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Dexmedetomidine and Fentanyl as Adjuvant to Bupivacaine for Postoperative Pain Management in Paravertebral Block after Surgery

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ABSTRACT

Aim: Our aim was to assess the efficacy of dexmedetomidine and fentanyl as adjuvant to bupivacaine for postoperative pain management by paravertebral block.**Methods:** Sixty American Society of Anaesthesiologists physical status I/II patients posted for surgery were randomly assigned into two groups of 30 each. Group BD received thoracic PVB with 20 mL of bupivacaine 0.25%. Group LD received thoracic PVB with 20 mL of bupivacaine 0.25% + 1 μg/kg dexmedetomidine. Group BF received paravertebral block with 20 ml of drug (18 ml bupivacaine (0.25%) + fentanyl 1 μg /kg diluted to 2 ml) with general anaesthesia. 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 BD in comparison to group BF. 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 BD compared to group BF. **Conclusion:** The addition of dexmedetomidine as adjuvant to bupivacaine in PVB in patients undergoing surgery improves the quality and the duration of analgesia postoperatively when compared to fentanyl.

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

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INTRODUCTION

Nearly 40% of postoperative surgery patients experience significant acute postoperative pain, with a pain score above 5 reflecting the inadequacy of conventional pain management.[1] Most of the responses of the human body to post-surgical pain have been proven to be detrimental to the patient's homeostasis and recovery. Moreover, the incidence of chronic postoperative pain in breast surgery patients is as high as 50% and inadequate analgesia is considered as an independent risk factor.[2]Hence, a number of therapeutic measures have been accepted as a part of the "multi-modal" approach to post-operative pain control. Regional anesthesia using paravertebral block has been suggested as an ideal adjunct to general anesthesia 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.Thoracic paravertebral block (PVB) is used for pain relief after thoracotomy and mastectomy.

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PVB can provide profound, analgesia resulting greater attenuation of surgical stress response may translate into reduced inotropic stimulation of the heart. Additionally, unlike general anesthesia, PVB can provide superior postoperative analgesia, less nausea and vomiting, shorter recovery time, require fewer analgesics, earlier mobilization, and earlier home readiness for discharge. The use of PVB in patients undergoing ambulatory breast surgery has a cost-saving potential.[2] There is little systematic research on the efficacy and tolerability of the addition of an adjunctive analgesic agent in paravertebral analgesia. 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-adrenoreceptor agonist Recently introduced to anesthesia; it produces a dose-dependent sedation, anxiolytics, and analgesia (involving spinal & supraspinal sites)without respiratory depression. α2- agonists are known to reduce anesthetic requirements and because of their sympatholytic properties, they provide hemodynamic stability during the intraoperative period.[17] The adverse effects of dexmedetomidine may include hypotension, hypertension, nausea, bradycardia, atrial fibrillation, and hypoxia. Fentanyl is an opioid agonist, it's a potent,synthetic analgesic which acts on mu opioid receptors. It is 75 to 125 times more potent analgesics and 800 times more lipid soluble than Morphine and is rapidly absorbed

from epidural space and CSF.[4] Its onset of action is very rapid which is about 15-30 minutes and its duration of action is 2-5 hours. The initial bolus dose of fentanyl is 5mcg/kg. Signs and symptoms of respiratory depression are very rare with this dose, although case reports of respiratory depression at these doses are very rare. Pruritis is the most common side effect, others like nausea, vomiting constipation etc. Its complementary and synergistic anti-nociceptive interaction results in analgesia with no respiratory depression, decrease incidence of tolerance, dependence and abuse.[5] Addition of Fentanyl to a local anaesthetic such as bupivacaine , decreases the concentration of bupivacaine to 0.125% or even 0.0625% instead of 0.5% or 0.25%. This would decrease the incidence of hypotension and unwanted motor blockade.The aim of this study was to investigate the safety and the analgesic efficacy of adding 1 µg/kg dexmedetomidine and 1 µg/kg fentanyl as adjuvant to 0.25% bupivacaine in thoracic PVB in patients undergoing modified radical mastectomy.

MATERIALS & METHODS

The study was conducted at SCB Medical College Cuttack. Sixty patients were studied after Hospital Ethical Committee approval. ASAI and ASAII patients (age-18-60yrs) scheduled to undergo elective modified radical mastectomy under general anesthesia were enrolled in this study.

Sample size: 60 patients

Study Period: September 2018 to 0ctober 2020

Sample Design: The study population were randomized via sealed envelopes technique into two groups asunder:-

1. **Group BD (n-30):-** received paravertebral block with 20 ml of drug (18 ml bupivacaine (0.25%) + dexmedetomidine 1mcg/kg diluted to 2ml) with general anesthesia.
2. **Group BF (n-30):-** received paravertebral block with 20 ml of drug(18 ml bupivacaine (0.25%) + fentanyl 1 mcg /kg diluted to 2 ml) with general anesthesia.

Inclusion criteria

1. Patients aged between 18-60yrs.
2. ASA I /II physical status.
3. Diagnosed cases of breast cancer.
4. Scheduled for elective modified radical mastectomy.

Exclusion criteria

1. Bleeding disorders.
2. Allergy to amide-type local anesthetics.
3. Infection at the thoracic paravertebral injection site.
4. Pregnancy or breast feeding females.
5. Severe obesity (BMI>35kg/sq–m).
6. Psychiatric disorders.
7. Patients with past history of musculoskeletal disorders.
8. Additional surgical procedure during the same surgical time.
9. Previous history of thoracic or abdominal surgeries.

Parameters to be studied

1. Intra operative Hemodynamics -HR, SBP, DBP
2. Postoperative HR
3. Pain severity-VAS(Resting/movement)
4. Post-operative pain profile
   A. Time of first analgesics request
   B. Total analgesic consumption
5. Side effects

Study Design

Ethical consent was obtained from the Institutional Ethics Committee. Informed consent was taken from the patients after detailed explanation of the nature of study.

Pre anesthetic checkup

The patients were examined one day prior to surgery. A detailed history was recorded as below:

- Present and past medical illness
- Past history of anesthetic exposure
- Concomitant history of drug allergy
- Any medications in preoperative period were recorded
  General physical examination, systemic examination and airway examination of all the patients were done.
- Basic investigations of Hb%, TLC, DLC and urine analysis were done for all patients and other investigations like ECG, blood sugar (fasting and postprandial) were done preoperatively.

Pre anesthetic advice

- The patients were premedicated with Tab Alprazolam 0.5mg and Tab Ranitidine 150mg orally at bedtime on the night before surgery.
- Pre-operative fasting for 8 hours were ensured.
- The patients were instructed how to use the Visual Analogue Scale (VAS 0-10).[6]

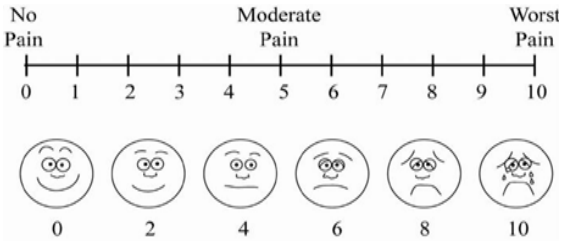

Figure 1: Visual Analogue Scale score for pain

- The patients were undergone postoperative assessment for pain, nausea and vomiting at 2hr (T2), 4hr (T4), 6hr (T6), 12hr (T12) and 24hr (T24) following surgery.

On the day of surgery, after the arrival of the patient, in the operating room18-gauge cannula was inserted

intravenously in the dorsum of the hand and lactated ringer's solution10mL/kg was infused intravenously over10 minutes before the initiation of anesthesia. 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 intravenous doses of midazolam (0.05mg/kg) and fentanyl (1.5µg/kg).Thoracic PVB were then performed as described by Moore and Katz.The superior aspect of the spinous processes of T1–T6 were marked. The skin entry points were 3 cm lateral to the marks. Intradermal lidocaine was used at the site of the needle insertion for local anesthesia. 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 in inferolateral direction for a further 1.5 to 2 cm. Paravertebral space was identified when a pop was felt,as there was loss of resistance to air then drug was injected. Patients were allocated into 2 groups of 30 patients each using a computer generated random number assignment in sealed opaque envelopes. A staff anesthesiologist not involved in the management of the patient or the study prepared the injectate according to randomization. The patients and all staff involved in patient management and data collection were unaware of the group assignment.

In group BD, the (Bupivacaine + Dexmedetomidine group), patients received 20mLof drug (18 ml bupivacaine (0.25%) + dexmedetomidine 1mcg/kg diluted to 2ml) paravertebrally,dividedinto3–4mLineachlevel. In group BF, the (Bupivacaine + Fentanyl group), patients received 20 ml of drug (18 ml bupivacaine (0.25%) +fentanyl 1µg/kg diluted to 2ml) paravertebrally dividedinto 3–4ml in each level.The time for performance of the block ranged from 10 to 15 minutes. The success of the block was tested by decrease pin prick sensation at the expected dermatomal level (fromT1-T6). Immediately after the block, the patients were placed in the supine position. General anesthesia was administered and patients were intubated by cisatracurium 0.15mg/kg. Anesthesia was maintained by isoflurane 1–1.5MAC.Fentanyl0.5µg/kg and cisatracurium 0.03mg/kg were given when indicated. Patients were mechanically ventilated to maintain ETCO2 between 30 and 35mmHg. Heart rate and systolic and diastolic blood pressures were recorded preoperatively and at 30minutes, 60minutes, and120minutes. Hypotension was defined as a 20% decrease in systolic blood pressure from the baseline. Bradycardia was defined as heart rates lower than 50 beats per minute or as an inappropriately slow heart rate despite hypotension. Hypoxia was defined as an oxygen saturation value<90%. Hypotension was treated with intravenous boluses of ephedrine 0.1mg/kg and normal saline 5mL/kg,the same doses were repeated as required and bradycardia was treated with intravenous atropine 0.01 mg/kg. At the end of surgery, neostigmine 0.05 mg/kg and glycopyrrolate 0.01mg/kg were used to reverse neuromuscular blockade and extubation was performed after full return of consciousness. At the end of the operation patients were transferred to the post anesthesia care unit and were monitored for vital signs (heart rate, noninvasive blood pressure, respiratory rate, and saturation of peripheral oxygen. 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 as rescue analgesia when the VAS was >4 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, also postoperative complications of the block such as accidental pneumothorax 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 a0.05level of significance,using a confidence interval of 95%.Analysis was performed using SPSS version 19(Chicago-USA). Data was presented as mean ± SD, numbers, and percentages.
- For continuous data independent samples t test was used.
- For categorical data Pearson Chi-square test was used.
- Repeated measures ANOVA test was used to test the change of different parameters having normal distribution over time in both study groups (time effect).
- $P < 0.05$ was considered significant.

RESULTS

Demographic parameters (age, weight, height, BMI) and duration of surgery were compared by independent samples t test.p-value >0.05 indicating that both the groups were comparable.

It was observed that the HR decreased in both the groups subsequently from the baseline. There was a significant reduction in HR starting at 30 minutes in both the groups but it was more significant in groupBD.After30 minutes, there was a greater increment in HR in group BF when compared to group BD, but it ended up almost being equal to the baseline in group BF while it ended up a bit lower than baseline in group BD. The P value for HR at 30

minutes and 60 minutes was <0.001 and at 120 minutes was 0.025 which were statistically significant. [Table 1]

Intraoperative systolic blood pressure showed a significant reduction at 30 minutes in both the groups; then significant increase occurred in group BF until 120 mins but it was more stable and below baseline in group BD (p value for group interaction was<0.001). [Table 2]

VAS.R score measured at rest showed significant reduction in group BD after 2 hours but did not show any significant difference in group BF. VAS.R score started to increase at 12 hours and thereafter in group BD whereas it increased at 6 hours and thereafter in group BF.

The p-value for VAS.R at 2 hours (0.036), 4hours (0.018), 6hours (0.005) and12hours (0.026) postoperatively were found to be statistically significant. [Table 3]

There was no significant changes in VAS.M in either study group postoperatively. [Table 4]

The time for the first rescue analgesic requirement was significantly delayed in group BD in comparison to group BF hours. The mean total consumption of intravenous tramadol (rescue analgesia) in the post anesthesia care unit in the first 24 hours postoperatively was significantly lower in group BD in comparison to group BF. [Table 5]

Table 1: Intraoperative changes in heart rate in study groups

Groups	HR 0 time	HR 30 mins	HR 60 mins	HR 120 mins	p value for time effect
BF	82.13±5.07	78.67±3.925	80.53±4.281	80.03±4.013	<0.001
BD	83.30±5.253	70.83±4.684	73.00±5.571	76.87±6.361	<0.001
P value	0.385	<0.001	<0.001	0.025	

Table 2: Intraoperative changes in systolic blood pressure in studied groups

Groups	SBP 0 time	SBP 30 mins	SBP 60 MINS	SBP 120 MINS	P value for time effect
BF	130.67±11.31	121.03±7.156	132.57±5.770	134.50±5.322	<0.001
BD	130.87±12.53	104.90±7.945	123.83±5.884	127.33±6.019	<0.001
P value	0.948	<0.001	<0.001	<0.001	

Table 3: Vas at rest

Group	VASR 0HR	VASR2 HR	VASR4 HR	VASR6 HR	VASR12HR	VASR24HR
BF	2.87±0.68	2.77±0.68	2.83±0.65	3.07±0.78	3.23±1.01	3.10±1.24
BD	2.60±0.72	2.37±0.76	2.43±0.63	2.47±0.82	2.60±1.13	2.90±1.45
P value	0.147	0.036	0.018	0.005	0.026	0.5678

Table 4: Vas on movement

Group	VASM0HR	VASM2 HR	VASM4 HR	VASM6 HR	VASM12 HR	VASM24 HR
BF	3.07±1.39	2.77±0.90	3.17±1.26	2.90±1.42	3.33±1.32	3.27±1.57
BD	2.57±1.33	2.43±0.77	2.57±1.30	2.80±1.13	2.97±1.33	3.03±1.13
P value	0.1598	0.1289	0.0754	0.7639	0.2878	0.5120

Table 5: Post-operative pain profile

Group	BF	BD	p value
Tramadol consumption(mg)	155.6±50.7	124±40.7	0.0346
Time to firstanalgesic request(hour)	6.52±2.9	8.4±2.1	0.0011

DISCUSSION

With TPVB, there is minimal risk of neurological damage, being unilateral with sympathetic blockade incidence of postural hypotension is less unless the patient is hypovolemic and thus ambulatory discharge is possible. Patient's satisfaction is better as compared to thoracic epidural or general anesthesia with lesser hospital stay and cost of treatment. Hence TPVB is considered as a safe alternative to epidural anaesthesia. Burlacu et al,[7] noted that paravertebral fentanyl and clonidine in combination with diluted levobupivacaine(0.05%) were effective analgesics as demonstrated by a significant decrease in supplemental postoperative morphine consumption. Furthermore, it appears that fentanyl and clonidine have a local anesthetic sparing effect. At the doses used, the addition of fentanyl is associated with nausea and vomiting, drowsiness, respiratory depression and clonidine with arterial hypotension. A study by Bhubaneswari et al8 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. In our study we found that addition of dexmedetomidine not only caused less side effects but also lowered the concentration of local anesthetic to be effective in PVB. Previous studies report that multiple injections do improve the

duration and quality of analgesia, with a higher probability of procedural complications. On the other hand, a single injection provides more patient comfort and lowers the need for sedation during performance of PVB, thereby improving patient satisfaction. Small doses of multiple injections are supposed to provide better consistency in the optimal spread of the injectate. In our study we have given 3-4ml of drug paravertebrally from T1 to T6 level. Our study showed that the addition of 1 mcg/kg dexmedetomidine to 0.25% bupivacaine in PVB before induction of general anesthesia induced significant reduction in pulse rate and systolic blood pressure at 30 minutes intraoperatively, also diastolic blood pressure showed a significant reduction at 30 minutes 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 24hours in the dexmedetomidine+ bupivacaine group. Mohamedetal.[9] Compared the effects of addition of dexmedetomidine 1 mcg/kg to 0.25% of bupivacaine in TPVB for modified radical mastectomies. They observed significant intraoperative hemodynamic stability, prolonged postoperative analgesia and decreased need of rescue analgesics for 48 hours after surgery. In another study with 0.5% ropivacaine and 0.5mcg/kg dexmedetomidine they found similar results of hemodynamic stability with postoperative analgesia of mean 6hours with lesser need of rescue analgesics,which corresponds to our study where we found that total tramadol consumption was less and time for first analgesic request was prolonged by addition of dexmedetomidine to bupivacaine in PVB which corresponds to the findings in our study. Our study is further strengthened by a study conducted by Mohta et al.[10]found that PVB using dexmedetomidine 1mcg/kg added to 0.5% bupivacaine in patients undergoing major breast cancer surgery along with general anesthesia provide analgesia of longer duration with decrease post-operative opiod consumption and lower incidence of nausea/vomiting as compared to PVB with bupivacaine or no PVB. Similar results were found by Ahmad Sabry et al,[12] Hassan, Mohamed Elsayed, and Essam Mahran,[13] Wang, Kai et al,[14] Mukherjee et al,[15]Ahmed et al,[11] Bakeer, Ahmed H, and Nasr M Abdallah.[16]

CONCLUSION

We can conclude that the addition of dexmedetomidine as an adjuvant to bupivacaine in PVB in patients undergoing breast cancer surgery improves the quality and the duration of analgesia postoperatively compared to fentanyl.

REFERENCES

1. Gunaydin B, Intravenous dexmedetomidine sedation for spinal anesthesia in the prone chest position for lumbar laminectomy surgery. TurkJMedSci;2004;34:353-355.
2. Klein SM, Bergh A, Steele SM, Georgiade GS, Greengrass RA. Thoracic paravertebralblock for breast surgery. Anesth Analg 200; 90:1402-1405.
3. Eamonn Coveney, Christina R.Weltz, Roy Greengrass, J, DirkIglehar, George s. Leight, Susan M Steele and H Kim Lyerly, Use of paravertebral block anaesthesia in the surgical management of breast cancer-Annals of Surgeryvol227,no4,496-501.
4. Poleshuck EL, Katz J, Andrus CH, Hogan LA, Jung BF, et al. Risk factors for chronic pain following breast cancer surgery: A prospective study.JPain2006;7:626-634.
5. Gartner R, Jensen MB, Nielsen J, Ewertz M, Kroman N, Kehlet H. Prevalence of and factors associated with persistent pain following breast cancer surgery .J am Med Assoc 2009;302:1985-1992.
6. Bajwa SJ, Arora V, Kaur J, Singh A, Parmar SS. Comparative evaluation of dexmedetomidine and fentanyl for epidural analgesia in lower limb orthopedic surgeries. Saudi J Anaesth. 2011;5:365–70.
7. Barlacu CL, Frizelle HP, Moriaty DC, Buggy DJ. Fentanyl and clonidine as adjunctive analgesics with levobupivacaine in paravertebral analgesiaforbreast surgery.Anaesthesia2006;61:932-993.
8. Bhuvaneswari V, Wig J, Mathew PJ, Singh G. Post-operative pain and analgesic requirements after paravertebral block for mastectomy: A randomized controlled trial of different concentrations of bupivacaine and fentanyl. Indian J Anaesth. 2012;56(1):34-39.
9. Mohamed SA, Fares KM, Mohamed AA, Alieldin NH. Dexmedetomidine asan adjunctive analgesic with bupivacaine in paravertebral analgesia for breast cancer surgery.PainPhysician2014; 17:E589–E598.
10. MohtaM,KalraB,SethiAK,KaurN.Efficacyofdexmedetomidine as an adjuvant in paravertebral block in breast cancer surgery. J Anesth2016;30:252–260.
11. Ahmed R. Morsy, Mervat M. Abd-elmaksoud, Rehab A. Abdel Aziz,MohamedMetwally Comparison between dexmedetomidine versus morphine added to bupivacaine in paravertebral block patients scheduled for modified radical mastectomy Research and Opinion in Anesthesia& Intensive Care, Vol. 4 No. 2, April-June 2017,p59-63
12. Ahmad Sabry, M. H. I. Aly, M.Ammar, R. Elgama N. Comparative Study Between Addition of Dexmedetomidine Or Fentanyl to Bupivacaine in Ultrasoun Guided Continous Paravertebral Block in Unilateral Renal Surgery., Anesthesia & Analgesia: September 2016 - Volume 123 – Issue 3S - p 609
13. Hassan, Mohamed Elsayed, and Essam Mahran. "Evaluation of the role of dexmedetomidine in improvement of the analgesic profile of thoracic paravertebral block in thoracic surgeries: A randomised prospective clinical trial." Indian journal of anaesthesia vol. 61,10 (2017): 826-831
14. Wang, Kai et al. "Dexmedetomidine combined with local anesthetics in thoracic paravertebral block: A systematic review and meta-analysis of randomized controlled trials." Medicine vol. 97,46 (2018): e13164.
15. Mukherjee, Anindya et al. "Comparative evaluation of analgesic sparing efficacy between dexmedetomidine and clonidine used as adjuvant to ropivacaine in thoracic paravertebral block for patients undergoing breast cancer surgery: A prospective, randomized, double-blind study." Saudi journal of anaesthesia vol. 12,4 (2018): 548-554.
16. Bakeer, Ahmed H, and Nasr M Abdallah. "Transdermal fentanyl as an adjuvant to paravertebral block for pain control after breast cancer surgery: A randomized, double-blind

controlled trial." Saudi journal of anaesthesia vol. 11,4 (2017): 384-389.

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