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Is Thoracic Epidural Anesthesia a Better Alternative to General Anesthesia in Modified Radical Mastectomy Surgeries?

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Abstract

Background and objectives: Though the breast surgeries are usually performed under general anesthesia (GA), it is not without any attendant risks. Thoracic Epidural anesthesia (TEA) is gaining more attention in view of better intraoperative conditions, postoperative recovery profile and fewer postoperative complications. This study was designed to determine the efficacy and safety of TEA as an alternative anesthetic technique to GA for Modified radical mastectomy (MRM). *Methodology:* Group G (n = 25) was administered conventional GA. The Group T (n = 25) received TEA with 0.25% Bupivacaine and Fentanyl. Postoperative pain management was provided with Tramadol for GA patients and epidural infusion for TEA patients. The need for anesthesia supplementation, sedation, hemodynamic changes, respiratory depression and other intercurrences like pruritus, nausea, vomiting were recorded. The duration of surgery, length of stay in the recovery room and quality of post-operative analgesia were also recorded. *Results:* In group T, Supplementation with axillary infiltration was required in 20% of patients and all patients required sedation. Hypertension was more frequent in group G, whereas hypotension and bradycardia were more frequent in group T. Postoperatively, the incidence of nausea and vomiting were observed frequently in group G. The group G patients had longer duration of stay in recovery room (202.32 vs 160.80 minutes). The Visual Analog scores and requirement of supplementary analgesics upto 24 hours of postoperative period were significantly lower in group T patients. *Conclusion:* TEA is a safe, reliable and better alternative to GA in patients undergoing MRM.

Keywords: General Anesthesia; Modified Radical Mastectomy; Postoperative Analgesia; Thoracic Epidural Anesthesia.

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Introduction

As the incidence of breast malignancies is on the rise, Modified Radical Mastectomy (MRM) is now frequently performed. Though the breast surgeries can be performed under Cervical Epidural Anesthesia, Thoracic Epidural Anesthesia (TEA), Thoracic Paravertebral Blocks and Intercostal Blocks [1-3], oncologic breast surgeries are usually performed under general anesthesia (GA) and is more acceptable by patients also. But GA does not eliminate the surgical stress response, may aggravate immunosuppression [4] and cause undesirable side effects such as nausea and vomiting [5-7]. Due to lack of residual analgesia, Postoperative pain is one of the most debilitating outcomes, often necessitating the use of opioids. This aggravates the incidence of nausea and vomiting, impaired ventilation and postoperative sedation [8], ultimately resulting in prolonged hospital stay [9]. In recent days, regional anesthesia particularly TEA, is gaining more

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attention in view of better intraoperative hemodynamic stability, fewer postoperative complications, early mobilization and thereby becoming an useful adjunct for fast track surgery. It reduces the overall costs of perioperative care of patients undergoing MRM.

TEA allows utilization of incremental doses of local anesthetic agent, which offers preservation of the respiratory function [4,10-12]. TEA also selectively blocks cardiac sympathetic fibers, thereby it attenuates surgical stress response, improves myocardial oxygen balance and stabilizes intraoperative hemodynamics [7,13]. It also avoids the problems of difficult tracheal intubation and hemodynamic changes associated with it. Thus TEA reduces perioperative cardiac complications and mortality [14]. Thereby it is more beneficial in patients with difficult airway, compromised cardiac and pulmonary reserve and elderly patients [15,16]. TEA decreases intraoperative blood loss and also allows early feeding. Postoperative pain relief can be provided through the epidural catheter [17]. All these factors positively affects the early mobilization and shorter duration of hospital stay [18]. But the technique of thoracic epidural requires special skill and expertise to avoid potential complications like inadvertent dural puncture, spinal cord trauma, and epidural hematoma/abscess.

Various studies had demonstrated the effectiveness and the decreased incidence of complications associated with TEA [5,6,8]. Still exclusive TEA for MRM surgeries is not frequently performed. Hence, this study was designed to determine the efficacy and safety of TEA as an alternative anesthetic technique to GA for mastectomy and axillary dissection.

Materials and Methods

After getting approval from institutional ethics committee, fifty cases of Carcinoma Breast scheduled for elective Modified Radical Mastectomy were enrolled in this Prospective randomized comparative study, after signing an informed consent. These patients were randomized into two groups by Sealed Envelope technique. Group G (n = 25) General Anesthesia group and Group T (n = 25) Thoracic Epidural Anesthesia group.

Inclusion Criteria

1. Female patients of carcinoma breast proven by FNAC or biopsy and mammogram.
2. Age between 30-65 years

Exclusion Criteria

1. Patient refusal
2. American Society of Anesthesiologists (ASA) physical status > III
3. Infection at the site of epidural placement
4. Difficult airway
5. Coagulation disorder
6. known allergy to bupivacaine
7. Hypovolemia
8. Vertebral column deformity

Procedure

Prior to the day of surgery, anesthesiologists had evaluated all patients and explained the anesthesia process and method. Demographic data were recorded. The patients were advised fasting as per ASA guidelines. Tab. Alprazolam 0.5mg, Tab. Ranitidine 150 mg and Tab. Metoclopramide 10 mg were administered orally the night before surgery. On arrival in the operating room, ECG (leads II and V5) for heart rate (HR) and ST segment changes, Pulse oximetry (SpO_2), and non-invasive blood pressure monitors were attached and baseline readings were recorded. After securing intravenous access with 18G cannula, the patient was preloaded with 10 mL/kg of lactated Ringer's solution slowly over 30 minutes. Oxygen was administered through facemask. The patients were sedated with intravenous Midazolam 2 mg, and Fentanyl 25 μg; After that the group G patients receiving GA were pre-medicated with inj. Glycopyrrolate 0.2mg, inj. ondanseteron 4 mg intravenously and induced with inj. Fentanyl 1.5mcg/kg followed by inj. Propofol 2 mg/kg intravenously. Tracheal intubation was facilitated using inj. Vecuronium 0.1 mg/kg. Anesthesia was maintained using Isoflurane along with admixture of oxygen and nitrous oxide (1:2) and additional doses of Vecuronium (1 mg), as required. Supplementation of Fentanyl was given as analgesia, whenever necessary. At the end of the surgery, the residual neuromuscular blockade was reversed with Neostigmine 0.05 mg/kg and glycopyrrolate 0.01mg/kg.

The group T patients received thoracic epidural block by a qualified anesthesiologist. Under strict aseptic precautions, with patient in lateral position, the area was cleaned and the T4-5 intervertebral space, or the one closer to this space considered to be an easier access, was anesthetized. An 18G Tuohy needle was introduced using midline approach and

epidural space identified by loss of resistance technique. The epidural catheter 20G was inserted 3 – 4 cms cephalad into epidural space. A test dose of 3ml 2% lignocaine with 1:2,00,000 adrenaline was given after careful aspiration. The patient was positioned supine and 17 mL of 0.25% bupivacaine with 100 µg fentanyl was administered incrementally. After testing the quality of anesthesia (adequate analgesia determined by pinprick method from the lower border of the clavicle to the inferior costal margin), the surgery was initiated. Whenever necessary, supplemental doses of midazolam 1 mg was administered for sedation. The procedure was considered as failure, if targeted dermatomal levels were not attained even after 10 minutes and GA was instituted. If the patient experienced pain or discomfort during axillary exploration, the surgeon infiltrated the area with with 5 to 10ml of 1% lignocaine with adrenaline. Anesthesia was maintained by injecting 5 mL of 0.25% bupivacaine every 60 to 90 minutes through the epidural catheter. Oxygen was administered through facemask. After the surgery, the patient was shifted to recovery room with continuous monitoring for vital parameters. After anesthesiologist clearance, the patient was then transferred to postoperative ward.

The need for supplementary sedation and anesthesia supplementation, hemodynamic changes [tachycardia (HR > 100 beats per minute), bradycardia (HR < 60 beats per minute), hypotension (20% drop in baseline blood pressure) and hypertension (20% increase in baseline blood pressure)], respiratory depression and other intercurrences like pruritus, nausea, and vomiting were recorded both intraoperatively and postoperatively upto 24 hours. The duration of surgery and the length of stay in the recovery room were also noted. Hypotension was treated with fluid boluses and 6 mg Ephedrine, bradycardia was treated with 0.3-0.6 mg Atropine and vomiting with 10 mg Metoclopramide intravenously.

In GA patients, postoperative pain management was provided with inj. Tramadol 50 mg intravenously every 6 hours for the first 24 hours and TEA patients were managed with epidural infusion of 0.125% bupivacaine 6 mL/h for 24 hours. Quality of post-operative analgesia was evaluated at 30 minutes, 2nd hour, 6th hour, 12th hour and 24th hour postoperatively, by using a 10 cm Visual Analog Scale (VAS), where zero represented no pain and 10 cm represented worst possible pain. A VAS score ≤ 4 cm was considered to be an acceptable level of pain. The VAS score > 4 was treated with rescue analgesics Diclofenac (iv or oral) and Paracetamol (i.v. or oral). All drug administrations were recorded.

Statistical Analysis

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS Inc., Chicago, Illinois, USA) version 23. Quantitative parameters were analysed using students' t-test whereas qualitative parameters are compared using Chi square test and fisher exact test. Data are shown as mean± standard deviation and in absolute numbers or percentages. $p < 0.05$ was considered statistically significant.

Results

The patients in both the groups are comparable with regard to demographic characteristics like age, height and weight. Baseline HR, Systolic and Diastolic blood pressure and the duration of surgery was also similar between both the groups (Table 1). The difference was not statistically significant.

In group T, Supplementation of anesthesia with axillary infiltration was required in 20% of patients and all patients required sedation, mostly at the beginning of surgery without any complaints of pain.

Table 1: Patient characteristics

Variable	Group G	Group T	p value
Age(years)*	49.64 ± 5.83	48.12 ± 6.52	0.195 NS
Height(cms)*	154.56 ± 5.12	153.68 ± 4.91	0.269 NS
Weight(kg)*	62.08 ± 9.79	58.84 ± 9.2	0.117 NS
Baseline systolic pressure (mmHg)*	127.56 ± 12.24	125.44 ± 10.38	0.256 NS
Baseline Diastolic pressure (mmHg)*	80.68 ± 8.40	77.72 ± 7.77	0.101 NS
Baseline Heart rate (beats per minute)*	85.2 ± 12.43	85 ± 13.28	0.478 NS

*Data as Mean ± Standard Deviation
NS – Not significant

Hypertension was more frequent in group G whereas hypotension and bradycardia were more frequent in group T (Table 2). Postoperatively, the incidence of nausea and vomiting were observed more frequently in group G. The group G patients had longer duration of stay in recovery room when compared to group T patients (202.32 vs 160.80 minutes) and the difference was statistically significant (Table 3). The VAS scores and requirement of supplementary analgesics upto 24 hours of postoperative period were significantly lower in group T patients (Table 4).

Discussion

With increasing trend of breast cancer, the current tendency is towards radical surgical procedures. The use of an anesthetic technique, which allows for optimal surgical conditions, reduced blood loss, rapid recovery and excellent postoperative analgesia may have a positive impact on the patient's recovery from this major surgical insult.

The TEA has been increasingly practiced in recent years. It offers protection against the

Table 2: Intraoperative patient Characteristics

Parameters	Group G	Group T	P value
Duration of surgery (minutes)*	159.72 ± 7.56	158.64 ± 7.97	0.313 NS
Axillary supplementation**	0(0%)	5(20%)	0.05 S
Supplementary Sedation**	0(0%)	25(100%)	0.05 S
Hypertension**	8(32%)	0(0%)	0.05 S
Hypotension**	3(12%)	13(52%)	0.002 S
Tachycardia**	3(12%)	7(28%)	0.157 NS
Bradycardia**	2(8%)	12(48%)	0.002 S

*Data as Mean±Standard Deviation
**Data as number of patients (percentage)
S – Significant NS – Not Significant

Table 3: Postoperative patient Characteristics

Parameters	Group G	Group T	P value
Nausea**	11(44%)	3(12%)	0.012 S
Vomiting**	15(60%)	2(8%)	0.0001 S
Pruritus**#	0(0%)	10(40%)	<0.05 S
Respiratory Depression**	0(0%)	0(0%)	NS
Duration of stay in recovery room (minutes)*	202.32 ± 20.23	160.8 ± 15.7	0.00001 S

*Data as Mean±Standard Deviation
**Data as number of patients (percentage)
perioperative
S – Significant NS – Not Significant

Table 4: Postoperative Visual Analog Scores(VAS)

VAS	Group G	Group T	P value
Postop 30 minutes*	3.44 ± 0.51	0.36 ± 0.64	0.00001 S
Postop 2 hours*	5.36 ± 1.0	2.92 ± 0.76	0.00001 S
Postop 6 hours*	5.16 ± 1.2	1.56 ± 0.65	0.00001 S
Postop 12 hours*	5.08 ± 0.81	1.52 ± 0.59	0.00001 S
Postop 24 hours*	3.64 ± 1.08	1.36 ± 0.57	0.00001 S

*Data as Mean±Standard Deviation
S – Significant

perioperative stress response and the beneficial effects have been attributed to the physiological changes caused by neuraxial anesthesia and better pain management. The benefits include an effective postoperative analgesia, lower incidence of pulmonary complications, stabilization of endothelial coronary function, improved hemodynamic stability, earlier return of bowel function, preservation of immune competence, early ambulation and a reduction in the cost of perioperative care [19,20]. TEA offers protection against arrhythmias, particularly of ventricular origin [21] and also maintains the myocardial oxygen demand /supply ratio along with maintenance of the coronary perfusion pressures even in the ischemic myocardial tissue [22], thereby having a positive impact on the cardiovascular status [23]. But the main apprehension behind its regular use are technical difficulty and spinal cord injury. With utmost precautions and experienced hands, dural puncture is rare and the incidence of neurological injury is 0.01–0.001% [24]. Brull et al had reported the incidence of permanent neurological sequelae related to TEA as <0.07% [25].

GA may increase the risk of impaired cardiac function [22] by decreasing myocardial blood flow and left ventricular function. It also increases the risk of alveolar barotrauma [26] and pneumonia. Neuromuscular blockade during GA increases atelectasis in the dependent lung, leading to a right-to-left shunt and increased risk of intraoperative hypoxia. In addition, difficult intubation and intubation-related trauma to teeth or vocal cords can also occur. Further these complications can be aggravated according to the comorbid conditions of the patient. Considering the risk benefit ratio, this study was designed to determine the efficacy of TEA as a safe and better alternative to GA in MRM surgeries.

The preoperative subject characteristics were statistically comparable between both the groups. The baseline hemodynamic variables and duration of surgery were also comparable. The T4-5 intervertebral space, or the next closer space, considered to be an easier access was selected. In similar other studies, Belzarena et al. [6], Sagiroglu G et al. [27] and Sundarathiti P et al. [8] had all selected T4-T5 space. The drug used was 0.25% Bupivacaine. As breast surgery does not need muscle relaxation, 0.25% concentration was chosen. Bupivacaine has an acceptable onset time, long duration of action, profound conduction blockade and significant separation of sensory and motor blockade. It provides safe, effective and hemodynamically stable analgesia. The volume used was 20ml (3ml as test dose followed by 17ml) in line with other similar studies [6,28]. None of the patients had difficulty or complications in instituting TEA.

The quality of anesthesia was adequate in most patients. But five patients in group T required complementation by local infiltration of axilla with 5-10ml of 1% lignocaine with adrenaline. This problem arose when dissection involved the second or third level (behind and medially to the pectoralis minor muscle), during which time along with second thoracic root, the other cervical roots (up to fourth cervical root) are involved in the innervation. On the surface, the territory of the fourth cervical root is above the second thoracic dermatome. Thus blockade up to the level of fourth cervical root is necessary and can be consistently achieved by administration of a large volume dose of local anesthetic with an opioid. Visser et al[29] had concluded that the total dose and volume of local anesthetic was the most important determinant factor for the extent of the blockade, while the site of epidural puncture controlled the pattern of distribution of sensory blockade. The median thoracic approach, as used in the present study, tends to cause greater caudal dispersion of the local anesthetic, justifying the use of larger volumes [30]. All the patients in TEA group received sedation, mostly before the beginning of surgery to allay apprehension. Few patients required intraoperatively either during axillary sparing or when the surgery was getting prolonged. Belzarena et al. [6] had observed axillary sparing and subsequent supplementation in 15% patients and complimentary sedation in 100% patients despite high level of blockade. Similar observation was made in many other studies [31,32]. None of the patients in TEA group had respiratory depression.

The incidence of hypotension (52%) and bradycardia (48%) were significantly high in TEA patients but were mild due to segmental blockade, lower concentration of local anesthetic used and preserved venous return. It was easily managed with fluid boluses, low doses of vasopressor and Atropine accordingly. Medium thoracic block is considered to cause hypotension and bradycardia by inhibiting sympathetic cardiac fibers. Tachycardia was encountered in both the groups and there was statistically significant incidence of hypertension in group G patients (32%). Tachycardia in group T might be secondary to hypotension. But hypertension and tachycardia noted in group G correlated with intubation and surgical stimulation especially after skin incision. Oktavia et al. [28] and many others

[6,31] had made a similar observation in their comparative study between TEA and GA on MRM surgeries.

When compared to GA group, TEA patients had a lower incidence of Postoperative nausea and vomiting (PONV), which had been demonstrated in several other studies [5-7,13,31]. Administration of Opioids during GA, can induce nausea and vomiting by direct stimulation [33] of the chemoreceptor trigger zone. Increased pain scores in GA group also could have resulted in more analgesic dosage with possible side effects. In high frequency, PONV will be distressing to patients and potentially detrimental to their postoperative recovery. Pruritus was noted in 40% of the patients in TEA group. Since pruritus was not severe, specific treatment was not required. Pruritus was encountered in studies which used fentanyl as epidural adjuvant [6,13].

GA patients stayed for a longer time in recovery room when compared to TEA patients (202.32 vs 160.8 minutes) and it was statistically significant. This finding correlates with the observation made by Belzarena et al. [6] and Bhardwaj et al. [31]. Apart from delayed recovery from anesthesia, other factors like nausea, vomiting, high pain scores and human factors, such as late discharge order from attending anesthesiologist might prolong the stay. But Sagiroglu G et al. [27] had observed that TEA patients stayed for a longer time in recovery room. Probably, the propofol infusion used to maintain intraoperative sedation in these patients might be the cause for delay.

Ineffective analgesia may result in harmful physiological and psychological effects and in turn these adverse effects may result in significant morbidity and even mortality [34]. Adequate postoperative control of pain is very important as it makes for a better postoperative period, early hospital discharge and can have a long-term effect of decreasing complications such as chronic pain [7,35]. Calimli S et al. [36] had found significantly high VAS scores in patients undergoing mastectomy under GA. Doss NW et al. [5] had observed that TEA patients experienced significantly less pain after surgery. Accordingly in our study also, the VAS scores were very significantly lower in TEA group for upto 24 hours postoperatively and required less parenteral analgesics. Lahiry et al. [37] also had found significantly lower VAS scores in TEA patients in the immediate postoperative period. The post-operative analgesia and opioid sparing effect can be demonstrated by administering local anaesthetic through the epidural route [38]. TEA may also have a role in controlling the scar pain and phantom pain [35].

Yeh CC et al. in his comparative study between GA and TEA for MRM patients concluded that TEA provided a more prolonged analgesic effect than GA after operation. Side effects were observed at a higher frequency in the GA group. The average bed rest time was significantly shorter in the TEA group. Overall satisfaction scores were significantly higher in the TEA group than in the GA group [13].

Although not specifically assessed in this study, intraoperative blood loss, duration of hospital stay and hospital costs were more in GA group than TEA group [39]. It was observed that patients in TEA group were ambulating early with more comfort and satisfaction than patients in GA group.

Few limitations of this study were a small sample size, and patients of ASA physical status IV were not assessed. So the efficacy of TEA in sicker patients remains under evaluated. A longer follow up of the patients may show the effect of TEA on the scar pain and phantom pain.

Conclusion

Both TEA and GA offered good operating conditions. TEA has no effect on inducing hypertension, but hypotension and bradycardia may occur. Postoperative recovery profile was better in TEA patients in terms of reduced incidence of nausea and vomiting, adequate postoperative analgesia and shorter stay in recovery room. Postoperative epidural infusion provided excellent analgesia without any major hemodynamic fluctuations which in turn contributed to reduced analgesic requirements and its attendant side effects.

Thus Thoracic epidural anesthesia is a safe, reliable and better alternative to General anesthesia in patients undergoing Modified Radical Mastectomy. However meticulous dosing and proper asepsis is of utmost importance for the success of TEA. Further extensive studies are needed to validate our conclusion.

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References

1. Kulkarni K, Namazi IJ, Deshpande S, Goel R. Cervical epidural anaesthesia with ropivacaine for modified

radical mastectomy. Kathmandu University Medical Journal. 2015 May 2;11(2):126-31.

2. Patel LP, Sanghvi PR, Agarwal MB, Prajapati GC, Patel BM. Thoracic paravertebral block for analgesia after modified radical mastectomy. Indian Journal of Pain. 2014 Sep 1;28(3):160.
3. Sidiropoulou T, Buonomo O, Fabbi E, Silvi MB, Kostopanagiotou G, Sabato AF et al. A prospective comparison of continuous wound infiltration with ropivacaine versus single-injection paravertebral block after modified radical mastectomy. Anesthesia & Analgesia. 2008 Mar 1;106(3):997-1001.
4. Stevenson GW, Hall SC, Rudnick S. The effect of anesthetic agents on the human immune response. Anesthesiology, 1990;72:542-552.
5. Doss NW, Ipe J, Crimi T, Raipal S, Cohen S, Fogler RJ, et al. Continuous thoracic epidural anesthesia with 0.2% ropivacaine versus general anesthesia for perioperative management of modiied radical mastectomy. Anesth Analg. 2001;92:1552-7.
6. Belzarena SD. Comparative study between thoracic epidural block and general anesthesia for oncologic mastectomy. Rev Bras Anesthesiol. 2008; 58: 561-8.
7. Lynch EP, Welch KJ, Carabuena JM, Eberlein TJ. Thoracic epidural anesthesia improves outcome after breast surgery. Ann Surg. 1995; 222: 663-9.
8. Sundarathiti P, Pasutharnchat K, Kongdan Y, Suranutkarin PE. Thoracic epidural anesthesia (TEA) with 0.2% ropivacaine in combination with ipsilateral brachial plexus block (BPB) for modified radical mastectomy (MRM). J Med Assoc Thai. 2005;88(4):513 20.
9. Oddby-Muhrbeck E, Jakobsson J, Andersson L et al. — Postoperative nausea and vomiting. A comparison between intravenous and inhalation anaesthesia in breast surgery. Acta Anaesthesiol Scand, 1994;38:52-56.
10. Andress M, Norbert R, Hugo VK. Thoracic epidural anesthesia and the patient with heart disease: benefit, risks and controversies. Anesth Analg, 1997;85:517-28.
11. Edwards MJ, Broadwater JR, Bell JL, Ames FC, Balach CM. Economic impact of reducing hospitalization for mastectomy patients. Ann Surg, 1988;208:330-6.
12. Lui S, Carpenter RL, Neal JM. Epidural anesthesia and analgesia their role in postoperative outcome. Anesthesiology, 1995;82:14774-506.
13. Yeh CC, Yu JC, Wu CT, Ho ST, Chang TM, Wong CS. Thoracic epidural anesthesia for pain relief and postoperation recovery with modified radical mastectomy. World J Surg, 1999;23:256–61.
14. Wijeysundera DN, Beattie WS, Austin PC, Hux JE, Laupacis A. Epidural anesthesia and survival after intermediate-to-high risk non-cardiac surgery: a population based cohort study. Lancet. 2008;372 (9638):562 9.
15. Ballantyne JC, Carr DB, deFerranti S, Suarez T, Lau J, Chalmers TC, et al. The comparative effects of postoperative analgesic therapies on pulmonary outcome: cumulative meta-analysis of randomized, controlled trail. Anesth Analg, 1998;86:589-612.
16. Liu S, Carpenter RL, Neal JM, Epidural anesthesia and analgesia. Anesthesiology 1995;82:1474-506.
17. Garcha HS, Walia C, Aujla KS, Gupta R. A Study to Compare Intravenous Fentanyl With Epidural Bupivacaine-Fentanyl Combination For Post Operative Analgesia in Patients Undergoing Modified Radical Mastectomy. International Journal of Scientific Research. 2016 Apr 12;5(2).
18. Singh AP, Tewari M. Singh DK, Shukla HS. Cervical epidural anesthesia: A safe alternative to general anesthesia for patients undergoing cancer breast surgery. World J Surg. 2006;30(11):2043-7.
19. Popping DM, Elia N, Marret E, Remy C, Tramer MR. Protective effects of epidural analgesia on pulmonary complications after abdominal and thoracic surgery: a meta-analysis. Arch Surg, 2008 Oct;143(10):990–9.
20. Waurick R, Van Aken H. Update in thoracic epidural anaesthesia. Best Pract Res Clin Anaesthesiol 2005; 19:201-13.
21. Meissner A, Eckardt L, Kirchhof P, Weber T, Rolf N, Breithardt G et al. Effects of Thoracic Epidural Anesthesia with and without Autonomic Nervous System Blockade on Cardiac Monophasic Action Potentials and Effective Refractoriness in Awake Dogs. Anesthesiology 2001;95:132–8.
22. Blomberg S, Emmanuel H, Kvist H, Lamm C, Ponten J, Waagstein F, et al. Effects of thoracic epidural anesthesia on coronary arteries and arterioles in patients with coronary artery disease. Anesthesiology 1990;73:840-7.
23. McLeod GA, Cumming C. Thoracic epidural anaesthesia and analgesia. Continuing Education in Anaesthesia, Critical Care & Pain 2004;4(1):16-9.
24. Tanaka K, Watanabe R, Harada T, Dan K. Extensive application of epidural anesthesia and analgesia in a university hospital: incidence of complication related to technique. Reg Anesth 1993;18(1):34–8.
25. Brull R, McCartney CJ, Chan VW, El-Beheiry H. Neurological complications after regional anaesthesia: contemporary estimates of risk. Anesthesia & Analgesia. 2007 Apr 1;104(4):965-74.
26. Clemente A, Carli F. The physiological effects of thoracic epidural anesthesia and analgesia on the cardiovascular, respiratory and gastrointestinal systems. Minerva Anesthesiol 2008;74(10):549-563.
27. Sagiroglu G, Sezer A, Cakcak E, Copuroglu E, Sagiroglu T and Hekimoglu S. Non-intubated thoracic epidural anesthesia for modified radical mastectomy as an alternative to general anaesthesia. J Surg Cl Res – Vol. 8 (2) 2017:140-150.
28. Oktavia E. A comparative study between thoracic epidural anesthesia and general anesthesia for patients who underwent modified radical mastectomy with axillary lymph node dissection in de la salle university medical center. Indones Biomed J. 2015;7(2):111-6.

29. Visser WA, Lee RA, Gielen MJM. Factors affecting the distribution of neural blockade by local anesthetics in epidural anesthesia and a comparison of lumbar versus thoracic epidural anesthesia. Anesth Analg. 2008;107:708-21.
30. Visser WA, Liem TH, van Egmond J et al. — Extension of sensory blockade after thoracic epidural administration of a test dose of lidocaine at three different levels. Anesth Analg, 1998;86:332-335.
31. Bhardwaj A, Singh B, Singh AP. Comparative study between thoracic epidural and general anesthesia for modified radical mastectomy. Indian Journal of Clinical Anaesthesia, 2017;4(1):13-15.
32. Vineetha P, Ramadas KT, Sajid B, Biji KP. A prospective observational study to assess the efficacy of thoracic epidural anaesthesia for mastectomy. Ann Int Med Den Res. 2017;3(3):09-13.
33. Borgeat A, Ekatodramis G, Schenker C. Postoperative nausea and vomiting in regional anesthesia: a review. Anesthesiology, 2003;98:530-547.
34. Cousin M. Acute and postoperative pain. In: Wall PD, Melzack R, eds. Text book of pain.3rd ed. London: Churchill Livingstone, 1994:357-86.
35. Kroner K, Knudsen UB, Lundby L. Long-term phantom breast syndrome after mastectomy. Clin J Pain, 1992;8:346-350.
36. Calimli S, Topal A, Erol A, Tavlan A, Otelcioglu S. The Effect of General Anesthesia and General Anesthesia Plus Epidural Levobupivacaine or Bupivacaine on Hemodynami Stress Response and Postoperative Pain. Pain Management - Current Issues and Opinions, Dr. Gabor Racz (Ed.), 2012; ISBN: 978-953-307-813-7, InTech.
37. Lahiry S, Sharma DN, Mund M, Dhaarini R, Deshmukh H. Thoracic epidural versus general anaesthesia for MRM surgeries. Int J Med and Dent Sci 2016;5(2):1125-31.
38. Block BM, Liu SS, Rowlingson AJ, Cowan AR, Cowan JA Jr, Wu CL. Efficacy of postoperative epidural analgesia: A metaanalysis. JAMA 2003;290:2455–63.
39. Tejler G, Aspegren K. Complications and hospital stay after surgery for breast cancer: a prospective study of 385 patients. BJS 1985;72(7):542-44.