ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

A Randomized Prospective Study Of Comparison Between Levobupivacaine And Combination Of Levobupivacaine With Nalbuphine As An Adjuvant In Thoracic Paravertebral Block For Postoperative Analgesia After Breast Surgeries.

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ABSTRACT

General anaesthesia is the traditional technique used for surgical treatment of breast surgeries. Incidence of postoperative pain in breast surgery patients is as high as 50% (8). Since the last two decades, there is a search for the best and ideal regional techniques for operative procedures on the breast and axilla, which would reduce post-operative nausea and vomiting caused by drugs such as Tramadol and also to provide prolonged post-operative sensory block, reducing the systemic narcotic requirements. To compare the effect of 0.125% of Levobupivacaine versus 0.125% of Levobupivacaine with Nalbuphine as an adjuvant in thoracic paravertebral block to manage postoperative pain after breast surgeries. Prospective randomized study involves ASA-I, II, III female patients of age group 18 to 60 years scheduled for breast surgery. Sample size was 60. These patients were assigned into two 30-members group: Group I who received 15ml of Levobupivacaine 0.125% and group II who received 15ml of Levobupivacaine 0.125% + 10mg (1ml) of Nalbuphine in thoracic paravertebral block using 16-gauge, 8 cm Tuohy needle by classical technique. Demographic data, intraoperative SPO2, HR, SBP and DBP were recorded. Time of onset of pain in the postoperative period were recorded during the initial 2 hours and 4, 8, 12, 16, 20, 24, 36, and 48 hours. Also, postoperative opioid consumption, time to the first analgesic request, and any complications were also recorded. There was no statistically significant differences among the two groups regarding demographic data, SPO2, HR, SBP and DBP intraoperatively. Moreover, no significant difference was found in HR, SBP and DBP postoperatively. Postoperative pain scores were significantly lower in group B, whether at rest or movement. There was a significantly lower postoperative opioid consumption in group B and a significantly longer time to the first analgesic request than group A. No complications were reported in any group. Addition of Nalbuphine 10 mg as an adjuvant to Levobupivacaine local anaesthetic in group B improved the quality of the block and decreased postoperative analgesic requirements than the Levobupivacaine only group. Adding Nalbuphine to Levobupivacaine increased the time to the first analgesic request without associated adverse effects.

Keywords: Levobupivacaine 0.125%, Nalbuphine, Paravertebral Block, VAS, Rescue analgesia.

https://doi.org/10.33887/rjpbcs/2024.15.3.37

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ISSN: 0975-8585

INTRODUCTION

Paravertebral block has been used for unilateral procedures such as thoracotomy, breast surgery, chest wall trauma, hernia repair and renal surgery. Hugo Sellheim of Leipzig was a pioneer in the concept of Paravertebral block in 1905 for obstetric surgeries. It was further refined by Lawen (1911) and Kappis (1919) [7]. Reappraisal on TPVB was presented by Eason and Wyatt [2]. The cortical responses to thoracic dermatomal stimulation can be particularly eliminated by paravertebral block. It is associated with reduced need for opioids for controlling pain, decreased nausea and vomiting and reduced pulmonary complications in the postoperative period [6], improved patient outcome and finally decreased duration of stay in the post-anaesthesia care unit [5]. Establishment of a block necessary for breast surgeries is easily done by the injection of local anaesthetic drug into the thoracic paravertebral space without any significant side effects. In our study we used Levobupivacaine which is an amino-amide local anaesthetic drug. It is the S-enantiomer of Bupivacaine [3]. Less hemodynamic variations and increased quality of block is seen with Levobupivacaine [4]. With its efficacy, lower propensity for motor block and reduced potential for cardiotoxicity and central nervous system toxicity, Levobupivacaine appears to be an important option for regional anaesthesia and management of postoperative pain. Nalbuphine is a synthetic opioid agonist-antagonist analgesic. Opioid induced respiratory depression is much reduced, in preoperative and postoperative analgesia it is used as a supplement to balanced anaesthesia [1]. Adjuncts to local anaesthetics can add value to the superiority and time length of analgesia [9].Therefore we conducted this study in order to evaluate the postoperative analgesic effects of levobupivacaine and combination of Levobupivacaine with Nalbuphine in thoracic paravertebral block in breast surgeries.

MATERIALS AND METHODS

This randomized, prospective study was carried out on total 60 patients of ASA I,II and III after obtaining approval from ethical committee and written informed consent from the patients.60 patients randomly divided into 2 groups (N=30)Group I: Received Levobupivacaine 0.125% (15ml) Group II: Received Levobupivacaine 0.125% (15 ml) +10 mg (1ml) of Nalbuphine. The study was carried out on female patients of 18-60 years who underwent breast surgeries.

Inclusion Criteria

- Female patients.
- Women giving informed consent.
- ASA I, II and III patients posted for elective breast surgeries.
- Females of age group 18-60 years.

Exclusion Criteria

- Women not giving consent.
- Women who are subjected to surgery on both sides or reconstruction of the breast.
- Infection at the site of injection.
- Anticoagulant use.
- Coagulopathy.
- Hypersensitivity to local anaesthetic agent.
- Pregnant women.
- Those with central neuropathy or those with renal or hepatic diseases.
- Individuals with psychiatric disorders.
- Overweight patients with a BMI > 30.
- ASA IV patients.

Pre-Anaesthetic Assessment

On the day of surgery patients who satisfy the inclusion criteria were selected and written informed consent obtained from all the patients. Preoperative evaluation including detailed history, clinical evaluation, investigations were done. The procedure was carried out in the operation theatre where facilities for resuscitation were available. Routine monitoring was done with ECG, Pulse Oximetry, NIBP, ETCO2. Intravenous cannulation done with 18G venflon and IV fluids started. Before block placement

incremental doses of IV midazolam(upto to a maximum dose of 0.06mg/kg) given to decrease anxiety and discomfort during the procedure.

Methodology

Patients were randomly divided into two groups as designated above and demographic data were noted. Baseline vital parameters were noted.

Technique

Anatomical landmark technique was used to identify the paravertebral space. Under strict aseptic precautions at the appropriate dermatome, 2.5-3 cms lateral to the most cephalad aspect of the spinous process, 16-gauge, 8 cm Tuohy needle is inserted and advanced perpendicular to the skin to contact the transverse process of the vertebra below depending on the built of the individual at a variable depth (2–4 cms). It is possible that the needle tip is lying between adjacent transverse processes if bone is not encountered at this depth. Before advancing the needle any further, it is important to locate the transverse process to prevent inadvertent deep insertion and possible pleural puncture. This is done by withdrawing the needle to the subcutaneous plane and redirecting it cephalad and caudad to the same depth until bone is encountered. The needle is advanced further centimetres if the bone is still not encountered, and the above process is repeated until the transverse process is contacted.

The needle is then walked above the transverse process and advanced gradually until a subtle "pop" or a loss of resistance to air or saline is felt as the needle tip pierces the thin superior costotransverse ligament usually within 1–1.5 cms from the superior edge of the transverse process. Local anaesthetic is injected after gentle aspiration in the thoracic paravertebral space.

Patients were observed for specific complications like,

- Pneumothorax.
- Horner's syndrome.
- Hypotension.
- Vascular puncture.

Pain severity was measured using

Visual Analogue Scale (VAS) rating from 0 to 10. 0 indicates no pain, 10 indicates worst intolerable pain.

Statistical Analysis

Data analysis was performed using Microsoft Access and SPSS software version 18. Two-way ANOVA test was used to compare quantitative parametric data. Chi square test was used to compare qualitative data .P value equal to or less than 0.05 was considered to be significant.

Demographic Data

Patient's age, weight, height, BMI and ASA physical status were considered as demographic parameters. Age, weight, height and BMI were analyzed by using ANOVA and chi-square test was used to analyze ASA physical status. Both groups were comparable in terms of age, weight, height, BMI and ASA physical status. [Table 1 &2]

ISSN: 0975-8585

Table 1: Demographic profile of the study population

	Group	N	Mean	Std. Deviation	Std. Error Mean	t value	P value
AGE	Group A	30	36.467	8.123	1.483	1.375	0.174
	Group B	30	39.367	8.211	1.499		
Ht in cms	Group A	30	156.467	3.491	0.637	1.048	0.299
	Group B	30	157.400	3.410	0.623		
Wt in Kg	Group A	30	59.267	6.313	1.153	1.82	0.074
	Group B	30	56.500	5.425	0.990		
BMI in Kgm2	Group A	30	24.200	2.415	0.441	2.35	0.453
	Group B	30	22.806	2.174	0.397		

Data are presented in Mean ± SD or absolute numbers. P value>0.05 is statistically insignificant.

The mean age of the patients in Group A and Group B was 36.467 and 39.367 years respectively. Statistically there was no significant difference between the groups (p=0.174).

The mean weight of the patients in Group A and Group B was 59.267 and 56.50 kgs respectively. Statistically, there was no significant difference between the groups (p=0.074).

The mean height of the patients in Group A and Group B was 156.467 and 157.400 cms respectively. Statistically, there was no significant difference between the groups (p=0.299).

The mean BMI of the patients in Group A and Group B was 24.200 and 22.806 respectively.Statistically, there was no significant difference between the groups (p=0.453).

American society of Anesthesiologists (ASA) physical status ratio (I/II/III) was 21/8/1 in patients of Group A and 17/13/0 in patients of Group B. Both groups did not differ significantly in their ASA Physical status (p=0.271).

Table 2: ASA PS status of the study population

			Group		Total
			Group A	Group B	
ASA Status	I	Count	21	17	38
		% within Group	70.0%	56.7%	63.3%
	II	Count	8	13	21
		% within Group	26.7%	43.3%	35.0%
	III	Count	1	0	1
		% within Group	3.3%	0.0%	1.7%
Total		Count	30	30	60
		% within Group	100.0%	100.0%	100.0%

Table 3: Duration of surgery and time of onset of pain

	Independent t test					
	Group	N	Mean	Std. Deviation	Std. Error Mean	t value
Duration of surgery in minutes	Group A	30	90.8333	30.31681	5.53507	4.254**
	Group B	30	119.8333	21.79384	3.97899	
Time of onset of pain postoperatively (minutes)	Group A	30	425.3333	57.99723	10.58880	18.550**
	Group B	30	917.0000	133.08411	24.29772	

ISSN: 0975-8585

Table 4: VAS of the study population

Descriptive Statistics				
	Group	Mean	Std. Deviation	N
6 Hrs	Group A	0.5667	1.30472	30
	Group B	0.0000	0.00000	30
	Total	0.2833	0.95831	60
8 Hrs	Group A	3.2667	1.14269	30
	Group B	3.0667	1.14269	30
	Total	3.1667	1.13745	60
12 Hrs	Group A	4.4667	0.81931	30
	Group B	3.3667	0.76489	30
	Total	3.9167	0.96184	60
16 Hrs	Group A	4.9000	1.68870	30
	Group B	3.6000	1.06997	30
	Total	4.2500	1.54728	60
20 Hrs	Group A	3.6333	1.44993	30
	Group B	3.1333	0.86037	30
	Total	3.3833	1.20861	60
24 Hrs	Group A	2.5333	1.10589	30
	Group B	2.2667	0.78492	30
	Total	2.4000	0.96023	60
48 Hrs	Group A	2.0000	1.20344	30
	Group B	1.2000	0.71438	30
	Total	1.6000	1.06086	60

Requirement Of Opioid Doses In 48 Hrs

Majority of the Group A patients required two doses of opioid in 48 hrs and Group B patients required one dose of opioid in 48 hrs. The association between the intervention groups and number of doses of opioid required in 48 hrs is considered to be statistically significant since the p value is 0.015 as per ANOVA test.

Table 5: Requirement of opioid doses in 48 hrs

Requirement of opioid doses in 48 Hrs					
			Group		Total
			Group A	Group B	
Requirement of opioid doses in 48 Hrs	.00	Count	7	11	21
		% within Group	23.3%	6.7%	35.0%
	1.00	Count	6	14	17
		% within Group	20.0%	46.7%	28.3%
	2.00	Count	12	3	15
		% within Group	40.0%	10.0%	25.0%
	3.00	Count	5	2	7
		% within Group	16.7%	6.7%	11.7%
Total		Count	30	30	60
		% within Group	100.0%	100.0%	100.0%

DISCUSSION

Pain in the postoperative period is the distressing period for any patient and many drugs are being used for it with varying safety concerns. NSAIDS and Paracetamol are used in many patients but intensity

of analgesia vary from patients to patients which may not be complete pain relief for those with minimal threshold. Opioids might provide better analgesia but leads to many complications particularly when large and cumulative doses are used which needs close hemodynamic and respiratory monitoring in the postoperative period. Nalbuphine, a 14-hydroxymorphine derivative, is a potent analgesic with opioid receptor k agonist and μ antagonist properties. Nalbuphine maintains or augments μ-receptor based analgesia and modifies the μ-receptor side effects. Subduing of serotonin uptake in the neurons causes augmentation of the inhibitory pathways in the spinal cord for pain. Excitation on the central nervous system neurons by opioid receptors causes suppression of intracellular adenylyl cyclase, opening of potassium channels, and closure of the calcium channels. This results in hyperpolarization of the cell membrane potential and also suppression of action potential spread of ascending pain pathways.This study is done to find out whether addition of Nalbuphine as an adjunct to Levobupivacaine in thoracic paravertebral block has real impact on the duration of postoperative pain relief which is the primary outcome measure by comparing with Levobupivacaine alone in patients undergoing breast surgery. In the present study, age group included was between 18-60 years and the mean age of Levobupivacaine only group is 36.467 years and Levobupivacaine and Nalbuphine group is 39.367 years. The association between the intervention groups and the age distribution is not statistically significant. In the study conducted by Omar Mostafa et al, the age groups selected were between 18 to 78 years and the mean age in Bupivacaine and Nalbuphine group is 55.2 years and that of the control group is 55.8 years. In our study and also in Omar Mostafa et al study, age distribution and intervention groups is not statistically ignificant and they were standardised. Hence selection bias was excluded. In the present study, the mean weight of Levobupivacaine only group is 59.267 kgs and Levobupivacaine and Nalbuphine group is 56.500 kgs. The association between the intervention groups and the weight distribution is not statistically significant. In the study conducted by Omar Mostafa et al, the mean weight in Bupivacaine and Nalbuphine group is 80.6 kgs and that of the control group is 80.3 kgs. There was no statistical significance difference between the groups in our study and Omar et al study and hence selection bias was excluded. In the present study, the mean height of Levobupivacaine only group is 156.467 cms and Levobupivacaine and Nalbuphine group is 157.400 cms. The association between the intervention groups and the height distribution is not statistically significant.In the study conducted by Omar Mostafa et al, the mean height in Bupivacaine and Nalbuphine group is 169.5 cms and that of the control group is 169.9 cms. There was no statistically significant difference in height selection between groups in both studies and hence selection bias was excluded.

In the present study, the mean BMI of Levobupivacaine only group is 24.200 and Levobupivacaine and Nalbuphine group is 22.806. The association between the intervention groups and the BMI distribution is not statistically significant. In the study conducted by Omar Mostafa et al, the mean BMI in Bupivacaine and Nalbuphine group is 28.1 and that of the control group is 27.8. There was no statistical significant difference in BMI in both studies. In the present study, American society of Anaesthesiologist (ASA) physical status I, II and III were enrolled and there is no statistical significant difference in both the groups. In Omar et al study, ASA I to III physical status were included and they were standardised in all three groups. In the present study, the mean duration of sensory blockade in Levobupivacaine only group is 425.333 minutes and in Levobupivacaine and Nalbuphine group is 917.000 minutes. The mean sensory block duration time was significantly longer in Levobupivacaine and Nalbuphine group compared to Levobupivacaine only group by a mean difference of 491.667 minutes. This difference is significant with a p value of <0.05 as per two way repeated measure ANOVA test.The present study showed that addition of 1ml of Nalbuphine of 10mg to 15mL 0.125% of Levobupivacaine in Levobupivacaine and Nalbuphine group improved the quality of the block and thus improvement in the pain scores and time to the first analgesic request was prolonged to 917.000 minutes with a statistical significance of $P<0.05$ compared to Levobupivacaine only group which was 425.333 minutes.In our study the VAS score was high at 6 to 8 hrs with a mean of 4.4667 in Levobupivacaine only group and the VAS score was high at 12 to 16 hrs with a mean of 3.3667 in Levobupivacaine and Nalbuphine group. The association between the intervention groups and the VAS score distribution is statistically significant. This indicates that the time of onset of pain in the postoperative period is prolonged in Levobupivacaine and Nalbuphine group compared to only Levobupivacaine group. In our study there was no intraoperative or postoperative complications related to the drug and the technique which was described earlier.

CONCLUSION

Addition of Nalbuphine as an adjuvant to Levobupivacaine in thoracic paravertebral block in breast surgeries provide intense sensory blockade for more than 12 hrs in the postoperative period. The

requirement of number of doses of opioids postoperatively is reduced considerably on addition of Nalbuphine to Levobupivacaine. Time to the first analgesic request was longer in Nalbuphine and Levobupivacaine group compared to Levobupivacaine only group in the postoperative period.Adverse effects such as postoperative nausea and vomiting and other complications like respiratory depression was significantly lower in Nalbuphine and Levobupivacaine group.

REFERENCES

[1] Blumberg H, Dayton HB, and Wolf PS. Analgesic properties of the narcotic antagonist EN -2234A Pharmacologist 10:1967.

[2] Eason MJ, Wyatt R. Paravertebral thoracic block-a reappraisal. Anaesthesia 1979;34(7):638–42.

[3] McLeod GA, Burke D. Levobupivacaine. Anaesthesia 2001; 56:331-41.

[4] Casati A, Santorsola R, Aldegheri G, Ravasi F, Fanelli G, BertiM,et al. Intraoperative epidural anesthesia and postoperative analgesia with Levobupivacaine for major orthopedic surgery: A double-blind, randomized comparison of racemic Bupivacaine and Ropivacaine. J Clin Anesth 2003; 15:126-31.

[5] Dabbagh A, Elyasi H. The role of paravertebral block in decreasing postoperative pain in elective breast surgeries. Med Sci Monit 2007;13:CR464-7.

[6] Joshi GP, Bonnet F, Shah R, Wilkinson RC, Camu F, Fischer B, et al. A systematic review of randomized trials evaluating regional techniques for post-thoracotomy analgesia. Anesth Analg 2008; 107:1026-40.

[7] Eid HEA. Paravertebral block: An overview. Curr Anaesth Crit Care 2009;20(2):65–70.

[8] 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; 302:1985-92.

[9] Hemati K, Zaman B, Hassani V, Imani F, Dariaie P. Efficacy of Fentanyl transdermal patch in the treatment of chronic soft tissue cancer pain. Anesth Pain Med 2015;5(1).e22900.

[10] Chatrath V, Attri JP, Bala A, Khetarpal R, Ahuja D, Kaur S.Epidural Nalbuphine for postoperative analgesia in orthopedic surgery. Anesth Essays Res. 2015;9(3):326–30.