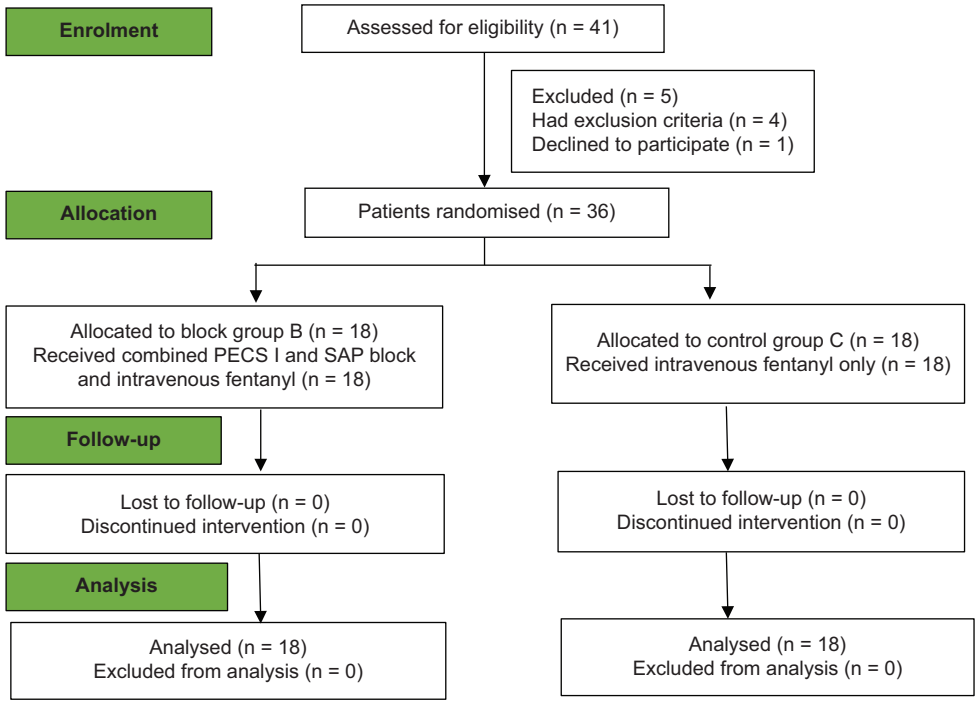

Figure 1: Consolidated standard of reporting trials (CONSORT) flow diagram

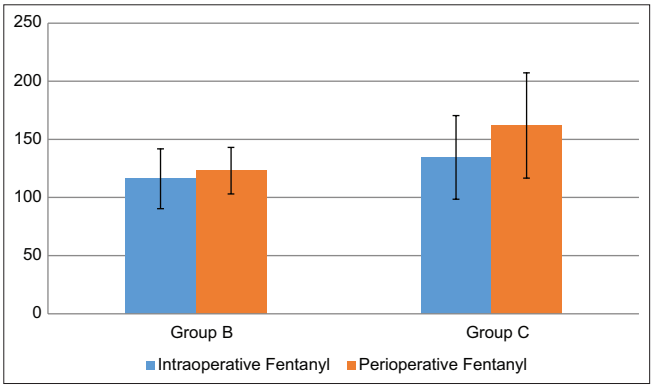

Figure 2: Intraoperative and perioperative fentanyl requirement. Values are expressed as mean±SD

Although apparently higher pain scores were noted in the control group (Figure 3) those were found to be statistically insignificant (Table 3).

Intraoperative vitals, MAC, duration of surgery, and incidence of PONV were similar in both groups (Table 3).

DISCUSSION

A combination of PECS I and SAP block can effectively attenuate the intraoperative surgical stress response as evidenced by significantly lower intraoperative fentanyl requirement to maintain stable vitals. In both groups, intraoperative vitals were well controlled, and the reduction in SBP and HR was significantly greater in the block group with the equivalent anesthetic requirements. Hence, greater attenuation of the stress response is achievable with blocks without using incremental dosages of opioids.

Although in a previous study by Wang et al., the Visual Analog Score was lower in the block group; this study has shown similar pain scores in both groups. However, the intraoperative fentanyl requirement was higher in the control group in our study which is similar to the findings of Wang et al.[14] The higher dosage of fentanyl along with pre-incision IV tramadol, paracetamol, and dexamethasone administration had led to equivalent

pain control in Group C patients. Postoperatively, in all patients, we used IV diclofenac initially and fentanyl thereafter whenever the pain score was ≥4. Hence, it can be concluded that a multimodal form of analgesia effectively reduces pain without causing significant PONV when blocks are not administered albeit with higher dose of opioids.

Table 3: Intraoperative and post-operative parameters

Variables	Group B (n=18)	Group C (n=18)	P-value
Intraoperative SBP (mm of Hg)	111.20±14.60	112.50±10.91	0.764
Intraoperative DBP (mm of Hg)	72.76±8.25	70.87±8.92	0.514
Intraoperative MBP (mm of Hg)	84.42±10.02	83.32±8.93	0.732
Intraoperative HR (mm of Hg)	73.59±8.52	75.33±8.58	0.546
Minimum alveolar concentration	1.02±0.08	1.01±0.10	0.888
Duration of surgery (min)	104.33±36.53	116.17±34.83	0.327
NRS score at 0 min	2 (0-2)	1.5 (0–2.75)	0.869
NRS score at 30 min	2.5 (2–4)	2.5 (2–5.75)	0.605
NRS score at 60 min	2 (2–3)	2 (2–5)	0.193
NRS score at 90 min	2 (1–2)	2 (1.25–4)	0.159
NRS score at 120 min	2 (1–2)	2 (1.25–2)	0.817
Diclofenac in recovery room % (yes/no)	50/50	55.6/44.4	0.739
Fentanyl in recovery room (μg)	0 (0–0)	0 (0-46.25)	0.105
PONV % (yes/no)	27.8/72.2	27.8/72.2	1.000

Values are in mean±SD, median with interquartile range, and percentage (%) of patients. SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MBP: Mean blood pressure, HR: Heart rate, NRS: Numeric rating scale, PONV: Post-operative nausea and vomiting

In PECS I, local anesthetic is injected in the fascial plane between the pectoralis major and pectoralis minor muscles and it targets the lateral (C5-7) and medial (C8-T1) pectoral nerves.[10,11] These are the major nerves supplying the pectoral muscles including fascia covering the pectoralis major muscle. Hence, PECS I can effectively block the pain arising from the dissection of the pectoralis major fascia and lymphadenectomy at various levels around the pectoralis minor muscle. In PECS II, in addition to PECS I, a second injection is made at the level of the fourth rib between the pectoralis minor and serratus anterior muscle. This second injection blocks the lateral cutaneous branches of upper intercostal nerves (T2-T6) causing dermatomal anesthesia to the anterolateral chest wall and also the long thoracic nerve (C5-C7), which is the motor supply of the serratus anterior muscle.[10] During the SAP block, dermatomal paresthesia of the anterolateral chest wall from T2-T9 is achieved by injecting local anesthetic either superficial or deep to the serratus anterior muscle.[12] Hence, both PECS II and SAP block can effectively block the anterolateral chest wall. Previous studies also suggest similar results.[16-19]

PECS II/serratus blocks utilize the same mechanism which is blocking the lateral branches of the upper intercostal nerves. Hence, their efficacy is related to their ability to reach the specific fascial plane.[20] In the

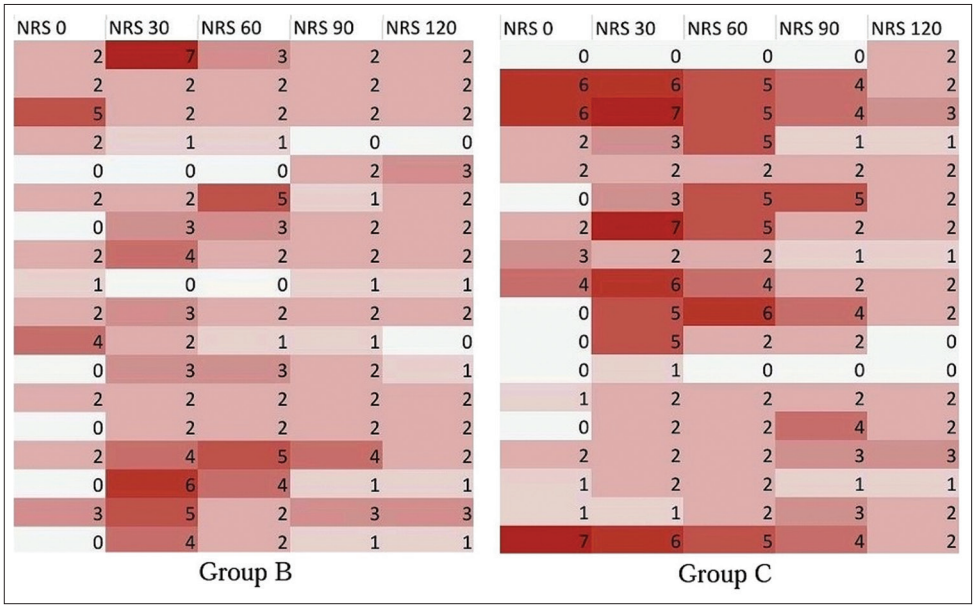

Figure 3: Postoperative pain score in the recovery room. Heat map representation using the white red colour scale (white represents lowest and red represents highest pain scores). Values are expressed as scores recorded at 0, 30, 60, 90, and 120 min in numeric rating scale

midaxillary line, the serratus plane is superficial and easier to identify during ultrasonography, making it a much simpler block compared to PECS II.[12] Hence, the combination of PECS I and SAP block is easier to perform and it provides adequate surgical stress response reduction and post-operative analgesia in patients posted for a post-chemotherapy modified radical mastectomy with complete axillary clearance.

Limitations of the study

A smaller sample size could be the limitation of this study. In this study, we have included only ASA I and II patients. The blocks could be effective in attenuating autonomic responses in poorly controlled hypertensive cancer patients where surgery is time-sensitive. Further studies on such patients are required to conclude the same.

CONCLUSION

A combined PECS I and SAP block attenuates intraoperative autonomic stress response due to the surgical stimulus with a lower opioid requirement. A multimodal form of analgesia is effective in reducing pain without causing significant PONV when blocks are not administered.

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