

Original Research Article

The effect of anesthesia technique on tumor recurrence rate after mastectomy

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ABSTRACT

Background: Breast cancer is most common cancer in women. Although surgical and chemotherapy methods have improved survival, mortality is seen secondary to metastasis and recurrence. Neuroaxial anesthesia has been shown to suppress neuroendocrine stress response due to surgery with sympathetic blockade and has a positive effect on tumor recurrence. In this study, the hypothesis was regional anesthesia may have a positive effect on patient comfort, surgical success rate and complications in the short term, tumor recurrence and metastasis in the long term.

Methods: Patients who underwent mastectomy for breast cancer were divided into two groups as thoracic epidural or general anesthesia retrospectively. Preoperative patient characteristics, intraoperative hemodynamic data and postoperative complications were recorded. Static and dynamic pain was evaluated at 12, 24 and 48 hours, at 1 week, 3 and 6 months, and at the end of 1 and 3 years. The presence of metastasis and recurrence was evaluated.

Results: In this study, no relationship between recurrence and anesthesia type ($p=1.0$) could be found. Intraoperative hemodynamic data and pain scores were lower in patients who underwent thoracic epidural anesthesia.

Conclusions: As a result, thoracic epidural anesthesia had hemodynamic effects and lower pain scores in postoperative pain control, but had no effect on tumor recurrence in breast cancer patients.

Keywords: Breast cancer, Regional anesthesia, Tumor recurrence

INTRODUCTION

Breast cancer is the second most frequently diagnosed malignancy and the most common female cancer in the world.¹⁻³ Surgery is the most effective treatment for solid tumors. Despite the increase in survival rates with developing surgical and chemotherapy techniques, mortality is still observed as a consequence of metastasis and recurrence. It has been reported that the recurrences most frequently in the first 5 years after surgery and the incidence rate is approximately 10%.¹⁻⁴ Many factors are responsible for tumor recurrence and metastasis. Immune system suppression, angiogenesis and micrometastases caused by the mediators (growth factors, cytokines, etc.)

are the non-immunological mechanisms. Sympathetic blockage that is as a result of regional anesthesia suppress neuroendocrine stress response.⁵⁻⁷ Tumor recurrence frequency is decreased with providing effective postoperative pain control and decreased opioid need with regional anesthesia.^{5,6,8}

An experimental study in rats was reported regional anesthesia reduces the suppression in neuroendocrine stress response and may be effective in postoperative tumor metastasis when administered with general anesthesia.⁹ In this study, to compare the effect of anesthesia technique on patient pain score, tumor recurrence and metastasis was aimed.

METHODS

After approval of Baskent University Research Board (KA20/11), female patients who underwent mastectomy with the diagnosis of breast cancer in this hospital were retrospectively analyzed. The patients were divided into general (G) and thoracic epidural (TE) anesthesia groups. In group TE, after sedation with 2 mg midazolam, a thoracic epidural catheter was inserted from the T4-T5 interval.

First, 15 ml of 0.5% bupivacaine, 20 minutes later 5 ml 0.5% bupivacaine was applied and surgery started. If necessary, 1 mg midazolam was added intraoperatively. In group G, anesthesia induced with 2.5 mg/kg propofol, 1 mcg kg⁻¹ fentanyl and 0.1 mg kg⁻¹ vecuronium. Maintenance of anesthesia was provided with sevoflurane (MAC 2%), 50% O₂ and N₂O. Bolus 0.5 mcg kg⁻¹ fentanyl and 0.025 mg kg⁻¹ vecuronium were administered intraoperative when necessary. Patients who had immunosuppressive and steroid therapy, additional plastic surgery and unsuccessful epidural anesthesia approaches were excluded.

In patients with group TE, patient-controlled analgesia (PCA) was provided with 0.625% bupivacaine concentration 4 ml of infusion, 6 ml of bolus and a 20 minute lock time protocol. In group G, intravenous patient controlled analgesia was provided with 1 mg bolus morphine and 10 minutes lock time protocol. PCA was continued until the patient was discharged in both groups. Patients' age, weight, ASA scores and

comorbidities; intraoperative vital parameters (heart rate, blood pressure, oxygen saturation), surgery during time, bleeding, fluid infusion, amount of blood transfusion; postoperative nausea-vomiting, hypotension, dysrhythmia and other complications in first 48 hour were recorded from the patient files.

Static (S) and dynamic (D) pain scores were evaluated with Visual Analogue Score (VAS) and were retrospectively recorded from PCA forms. Twelfth, 24th and 48th hours and 1st week VAS scores were recorded. Authors made phone calls with patients to learn VAS scores at the 3rd and 6th months, at the end of the 1st and 3rd years after surgery. During the 3 years follow-up period, the presence of metastases and recurrence was recorded every year.

Statistical program SPSS 20 was used for statistical analyses of the data. Chi-square test was used for demographic data analysis and Student's t-test was used to compare two groups. Mann-Whitney U test was used for numerical variables and chi-square test was used for categorical data p<0.05 were accepted significant.

RESULTS

Between November 2010 and September 2014, 31 female patients with a diagnosed breast cancer and underwent mastectomy were included in this study. The mean age of the patients was 56.2 ± 13.2. Fourteen patients were in group TE and 17 patients were in group G. The demographic data of the patients were given in Table 1.

Table 1: Patient characteristics variable.

	Group E	Group G	p
Age (year)	60.1±12.4	52.8±13.4	0.33
Co-existing disease (N/%)	10/32.3	12/38.7	0.64
Hypertension (N/%)	7/22.6	6/19.4	0.32
Hyperlipidemia (N/%)	2/6.5	5/16.1	0.30
Diabetes mellitus (N/%)	1/3.2	2/6.5	0.57
Asthma (N/%)	1/3.2	2/6.5	0.57
Obesity (N/%)	1/3.2	0/0	0.45

Table 2: Static and dynamic pain scores of patients.

	VAS Static		p	VAS Dynamic		p
	Group E	Group G		Group E	Group G	
12 hour	3.43±2.5	4.35±3.9	0.43	4.64±2.6	4.94±3.8	0.80
24 hour	2.57±1.9	2.82±2.4	0.75	3.57±2.3	3.76±2.9	0.84
48 hour	1.36±1.8	2.12±1.9	0.26	1.79±1.9	2.88±2.4	0.17
1 week	0.77±1.9	1.82±2.2	0.17	1.46±2.5	1.65±2.1	0.83
3 month	0.38±1.4	0.35±0.8	0.76	0.38±1.4	0.75±1.4	0.49
6 month	0.38±1.4	0.06±0.3	0.42	0.62±1.7	0.38±0.9	0.64
1 year	0.17±0.6	0.0±0.0	0.34	0.08±0.3	0.19±0.8	0.62

VAS: visual analogue score, p<0,05 significantly

There were no mortality was seen in both groups during the follow-up period. In the general anesthesia group, one person had tumor recurrence in her third year follow-up, and it was not statistically significant (p=1.0).

When the static and dynamic pain scores were compared between two group postoperative 48th hour and 1st week, both pain scores were lower in the group E. However, this difference was statistically similar (Table 2).

When compare the two groups, systolic blood pressures (SBP) were lower in group E during the surgery and diastolic blood pressures (DBP) after the 15th minute of surgery. These differences was significantly both SBP and DBP at the 45th (p = 0.05; p <0.05), 60th (p <0.05; p <0.05) and 90th (p <0.05; p <0.05) minutes of surgery; only DBP at the 105th minute (p=0.82; p<0.05). There was a statistically significant in the group E decrease in heart rate at the 60th (p<0.05), 75th minutes (p<0.05), 120th (p <0.05) minutes of surgery (Table 3).

Table 3: Compare intraoperative hemodynamic parameters of two group.

	Time (min)	E	G	p
SBP (mmHg)	15	109.6±20.1	110.0±22.6	0.96
	30	108.3±14.5	117.8±18.8	0.12
	45	103.8±18.4	122.5±15.2	<0.05
	60	105.3±18.6	131.2±19.0	<0.05
	75	112.2±24.3	124.8±18.8	0.11
	90	108.7±15.8	130.4±24.5	<0.05
	105	109.5±16.4	121.1±18.1	0.08
	120	123.4±15.8	126.0±21.8	0.20
DBP (mmHg)	15	62.3±12.5	61.2±11.8	0.80
	30	62.1±17.8	66.0±11.0	0.38
	45	53.7±11.1	67.2±11.0	<0.05
	60	61.5±14.5	73.4±11.2	<0.05
	75	63.1±15.8	69.8±16.2	0.26
	90	58.7±11.1	76.2±19.0	<0.05
	105	57.0±11.5	71.2±12.2	<0.05
	120	61.7±10.2	68.7±15.8	0.16
Heart rate (pulse/min)	15	68.3±16.7	69.6±13.6	0.82
	30	64.8±12.5	64.6±12.0	0.42
	45	61.4±11.5	69.8±13.4	0.93
	60	61.0±12.1	76.7±19.8	<0.05
	75	62.2±10.1	71.1±13.0	<0.05
	90	64.6±14.2	71.1±11.2	0.16
	105	62.0±14.8	71.2±10.3	0.08
	120	60.8±10.3	76.8±12.8	<0.05

SBP: systolic blood pressure, DBP: diastolic blood pressure, min: minute p<0,05 significantly

DISCUSSION

In this study to define the relationship between regional anesthesia and tumor recurrence was aimed, tumor recurrence was seen only one patient during the 3-year follow-up period of. There were no relationship found between tumor recurrence and anesthesia type. Authors found that Intraoperative hemodynamic data and postoperative first 48 hours pain scores were found lower in patients who underwent regional anesthesia during the first two hours of surgery.

Drugs that used in general anesthesia cause the immune system suppression. It has been reported that regional anesthesia decreases tumor precursor cytokines, metalloproteinases and antitumor cytokines (IL-10) as a

consequence of a decrease in stress response and immune system suppression in vitro.^{6,10} In addition to these effects, Ravi et al, reported in their meta-analysis that include 28 study, regional anesthesia wasn't effective on tumor metastasis and recurrence.¹⁰ In this study, regional anesthesia and tumor recurrence were not related to each other for three-year period. Authors found a decrease in hemodynamic data of patients in the regional anesthesia group at the 45th minutes of surgery. Peripheral vasodilation, ventricular filling decreases, bradycardia and hypotension are observed as a result of inhibition in the sympathetic system. The effect of neuroaxial anesthesia on the cardiovascular system determines with relationship between preload and afterload and sympathetic blockage and cardiac reflexes.¹¹ This side effect can be observed more frequently in surgeries that

with a high thoracic epidural level target (especially at T4 level), including this study group.

When the postoperative pain of this patients was compared, it was observed that pain control was better in the group E in the early period, but this difference was not statistically significant. In the literature, regional anesthesia has been reported to be more successful in postoperative pain control than general anesthesia.¹² Deegan et al, compared the effect of opioid and regional anesthesia with general anesthesia on postoperative pain in their study, they found lower VAS scores with the first 24 hours of postoperative propofol/paravertebral anesthesia.⁶ In this study, there was a decrease in pain scores in the first 48 hours and 1st week in the group E, but it was not statistical significant. This difference may be as a consequence of the low number of patients.

Limitations of this study the tumor stage at the time of diagnosis and the surgical method can be effective in tumor recurrence and metastasis. Tumor stages and the effect of surgical method were not analysed in this study. In this study include 31 patients only, the studies with higher number of patients could make the analysis more reliable. Although it is known that the tumor recurrences most frequently occur in the first 5 years, three years data of this patients' after surgery were reached.

CONCLUSION

In conclusion, there were no relationship between thoracic epidural anesthesia and tumor recurrence detected in this study. The thoracic epidural anesthesia provides a more stable hemodynamics intraoperatively and lower pain scores in postoperative pain control due to study result.

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