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Dexmedetomidine as an Adjuvant to Levobupivacaine in Paravertebral Block For Postoperative Analgesia After Breast Cancer Surgery

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ABSTRACT

Background & Aim: Currently regional technique like thoracic paravertebral block for postoperative analgesia after breast surgery is gaining popularity. The addition of adjunctive analgesics, like fentanyl and clonidine, to local anaesthetics has been shown to enhance the quality and duration of postoperative analgesia. But each one has its own limitations. Our aim of the study was to find out the safety and the analgesic efficacy of 1 µg/kg dexmedetomidine when added to levobupivacaine 0.25% in paravertebral blocks (PVB) in patients undergoing breast cancer surgery. **Methods:** Sixty American Society of Anaesthesiologists physical status I/II patients posted for breast cancer surgery were randomly assigned into two groups of 30 each. Group L received thoracic PVB with 20 mL of levobupivacaine 0.25%. Group LD received thoracic PVB with 20 mL of levobupivacaine 0.25% + 1 µg/kg dexmedetomidine. Time of first analgesics request, total analgesic consumption, VAS score, hemodynamic, sedation score and side effects in the first 24 hours were recorded. **Results:** The time of the first rescue analgesic requirement was significantly prolonged in the group LD (8.15 ± 2.21 hours) in comparison to group L (6.34 ± 2.83 hours). The mean total consumption of intravenous tramadol as rescue analgesia in the postanesthesia care unit in the first 24 hours postoperatively was significantly decreased in group LD (120 ±40.68 mg) compared to group L (146.67 ± 50.74 mg). No significant serious complications were recorded during the study. **Conclusion:** The addition of dexmedetomidine 1 µg/kg to levobupivacaine 0.25% in PVB in patients undergoing breast cancer surgery improves the quality and the duration of analgesia postoperatively.

Keywords: Dexmedetomidine, levobupivacaine, paravertebral block, postoperative analgesia, breast cancer surgery.

INTRODUCTION

Breast cancer is perhaps the most common cancer in women that requires surgery. General anaesthesia is currently the standard technique used for modified radical mastectomy used for surgical treatment of breast cancer. However it has its limitations in the form of poor postoperative pain control. Poor postoperative pain control in turn leads to greater incidence of nausea and vomiting and prolongs recovery room stays and necessitates prolonged hospitalization. Parenteral narcotic is used commonly during the early postoperative period, which further increases the incidence of nausea, vomiting and sedation.[1]Nearly 40% of postoperative breast surgery patients experience significant acute postoperative pain. A number of therapeutic measures have been accepted as a part of the "multi-modal" approach to postoperative pain control.Regional anaesthesia using paravertebral block has been suggested as an ideal adjunct to general anaesthesia for modified radical mastectomy. Benefits include a reduction in postoperative pain relief indirectly leading to a reduction of postoperative nausea and vomiting. Most importantly, by reducing postoperative pain, nausea and vomiting, paravertebral block markedly improves the quality of operative recovery for patients.[2]There is little systematic research on the efficacy and tolerability of the addition of an adjunctive analgesic agent to local anesthetics in paravertebral block. The addition of adjunctive analgesics, such as fentanyl and clonidine, to local anesthetics has been shown to enhance the quality and duration of sensory neural blockade, and decrease the dose of local anesthetic and supplemental analgesia.[3]Dexmedetomidine is a highly selective α2- adrenorceptor agonist recently introduced to anesthesia; it produces a dose-dependent sedation, anxiolysis, and analgesia (involving spinal and supraspinal sites) without respiratory depression.[4] α2-agonists are known to

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reduce anesthetic requirements, and because of their sympatholytic properties, they afford hemodynamic stability during the intraoperative period. Administration of an α2-agonist via an intrathecal or epidural route provides an analgesic effect in postoperative pain without severe sedation. This effect is due to the sparing of supraspinal central nervous system (CNS) sites from excessive drug exposure, resulting in robust analgesia without heavy sedation.[5] The aim of this study was to investigate the safety and the analgesic efficacy of adding 1 µg/kg dexmedetomidine to levobupivacaine 0.25% in thoracic PVB in patients undergoing breast cancer surgery.

Primary aim-

1. To assess efficacy of dexmedetomidine as adjuvant to Levobupivacaine for postoperative pain management by paravertebral block.
2. Postoperative VAS score
3. Time to 1st rescue analgesia
4. Total rescue analgesia consumption

Secondary aim-

1. Intraoperative hemodynamic parameters like heart rate and blood pressure.
2. Incidence of postoperative sedation, nausea and vomiting.

MATERIALS AND METHODS

The study was conducted at a tertiary care hospital from Sept 2017 to Sept 2018. Sixty patients were studied after Institutional Ethical Committee approval and after giving written informed consent. ASA I /II patients scheduled to undergo elective breast cancer surgery under general anesthesia were enrolled in this study.

Inclusion criteria

1. Adult patients aged between 18-70 yrs.
2. ASA I and ASA II physical status.
3. Diagnosed cases of breast cancer.

Exclusion criteria

1. Bleeding disorders.
2. Allergy to amide-type local anaesthetics.
3. Infection at the thoracic paravertebral injection site.
4. Pregnancy or breast feeding females.
5. Severe obesity (BMI>35 kg/sqm).

The patient was examined one day prior to surgery and standard institutional preoperative advice was offered. A preoperative assessment was done. Basic investigations of Hb%, TLC,DLC and urine analysis was done for all patients and other investigations like ECG, blood sugar was done preoperatively depending on the ASA status, age and clinical profile of the patient. At the pre-operative visit, the patients were instructed how to use the Visual Analogue Scale (VAS 0-10).

On the day of surgery, after the arrival of the patient, in the operating room a 18-gauge IV cannula was inserted and lactated ringer's solution 10 mL/kg was started.Basic monitoring probes (electrocardiography, noninvasive blood pressure, O2 saturation, and temperature) were applied. The patients were seated for placement of the block and were sedated with incremental intravenous doses of midazolam (1 – 3 mg) and fentanyl (50 – 100 µg). Thoracic PVB were then performed as described by Moore and Katz.[6] The superior aspect of the spinous processes of T1 – T6 were marked. The skin entry points were 3 cm lateral to the marks. A 22-gauge quincke spinal needle attached through extension tubing to a syringe containing the study drugs was used. The needle was inserted perpendicular to the skin for a distance of 2 to 4 cm until the transverse process was contacted. The needle was withdrawn and walked cephalad off the transverse process and advanced for a further 1.5 to 2 cm. Patients were allocated into 2 groups of 30 patients each using a computer-generated random number assignment in sealed opaque envelopes. Anesthesiologist not involved in the management of the patient or the study prepared the study drug according to randomization. The patients and all staff involved in patient management and data collection were unaware of the group assignment. In group L, the patients received 20 mL of levobupivacaine 0.25% paravertebrally, divided into 3 – 4 mL in each level. In group LD, the patients received 20 mL of levobupivacaine 0.25% + 1 µg/kg dexmedetomidine paravertebrally divided into 3 – 4 mL in each level. The time for performance of the block ranged from 10 to 15 minutes. The success of the block was checked by decrease pin prick sensation at the expected dermatomal level (from T1- T6). Immediately after the block, the patients were placed in the supine position. General anesthesia was induced by fentanyl 1.5 µg/kg, and propofol 2 – 3 mg/kg. Endotracheal intubation was facilitated by vecuronium 0.08 mg/kg. Anesthesia was maintained by isoflurane 1 – 1.5 MAC. Heart rate and systolic and diastolic blood pressures were recorded preoperatively and after 30 minutes, 60 minutes, and 120 minutes and up to 24 hrs. Hypotension was defined as a 20% decrease in systolic blood pressure from the baseline. Bradycardia was defined as a heart rate slower than 50 beats per minute. Hypoxia was defined as an oxygen saturation value < 90%. Hypotension was treated with intravenous boluses of ephedrine 0.1 mg/ kg and normal saline 5mL/kg. Bradycardia was treated with intravenous atropine 0.01 mg/kg. At the end of the operation patients were extubated after giving reversal agent and were transferred to the postanesthesia care unit. They were monitored for vital signs (heart rate, noninvasive blood pressure,

respiratory rate, and saturation of peripheral oxygen. The level of sedation was recorded using a modified observer's Assessment of Alertness/ Sedation Scale where 1 = awake/alert to 5 = sleep/unarousable. VAS at rest (VAS.R) and during movement or ipsilateral arm abduction (VAS.M) were assessed immediately postoperatively and at hours 2, 4, 6, 12, and 24 of the postoperative period. Intravenous tramadol 100 mg was given when the VAS was ≥ 5 or upon patient request. The time of the first request for analgesia and the total analgesic consumption in the first 24 hours were recorded. Postoperative adverse effects such as nausea, vomiting, hypotension, bradycardia, and cardiac arrhythmia were recorded and treated.Any postoperative complications of the block such as accidental pnemothorax and vascular puncture were recorded and treated. Statistical analysis-The power of the study was based on a calculated sample size of 30 patients which would have 80% power of detecting a difference at a 0.05 level of significance, using a confidence interval of 95%. Analysis was performed using SPSS version 17 (Chicago-USA). Data was presented as mean ± SD, numbers, and percentages. Repeated measures ANOVA was used to test the change of different parameters having normal distribution overtime in both study groups (time effect) and also to test the difference between group L and LD over time (group interaction). Bonferroni test was used for multiple pairwise comparisons. For VAS score, Friedman test was used to show effect of time in each study group. Pairwise comparisons were done using Wileoxan rank test. P < 0.05 was considered significant.

RESULTS

Table 1: Demographic data and duration of surgery

Variable	Group L(N=30)	Group LD(N=30)	P-value
Age(years)	52.33±7.937	51.73±8.944	0.784
Weight(kg)	51.57±6.831	53.43±8.059	0.337
Height(cm)	157.80±5.939	159.23±5.463	0.335
BMI (kg/sqm)	21.544±2.268	22.57±2.787	0.123
Surgical time(hours)	2.19±0.132	2.226±0.14	0.312

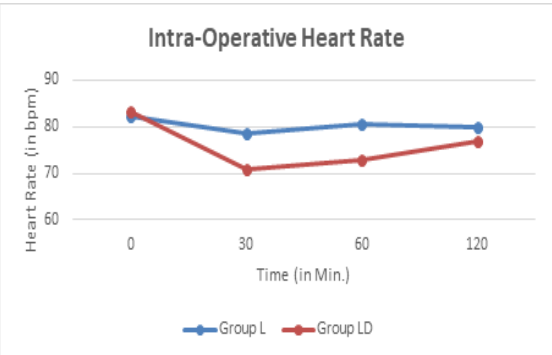

Figure 1: Intraoperative changes in heart rate in studied group

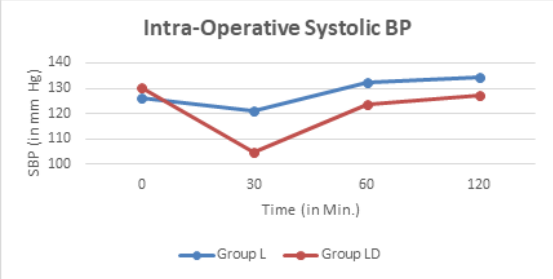

Figure 2: Intraoperative changes in systolic blood pressure in studied group

There were no significant differences among the 2 groups in demographic data as regard to age, weight, height, BMI, and duration of surgery (P > 0.05) [Table1]. There was a significant reduction in pulse rate starting at 30 minutes in both groups, but more evidenced in group LD [Figure 1].

Intraoperative Systolic blood pressure showed a significant reductionat 30 minutes in both groups then returned to baseline level at 120 minutes in both groups [Figure 2]. Changes in intraoperative diastolic blood pressure were similar to pulserate where a significant drop occurred at 30 minutes,but more evidenced in group LD, then became stable until 120 minutes in group L and increased but not to baseline in group LD. [Figure 2] There was a significant increase in pulse rate starting 2 hours postoperative until 24 hours postoperatively in group L but only after 12 hours until 24 hours in group LD. [Figure 3].

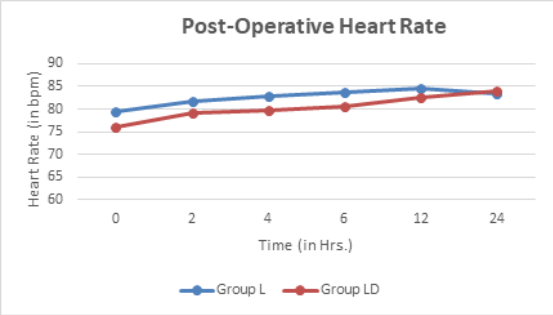

Figure 3: Postoperative changes in heart rate in studied group

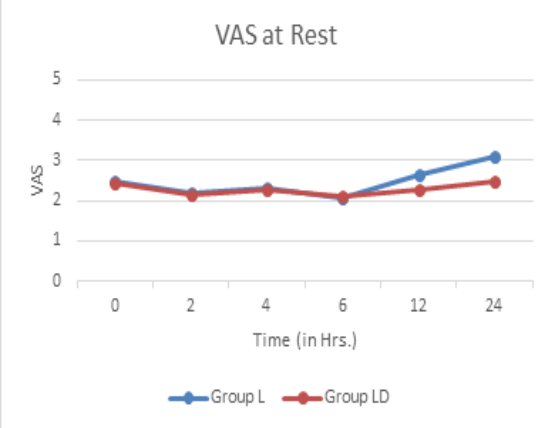

Figure 4: VAS at rest

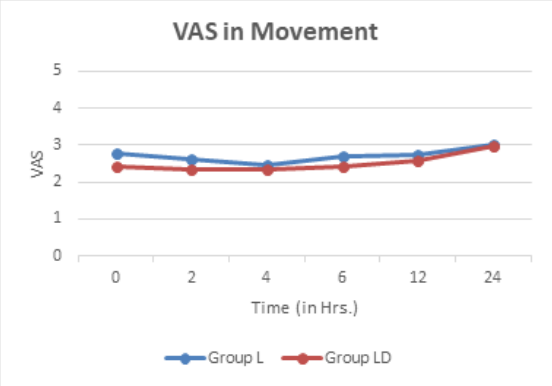

Figure 5: VAS in movement

Table 2: Post operative pain profile

Variable	Group L	Group LD	P value
Tramadol consumption(mg)	146.67±50.74	120±40.68	0.0285
Time to first analgesic request(hour)	6.34±2.83	8.15±2.21	0.0079

VAS.R measured showed significant reduction in both groups up to 6 hrs but VAS started to increase significantly after 6 hrs in L group compared to LD group. [Figure 4] There was no significant changes in VAS.M in both study group postoperatively [Figure 5]. The time of the first rescue analgesic requirement was significantly prolonged in group LD in comparison to group L. [Table 2]. The mean total consumption of intravenous tramadol as rescue analgesia in the postanesthesia care unit in the first 24 hours postoperatively was significantly lower in group LD in comparison to group L [Table 2]. Regarding adverse effects noted in the first 24 hours postoperatively6 patients in group L and 6 patients in group LD had postoperative nausea and vomiting. There was no significant difference in the incidence of postoperative complications between the two groups[Table 3].

Table 3: Complications

Variable	Group(L) N=30	Group(LD) N=30	P-value
1.Nausea	4(13.33%)	3(10%)	0.688
2.Vomiting	2(6.6%)	3(10%)	0.640
3.Pneumothorax	1(3.3%)	0	0.313
4.Bradycardia	0	2(6.6%)	0.536
5.Hypotension	0	2(6.6%)	0.349

DISCUSSION

Post operative pain delay ambulation,and prolongs the hospital stay. Regional anesthesia can decrease episodes of nausea ,vomiting and postoperative pain. Various methods of regional anesthesia for breast surgery are in practice. Simple infiltration methods can provide adequate anesthesia for minor procedures but patient discomfort, frequent supplementation and distortion of anatomy may preclude their use for major procedures. Thoracic epidurals are associated with cardiorespiratory and physiological changes, which required an increased level of monitoring when used for postoperative analgesia.[7] Paravertebral block can achieve superior analgesia and inhibit the surgical stress response at greater extent than epidural anesthesia.PVB is indicated as a primary anaesthetic technique for simple chest wall surgeries, rib resection and for breast augmentation surgeries.[8] More often it is utilized as an analgesic for breast carcinoma surgery, minimally invasive cardiac surgery, post thoracotomy pain, multiple rib fractures, acuteherpetic neuralgia and other chronic pain conditions.In this study, we have demonstrated that patientswho received PVB with 0.25% levobupivacaine and 1 µg/kg dexmedetomidine in addition to general anesthesia experienced superior postoperative analgesia, prolongation of the time to the first rescue analgesic requirement, and decreased mean total intravenous tramadol consumption as compared with PVB with 0.25% levobupivacaine alone. Burlacu et al,[9] noted that paravertebral fentanyl and clonidine in combination with diluted levobupivacaine (0.05%) are effective analgesics as demonstrated by a significant decrease in supplemental postoperative morphine consumption. At the doses used, the addition of fentanyl is associated with nausea and vomiting, and clonidine with arterial hypotension. A study by Buhuvaneswari et al,[10] demonstrated that the rescue analgesic consumption as well as cumulative pain scores at rest and on movement were significantly lower in 0.25% bupivacaine + epinephrine with fentanyl and 0.5% bupivacaine groups. They concluded that lower concentrations of bupivacaine can be combined with fentanyl to achieve analgesic efficacy similar to bupivacaine at higher concentrations, decreasing the risk of toxicity in PVB. Few clinical studies have examined the epidural usual dose of 1 – 2 µg/kg dexmedetomidine in thoracic and upper abdominal surgery. Epidural dexmedetomidine potentiates neuroaxial local anesthetics, decreases intraoperative anesthetic requirements, and improves postoperative analgesia hence reducing pulmonary complications associated with thoracotomy. Local anesthetic acts by blocking sodium channels, whereas an α2-adrenoceptor agonist acts by binding to presynaptic C- fibers and postsynaptic dorsal horn neurons; they produce analgesia by depressing the release of C-fiber transmitters and hyerpolarization of postsynaptic dorsal horn neurons. On the other hand, Gupta et al,[11] compared the role of intrathecal dexmedetomidine and fentanyl as adjuvants to bupivacaine, and concluded that intrathecal dexmedetomidine is associated with prolonged motor and sensory block, hemodynamic stability, and reduced demand for rescue analgesics in 24 hours as compared to fentanyl. Kairaluoma et al,[12] reported that preincisional PVB provided good acute

postoperative pain relief and prevented pain conditions for up to one year after breast cancer surgery. In our study, there were no significant differences in sedation scores between the 2 groups. Also our study showed that the addition of 1 µg/kg dexmedetomidine to 0.25% levobupivacaine in PVB before induction of general anaesthesia induced significant reduction in pulse rate and systolic blood pressure at 30 minutes intraoperatively, also diastolic blood pressure showed a significant reduction at 30minutes intraoperatively. In the postoperative period systolic and diastolic blood pressure showed no significant difference between the 2 groups, but heart rate significantly increased 12 hours postoperatively until 48 hours in the levo bupivacaine group. In agreement with finding of the present study, Mohta et al.[13] found that the time to first analgesic request was significantly longer and total morphine consumption was low in when dexmedetomidine was used as adjuvant to local anaesthetics in PVB.Our study was also in agreement to study by Ahmed R et al,[14] and Mohamed SA et al.[15]

CONCLUSION

Addition of dexmedetomidine 1µg/kg to levobupivacaine 0.25% in PVB in patients undergoing breast cancer surgery improves the quality and the duration of analgesia and also provides an analgesic sparing effect with no serious complications.

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