Introduction

Breast cancer is a common oncologic diagnosis in women of a productive age group. Modified radical mastectomy (MRM) with axillary clearance of lymph nodes is traditionally performed under general anesthesia with intra and postoperative opioid-based analgesia. It is associated with more than 30% incidence of postoperative nausea vomiting (PONV) and 40% acute postoperative and chronic debilitating pain. Opioid-based anesthesia is associated with increased nausea and vomiting, respiratory depression, prolonged sedation, urine retention, ileus, increased postoperative pain (hyperalgesia), tolerance, and chronic pain. The possibility of higher risk of metastasis has also been reported.

In recent times, there has been a move toward opioid-free anesthesia (OFA) to achieve the goals of hypnosis with amnesia and sympathetic stability without the adverse effects of opioids. Various methods, such as regional blocks, and...
drugs, such as lignocaine, dexmedetomidine, ketamine, etc., can be employed to preclude the use of opioids.\textsuperscript{[10]}

Studies have shown that when used in conjunction with opioid-based general anesthesia, nerve blocks can reduce postoperative pain and opioid requirement.\textsuperscript{[11-13]} Single-injection paravertebral block (PVB) has been shown to be an alternative to general anesthesia for breast surgeries.\textsuperscript{[14]} Recent studies have found greater opioid sparing and analgesic benefits of the PECS block (a combination of PECS 1 and 2 blocks) over the PVB.\textsuperscript{[15-17]}

With this background in mind, we hypothesized that we may be able to perform breast surgery without using any opioids at all, thereby reducing morbidity. The purpose of our study was to find out if an opioid-free PECS block-based anesthesia technique is feasible and even beneficial compared to the opioid-based general anesthesia regimen that is routinely undertaken at our center with respect to the primary outcome measures of postoperative nausea, pain relief, and analgesic requirement and secondary outcome measures of length of stay in postanesthesia care unit (PACU) and hospital and satisfaction of patients and surgeons.

**Material and Methods**

This study was conducted as a part of a larger trial planned to assess two modalities of analgesia for breast cancer study (registered under CTRI/2017/02/007897). It involved adult patients of American Society of Anesthesiologists I–III category with breast cancer posted for MRM with axillary dissection. The setting was the in-patient unit and the operative suite of a 450-bedded tertiary care university (public) hospital. Following written informed consent, patients were screened for and recruited to the study.

After recruitment, the patients were administered one of two types of anesthesia in the operation suite (the days and procedures being arbitrary). One anesthetist routinely administered nonopioid anesthesia with PECS block, while two others administered opioid-based general anesthesia.

Patients were followed up for 24 h after surgery for PONV, pain scores, analgesic requirement, length of stay in recovery room, and readiness for discharge on day of surgery. A follow-up call was made at 7 days after surgery to enquire about the patients’ pain and quality of life (QOL).

The study protocol conformed to the ethical guidelines of the Declaration of Helsinki and was approved by the Research Ethics Committee of the institution.

**Patient selection and anesthesia technique**

Patients with a history of postoperative nausea, chronic pain, prior allergy to local anesthetics (LA) or coagulopathies, or those not consenting were excluded from the study, all others being included.

After application of standard monitoring, including ECG, noninvasive blood pressure, and pulse oximetry, all patients were administered intravenous midazolam 1–2 mg and ondansetron 4 mg.

In the patients of the nonopioid group (Gr NO) an i-gel was inserted after induction with intravenous propofol (2–3 mg/kg). Patient was maintained on spontaneous ventilation (assisted if needed with pressure support to keep EtCO\textsubscript{2} 30–40 mm Hg). Isoflurane was delivered to achieve 0.8–1.0 minimum alveolar concentration (MAC). After LA infiltration under ultrasound guidance, PECS block was administered at the level of the fourth rib in the mid-axillary line. A single-prick technique (modified from the original description of Blanco et al.) was used. Keeping the needle tip in view, 20 and 10 ml of the solution (0.3 ml/kg 0.5% bupivacaine, 0.3 ml/kg 2% lignocaine with adrenaline, and 1 mcg/kg dexmedetomidine – not exceeding toxic dosage of either LA agent) was administered: first, at the level of fourth rib, below the serratus anterior and then by withdrawing the needle to lie in between the pectoralis minor and major muscles, respectively. Drug spread in the correct plane was documented and incision was allowed in 10–15 min after testing for absence of response to skin pinch stimulus with forceps. If one or more of three predefined signs (20% rise in the baseline heart rate or blood pressure, purposeful movement of limbs, or facial grimacing) was noted on incision, rescue analgesia was administered – this included Inj. paracetamol 1 g, local infiltration with 5–10 ml 1% lignocaine, and deepening of the plane of anesthesia up to 1.2 MAC. Incision was attempted again in 5 min. Block inadequacy was defined as recurrence of any of the three predefined signs after the rescue. In case of block failure, the anesthetist could administer opioids as required.

In the patients who received opioid-based general anesthesia (Gr O), the patient was induced with propofol 1–2 mg/kg, Inj. morphine 0.1–0.2 mg/kg, and vecuronium 0.8–1 mg/kg. Anesthesia was maintained with isoflurane delivered at 1.0–1.5 MAC. Additional 3–6 mg bolus of morphine or any other opioid at the discretion of the anesthetist was administered if a 20% rise in heart rate (HR) or blood pressure (BP) was observed at incision and titrated to effect.

For postoperative analgesia in Gr NO infusion, paracetamol 1 g IV was given if visual analog scale (VAS) score was 4.

**Funding**

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**Conflicts of Interest**

None.
or more (at rest or on arm movement) or on patient demand. In case the dose exceeded 4 g of paracetamol or if VAS >6, then Inj. diclofenac 75 mg IV was supplemented.

In Gr O, the advice was fourth-hourly administration of Inj. paracetamol. Inj. diclofenac could be administered on patient demand or if VAS was >4.

**Assessment of outcomes**

**Postoperative nausea and vomiting**

PONV was defined as any nausea, retching, or vomiting occurring during the first 24 h after surgery. In the PACU and the ward, patients were asked to report nausea “which makes you uncomfortable” or an event of retching or vomiting in a yes/no format at 4-h intervals. Data were entered as PONV present/absent per patient.

**Pain**

VAS pain scores were recorded on a 10 cm scale half-hourly for the first hour, hourly for next 2 h, and second-hourly thereafter for 24 h. Data were entered as the VAS scores and the total number of times that analgesic was administered.

**Satisfaction scores**

Surgeon and patient satisfaction scores were obtained at the end of surgery and at 24 h, respectively, on a Likert scale of 1–5, with 1 being most dissatisfied and 5 being very satisfied. Overt recall of intraoperative events was also enquired of the patient.

**Quality of life**

A follow-up call was given at 7 days postoperatively, to assess the QOL with a validated version of the EuroQOL-5D questionnaire.\(^{[18]}\)

**Others**

Observers who were blinded to the study groups recorded the intraoperative hemodynamics (noted from the anesthesia charts), volume of breast tissue excised, and length of stay in PACU.

**Bias and sample size**

As the patients in the two subgroups of the cohort were similar with respect to age, sex, duration of anesthesia and surgery, and area in which the tumor was located [Tables 1 and 2], propensity matching was not deemed necessary. Nurses in the recovery room and the general ward who assessed the nausea and pain were blinded to the treatment groups. As the block had been administered after induction and was covered under the dressings, chance of bias was reduced. Confounding was reduced by restriction-excluding patients with high risk of postoperative nausea or chronic pain (previous history of PONV, opioid medications, etc.). Nonroutine rotation of anesthetists helped in reducing patient selection bias. The sample size was estimated to have a two-sided significance level of 95%, power of 80%, and to detect a risk difference in PONV of 30% between the two groups.

**Statistics**

Descriptive parameters were represented as means (SD) or median and range (if in skewed distribution). Continuous variables were compared using unpaired t-test (or Mann–Whitney U test) and categorical variables by Chi-square test. Statistical significance was set at \( P < 0.05 \). Missing data were handled by the multiple imputation method.

Quantitative data were categorized to allow calculation of relative risk (RR) as follows: PONV – Present/Absent; Early discharge – Was the patient considered fit for discharge within 24 h of surgery? – Yes/No; Analgesia – Did the patient require one or fewer doses of analgesia in the first 24 h after surgery? – Yes/No.

**Results**

Of 48 patients included in the study, 24 underwent surgery under nonopioid anesthesia and PECS block. Twenty-four underwent surgery under general anesthesia with opioid analgesia. The patient, surgery characteristics, and intraoperative hemodynamics were similar in both the groups [Tables 1 and 2].

The incidence of postoperative analgesia requirement, PONV, and early discharge were compared by Chi-square test and were significantly less in Gr NO than Gr O [Table 3].

VAS scores between the two groups were compared using Mann–Whitney U test as the Shapiro–Wilk test (\( P < 0.05 \)) and a visual inspection of their histograms showed that the values were not normally distributed for both the groups. A Mann–Whitney test indicated that the average VAS score was greater for Gr O than the NO group. No patient in the OFA group required diclofenac injection as compared to six patients in the O group. An independent samples t-test was used to compare the (normally distributed) time of stay in the PACU. It was shorter in Group NO than in Group O [Table 4].
Satisfaction scores of the patients were significantly better in the NO group ($P < 0.05$); the first demand for analgesia was at a median of 350 min (0–1560 min) after the administration of the block. The surgeons were more satisfied with the intraoperative conditions provided in Gr O ($P > 0.05$).

There were no complications attributed to the PECS block. There was no incidence of bradycardia or hypotension requiring treatment in the PECS group. The EuroQOL 5D scores between the two groups were better for the NO group at 7 days of surgery (not reaching level of significance).

### Discussion

We studied a cohort of patients undergoing MRM with axillary dissection for breast cancer and compared breast surgery done under PECS block without opioids with surgery done under general anesthesia with opioids. OFA under PECS block provided better analgesia (less VAS score and decreased requirement of supplemental analgesics) and reduced the PONV and duration of stay in PACU.

Previous studies involving anesthesia for breast cancer surgery aimed at identifying the best nerve block (route, dosage, site, technique, etc.), which could decrease the perioperative opioid requirement and provide better analgesia.\[11-17\] Although most studies found significant decrease in postoperative opioid requirement, none have tried to avoid opioids altogether. OFA techniques are currently gaining acceptance over the world, especially in areas of bariatric surgery and oncosurgery.\[19,21\]

We demonstrate a scope for adopting this technique for breast cancer surgery as well. The benefits include avoiding respiratory depression, central muscle rigidity, pharyngeal muscle weakness, obstructed breathing, negative inotropism, nausea, vomiting, ileus and constipation, urinary retention, tolerance and addiction, dizziness, and excessive somnolence.\[10\]

Our method of anesthesia was finalized after some trial cases: We observed that female patients, usually anxious, find an ultrasound-guided nerve block in the chest (or back) distressing and embarrassing when awake. PECS block was chosen over PVB or other blocks as it was quicker and easier to perform and did not require a change in patient position after i-gel insertion. Recent studies have reported better block characteristics with PECS as compared to PVB.\[16,17\] We chose a single-point insertion nerve block technique, which gave good block results from among the many variations available for anterior chest wall nerve blocks.\[21-24\]

We needed a drug mixture that could provide rapid onset of block with a long duration within acceptable levels of toxicity; a mixture of lignocaine with adrenaline and bupivacaine was chosen. We added dexmedetomidine (1 mcg/kg body weight) shown to prolong block duration in nerve blocks and provide good sympathetic blockade in OFA techniques.\[25,26\]

We used isoflurane (age adjusted MAC of 0.8–1.0) for maintenance of anesthesia. Our choice was determined by the following factors: First, a large volume of propofol is required to keep patients sedated in OFA techniques.\[27\] Second,

### Table 2: Intraoperative hemodynamic parameters

| Hemodynamic data | 0 min | 5 min | 15 min | 30 min | 45 min | $P$ |
|------------------|-------|-------|--------|--------|--------|-----|
| NIBP (mmHg)      |       |       |        |        |        |     |
| Gr O             | 84 (14.3) | 74 (23.6) | 69 (13.7) | 74 (16.5) | 74 (11.8) | >0.05 |
| Gr NO            | 88 (12.6) | 78 (24.6) | 70 (18.3) | 70 (14.4) | 71 (12.6) | >0.05 |
| HR (beats/min)   |       |       |        |        |        |     |
| Gr O             | 88 (12.6) | 86 (28.8) | 82 (18.4) | 76 (21.8) | 78 (18.0) | >0.05 |
| Gr NO            | 86 (11.8) | 78 (10.2) | 74 (10.5) | 70 (8.7)  | 72 (6.8)  | >0.05 |

Data is presented as mean (standard deviation); NIBP (noninvasive blood pressure) and HR (heart rate) before (0) and 5, 15, 30, 45 min after induction of anesthesia in the two groups

### Table 3: Postoperative outcome I

| PONV | Group O | Group NO | RR (95% CI) | NNT (95% CI) | Benefit | $P$ |
|------|---------|----------|-------------|--------------|---------|-----|
|      |         |          | 0.12 (0.17-0.9) | 3.4 (2-11.8) | 0.04    |     |
| Early discharge | 18 | 9       | 0.4 (0.18-0.85) | 2.6 (1.6-8.7) | 0.01    |     |
| 0/1 dose analgesia | 10 | 0       | 0.58 (0.4-0.8) | 2.4 (1.6-4.5) | 0.002   |     |

*P<0.001

| Group NO | Group O | Time in postoperative recovery room min (mean, SD) | 72.6 (17.2) | 137.3 (50.6)* |
|----------|---------|-----------------------------------------------|------------|--------------|
|           |         |VAS score over 24 h median (R)                  | 2.3 (2.5)  | 3.5 (2)*     |

*P<0.001

*PONV, Postoperative nausea and vomiting*
as our patients are not paralyzed, self-regulation of MAC and depth is possible with inhalation agents as compared to intravenous agents.

We noticed a steep learning curve in mastering the technique of anesthesia: Prophylactic infiltration of LA in tumors involving the upper-medial quadrant prevented the occasional arm movement at incision and gradually decreasing the inhalation agent over the course of the surgery allowed removal of i-gel by skin closure. As the patients in Gr NO recovered in the PACU, some woke up accepting the nerve block and surgery-related paresthesia quite well, whereas others appeared to have VAS pain scores >4. Some of these latter women became very comfortable once they were purposefully woken up and explained about the surgery being over; the rest needed a dose of paracetamol, often the only dose in the next 24 h.

The patient satisfaction was better in the NO group, with near pain-free arm movements. Pusch et al.\(^1\) reported similar findings with PVB and spontaneous breathing patients. The surgeons rated the Gr O surgical experience better; this was attributed to the occasional (2 cases, early in the series) nonpurposeful movements and muscle contractions during incision and axillary clearance, respectively, in Gr NO.

There are certain limitations of our study. No attempt was made to change established practice of surgery and anesthesia in the Gr O. It is possible that use of an i-gel and avoidance of muscle relaxants may have decreased time in the recovery room in Gr O. As there was no background nerve block providing analgesia in Gr O and our group of surgeons did not desire to change practice by instituting field infiltration with LA, it was considered unethical to not provide a background cover with analgesics to this group. Thus, medical surveillance bias cannot be ruled out, as Gr O was receiving fixed eighth-hourly dose of paracetamol as opposed to Gr NO who received analgesic based on VAS. Morphine was the opioid chosen during induction based on the present theatre protocol. Although this might affect the external validity of our study (more centers use fentanyl), we hoped to mitigate the effect by avoiding postoperative patient control analgesia with morphine in both groups. Finally, observational studies are vulnerable to methodological issues, but in “first of kind” studies they help in strengthening hypothesis and enabling sample size calculations for future randomized trials.

**Conclusion**

A PECS block-based anesthesia without any opioids is safe and effective. Breast surgery with axillary clearance. It appears to reduce postoperative PONV and analgesic requirement, improves the surgical experience for the patient, and may allow earlier discharge. Further studies will be needed to assess the long-term benefits of avoiding opioids.

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Nil.

**Conflicts of interest**
There are no conflicts of interest.

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**CONFERENCE CALENDAR January-March 2018**

| Name of conference | Dates                  | Venue                                | Name of organising Secretary with contact details |
|--------------------|------------------------|--------------------------------------|--------------------------------------------------|
| 15th CONFERENCE OF ASIAN SOCIETY OF PAEDIATRIC ANAESTHESIOLOGISTS (ASPA 2018) | 17th - 19th August 2018 | Shangri-La Hotel Bangkok                  | CONGRESS SECRETARIAT: Mind MAP Organizer Co., Ltd. Address: 39 Tiwanon 24, Tiwanon Rd., Muang, Nonthaburi 11000, Thailand. Phone: (66)81-701-8345 Fax: (66)2-950-7423 Email: 2018aspa@gmail.com |
| National Airway Conference 2018 of the All India Difficult Airway Association (AIDAA) | 7th - 9th September 2018 | The Heritage Plaza, Narkeldanga Main Road, 89C Moulna Abul Kalam Azad Sarani, Kolkata, West Bengal 700 054 | Dr. Jyotsna Goswami M: +91 98303 27187 Dr. Sarbani Swaika M: +91 84204 05962 Dept. of Anesthesia & Critical Care Institute of Post Graduate Medical Education & Research 244, AJC Bose Road Kolkata 700020, West Bengal Email: secynac2018@gmail.com |
| 11th Annual National Conference of the Association of Obstetric Anesthesiologists (AOA 2018) | 28th - 30th September 2018 | Jodhpur, Rajasthan                      | Dr Bharat Maheshwari Org. Chairman Dr Kusum Agarwal Org. Secretary 9414153719 Email: aoa@jodhpur2018@gmail.com www.aoa2018.com |
| 66th Annual National Conference of Indian Society of Anaesthesiologists, India (ISACON 2018) | 25th - 29th November 2018 | Jaypee Palace & Convention Centre, Agra, India | Organizing Secretary: Dr. Ranvir Singh Tyagi Mobile No.: 9837047812 Email ID: isaconagra2018@gmail.com WebSite: http://isacon2018.org/ |