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Research Article

Comparision of Postoperative Analgesia Provided By Multilevel Thoracic Paravertebral Block Using Bupivacaine (0.5%) Alone & With Clonidine in Breast Surgery: A Prospective Double Blind Study

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Abstract: **Objectives**: Paravertebral nerve block is an anaesthetic technique that results in less postoperative pain, nausea and vomiting. The aim of our study was to compare the postoperative analgesia provided by multilevel thoracic paravertebral block (TPVB) of bupivacaine alone and with clonidine in various breast surgeries without axillary dissection. **Methods:** The prospective study of 50 patients posted for various breast surgeries were randomly divided into 2 groups. Group B received TPVB using 0.5% bupivacaine 19 ml + 1 ml NS to make 20 ml solution; Group BC received TPVB using 0.5% bupivacaine 19ml + clonidine (1µg/kg) + NS to make 20 ml solution, given 5 ml at each of four injection sites (T_1, T_3, T_5, T_7). Variables of efficacy [VAS up to 24 hrs, time for first rescue analgesic (whenever VAS≥3) and amount of tramadol consumption in 24 hours] were noted. Sedation and duration of analgesia were also noted. **Results:** Patients characteristics, vital parameters and anaesthetic techniques were comparable between the two groups. Duration of analgesia was significantly longer in group BC as compared to group B (p=0.005). The VAS scores were significantly low in group BC at 8 and 12 postoperative hours. Patients in group BC were sedated postoperatively at 0 hour (at time of shifting), which was statistically significant when compared to group B. **Conclusion:** We concluded that bupivacaine (0.5%) with clonidine (1µg/kg) produces significantly higher duration of analgesia and less postoperative pain as compared to bupivacaine (0.5%) alone when used in thoracic paravertebral nerve block for breast surgeries.

Keywords: Breast surgery, Thoracic paravertebral nerve block, Analgesia, Bupivacaine, Clonidine.

INTRODUCTION:

Breast cancer is the second most common cancer among Indian women, a study conducted by the International Association of Cancer Research, reported 1 lac breast cancer cases annually in India and projected a 3 percent increase per year. (Bagchi S., 2008).After diagnostic confirmation, vast majority of breast disease patients undergo definitive surgery, most commonly modified radical mastectomy or lumpectomy with axillary dissection.(Osteen RT, Winchester DP, 1995).

Acute postoperative pain can adversely affect coughing & deep breathing which can result in respiratory complications such as hypoxia, atelectasis, chest infection and respiratory failure that may delay recovery and if severe could be life threatening and may also contribute to development of chronic pain syndrome.(Kavanagh BP *et al.*, 1994).

Patient controlled intravenous analgesia with opioids remains a common strategy for management of postoperative pain (Macintyre PE., 2001). However, this method is far from ideal because efficacy is suboptimal and side effects such as nausea, vomiting and sedation, are frequent. Systemic opioids are not potent enough to control neurogenic pain without detrimental effects on respiratory outcome. This lead to the search for alternative analgesic regimens without above mentioned adverse effects.

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TPVB is a regional anaesthetic technique that can uniquely eliminate cortical responses to thoracic dermatomal stimulation. It is the technique of injecting local anaesthetic adjacent to thoracic vertebra close to where the spinal nerves emerge from intervertebral foramina. This results in ipsilateral somatic and sympathetic nerve blockade in multiple contiguous thoracic dermatomes above and below the site of injection.(Cheema SP *et al.,* 1995) It is effective in treating acute and chronic pain of unilateral origin from chest and abdomen.(Carabine UA *et al.*,1995; Eason MJ *et al.*,1979) Bilateral use of TPVB has also been described.(J. Richardson *et al.*, 2011). Understanding of safety and efficacy of TPVB has improved significantly in last two decades prompting its use in children and neonates and for surgical anaesthesia.(Cheung SL *et al.*, 1997; Down CS *et al.*, 1997; Greengrass R *et al.*, 1997; Ebrahimy M *et al.*, 2009). TPVB appears promising due to reduction in postoperative pain, decreased opioid consumption which leads to reduction in postoperative nausea and vomiting (PONV), drowsiness, risk of respiratory depression and cost saving.(Gilbert J *et al.*, 1989). This study is planned to evaluate efficacy of clonidine (1µg/kg) as an adjuvant to 0.5% bupivacaine in TPVB by 4 injection technique at T_1,T_3,T_5,T_7 level for postoperative analgesia in patients undergoing different breast surgeries.

METHODS:

This study was conducted in department of anaesthesiology, MB Govt. Hospital attached to RNT medical college udaipur, after obtaining approval from the institutional ethical committee. Written informed consent was taken from patients scheduled to undergo various breast surgeries. Type of breast disorders that was included in this study were fibroadenomas, fibrocystic diseases, sclerosing disorders, periductal mastitis, nipple inversion, duct ectasia, intraductal papillomas, atypical lobular hyperplasia and atypical ductal hyperplasia.

Exclusion Criteria Were:

Patient refusal for PVB, age < 18 years, ASA grade> II, patient having severe respiratory/cardiac or renal disorders, infection at the injection site, any acute psychiatric illness, allergy to drugs used, morbid obesity (body mass index>35), coagulation disorders, severe spine and chest wall deformities, pregnancy, lactating mothers and mastectomy with axillary dissection.

All patients were randomly allocated to one of two groups using random number in opaque sealed envelopes:

- Group B- Multilevel TPVB using 0.5% bupivacaine (19ml) + 1 ml normal saline to make 20 ml solution: 5 ml at each of four injection sites (T_1, T_3, T_5, T_7)
- Group BC- Multilevel TPVB using 0.5% bupivacaine (19ml) + clonidine(1µg/kg) + normal saline to make 20 ml solution: 5 ml at each of four injection sites (T_1, T_3, T_5, T_7).

All patients received Inj. Diclofenac 75 mg i.m and inj. Midazolam 2 mg i.v 1/2 hour before block. After standard monitoring (ECG, NIBP, SpO_2) and peripheral venous access with 18G cannula, all patients were given TPVB on ipsilateral side to the breast being operated as described below under all aseptic precautions.

Block Procedure:

The block was performed in sitting position by using the technique described by **Moore (1965) and Katz (1994).** Superior spinous process of thoracic level T_1-T_7 were identified. Block was given in our study at T_1, T_3, T_5, T_7 levels. Entry site was marked 2.5 cm lateral to each spinous process ipsilateral to operative breast. All injection site got infiltration of 1% lignocaine (2-3ml) and PVB was given by using a 22 gauge, 3.5 inch long Quincke spinal needle. The shaft of needle grasped by dominant hand and was inserted through entry site and advanced anteriorly in parasagittal plane (perpendicular to the back in all direction) until it contacts transverse process. The needle was then withdrawn to subcutaneous tissue and angled to walk off the caudal edge of transverse process. From caudal edge, it was then advanced anteriorly approximately 1cm. Loss of resistance or a subtle "pop" was felt as needle passed through superior costotransverse ligament. After aspiration of syringe, drug was given at each level according to group (T_1, T_3, T_5, T_7).

General anaesthesia was then induced using propofol (2-3 mg/kg) and fentanyl (1-2µg/kg) followed by vecuronium (0.1mg/kg). Three minutes after vecuronium administration, a laryngeal mask airway (LMA, No. 3-4) inserted & patient ventilated with 100% oxygen through bain's circuit. Anaesthesia was maintained with isoflurane (0.8-1.2%) titrated to signs of an adequate depth of anaesthesia. Boluses of fentanyl (50-100µg) i.v. were given intra operatively if heart rate and mean blood pressure increases more than 20% from baseline. If heart rate and mean blood pressure remain persistently>20% from baseline even after 2 boluses of fentanyl then that case were excluded from study. Isoflurane was stopped 5 minutes prior to last suture. Neuromuscular blockade was reversed with neostigmine 0.05mg/kg and glycopyrrolate 0.01mg/kg. Suction of oral cavity was done and LMA removed on recovery from anaesthesia. Orientation to time, place and person was assessed.

Parameters like pulse rate (PR), mean blood pressure (BP) and oxygen saturation (SPO_2) were recorded before blockade, after blockade, after induction and after insertion of LMA, intraoperatively, before shifting patient to postoperative ward and thereafter at 4^{th}, 8^{th}, 12^{th} and 24 hrs.

The primary outcome was cumulative consumption of intravenous tramadol (2 mg/kg**)** over 24 hours in both groups. Pain score was measured using a 10 points (0-10) Visual Analogue Scale (VAS). The VAS was recorded on rest (R), cough(c), movement (M-forward hand movement) at 0, 4, 8, 12, 24hours postoperatively (0 hours - the time when patient shifted from operation theatre to ward). Time for first rescue analgesic (tramadol 2mg/kg) was also noted, which was to be given whenever VAS ≥ 3, as well as any complications were noted down.

Observer assessment of alertness and sedation (OAA/S) score (1-5) was used to assess level of postoperative alertness and sedation, where 5= patient responds readily to name spoken in normal voice; 4= patient asleep but arousable to normal tone voice; 3= patient asleep but arousable to loud or repeated verbal stimulation; 2= patient asleep but arousable by mild prodding or shaking; 1= comatose patient.(Bhatnagar S *et al.*, 2006)

Sample size& Statistical Analysis:

Based on previous study done by CL Burlacu et al.(2006), minimum sample size of 23 patients in each group was required to detect a differrence of 10 mg consumption of rescue analgesic with a power of 90% (β = 0.10) and confidence interval of 95%(α = 0.05%). Considering the possibility of drop outs, we took 25 patients in each of 2 groups. Statistical data were entered and analyzed by using MS excel, Epi Info 6 and SPSS. Quantitative data were represented as arithmetic mean or standard deviation and analyzed by using Student t- test or ANOVA as per need. Qualitative data was represented as number (proportion or %) and analyzed with chi square test. [P<0.05 was considered statistically significant].

RESULTS:

Table 1 shows that both the groups were comparable regarding demographic profiles and baseline vitals (pulse rate, mean arterial pressure and SpO_2) [P>0.05].

Table 1: Demography and baseline vital parameters

Variables	Group B (n=25)	Group BC(n=25)	P value
Mean Age (years)±SD	49.20±12.75	46.80±14.10	0.53
Mean Weight (kg)±SD	56.76±4.20	56.20±5.35	0.68
Baseline pulse rate (per minute)	83.28±7.27	86.68±11.43	0.22
Baseline mean blood pressure (mm hg)	96.96±7.29	96.28±7.80	0.75
Baseline SpO_2(%)	98.24±0.83	98.00±0.64	0.26

Table 2 summarises the intra-operative vital parameters at 30 minutes of surgery and mean dose of fentanyl used intraoperatively. No statistical significant difference was found in between the groups. Both the groups were comparable with respect to intraoperative pulse rate, mean arterial pressure, spo_2 and fentanyl dosage.[P>0.05].

Table 2: Intra-operative parameters

Parameters	Group B (n=25)	Group BC (n=25)	P value
Pulse rate at 30 min. (per min.) (mean ±SD)	85.40±8.47	83.84±11.60	0.59
Mean arterial pressure at 30 min. (mmHg) (mean ±SD)	98.60±7.31	96.32±6.14	0.24
SpO_2 at 30 min.(%) (mean ±SD)	99.44±0.50	99.40±0.50	0.78
Fentanyl dose(µg) (mean±SD)	190.00±57.28	189.00±64.58	0.95

Pain intensity at rest, cough, and forward hand movement measured using VAS score (0-10 cm scale) was significantly low in group BC at 8 and 12 postoperative hour, as compared to group B(P=0.000 and P=0.050 respectively at 8 and 12 postoperative hour). OAA/S score was significantly lower in group BC at time of shifting (0 hrs) as compared to group B (P=0.01) [Table 3].

Table3: VAS score and OAA/S score

Variables	Group B (n=25)	Group BC (n=25)	P value
VAS score at 8 hrs (at rest)	0.28±0.61	0.00	0.03
VAS score at 12 hrs (at rest)	0.44±0.65	0.08±0.28	0.01
VAS score at 8 hrs (at cough)	1.24±0.88	0.00	0.00
VAS score at 12 hrs (at cough)	1.36±0.81	0.56±0.58	0.00
VAS score at 8hrs (at FHM)	1.56±0.77	0.00	0.00
VAS score at 12hrs (at FHM)	1.56±0.87	1.12±0.67	0.05
OAA/S Score at 0 hrs	5.00	4.76±0.44	0.01
OAA/S Score at 4 hrs	5.00	4.92±0.28	0.15

VAS- Visual analogue score, OAA/S- Observer's Assessment of Alertness and Sedation score and FHM- Forward hand movement.

Mean duration of analgesia (as calculated by time when first rescue analgesic was given) was significantly higher in group BC (23.53hrs) as

compared to group B (19.37hrs).(P=0.005). Both groups were comparable in terms of mean total dose of rescue analgesics required in 24 hrs postoperatively. However, rescue analgesic requirement was lower in group BC as compared to group B but this could not reach value for significance (P =0.060).[Figure I and II]

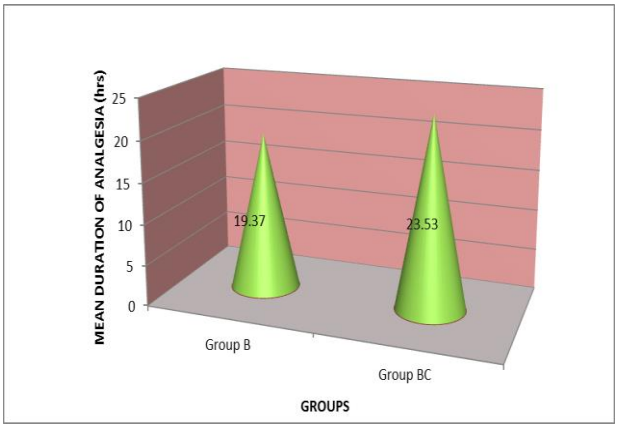

Figure I: comparison of duration of analgesia in both groups.

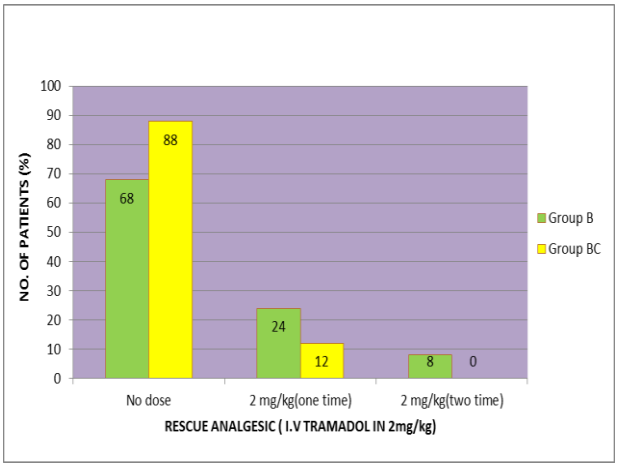

Figure II: comparison of rescue analgesic requirement in between the groups

DISCUSSION:

The increasing popularity of paravertebral analgesia as an effective method of intra and postoperative pain relief for breast surgeries warrants more research on combinations of local anaesthetics and adjuvant analgesics. Bupivacaine 0.5% is used traditionally for this block. The major disadvantage is its relatively short duration of analgesia which can be solved by addition of analgesic adjuvant to bupivacaine. The addition of adjuvant such as fentanyl and clonidine to local anaesthetics has been shown to enhance the quality and duration of sensory neural blockade and decrease the dose of local anaesthetic.(Burlacu CL *et al.*, 2006; Bhatnagar S *et al.*, 2006; Eisenach JC *et al.*, 1996).

Clonidine, a partial α_2 adrenergic agonist, produces an anti-nociceptive effect and improves analgesic efficacy when combined with local anaesthetic. Clonidine enhances both sensory and motor blockade from local anaesthetic used for epidural or peripheral nerve block. A postulated mechanism for this is that clonidine blocks conduction of C and A-delta fibres and increases potassium conductance in isolated neurons in vitro, thus intensifying conduction block. Secondly, clonidine causes local vasoconstriction in the clinical setting, thereby reducing vascular uptake of local anaesthetic from around the neural structures.(Burlacu CL *et al.*, 2006; Bhatnagar S *et al.*, 2006).

In our study both groups were comparable to each other in terms of demographic data and type of breast disease for which surgery was being performed. There were no significant differences in terms of the time required for performance of the block and intraoperative fentanyl consumption in both groups. Both groups were comparable in terms of perioperative vital parameters and side effects such as arterial hypotension, bradycardia and fall in oxygen saturation.

Pain intensity measured postoperatively using VAS (0-10) score at rest, cough and forward hand movement was significantly low in group BC at 8 and 12 postoperative hour, as compared to group B. For rest of the time intervals, both groups were comparable in terms of pain intensity. This was in accordance with the study by Bhatnagar S *et al.*, (2006) who found that mean of all VAS scores at rest and on coughing was significantly lower in bupivacaine+ clonidine group as compared to the group receiving bupivacaine alone at all time points. This may be attributed to continuous infusion of clonidine through paravertebral catheter besides a loading bolus.

Mean total dose of rescue analgesic in group BC was lower as compared to group B. However, this could not reach value for statistical significance. This is consistent with study done by Burlacu CL *et al.*, (2006) who found that mean 24 hrs rescue morphine consumption was significantly decreased in group using clonidine (5.9±3.5mg v/s 27.7±8.6 mg with P value<0.01), this was also consistent with the study by Bhatnagar S *et al.*,(2006).They observed that two patient in group bupivaciane+clonidine requested analgesia on first postoperative day and this was achieved with intravenous morphine 6mg. Among bupivacaine group three patients requested analgesia on first postoperative day and they required i.v morphine 15 mg, 9 mg and 6 mg respectively.

Duration of analgesia was also higher in group BC (mean- 23.54± 1.32 hrs.) as compared to group B (19.38±6.85 hrs.) which was statistically significant. Similarly in a study by Kulkarni *et al.*, (2012) duration of analgesia in group bupivacaine +clonidine (386±38

min.) was found to be longer as compared to 198±28 min. in group bupivacaine (P value<0.001).

No statistically significant difference in between the groups was found in respect to pulse rate, mean arterial pressure and respiratory rate measured postoperatively at varied time intervals. In contradiction, study done by Burlacu CL *et al.,* ; Bhatnagar S *et al.,* (2006) showed that systolic blood pressure at any measured time interval was significantly lower in group using clonidine as compared to other groups. This difference in these two studies regarding blood pressure may be attributed to continuous infusion of clonidine in both the studies via a catheter left in paravertebral space as opposed to single shot injection in our study.

Patients in group BC were sedated (mean-4.76, 1-5 grade of sedation as per OAA/S score) postoperatively at 0hr (at time of shifting) which was statistically significant when compared to group B (mean-5). For rest of the time intervals postoperatively, both groups were comparable regarding sedation scores. Higher sedation scores in group given clonidine were also seen in studies done by Bhatnagar S *et al.,* (2006) and Chakraborty S *et al.,* (2010) However, in study done by Bhatnagar S *et al.,* (2006) sedation score were significantly higher in group using clonidine at each point of time postoperatively as opposed to higher sedation only in immediate postoperative period in our study. This can again be attributed to continuous infusion of clonidine through paravertebral catheter in their study as opposed to a single bolus dose given in our study.

CONCLUSION:

We advocate that addition of clonidine in dose of 1µg/kg may be used as an adjuvant to 0.5% bupivacaine for multilevel thoracic paravertebral block as it significantly reduces postoperative pain and total analgesic consumption and prolong postoperative analgesia in patients undergoing breast surgeries without added problems apart from low grade sedation in early postoperative period.

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