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Effect of Dexmedetomidine and Nalbuphine as an adjuvant to bupivacaine in paravertebral block for postoperative pain after modified radical mastectomy

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Abstract

Background & aim

Paravertebral block (PVB) is a commonly used technique, for postoperative analgesia after modified radical mastectomy(MRM).Though many adjuvants to bupivacaine in PVB have been tried for postoperative analgesia, none has been found ideal. We have compared the duration of analgesia in PVB using adjuvant like dexmedetomidine and nalbuphine with bupivacaine after MRM.

Methods

Sixtyfive female patients posted for MRM were divided into two groups. Group BN received ultrasound guided PVB with 20 ml bupivacaine 0.25% with nalbuphine 10mg and Group BD received 20 ml bupivacaine 0.25% with dexmedetomidine 1 μg/kg. After confirming PVB, surgery was done under general anesthesia in all patients. Time for 1st rescue analgesic request was the primary aim of our study. Secondary aim of our study was numerical rating scores

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(NRS) for pain at rest and on movement and total analgesic consumption. Side effects like nausea and vomiting ,hemodynamics and sedation in post operative 24 hrs were also assessed.

Results

The time of the first rescue analgesic requirement was prolonged in the group BD (7.32 ± 1.75 hours) in contrary to group BN (4.94 ± 2.12 hours). The mean total paracetamol consumption as rescue analgesia in the in the first 24 hours postoperatively was significantly reduced in group BD (2.7 ±0.94 gm) in contrary to group BN (3.6 ± 0.98 gm). ($p<0.001$) Decrease in hear rate and mean arterial pressure was more in BD group compared to BN group intraoperatively. ($p<0.001$)

Conclusion

Dexmedetomidine provides prolonged analgesia when used as additive to bupivacaine in PVB for modified radical mastectomy compared to nalbuphine.

Keywords- Nalbuphinel, Dexmedetomidine, bupivacaine, paravertebral block, analgesia

Introduction

Breast cancer is the commonest cancer in women that frequently requires surgical intervention and they suffer from pain postoperatively.[1] Though general anesthesia is commonly used for this surgery, it doesn't provide any relief for postoperative pain control. Also this is associated with a very high incidence of postoperative nausea and vomiting.[2] Inadequate control of postoperative pain and PONV can lead to poor recovery, increase the duration of hospital stay, and increased risk of developing chronic post-surgical pain (CPSP).Various modalities, like intercostal block, thoracic epidural anesthesia, local anesthetic infiltration paravertebral block,

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pectoral nerve blockage and opioids , have been suggested to reduce postoperative pain, but have shown variable efficacy.[3] Schnabel A et al and Tahiri et al [4],[5] have showed that PVB may be an efficient modality for providing postoperative analgesia after breast cancer surgery. PVB not only reduce postoperative pain,and postoperative opioid consumption but also reduces incidence of PONV.To avoid toxicity, local anesthetic agents like bupivacaine requires additives to prolong the analgesia in PVB. Various adjuvants like fentanyl,clonidine, magnesium, epinephrine, tramadol, dexamethasone, opioids, and dexmedetomidine are used with bupivacaine for enhancing the quality as well as the duration of the analgesia in PVB.[6]Dexmedetomidine has proved its efficacy in paravertebral block as it reduces the postoperative pain with reduced consumption of opioids but it has produced significant reduction in heart rate and mean arterial pressure intraoperatively.[7] Nalbuphine, derived from 14-hydroxymorphine, is considered a potent analgesic possessing a mixture of k agonist and μ competitor profiles. The pain-relieving potency considering nalbuphine had been reported to be identical to morphine but dissimilar from it in exhibiting a top limit effect on respiratory depression. Nalbuphine possesses the effect of maintaining or even augmenting the opioid μ receptor centered analgesia and at the same time mitigating the μ-opioid side effects.[8] There was also controversy in literature regarding efficacy of dexmedetomidine and opiods like morphine and fentanyl as additive in PVB.[9] We compared the efficacy of additive like dexmedetomidine and nalbuphine with bupivacaine in paravertebral block for postoperative pain in patients undergoing breast surgery.

Methods

The study prospective trial was conducted at a tertiary care hospital after taking Institutional Ethical Committee approval. Written informed consent was obtained from all patients. Sixty patients of ASA I /II and aged 18-70 yrs posted for elective breast cancer surgery were enrolled

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in this study. Patients having coagulopathy,allergy to study drug,infection at site of paravertebral block.pregnancy and severe cardiopulmonary diseases were excluded from the study.During pre anesthetic chekup,after taking history all the patients were examined and investigations were checked. Al the patients were explained regarding use the visual analog scale (VAS 0-10). All the patients were split into 2 groups of 30 patients each using a computer-generated random number assignment in sealed opaque envelopes. Anesthesiologist not involved in the study prepared the study drug according to randomization. The patients and investigator involved in data collection were blinded to allocation. On the arrival in the operating room, a 18-gauge IV cannula was inserted and lactated ringer's solution 10 ml/kg was started. Monitoring like electrocardiography, noninvasive blood pressure, O2 saturation, and temperature were done. Patients were seated for block and were premedicated with iv midazolam (0.03 mg.kg) and tramadol1mg/kg . Needle entry point was marked at 2.5 cm lateral to the spinus process from the intercostal gap between the T5 and T6 ribs and 2 mL of 2% lidocaine infiltration was given. Paravertebral block was given by a 23 G 100 millimeter (Stimupleks® Ultra, B. Braun, Melsungen, Germany) peripheral blockade needle. The thoracic paravertebral area was determined using the internal intercostal membrane at the top and the pleura at the bottom. Perpendicular entry was made to the skin via a nerve block needle with ultrasonography until the transverse process is reached. Paravertebral blockade was applied by injecting 21 ml of the prepared agent following the verification of the paravertebral space. In group BN, the patients received 19 ml of bupivacaine 0.5% with 10 mg (1 mL) nalbuphine,In group BD, the patients received 19 ml of bupivacaine 0.5% + 1 µg/kg dexmedetomidine(diluted to 1ml). After 10 min,the success of the block was checked and all patients having successful block were included in this study. Immediately after the block, the patients were placed in the supine position. Preoperative spo2,mean arterial pressure (MAP) and heart rate (HR) were recorded and also monitored intraoperatively. General anesthesia was

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administered with propofol 2mg/kg and tramadol 1mg/kg. Endotracheal intubation was facilitated by rocuronium 0.6 mg/kg. Anesthesia was maintained byoxygen,nitrous oxide and isoflurane 1 – 1.5%. Anesthesia was deepened by increasing the perentage of sevoflurane when MAP and HR values increased by 20% over basal values before induction. A MAP decrease of more than 20% was taken as hypotension which was managed by reducing sevoflurane concentration and iv 5 mg ephedrine if necessary. A heart rate less than 50 beats.min^{-}was taken as bradycardia.At the end of the operation,residual block was reversed using 0.02 mg.kg^{-}atropine and 0.04 mg.kg neostigmine and patients were extubated and were transferred to the postanesthesia care unit and vital parameters were monitored. VAS at rest (VAS.R) and during movement or ipsilateral arm abduction (VAS.M) were postoperatively at 0,0.5,1, 2, 4, 6, 12 and 24 hrs of the postoperative period. Intravenous paracetamol 15mg/kg100 was given as rescue analgesia when the VAS was ≥ 4. The time of the first request for analgesia and the total analgesic consumption in the first 24 hours were recorded. Heart rate and mean arterial blood pressures were recorded and sedation was assessed by Ramsay sedation score. Complications like hypotension, bradycardia ,respiratory depression, pruritus, and postoperative nausea vomiting were assessed. Ondansterone(4mg) was given to all patients with nausea, retching or vomiting. Statistical analysis-Sample size calculation was based on an initial pilot study involving ten patients with 'time needed for first rescue analgesic' as the primary end point of the study. Time to first analgesic request was 3.51 ± 1.13 hrs in BN group and 5.92 ± 1.15hrs in BD group. With α error of 0.05 and power of the study (1− α) at 80%, to detect a minimum of 120 min difference in time needed for rescue analgesia between the two groups, the sample size was calculated to be approximately 28 in each group. We included thirty patients in each group to compensate for possible dropouts. The patients, who were part of the pilot study, were not included in the study. The patients' data and characteristics, the time of onset and duration of the block were categorized and analyzed

appropriately using student's unpaired t-test and Chi-square test. A $P < 0.05$ was considered as statistically significant and a $P< 0.001$ as statistically highly significant.

Result

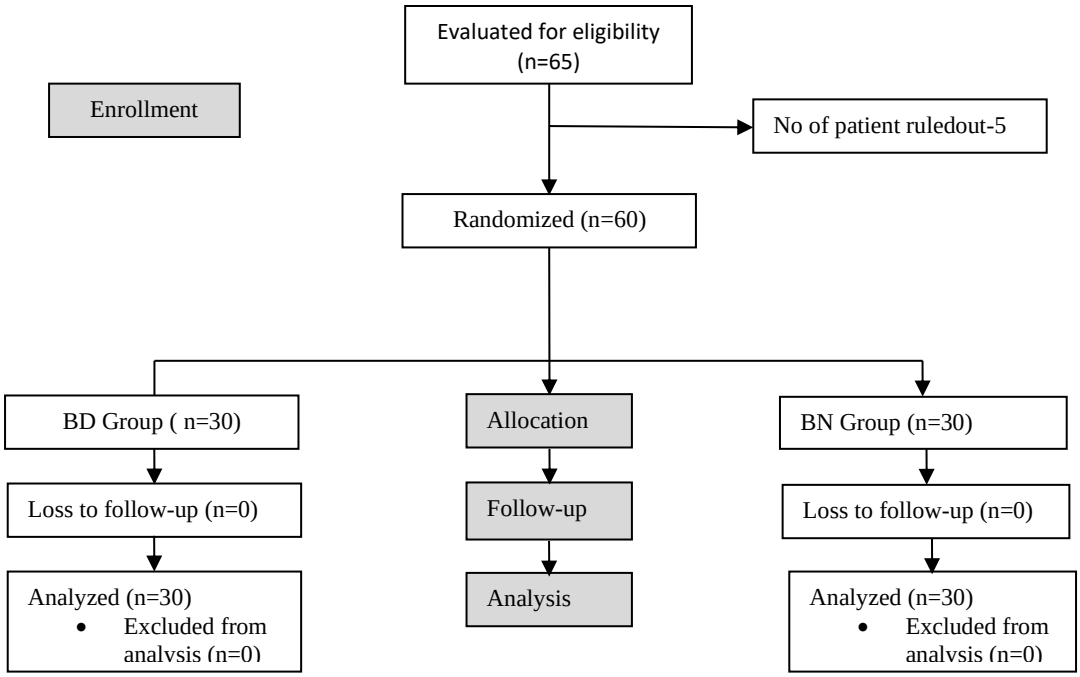

Fig 1:Consort flow diagram

65 patients were included in our study and 5 patients were excluded for not following inclusion criteria.Block was successful in all the patients, and all the enrolled patients completed the study (Fig 1). Demographic data such as age, sex, weight and duration of surgery between two groups were comparable (Table 1). The request for first rescue analgesic was significantly earlier in Group BN than Group BD. Group BD showed statistically significant prolonged analgesia (7.32 ± 1.75 hours) compared to 4.94 ± 2.12 hours in group BN. The mean total consumption of intravenous paracetamol as rescue analgesia in the postanesthesia care unit in the first 24 hours postoperatively was significantly decreased in group BD (2.7 ±0.94 gm) compared to group BN (3.6 ± 0.98 gm).

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VAS.R measured showed significant reduction in both groups up to 4 hrs but VAS started to increase significantly after 4 hrs in BN group compared to BD group. There was no significant changes in VAS.M in both study group postoperatively. (fig 2,3)There was a significant decrease in HR and MAP throughout the intraoperative period,in group BD compared to group BN which was statistically significant.(fig 4,5) HR and MAP in postoperative period in both group were comparable. Sedation score were comparable in both groups postoperatively.

Table 1:Demographic data and duration of surgery

Variable	Group BD (n=30) mean±sd	Group BN (n=30) mean±sd	P- value
Age(years)	58.13±4.96	57.83±8.39	0.383
Weight(kg)	57.13±8.24	56.92±8.11	0.228
Height(cm)	156.18±5.25	156.19±5.39	0.283
ASA I/II	18/12	20/10	0.372
BMI (kg/sqm)	23.25±1.32	22.67±.41	0.253
Surgical time(hours)	1.98±0.54	2.62±0.43	0.208

Table 2:Post operative pain profile

Variable	Group BD (n=30) mean±sd	Group BN (n=30) mean±sd	P value
Time to first analgesic request(hour)	7.32±1.75	4.94±2.12	<0.001
Paracetamol consumption(gm)	2.7±0.94	3.6±0.98	<0.001

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Table 3: Complications

Variable	Group BD n=30	Group BN n=30	P- value
1.PONV(n)	4	6	0.218
4.Bradycardia(n)	2	1	0.294
5.Hypotension(n)	3	1	0.338

Figure 4: Intraoperative changes in heart rate in studied group

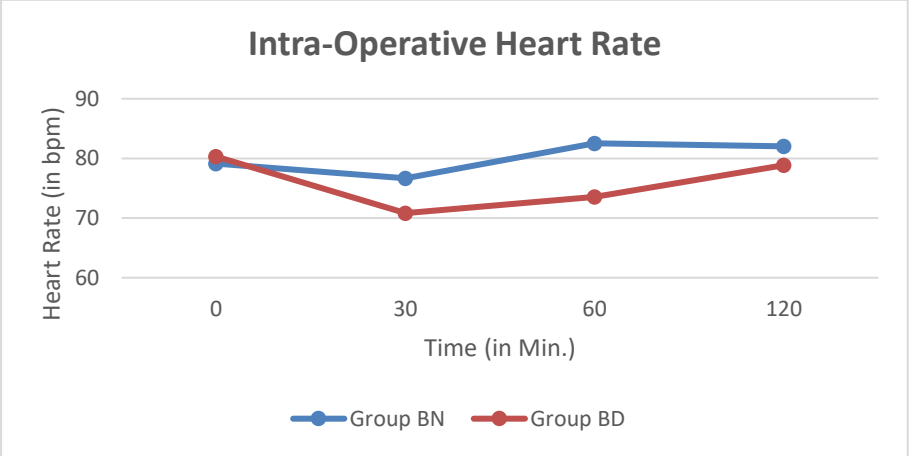


Figure 5: Intraoperative changes in MABP in studied group

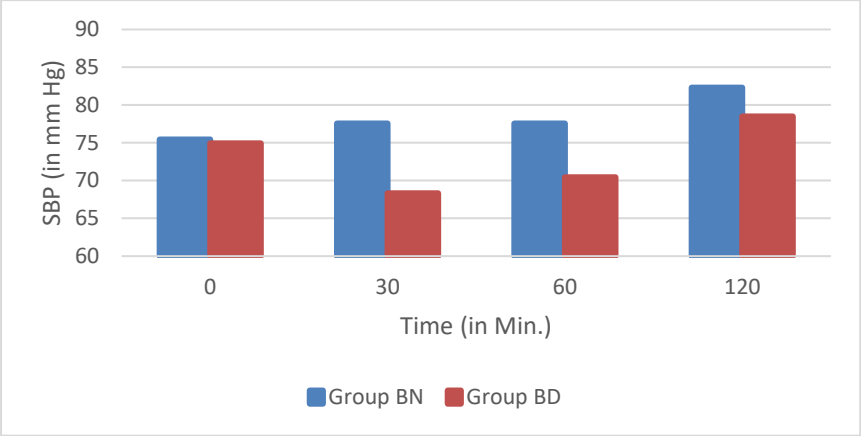


Figure 2:VAS at rest

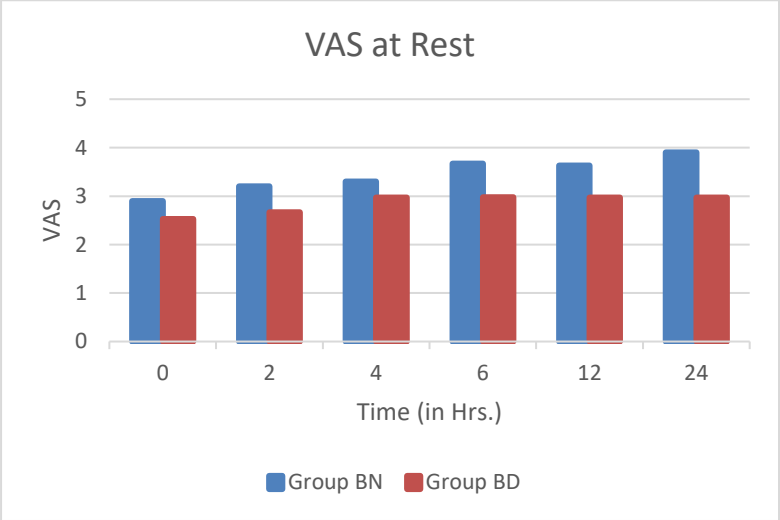
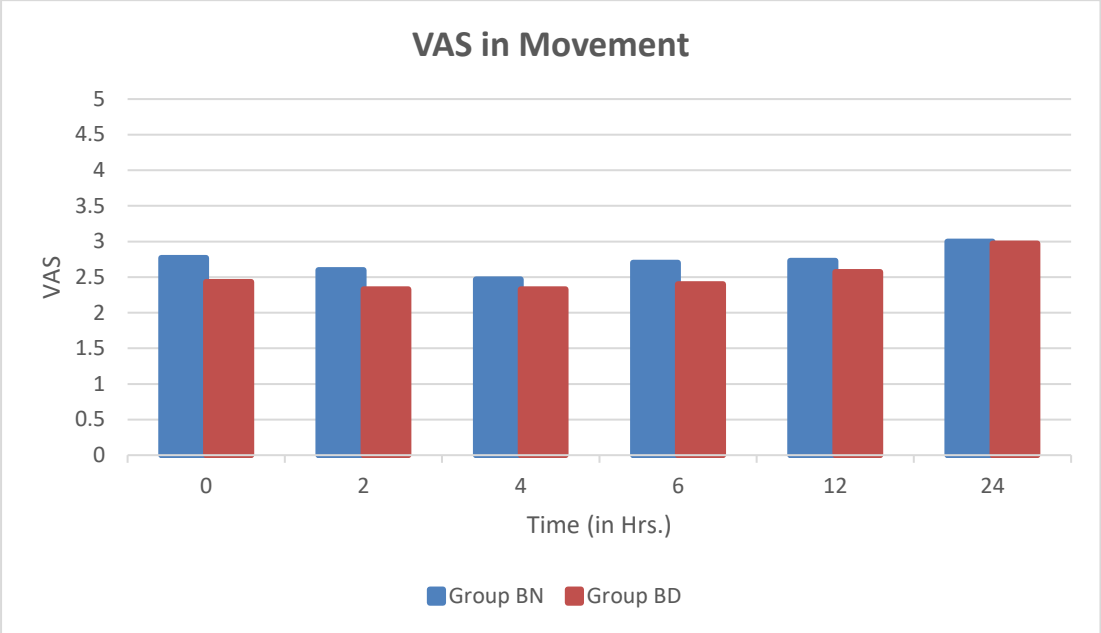


Figure 3:VAS in movement



Regarding adverse effects noted in the first 24 hours postoperatively4 patients in group BD and 5 patients in group BN had postoperative nausea and vomiting. There was no significant difference in the incidence of other postoperative complications like,sedation,bradycardia and hypotension between the two groups. (Table 3)

Discussion

The results of our study shown that dexmedetomidine as adjuvant to bupivacaine in paravertebral block produced prolonged analgesia and delayed the first request of rescue analgesia in patients posted for MRM compared to nalbuphine. It also produced significant reduction in the total consumption of rescue analgesia in the first 24 h postoperatively. Dexmedetomidine was associated with significant decrease in the postoperative VAS score after 4 hours postoperatively compared to nalbuphine.The paravertebral block was first used to induce unilateral analgesia along the thorax and the abdomen without severe hemodynamic changes. Kairaluoma et al,[10] showed that single dose PVB application decreases severe pain at postoperative 6 h after breast surgery at a statistically significant level in comparison with placebo, and also showed that PVB also decreases the minimal pain score within postoperative

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24 hrs. In paravertebral block, local anesthetic penetrates not only into the spinal nerves, sympathetic chain, but also the dorsal ramus. Local anesthetics penetrates into the spinal nerves as they are present in the form of small bundles without a fascial sheath. Certain opinions suggested that epidural migration may explain its mechanism of action.[11] Bhuvaneswari et al,[8] in their trial opined 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 but fentanyl can produce nausea and vomiting. Mohta et al,[12] studied the analgesic effect of the continuous paravertebral block using either ropivacaine alone and ropivacaine added to fentanyl in the patients with multiple fractured ribs and revealed that fentanyl provided good analgesia but few cases developed nausea and vomiting in fentanyl group. Burlacu et al,[13] conducted a randomized controlled study on 53 patients undergoing breast surgery under general anesthesia to compare the use of fentanyl, clonidine, or normal saline as an adjuvant to levobupivacaine in the paravertebral block. They found that fentanyl improved the quality and duration of postoperative analgesia,but it was associated with significant increase in the incidence of nausea and vomiting and pruritus. All the above studies suggested that fentanyl may be acting on opioid receptors found in dorsal root ganglia and also produce symptoms like nausea and vomiting. Dexmedetomidine is a selective α2-adrenal receptor agonist whose selectivity(α2 : α1) ratio is 1600 : 1. It has various pharmacological properties like sedation and anesthesia sparing action without respiratory depression. Additional properties include analgesia, anxiolysis, hemodynamic stability, antishivering effects, and reduced incidence of postoperative nausea and vomiting.[14] So we have compared dexmedetomidine as adjuvant with fentanyl in PVB. Bicer et al,[15] in their study opined that the addition of dexmedetomidine to bupivacaine lowers postoperative pain scores and morphine consumption in thoracotomy patients who receive ultrasonography guided paravertebral blockade.Morsy et al,[7] found that the addition of dexmedetomidine to

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bupivacaine in PVB decreased the VAS score, postoperative analgesics consumption, and delays the postoperative analgesic requirement without any side effects and found better than morphine. Also, Hassan et al[16] found that addition of dexmedetomidine to paravertebral bupivacaine in patients undergoing thoracic surgeries provides more effective analgesia with improvement in post-operative pulmonary functions.Dutta et al[17] evaluated the role of dexmedetomidine when added to ropivacaine in the paravertebral block, found significant improvement of the duration of postoperative analgesia and decreased rescue analgesia consumption.Mohta et al,[18] in their study concluded that bupivacaine with dexmedetomidine increased the duration and the quality of postoperative analgesia without any alteration in hemodynamic parameters and side effects.In addition, Sinha et al,[19] concluded that the use of dexmedetomidine as an adjuvant to ropivacaine in the paravertebral block in patients presented for renal surgeries led to significant improvement of the duration of postoperative analgesia and reduction of opioids consumption. The mechanism of action of dexmedetomidine as an adjuvant in local and regional anesthesia isn't fully clear until now. Dexmedetomidine acts centrally at the dorsal root neuron through inhibition of the release of substance P at the nociceptive pathway; also, it stimulates the adrenergic alpha 2 receptors of the locus coeruleus. Peripherally, it stimulates the peripheral adrenergic 2 receptors to decrease the release of norepinephrine and inhibition of nerve fiber action potential.[20] All above studies are in agreement with our study.In our study we found that dexemedtomidine was better than fentanyl in providing prolonged analgesia compared to fentanyl in PVB.In TAP block Chen et al,[21] has concluded that dexemedtomidine provided prolonged analgesia compared to fentanyl which was similar to our findings.Ahmed et al.[22] in their study concluded that both fentanyl and dexemedetomidine showed comparable efficacy in PVB in renal surgeries. We found similar finding in our studies.But few studies have also shown morphine as superior to dexemedetomidine in PVB.Megha et al,[23] concluded that morphine is superior adjuvant to

bupivacaine in PVB for modified radical mastectomy than dexmedetomidine. Also Ahmed et al,[24] As an adjunct to bupivacaine in PVB for MRM, morphine is superior to dexmedetomidine.In both above studies they have used higher dose (3mg) of morphine which could led to its superiority. There was statistical significant reduction in hear rate and mean arterial pressure in dexmedetomidine group intraoperatively in comparison to fentanyl group. This finding was in agreement with the one obtained by Mohamed et al, [25] who performed thoracic PVB with either bupivacaine alone and bupivacaine with dexmedetomidine and found that there was a significant reduction in intraoperative pulse rate and mean arterial pressure in dexmedetomidine groups. As there are a relatively low number of available studies in literature evaluating the use of nalbuphine or dexmedetomidine as adjuvant to bupivacaine in the paravertebral block, further large scale studies may be required to validate our findings. Omar et al[26] concluded that time to first analgesic request was longer in dexmedetomidine group, but tramadol consumption was lower in nalbuphine group, but both were statistically insignificant which was similar to our study.

Conclusion

When compared to nalbuphine ,the addition of adjuvant like dexmedetomidine to bupivacaine in PVB in patients posted for modified radical mastectomy not only improves the duration of analgesia but also reduces the rescue analgesic consumption with no serious side effects.

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