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Comparative Study To Show The Efficacy Of Throacic Paravertebral Block, With And Without Dexmedetomidine, Versus General Anesthesia In Modified Radical Mastectomies.

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ABSTRACT

In National Cancer Institute, most of the patients diagnosed to have breast cancer undergo modified radical mastectomy operation. In our study, we are searching for new anesthetic modalities that may decrease the postoperative complications (as PONV and pain) as well as the postoperative hospital stay with minimal associated complications. To assess safety and efficacy of the regional paravertebral block anesthetic technique, with and without dexmedetomidine, for operative management of breast cancer. 150 patients divided into three equal groups, the first group (control) received general anesthesia, the second group (TPVB) received thoracic paravertebral block with bupivacaine and sedation, the third group (TPVBD) received thoracic paravertebral block with bupivacaine and dexmedetomidine and sedation. Need for extra sedation or conversion to GA was detected. Also serial measurements of SBP, DBP, HR, VAS was done, monitoring for occurrence of complications, PACU and hospital stay and finally opioid consumption were detected. There were significant differences between TPVB and TPVBD groups on one side and control group on the other side as regards the haemo dynamics, VAS, opioid consumption and LOS in PACU denoting that the use of PVB is preferable, yet there was increased need for either sedation or general anesthesia in the TPVB and TPVBD groups specially on elevating the upper flap and in the axillary evacuation. There was significant difference between TPVB and TPVBD groups in HR measurements. we could conclude that the paravertebral block with single injection and a catheter placement as an isolated modality of anesthesia for cases undergoing modified radical mastectomy could be insufficient as the spectrum of nerve supply needed to be blocked is far beyond that could be blocked by single injection. Yet, it could be sufficient in other types of breast surgeries in which there is no encroachment over cervical supply.

Keywords: Paravertebral block, mastectomies, dexmeditomidine, breast surgeries

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INTRODUCTION

In the National Cancer Institute, as in most of other places, most of cases which are diagnosed to have breast cancer undergo definitive surgery, most commonly modified radical mastectomy (MRM) or lumpectomy with axillary dissection. Generally, these surgical procedures are used to be performed using general anesthesia which is supposed to be followed by inpatient hospitalization. Great effort was done decrease the hospital costs by reducing the length of hospital stay [1]. For this reason, in the l980's, early discharge of these patients postoperatively with closed suction in place was established as safe, properly tolerated, and had resulted in significant reduction of the costs [1]. However, performing breast cancer surgery on an ambulatory basis used to be limited due to postoperative nausea, vomiting and incisional pain, which are all issues related more to the anesthetic experience.

Nausea and vomiting are common complications that occur in 20% to 50% of all operative procedures [2]. The incidence increases in patients undergoing general anesthesia, in patients experiencing postoperative pain and in female patients specially undergoing breast surgeries [2]. The incidence of nausea and vomiting in the first 24 hours postoperatively was found to be 59% especially with general anesthesia. This was found to prolong the length of the recovery room stay and hospital stay for patients otherwise able to undergo ambulatory surgery [2]. Nausea and vomiting have been described as more debilitating than the operative procedure itself by patients [3]. In addition, general anesthesia cannot achieve adequate postoperative pain control. That is why parenteral narcotic use is routine during the early postoperative period, which increases the incidence of nausea, vomiting, sedation, resulting in increasing recovery room and hospital stays.

Thoracic paravertebral block (TPVB) is now considered to be an ideal alternative to general anesthesia for breast cancer surgery [4]. Its benefits include decreasing the postoperative vomiting and nausea, prolonging postoperative pain relief and potential for ambulatory discharge. Thoracic para- vertebral block is known to relieve acute chest wall pain arising from rib fractures, herpes and pleurisy as well as chronic and acute post-thoracotomy pain [5], in addition to being an anesthetic technique for shoulder and chest surgeries [6]. Recently, many anesthetists have described their experience with paravertebral block for the anesthetic management of breast cancer surgeries, and demonstrated its benefits related to length of stay and pain management [7]. However, its role was mainly confined to analgesia in addition to general anesthesia.

Dexmedetomidine is an alpha-2 agonist that has been recently used in the anesthetic practice, it acts on pre and post synaptic sympathetic nerve terminal as well as central nervous system leading to a decrease in the sympathetic outflow and nor-epinephrine release causing anti-anxiety, sedative, analgesic, sympatholytic and haemodynamic effects [8]. Dexmedetomidine causes an accepted bradycardia and hypotension but the main benefit of this drug is reducing the use of opioid decreasing its side effects which include nausea, and vomiting other than pruritis and respiratory depression [9].

Concerning MRM operations, they involve the complete removal of the breast, together with the thin covering overlying the pectoralis muscles, and most of the lymph nodes located in the axilla. The incision typically measures 15-20 cm and is made in a horizontal fashion unless the tumor is located high in the breast. The chest wall muscles are left intact and not removed. The nipple and areola are removed but most of the skin is left intact, yet a flap is elevated surgically on the upper and lower side to be able to cover the defect after the breast removal (figure 1) [10].

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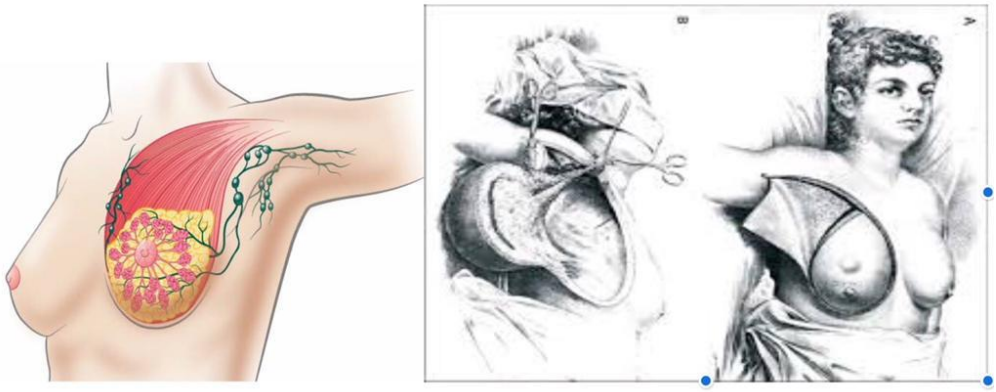

Figure 1: Modified Radical Mastectomy (removal of breast tissue and lymph nodes)(13)

Thoracic paravertebral blockade results in ipsilateral anesthesia. The location of the resulting dermatomal distribution of analgesia or anesthesia is the function of the level blocked and the volume of local anesthetic injected (figure 2)[11].

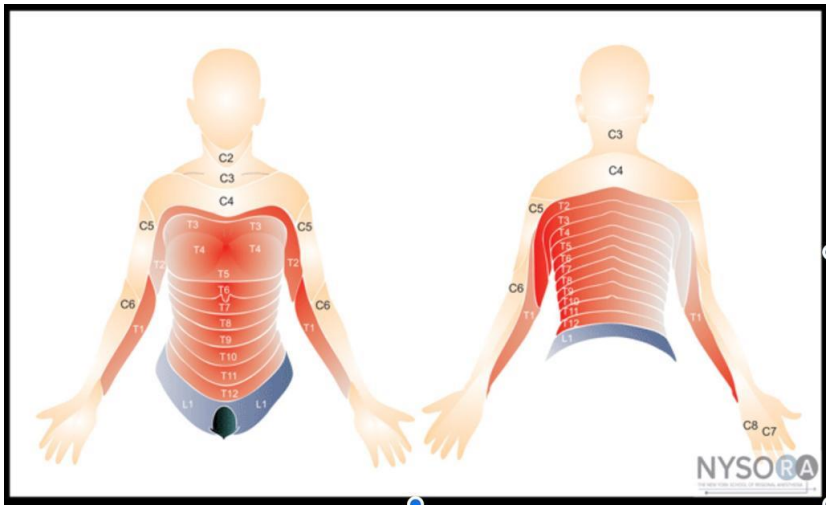

Figure 2: Thoracic dermatomal levels.(14)

Aim of study

To assess safety and efficacy of the regional paravertebral block anesthetic technique, with and without dexmedetomidine, for operative management of breast cancer.

PATIENTS AND METHODS

This study was conducted in National Cancer Institute hospital from May 2015 to May 2017. It was conducted on patients with physical statusII or III according to The American Society of Anesthesia (ASA) classification [12]. They were all scheduled for elective modified radical mastectomy operations.

A randomized controlled, non blind study was conducted. They were randomly divided, by closed envelope technique, into three equal groups of 50 patients each. The first group received general anesthesia (control group), the second group received thoracic paravertebral block regional anesthesia with local anesthetic and dexmedetomidine (TPVBD group), and the third group received thoracic paravertebral block regional anesthesia with local anesthetic only (TPVB group)

Inclusion Criteria:

1. Female patients with an age range of 20 and 55 years old.
2. ASA II or III.
3. Female patients between age of 20 and 55 years old.
4. Undergoing unilateral modified radical mastectomy surgery.
5. Acceptance to be enrolled in the study.

Exclusion Criteria

1. Refusal of enrollment in the study.
2. Coagulopathy.
3. Infection at site of injection.
4. Central neuropathy.
5. Cardiovascular diseases.
6. Allery to local anesthetics.
7. Severe chest diseases.

Anesthetic management: After application of standard monitoring (pulse oximetry, ECG, and non-invasive arterial pressure), all patients were premedicated with 0.02 mg/kg of midazolam and 0.01 mg/ kg atropine intravenously in the holding area. Preoperatively, patients in the (TPVB group) and (TBVBD group) were counseled for awake surgery under sedation. Details of the procedures with the potential to cause discomfort was discussed. Paravertebral block was performed in a monitored preoperative holding area by an attending anesthesiologist using continuous epidural anesthetic set (with low resistance syringe and 18g tougy needle with Weiss modification with epidural catheter 20g, with filter, prefix by B-Braun company). It was placedultrasound guided (by Philips EPIQ 7 G, Philips Ultrasound, WA, USA). The technique used was Transverse In-Line Technique, at the level of T1-2 or T2-3, and a catheter was placed. 20 ml of bupivacaine 0.5% were injected as aloading dose, and infusion with 8ml/hour was kept as maintenance. Intra-operative sedation was provided by titrated doses of propofol (20-50µg/kg/min) so as to allow patients to be arousable on command. Extra sedation was given to patients according to the situation in incremental doses of 30-50 mg propofol upon need. In resistant cases, general anesthesia was shifted to.

Control group received general anesthesia with endotracheal intubation. Induction of anesthesia was done using propofol (2mg/kg), fentanyl (1µg/kg) and atracurium (0.5mg/kg). Maintenance of anesthesia was done by sevoflurane (MAC2%), morphine (0.1mg/kg) and atracurium (0.1mg/kg/20-30minutes).

After surgery, all patients were brought to the recovery room and the length of stay there was documented. All patients were scheduled for overnight stay according to the surgical guidelines followed in the institute. Provision of pain medication was based on assessment of patient need in each case, and all narcotic use was documented. With initiation of solid food intake, all patients were prescribed Naprosyn (500 mg twice daily) as a standing order for 4 days. Postoperative nausea and vomiting was treated with intravenous or intramuscular antiemetics. and the use of these medications was also documented. Patients were discharged when they were able to tolerate oral intake and when adequate pain control on oral analgesia was achieved, yet not before 24 hours post-operative. All patients were given written documentation and were instructed regarding home care of drains and wounds and expected drain output during their preoperative clinic visits. These instructions were reviewed before discharge.

Study Objectives

Our primary end point was detecting the feasibility of undergoing the MRM operation with only thoracic paravertebral block either with or without dexmeditomidine as a single modality of anesthesia, so the percentage of need for either heavier sedation or general anesthesia was detected

Our secondary end point was:-

1) Visual Analogue Score (VAS)post-operative 4 times (([Time 1]: 30 minutes, ([Time 2]: 2 hours, ([Time 3]: 8 hours and ([Time 4]: 24 hours post-operative).

2) Systolic blood pressure (SBP), diastolic blood pressure (DBP) and Heart Rate (HR) 8 times perioperative ([Time 1]: baseline measure, ([Time 2]: immediately post-induction for control group and after block for the two other groups, ([Time 3]: 90 minutes after start of operation, ([Time 4]: during skin suturing at end of operation, ([Time 5]: post-extubation in control group and after operation in the two other groups, ([Time 6]: 1 hour post-operative, ([Time 7]: 4 hours post-operative and finally ([Time 8]: 24 hours post-operative).

3) Incidence of peri-operative complications in the 3 groups (bradycardia, hypotension, nausea, vomiting, incidence of pneumothorax, incidence of infection at site of injection and incidence of respiratory depression)

4) Opioid consumption

Basis of sample size estimation

A sample size of 28 in each group was sufficient to depict a clinical difference of 1.5 points on the mean VAS assuming a standard deviation of 2 points, using two-tailed difference between mean VAS, a power of 80%, and a significance level of 5%. This was based on the assumption that the measurement of VAS is normally distributed. This number had been increased to 50 per group (total 150) to allow for a predicted dropout or withdrawal from the procedure.

Statistical Analysis

Data were analyzed using Statistical Program for Social Science (SPSS) version 20.0. Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done:

- A one-way analysis of variance (ANOVA) when comparing between more than two means.
- Chi-square (X2) test of significance was used in order to compare proportions between two qualitative parameters.
- Probability (P-value)
  - P-value <0.05 was considered significant.
  - P-value <0.001 was considered as highly significant.
  - P-value >0.05 was considered insignificant.

RESULTS

The study included 150 patients; 50 patients for each group. There were 111 ASA-II patients and 39 ASA-III patients. There was a non-significant difference between patients enrolled in both groups as regards demographic and pre-operative data.

The results showed highly statistically significant difference between groups 1 and2 in times 2-8 according to systolic blood pressure, where it was higher in group 2 in time 2 and higher in group 1 in times 3-8. There was also highly statistically significant difference between groups 1 and3 in times 2-8, where it was higher in group 3 in time 2 and higher in group 1 in times 3-8 (figure 3). It also showed highly statistically significant difference between groups 1 and2 in times 2-8 according to diastolic blood pressure, where it was higher in group 2 in time 2 and higher in group 1 in times 3-8. There was also highly statistically significant difference between groups 1 and3 in times 2-8, where it was higher in group 3 in time 2 and higher in group 1 in times 3-8 (figure 4). Also the results revealed highly statistically significant difference between groups 1 and2 in times 3-8 according to heart rate, where it was higher in group 1 in these times. It also showed highly statistically significant difference between groups 1 and3 in times 3-8, where it was higher in group 1 in these times (figure 5).

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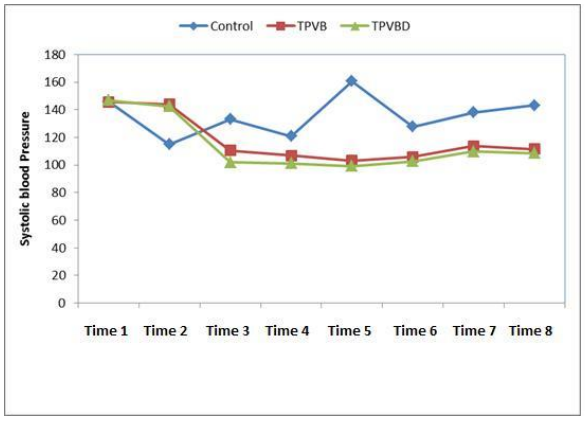

Figure 3: Relationship between groups according to systolic blood pressure (SBP).

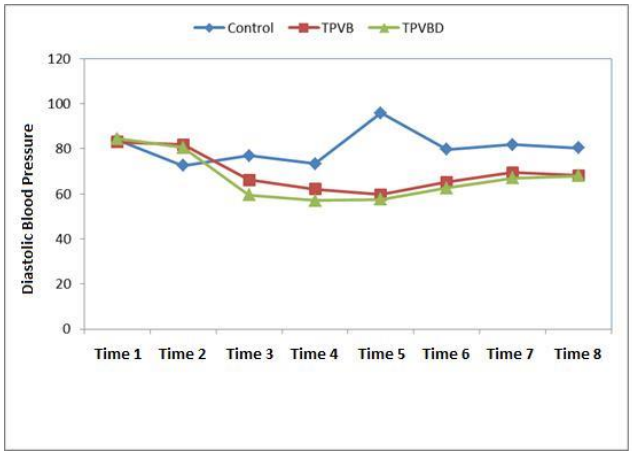

Figure 4: Relationship between groups according to diastolic blood pressure (DBP).

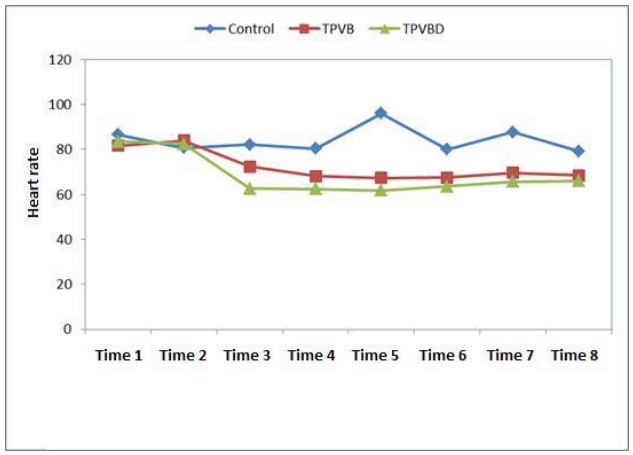

Figure 5: Relationship between groups according to heart rate.

There was highly statistically significant difference between groups 1 and2 according to VAS postoperative (higher in group 1). Also there was highly statistically significant difference between groups 1 and3 (higher in group 1). On the other hand, there was no statistically significant difference between groups 2 and3 (Table 1).

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Table 1: Comparison between groups according to VAS postoperative

VAS Posoperative	Control Group 1	TPVB Group 2	TPVBD Group 3	Kruskal Wallis Test		LSD		
				K	p	I vs. II	I vs. III	II vs. III
Time 1 Range Median	1-8 4(2)	0-3 1(1.75)	0-3 1.5(1)	69.060	<0.001 *	<0.001*	<0.001*	0.204
Time 2 Range Median	2-9 3.5(2)	0-3 1(1)	0-3 1(1)	76.185	<0.001 *	<0.001*	<0.001*	0.565
Time 3 Range Median	2-6 4(1.75)	0-3 0.5(1)	0-2 1(1.75)	83.741	<0.001 *	<0.001*	<0.001*	0.260
Time 4 Range Median	1-7 3(1)	0-3 0(1.75)	0-1 0(1)	88.052	<0.001*	<0.001*	<0.001*	0.241

(*): statistically highly significant

Also there was highly statistically significant difference between groups 1 and 2 according to post-operative opioid consumption (higher in group 1), highly statistically significant difference between groups 1 and 3 (higher in group 1). Whereas there was no statistically significant difference between groups 2 and3 (figure 6).

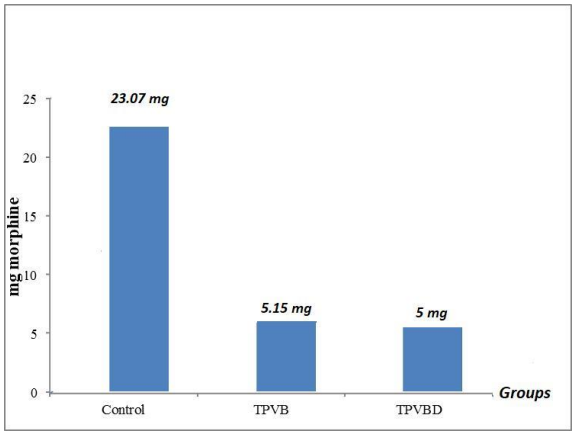

Figure 6: Relationship between groups according to Post-Op. Opioid Consumption (mg morphine in 1st 24hrs).

Concerning complications, according to bradycardia and hypotension, there was highly statistically significant difference between groups 1 and 2 (higher in group 2), also there was highly statistically significant difference between groups 1 and 3 (higher in group 3) and finally highly statistically significant difference between groups 2 and 3 (higher in group 3) (table 2).

According to post-operative nausea and vomiting, there was highly statistically significant difference between groups 1 and 2 (higher in group 1), also there was highly statistically significant difference between groups 1 and 3 (higher in group 1), while it showed no statistically significant difference between groups 2 and 3 (table 2).

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Table 2: Comparison between groups according to complications

Complications	Control Group 1	TPVB Group 2	TPVBD Group 3	x2	p
Bradycardia	0 (0.0%)	2 (4.5%)	19 (43.2%)	37.035	<0.001*
Hypotension	0 (0.0%)	6 (13.6%)	28 (63.6%)	51.659	<0.001*
Nausea & Vomiting	12 (27.3%)	2 (4.5%)	2 (4.5%)	14.224	<0.001*
Resp. Dep.	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	-
Pneumo Thorax	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	-
Inj. Site Infection	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	-

(*): statistically highly significant

We found statistically insignificant difference between groups 2 and 3 according to need for GA and need for extra sedation (table 3).

Table 3: Comparison between groups according to need for GA and need for extra sedation

	TPVB	TPVBD	x2	p
Need for GA	17 (38.6%)	13 (29.5%)	20.447	0.504
Need for Extra Sedation	28 (63.6%)	27 (61.4%)	47.19	0.937

DISCUSSION

The results of this study showed that paravertebral block is an excellent modality of analgesia in the intra-operative and post-operative period, meanwhile as a solo modality of anesthesia, it needed extra sedation or even shifting to GA in most of the cases in both TPVB and TPVBD groups, as mentioned previously in the results.

Concerning haemodynamics, our study showed significant lowering in SBP, DBP and HR in both groups TPVB and TPVBD rather than the control group on the times 3-8 which indicates that using PVB is accompanied with much decrease in pain and stress response. This goes hand in hand with Kulkarni [13]. He performed his study on 25 patients undergoing radical mastectomy surgeries. Thoracic paravertebral block and catheter insertion in which 20 ml ropivacaine 0.5% with 0.5mcg/kg dexmeditomidine was given. All the patients had good to excellent surgical anaesthesia. No significant hemodynamic changes noted. Four patients required IV fentanyl 0.5-1 mcg/kg for mild discomfort intraoperatively. The level of sedation was adequate with minimal side effects.

There was significant difference between both groups in the HR which showed to be less in TPVBD group. This goes hand in hand with Mohamed et al [14] who performed their study on 60 patients, 30 of them received 20 ml pubivacaine 0.25% while the others received 20 ml pubivacaine + 1µg/kg dexmeditomidine. The study showed that there was a significant reduction in pulse rate and diastolic blood pressure starting at 30 minutes in both groups, but more evidenced in the group with dexmeditomidine, followed by significant increase in pulse rate starting 2 hours postoperative until 48 hours postoperatively in the group without dexmeditomidine but only after 12 hours until 48 hours in the group using dexmeditomidine ($P < 0.001$).

Concerning VAS, our study showed that using PVB with or without dexmeditomidine showed significant decrease in VAS score in nearly all measurements. This goes hand in hand with Klein et al [15] and Schnabel et al [16]. The latter performed a meta-analysis of randomized controlled studies that included fifteen trials between 1999 and 2007 with 877 patients. It showed that there is considerable evidence that PVB in addition to GA or alone provide a better postoperative pain control with little adverse effects compared with other analgesic treatment strategies.

That was reflected on the opioid consumption that showed to be significantly less in TPVB and TPVBD compared to the control group. This goes hand in hand with Lijian Pei et al [17]. who performed their study on 247 patients in which 121 patients received TPVB with propofol general anesthesia (GA), (PPA group), while

126 patients received fentanyl and sevoflurane GA (GA group). Results showed that patients in the PPA group required less sevoflurane than those in the GA group.

Concerning complications, our study proved that using TPVB, either with or without dexmeditomidine, showed to decrease the incidence of post operative nausea and vomiting (PONV). This goes hand in hand with Coveney et al [18] and Klein et al [15]. The latter performed his comparative study on 60 patients undergoing breast augmentation or reconstruction surgeries, 30 of them received general anesthesia while the other 30 received thoracic paravertebral block. It showed that nausea was less severe in the PVB group. While our study didn't show occurrence of significant bradycardia, hypotension, pneumothorax, respiratory depression nor infection at site of injection

What concerned us much in our study was the much increased need to extra-sedation and general anesthesia in both TPVB and TPVBD groups. There was increased percentage of cases that needed either extra-sedation or general anesthesia that was not found in comparative studies as Coveney et al [18], whose retrospective study enrolled 145 patients undergoing breast surgeries using TPVB and 100 patients undergoing GA in 2 years duration. It showed that paravertebral block can be used to perform major breast surgeries with minimal complications and a low rate of conversion to general anesthesia. Also Klein et al [15] who performed their comparative study on 60 patients undergoing breast augmentation or reconstruction surgeries, 30 of them received general anesthesia while the other 30 received thoracic paravertebral block. It showed that paravertebral nerve block has the potential to offer long-lasting pain relief and few postoperative side effects when used for breast surgery. They demonstrated that paravertebral nerve block, when compared with general anesthesia, was an alternative technique for breast surgery that may offer pain relief superior to general anesthesia. Also Kulkarni [13] who performed his study on 25 patients undergoing radical mastectomy surgeries. He found that thoracic paravertebral block and catheter insertion in which 20 ml ropivacaine 0.5% with 0.5mcg/kg dexmeditomidine was given. It showed that continuous thoracic paravertebral block using ropivacaine 0.5% with dexmeditomidine 0.5 µg/kg as a sole anesthetic management provided satisfactory surgical anesthesia with minimal hemodynamic changes and adverse effects in 25 cases of radical mastectomies.

All of these conflicts made us look thoroughly to the type of the operation in our and their studies. Our study was restricted to modified radical mastectomy, while most of the studies included breast surgeries in general, breast augmentation, cosmetic breast surgeries, lumpectomies or abscess evacuation.

In MRM operation, as mentioned before, a flap is elevated surgically on the upper and lower side to be able to cover the defect after the breast removal (See Figure 1)

As the thoracic paravertebral blockade results in ipsilateral anesthesia. The location of the resulting dermatomal distribution of anesthesia or analgesia is a function of the level blocked and the volume of local anesthetic injected (Figure 2) [11]. From this figure, we can conclude that in the operation of modified radical mastectomy, while elevating the upper flap of the skin, as well as evacuating the lymph nodes in the apex of the axilla, the nerves that could be targeted are C4 andC3. This means that in order to make the paravertebral block effective in such operation, it should cover from C3 till T6.

Coveney et al. stated that a single injection of 15 ml of local anesthetic (LA)in the TPV space provides a sympathetic block to about eight dermatomes and somatic block over about three dermatomes. The spread of LA in the paravertebral space was found to be less in women thanin men [18]. Also there was other forms of distribution that have been observed other than longitudinal spread. Conacher et al reported that he found lateral and cloud-shaped spread of contrast when injected in the thoracic paravertebral space, indicating inter costal spreading pattern [19]. Karmakar et al found that there was a contralateral spread of contrast after successful paravertebral block for multiple fractured ribs anterior to the vertebral bodies [20]. The variability in spread following PVB was explained by Karmakar and Chung [21]due to the existence of the endothoracic fascia. This assumption was further confirmed by Naja et al. He used a nerve-stimulator guided technique to confirm that paravertebral injections dorsal to the endothoracic fascia result in more unpredictable spread while those ventral to the fascia facilitate longitudinal spread [22].

From all of these studies we could conclude that the paravertebral block with a single injection and a catheter placement as an isolated modality of anesthesia for cases undergoing modified radical mastectomy

could be insufficient as the spectrum of nerve supply needed to be blocked is far beyond that could be blocked by single injection. Yet, it could be sufficient in other types of breast surgeries in which there is no encroachment over cervical supply, done by upper flap elevation and axillary apex evacuation.

Also, we assume that multiple injections at different levels can be more effective, even if placement of catheter is planned for postoperative analgesia.

Combining paravertebral block, with single injection as done in our study, with superficial cervical plexus block could be tried to cover the defective area that couldn't be reached in our study.

CONCLUSION

From our study, we could conclude that the paravertebral block with a single injection and a catheter placement as an isolated modality of anesthesia for cases undergoing modified radical mastectomy could be insufficient as the spectrum of nerve supply needed to be blocked is far beyond that could be blocked by single injection. Yet, it could be sufficient in other types of breast surgeries in which there is no encroachment over cervical supply, done by upper flap elevation and axillary apex evacuation.

RECOMMENDATIONS

We assume that multiple injections at different levels can be more effective, even if placement of catheter is planned for postoperative analgesia.

Combining paravertebral block, with single injection as done in our study, with superficial cervical plexus block could be tried to cover the defective area that couldn't be reached in our study.

What is already known about this topic

- Thoracic paravertebral block is an excellent modality of analgesia in modified radical mastectomy operations
- Thoracic paravertebral block was being tried as an isolated modality of anesthesia in modified radical mastectomy operations yet it was not tested enough to be accepted as though

What this study adds

- Our study proved that thoracic paravertebral block with a single injection and a catheter placement as an isolated modality of anesthesia for cases undergoing modified radical mastectomy could be insufficient.

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