SPECIFIC ANESTHETIC APPROACHES IN PATIENTS WITH BREAST CANCER

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ABSTRACT

Objectives: The latest research shows an influence of some anesthetics and anesthetic techniques on patient's outcome who underwent breast cancer surgery. Surgery remains a golden standard in breast cancer therapy. The proper choice of type of anesthesia is crucial for a patient's safety and outcome.

Aim: To analyze which type of anesthesia for patients undergoing breast cancer surgery was the most preferable during 3-years period and to compare data with those in literature. **Material and Methods.** A three-years retrospective analysis (2019-2021) at Thoraco-vascular Surgery Clinic was done. Out of 1304 patients hospitalized for breast cancer surgery, a group of 60 patients were selected for analysis, divided into two groups according to the type of anesthesia (total intravenous anesthesia (TIVA) or TIVA + lidocaine). The effects of types of anesthesia on hemodynamic parameters, respiration and postoperative comfort were analyzed. Data were discussed with data from PubMed, Cochrane database. **Results:** All 1304 patients received TIVA. There was increasing use of TIVA over the years. TIVA + intravenous lidocaine 60mg was used in 25% of all patients in year 2020 and 30.4% in 2021. Blood pressure showed a significant decrease in both groups, without change in the heart rate. There was a significant reduction in postoperative respiratory rate (12,7±1,1vs13,7±1,6; P=0,04) and better postoperative comfort (2±0,38vs1,56±0,62; P=0,01) in the lidocaine group. The TIVA patients were more tachypneic and less satisfied. **Conclusion:** Using less harmful anesthetics and anesthetic techniques in everyday practice is imperative. TIVA+ lidocaine is a safe anesthesia in breast cancer surgery and can increase a patient's survival.

Key Words: *anesthesia, breast surgery, immune function, local anesthetics.*

Introduction

The Brest cancer remains as a leading cause for morbidity and mortality among the female population in the world and in our country. The annual incidence of Brest Cancer in the world depends on the level of development of the country (1). During 2020 in EU 13.3% of all newly diagnosed malignancies belonged to the breast cancer. The data obtained from the Institute for Public Health of Republic of North Macedonia shows 1200 new cases per year, with a mortality rate of 26.4 on 100000 (2).

Surgery and modified radical mastectomy remain the gold standard of treatment of the breast cancer. The anesthesiologic approach is delicate because the patients with malignancy are female, vulnerable population, under psychological stress, and can undergo repetitive operations. Unfortunately, surgical manipulation over the tumor inevitably provokes dissemination of the tumor cells through blood in the lymphatic system, with an impact to the outcome of the patients

with breast carcinoma. Recent research shows that some anesthetics and anesthetic techniques contribute to the outcome (3, 4). This knowledge increased the interest of anesthesiologists to discover more data about the anti-stress effects of anesthetic agents and its effects in breast surgery. Until today there is no present ideal anesthesia or anesthetic technique for breast surgery, the most of them have advantages or some unwanted effect (5).

During surgery the surgical trauma provokes a stress response of the body with an increase in the catecholamines, prostaglandins, cortisol, cytokines and others. Those products produce immunosuppression with decreased cells immunity. The dissemination of the tumor cells, inflammation, growth factors and impaired immunity are the key factors responsible for the long-time prognoses of the patients with breast tumor (6). The operative stress and the anesthetic agents activate a state of molecular mechanisms which reflects the genetic transcription of the patients with breast carcinoma (7). Current references show that volatile anesthetics and opioids suppress the immune function and play a role in the dissemination of the tumors. Otherwise, several new randomized studies affirm that the use of Propofol, local anesthetics, NSAID-analgesics and tramadol have either positive effect or no effect on the immune function (8). This problem is still under scope and additional research is needed. Those data motivated us to make a retrospective study to find out what anesthetic protocol is used for breast surgery in our department and to discuss if it is safe for the patients or something should be changed.

Goal

The main aim of this study was to find out which type of anesthesia was the most likely and preferable for patients undergoing breast surgery in our department and to compare the obtained data with those in the literature. To complete the secondary outcome, an overview of the medical literature was made. The obtained data were compared to those from the literature and the last data about the unwanted effects of anesthetics on tumor growth, as well as which possible markers are the most appropriate for use were discussed.

Results

The data of the given anesthesia in a three-years period is demonstrated below in Table 1. In this period 4035 patients were anesthetized for operations in thoraco-vascular surgery, and out of them 1304 cases were anesthetized for mastectomy. The type of anesthesia was general: total intravenous anesthesia (TIVA) with propofol, Fentanyl/ remifentanil and pancuronium/ rocuronium. It was obvious that in 2020, with the aim of decreasing the perioperative stress, during the introduction to anesthesia to TIVA, i.v. bolus of 60mg lidocaine 1% was added. In 2021 in order to prevent postoperative pain, preoperatively were added "dorsal rectus plane" block and Pectoralis major and minor blocks (Pictures 1&2).

Table 1. The total number of anesthesia and anesthesia of Ca mammae at a three-years period (n=4035).

Year	2019	2020	2021	N
Total N/%	1798/44.5	1009/25	1228/30.4	4035
Ca mammae /Year	530 (29.4%)	368 (36.47%)	406 (33.06%)	1304
Type of anesthesia for Ca mammae	General TIVA	TIVA + iv lidocaine	TIVA + Lid + blocks	

The data show that in 2019, 29.4% of all surgical interventions in the UC for thoraco-vascular surgery, were modified radical mastectomies. This number increases in 2020 and 2021 to 36.4 and 33.06 respectively.

The data of 60 representative patients in demographics and hemodynamic response anesthetized with TIVA and TIVA with lidocaine are presented in Tables 2 and 3.

Table 2. Demographics of the Groups (N, %, M±SD)

Groups	N	Sex (N/%)		Ages (Years)	Weight (kg)
		Female	Male		
TIVA	30	29 (96.66%)	1 (3.34%)	60.47±6.12	72.29±11.79
TIVA +lidocaine	30	30 (100 %)	0 (0%)	60.43±8.59	73.82±17.25
p		>0.05	>0.05	0.51	0.000

Demographic data show that most of the patients were female, in good condition, and approximately of same age @60 year. The differences between the groups were unsignificant >0.005.

Blood pressure (BP) and heart rate (HR) in the two groups were noted in 5 times periods (To-T5), where Mean BP was used as the most accurate. The times of measurement were as follows: T0 – before the induction to anesthesia. T1 after the induction to anesthesia, and T2, T3, T4, T5 every ten minutes after surgical incision. The approximate time of anesthesia was from 40 to60 minutes. The values of BP and HR in the time T0, were similar in both groups without significant differences.

Table 3. Hemodynamic disorders according to the type of anesthesia.

Variables	N	Mean BP		N	HR	
Groups/Timing	R	TIVA	TIVA + Lido	L	TIVA	TIVA + Lido
T0	30	101.43±16.89	106.43±15.73	30	83.63±15.80	84.13±12.88
T1	30	91.77±15.58	96.90±14.31	30	79.80±14.52	80.87±10.87
T2	30	88.87±14.15	94.47±15.27	30	77.93±13.38	80.97±11.65
T3	30	85.87±16.33	94.40±13.69	30	78.40±15.13	80.77±13.29
T4	28	83.43±13.60	92.83±10.36	23	78.43±14.74	80.26±12.90
T5	20	91.55±12.63	94.09±14.94	11	74.45±14.84	78.09±13.85
p		p = 0.001	p = 0.01		p = 0.42	p = 0.75

Kruskal-Wallis test: H (%, N= 154) =14.89 и p<0.05(p = 0.01)

The analysis of the BP in the studded periods shows a significant decrease in the TIVA group (p=0.001), and in the TIVA +Lidocaine group (p=0.01). The heart rate was not significantly changed in the groups (p=0.42 Vs p=0.75).

The effect of applied anesthesia on postoperative respiration was evaluated by the values pSO_2 and the respiratory rate, for postoperative pain visual analogue scale (VAS) was used, and the comfort was measured by three digits (1 - uncomfortable; 2 - mild comfort; 3 - comfort). The results are presented in the table below (Table 4.).

Table 4. Postoperative respiration, pain, and comfort in the studied groups (M±SD)

Anest	Resp/min	SpO_2	Pain	Comfort
TIVA	13.7 ± 1.6	96.1 ± 1.5	7.3 ± 1.1	2 ± 0.38
TIVA + lidocaine	12.7 ± 1.1	96.8 ± 1.3	6.8 ±1.08	1.56 ± 0.62
p	P=0.04	P=0.19	P=0.18	P=0.01

There was a significant difference in postoperative respiration/ minute and postoperative comfort (P<0.05). The TIVA patients were more tachypneic and less satisfied. The values of SpO_2 and postoperative pain were similar, but with lower VAS scores in the TIVA + Lidocaine group.

Discussion

According to the data from the recent literature, it appeared that volatile anesthetics and opioids suppress the immune function and could affect the long-term prognosis of patients with breast cancer (5). But other studies show that the use of Propofol, local anesthetics, NSAID-analgesics and tramadol have benefits, either positive effect or no effect on the immune function (8). The data from this study show a continuous improvement in the type of anesthesia, without the use of volatile anesthetics for breast surgery. Propofol with its beneficial properties was used in all anesthetized patients. The involvement of i.v. lidocaine is an unpretending beginning of the use of multimodal anesthesia as an opioid sparing technique. All of them with the main goal of achieving a safe anesthesia for patients with cancer.
It is known that surgery as a surgical trauma produces a severe stress response of the body, which is complex including the release of catecholamines, inflammation and growth cells (9). For this reason, less invasive surgical techniques are developed and new anesthetic techniques, such as: balanced anesthesia, multimodal anesthesia, regional and combined anesthesia. In all those surgical and anesthesiologic technics the patients are in the first line, using the multidisciplinary teams, whose main goal is to decrease the surgical stress, to optimize the physiological functions and to facilitate the postoperative recovery.

The surgery for breast carcinoma - partial or radical mastectomy, has a direct influence on the stress response and cells immunity, producing immunosuppression. Therefore, the activity of natural Killer Cells (NKC's) which are the main defense mechanism against the spread of tumor cells, is decreased, the relation of T2/T1 is impaired, and the activity of cytotoxic lymphocytes (CTL's) is suppressed (15-10).

The data in the literature about the effects of some Anesthetics on the tumor growth are still controversial (11).

In 2020, it was referred that volatile anesthetics, as isoflurane and sevoflurane, decrease the cytotoxicity NKC's, CTL's and the relation of T1/T2 cells, and they have tumorigenic effects because they inhibit the cellular apoptosis and stimulate the cells proliferation and migration (12). Other authors show that those attributes are dose dependent (13). Contrary to these findings are the results of some in vitro studies, where the authors assure that there are not significant differences and without invasive characteristics (14,15).

The situation about the agents used for total intravenous anesthesia (TIVA) is less alarming. The use of propofol for anesthesia in breast surgery shows several beneficial effects. It has limited influence on the immune function and NKC's, it can inhibit the systemic inflammatory response (SIRS) and the activity of hypoxia induced factor 1 alfa (HIF1α) (23,24). Propofol helps the

cellular apoptosis of tumors, what makes it to be one of the preferable agents in anesthesia of breast surgery (16).

Dexmedetomidine, a selective α2 agonist with simpaticoliticos and anti-inflammatory effects used still in anesthesia for sedation, is not convenient agent for cancer surgery. Experimental studies confirm that it stimulates the appearance of metastasis (17).

Opioids such as fentanyl, remifentanil, alfentanil or sufentanil have immunosuppressive effects. They decrease the activity of the NKC's, cytokines production, phagocyte's activity, and the release of antibodies (18). Those effects are decreased if they are used in combination with propofol, what was used as a preferred TIVA anesthesia in this studied material (19,20)

Conclusion

The ideal anesthesia does not exist, but the tendency in everyday practice should be to use the less harmful agents. With this study was shown that the most preferable anesthesia was general anesthesia (TIVA) where induction was done with propofol. The combination with local anesthetics (i.v. lidocaine) or regional techniques confirmed its benefits for patients with breast cancer. It is expected that such combinations could suppress the changes in immune function and can increase the survival of the patients with breast carcinoma. Further research in this field is necessary.

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