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Review Article

Analysis of thoracic nerve block combined with transversus thoracic muscle plane block in breast cancer

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Abstract: This paper aimed to explore the effects of thoracic nerve block (TNB) combined with transversus thoracic muscle plane block (TTMPB) for analgesic effect, inflammatory responses, and stress responses in patients with breast cancer after operation. Patients in the research and control groups were assessed and compared in their postoperative pain score. They were observed for their preoperative and postoperative hemodynamics, changes in respiratory function indices before and after operation, adverse reactions, and postoperative inflammatory and stress responses. Visual Analogue Scale (VAS) scores at resting state and after shoulder abduction in the research group were lower than those in the control group at 8, 12, and 24 hours after operation ($P<0.05$). The heart rate (HR), mean arterial pressure (MAP), and central venous pressure (CVP) were lower in the research group at 1 hour after operation ($P<0.05$). Patients in the research group had remarkably higher postoperative minute ventilation (MV) ($P<0.05$), remarkably lower incidence of adverse reactions ($P<0.05$), lower levels of IL-6, TNF-α, and CRP ($P<0.05$), remarkably higher superoxide dismutase (SOD) ($P<0.05$), and remarkably lower malondialdehyde (MDA) ($P<0.05$). In conclusion, TNB combined with TTMPB has better analgesic effects on patients with breast cancer after operation. The combination reduces inflammatory responses and avoids stress responses, so it is worthy of clinical application and promotion.

Keywords: TNB, TTMPB, combination, breast cancer

Introduction

Breast cancer is an extremely common malignant tumor found in clinical practice, and the total number of affected patients accounts for approximately 9%-12% of all malignant tumors [1]. It is estimated that the incidence of the disease has been on the rise in recent years and will surpass that of lung cancer; so this disease may become the malignant tumor with the highest worldwide incidence after gastric cancer in the next 50 years [2]. Its pathogenesis remains unclear, and the early stages usually have no clear symptoms, so most patients will have reached the middle and advanced stages when they are diagnosed; which therefore increases the treatment difficulty [3, 4]. Currently, breast cancer is mainly treated by surgical resection, which often causes severe trauma, intense pain, and other adverse reactions; thereby seriously affecting surgical efficacy and aggravating patients' psychological burden [5]. After radical mastectomy, intravenous opioids combined with non-steroidal anti-inflammatory drugs are mostly used for pain relief [6], but this method has a poor analgesic effect with a high incidence of adverse reactions [7]. Therefore, the search for a good analgesic method is still a clinical research hotspot, and significant to postoperative efficacy of patients with breast cancer and to their recovery.

First proposed by Blanco in 2011, thoracic nerve block (TNB) is a method that injects anesthetics between the pectoralis minor muscle and pectoralis major muscle; so as to block the lateral pectoral nerve, anterior external chest wall, medial pectoral nerve, axilla, and medial upper arm sensation [8]. It has been clinically confirmed that this method has a good analgesic effect on thoracic closed drainage, cardiac pacemakers, breast surgery, and axillary lymph node dissection [9]. Transversus thoracic muscle plane block (TTMPB) is a method that injects local anesthetics into the gap between the internal intercostal muscle (between the fourth and fifth ribs) and musculus transversus thoracis [10]. It can block sensation of the anterior branches of T2-T6 intercostal nerves, laying a good analgesic foundation for the anterior medial region of breast [11]. According to previous studies, TNB combined with TTMPB has a good analgesic effect on patients with breast cancer after operation [12]. For further determining the application value of this combination, its effects on the analgesic effect, inflammatory responses, and stress responses in patients with breast cancer after operation were explored in this research, to provide a reliable theoretical basis for the clinical application of this method.

Materials and methods

General information

One hundred and twenty-eight patients undergoing radical mastectomy, admitted to our hospital from June 2016 to June 2018 were enrolled as research subjects, in which 60 patients received TNB (control group), while 68 patients received TNB combined with TTMPB (research group). This research has been approved by the Ethics Committee of our hospital. All research subjects or their immediate families have signed an informed consent form.

Inclusion and exclusion criteria

Inclusion criteria: Those included were in accordance with the clinical manifestations of breast cancer [13], and were confirmed by biopsy in the pathology department of our hospital, and underwent breast cancer resection in our hospital after confirmation and participated in follow-up treatment; those who were in line with indications for breast cancer resection were included [14]; those with complete patient data were included; those willing to cooperate with and assist the medical staff in our hospital were included.

Exclusion criteria: Those with central or peripheral nervous system diseases, hepatic and renal dysfunction, or allergy to local anesthetics or opioids; those allergic to general anesthetic drugs; those with analgesic and sedative drug therapy for a long period; those with a history of drug abuse; those with coagulation dysfunction or puncture site infection; those complicated with multiple tumors; those who could not take care of themselves because of physical disabilities and who stayed in bed for a long time; and those who were transferred to other hospitals.

Methods

Anesthesia methods: Patients in the two groups were conventionally monitored after operation. General anesthesia induction was performed with fentanyl (1 μg/kg), propofol (2 mg/kg), and rocuronium (0.6 mg/kg). Mechanical ventilation was conducted after tracheal intubation. Patients in the research group received ultrasound-guided TNB combined with TTMPB after anesthesia induction, and 0.375% ropivacaine (number of imported drug registration: H20140763; AstraZeneca) was used for ultrasound-guided peripheral nerve block. Patients in the control group received only TNB. All operations were performed by senior anesthesiologists. TNB: Mindray ultrasound (UMT-400, Shenzhen Mindray Biomedical Electronics Co., Ltd.) high-frequency linear array probe was positioned at the level of the third and fourth ribs. Ultrasound images showed the pectoralis major muscle, pectoralis minor muscle, and serratus anterior tissues, as well as pleura. In-plane needle insertion was adopted to avoid the thoracic wall branch of thoracoacromial artery. After a local anesthetic (10 mL) was injected between pectoralis major muscle and pectoralis minor muscle, needle insertion was continued to penetrate the pectoralis minor muscle, and then the local anesthetic (15 mL) was injected between pectoralis minor muscle and serratus anterior. The anesthesiologist was careful not to insert the needle too deeply, to avoid breaking the pleura. TTMPB: The ultrasonic probe was placed between the fourth and the fifth ribs, parallel to the sternum. Next, the local anesthetic (15 mL) was injected between the internal intercostal muscle and the musculus transversus thoracis for TTMPB. After the operation, the patients' blood pressure, heart rate (HR), and oxygen saturation were monitored. Parecoxib sodium (40 mg) was injected once every 8 hours as an additional remedy for analgesia when the patients suffered from pain, and tropisetron (5 mg) was intravenously injected for treating nausea and vomiting. After the patients were fully awake, acupuncture test was conducted in the medial and lateral skin areas of the chest at T2-6 level, to evaluate the level of anesthesia.

Detection methods: The HR, mean arterial pressure (MAP), and central venous pressure (CVP) were measured before and at 1 hour after operation. SpO_2 and minute ventilation (MV) were analyzed by a blood gas analyzer. Before treatment (on admission) and after treatment (at 2 hours after operation), fasting venous blood (4 mL) was drawn from the patients, placed at room temperature for 30 min, and then centrifuged (1500 × g) for 10 min, to obtain the upper serum. Enzyme-linked immunosorbent assay (ELISA) was used to detect concentrations of IL-6, TNF-α, and CRP in the serum. Superoxide dismutase (SOD) and malondialdehyde (MDA) expression was also measured after treatment.

Outcome measures

Postoperative pain score: Visual Analogue Scale (VAS) was used to assess the patients' postoperative pain [15]. Adverse reactions: The adverse reactions (such as nausea, vomiting, and urinary retention) that occurred during hospitalization were recorded. The incidence of adverse reactions was calculated = The number of cases of adverse reactions/total number of cases × 100%. Inflammatory responses: The venous blood was extracted from the patients before operation and at 1 hour after operation, and then centrifuged to obtain the upper serum. ELISA was used to detect concentrations of IL-6, TNF-α, and CRP in the serum. Stress responses: SOD and MDA expression in the serum was measured as above. Hemodynamic changes: The patients' HR, MAP, and CVP were detected before and after operation. Respiratory function: SpO_2 and MV were detected as above.

Statistical methods

The results of this experiment were statistically analyzed by SPSS 24.0 (Shanghai Yuchuang Network Technology Co., Ltd.). Count data were expressed by (rate), and chi-square test was used for their comparison between groups. Measurement data were expressed by (mean ± standard deviation), and t test was used for their comparison between groups, one-way analysis of variance and LSD post hoc test was used for comparisons between multiple groups. When $P<0.05$, the difference was statistically significant.

Results

Comparison of general information

The differences were not significant between the research and control groups in terms of their age, course of disease, body mass index (BMI), combined diseases, smoking, exercise, living environment, anesthesia time, and operative time ($P>0.05$). See **Table 1**.

Comparison of postoperative pain scores

VAS scores at resting state and after shoulder abduction in the research and control groups were assessed at 8, 12, and 24 hours after operation. The scores were lower in the research group ($P<0.05$). See **Figure 1**.

Changes in hemodynamics before and after operation

The patients' HR, MAP, and CVP were observed before and at 1 hour after operation. Before operation, the differences were not significant between the research and control groups in the three indicators ($P>0.05$); but they were lower in the research group at 1 hour after operation ($P<0.05$). See **Figure 2**.

Comparison of respiratory function indices before and after operation

Changes in respiratory function indices were observed before and after operation. The difference was not statistically significant in SpO_2 between the research and control groups before and after operation ($P>0.05$), while MV was remarkably higher in the research group after operation ($P<0.05$). See **Figure 3**.

Comparison of adverse reactions

The incidence of adverse reactions in the research and control groups was observed. The incidence in the research group was 8.82%, remarkably lower than 23.33% in the control group ($P<0.05$). See **Table 2**.

Table 1. Comparison of general information [n (%)]

Factors	research group (n=68)	Control group (n=60)	X^2/t	P
Age	55.2±6.7	56.2±7.1	0.819	0.414
Course of disease (Years)	0.54±0.24	0.53±0.30	0.209	0.835
BMI (KG)	25.31±3.94	25.43±3.76	0.205	0.838
Combined diseases			1.052	0.591
Hypertension	15 (22.06)	18 (30.00)		
Diabetes	20 (29.41)	16 (26.67)		
No	33 (48.53)	26 (43.33)		
Smoking			2.654	0.103
Yes	14 (20.59)	25 (33.33)		
No	34 (79.41)	23 (66.67)		
Exercise			0.003	0.955
Yes	28 (41.18)	25 (41.67)		
No	40 (58.82)	35 (58.33)		
Living environment			0.328	0.567
City	56 (82.35)	47 (78.33)		
Countryside	12 (17.65)	13 (21.67)		
Anesthesia time (min)	132.52±17.36	135.36±15.58	0.969	0.335
Operative time (min)	96.52±10.47	95.77±11.34	0.389	0.698

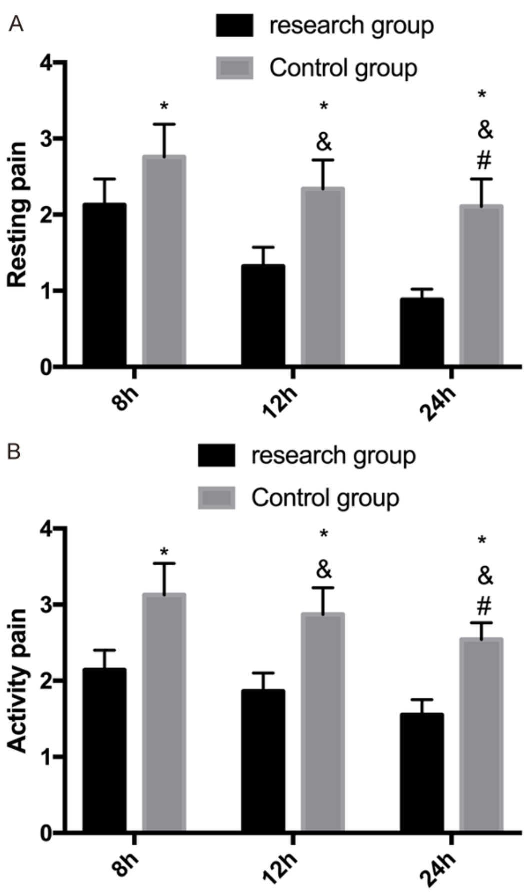

Figure 1. Comparison of postoperative pain scores. A. The comparison of postoperative resting pain scores between the two groups. B. The comparison of postoperative active pain scores between the two groups. Note: * indicates the comparison with the research group at 8 hours after operation. & indicates the comparison with the research group at 12 hours after operation. # indicates the comparison with the research group at 24 hours after operation.

Inflammatory responses after operation

Inflammatory responses before and after operation were observed. Before operation, the differences in IL-6, TNF-α, and CRP expression were not significant between the research and control groups ($P>0.05$). After operation, their expression in the two groups rose, and the expression was lower in the research group ($P<0.05$). See **Figure 4**.

Stress responses

The expression of SOD and MDA (the final product of lipid oxidation) was observed after operation. SOD expression was remarkably higher in the research group ($P<0.05$), while MDA expression was remarkably lower in the research group ($P<0.05$). See **Figure 5**.

Discussion

As a clinically common gynecologic malignant tumor, breast cancer has a high incidence [16],

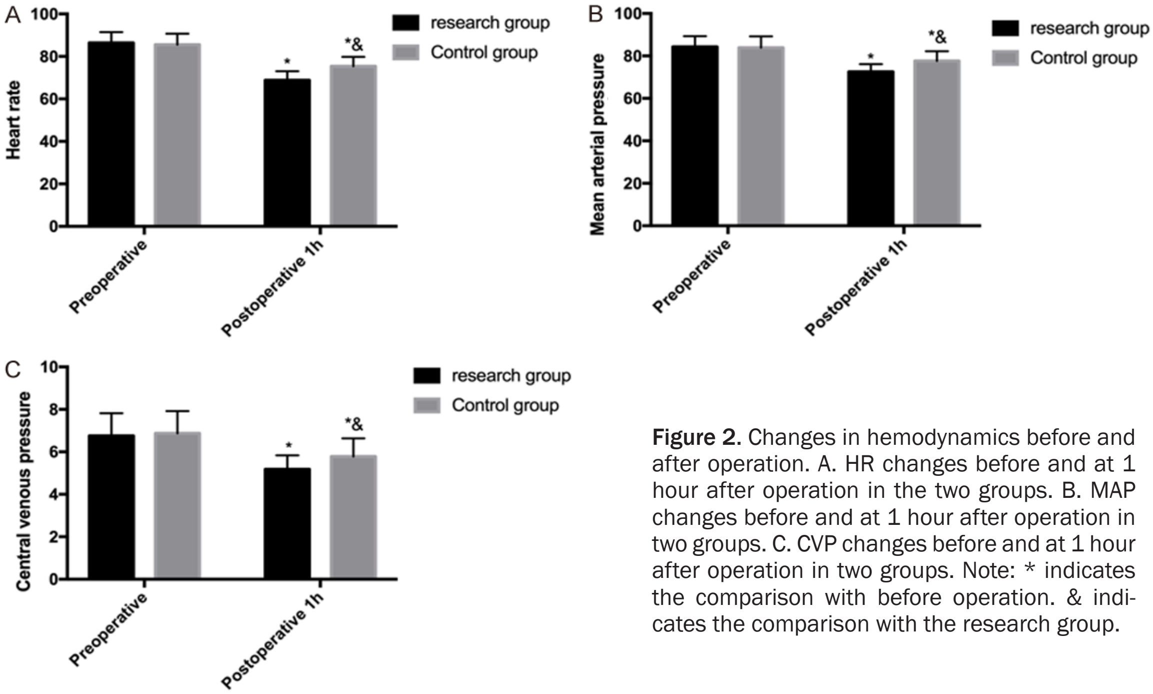

Figure 2. Changes in hemodynamics before and after operation. A. HR changes before and at 1 hour after operation in the two groups. B. MAP changes before and at 1 hour after operation in two groups. C. CVP changes before and at 1 hour after operation in two groups. Note: * indicates the comparison with before operation. & indicates the comparison with the research group.

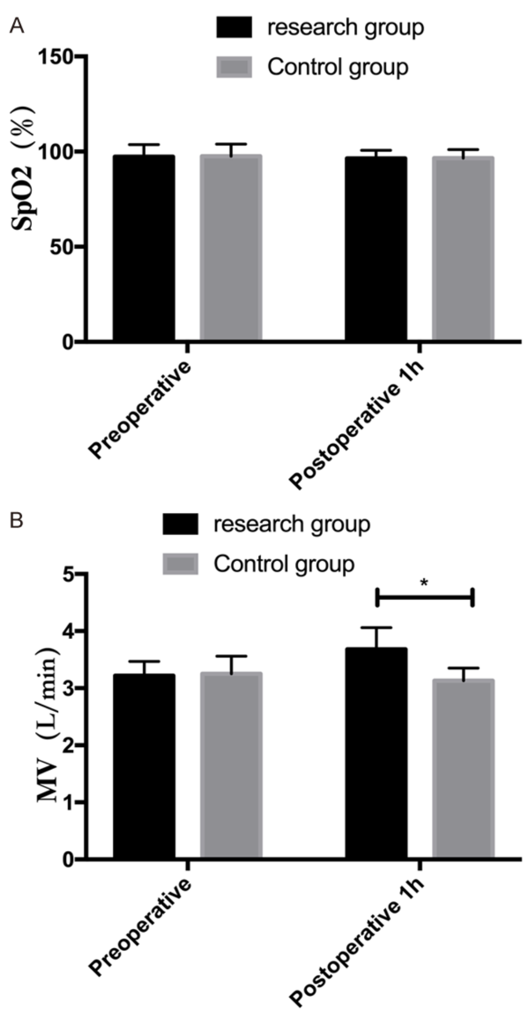

Figure 3. Comparison of respiratory function indices before and after operation. A. The comparison of SpO_2 changes between the two groups before and after operation. B. The comparison of MV changes between the two groups before and after operation.

and patients with the disease are usually treated by modified radical mastectomy [17]. However, invasive operations cause damage to chest wall nerves and the surrounding tissues of breast, thus resulting in painful sensations [18]. Postoperative pain makes the patients unwilling to undergo deep-breathing exercises which reduce their cough; thereby leading to pulmonary atelectasis, pneumonia, and residual pulmonary secretions, limiting their exercise capacity, and increasing the incidence of perioperative complications [19]. According to an investigation, more than 50% of patients undergoing modified radical mastectomy experience moderate or severe pain, which seriously affects their social adaptive capacity and postoperative quality of life [20]. Therefore, good analgesic methods are particularly important for the postoperative recovery of patients. In this study, effects of TNB combined with TTMPB on the analgesic effect, inflammatory responses, and stress responses in patients with breast cancer after operation were explored.

The postoperative pain scores were remarkably lower in the research group, indicating that the

Table 2. Incidence of adverse reactions [n (%)]

	research group (n=68)	Control group (n=60)	X^2	P
Remedial analgesia	2 (2.94)	5 (8.33)		
Nausea and vomiting	2 (2.94)	4 (6.67)		
Lethargy	1 (1.47)	2 (3.33)		
Urinary retention	1 (1.47)	3 (5.00)		
Total incidence	6 (8.82)	14 (23.33)	5.090	0.024

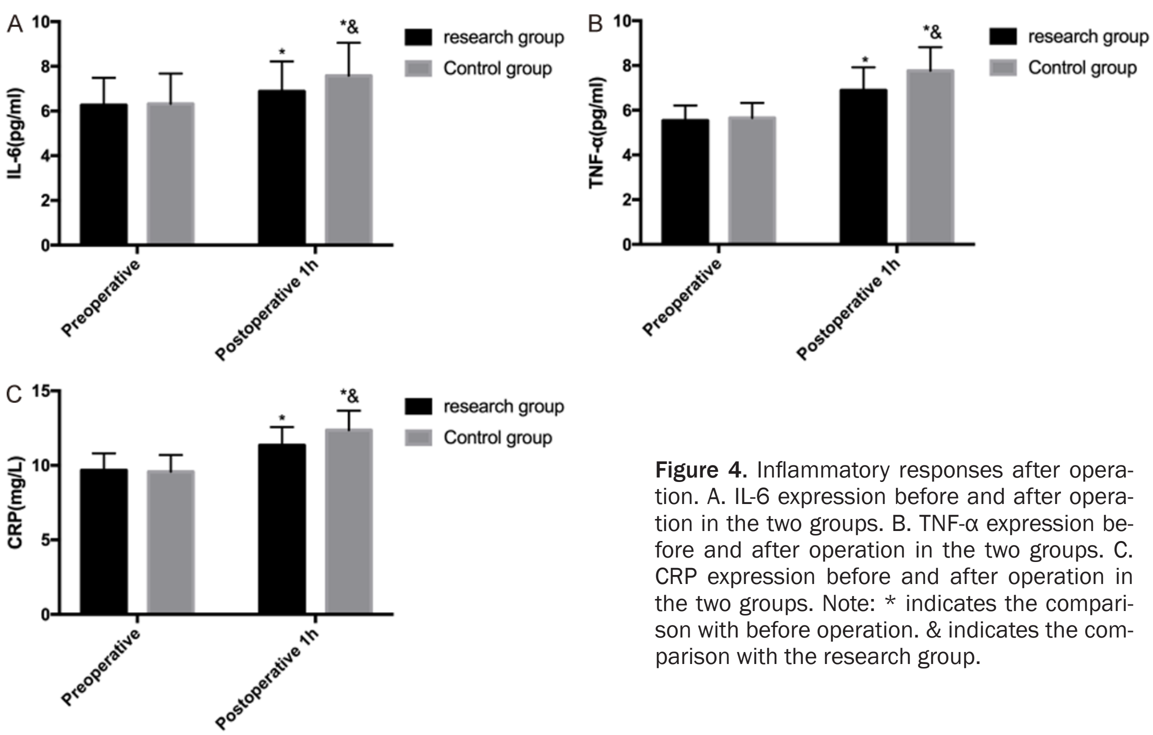

Figure 4. Inflammatory responses after operation. A. IL-6 expression before and after operation in the two groups. B. TNF-α expression before and after operation in the two groups. C. CRP expression before and after operation in the two groups. Note: * indicates the comparison with before operation. & indicates the comparison with the research group.

combination has a more satisfactory postoperative analgesic effect than TNB alone. TNB is a method which injects local anesthetics into the space between the pectoralis minor muscle and pectoralis major muscle, as well as between the serratus anterior and pectoralis minor muscle [21]. It blocks the intercostobrachial nerve and lateral cutaneous branch of the intercostal nerve, the medial cutaneous nerve of the arm and forearm, long thoracic nerve, and thoracodorsal nerve; thus providing an analgesic effect to the lateral mammary gland region. However, it does not provide any analgesic effect to the internal mammary gland region, which results in incomplete analgesia [22]. This is possibly the main reason for relatively high postoperative VAS score. TTMPB blocks the anterior branches of multiple intercostal nerves (the 2nd to 6th ribs) that dominate the internal mammary gland region, thereby providing better analgesic effect for this region [23]. Therefore, their combination has a more comprehensive and effective analgesic effect on the mammary gland region, which also confirms our research results. The HR, MAP, and CVP in the research group were lower than those in the control group at 1 hour after operation, and the postoperative MV was remarkably higher in the research group. Based on the results of hemodynamics, we speculate that TNB combined with TTMPB can inhibit the central nerve conduction of nociceptive stimulus and avoid the occurrence of stress responses. As an important physiological parameter of respiratory circulation, SaO_2 is the percentage of oxyhemoglobin (HbO_2) bound by oxygen in blood to the total bound hemoglobin (Hb), i.e. the concentration of blood oxygen in blood [24]. As an important indicator reflecting exhalatory function, MV refers to the total amount of gas entering or

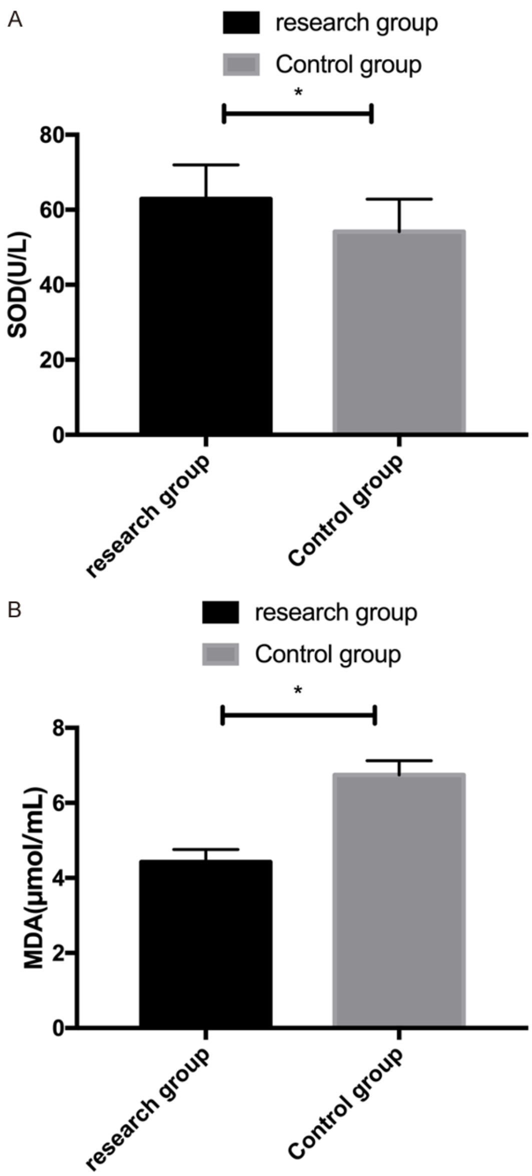

Figure 5. Stress responses. A. The comparison of SOD expression between the two groups. B. The comparison of MDA expression between the two groups.

exiting the lung every minute [25]. The inspiratory function of the human body mainly depends on the diaphragm controlled by C3-4 nerves, and certain cervical muscle groups are involved in the function of deep breathing [26]. Therefore, we suspect that TNB combined with TTMPB has a better analgesic effect on motor and sensory block. It avoids block on motor nerves, and relieves postoperative dyspnea and chest tightness, thus reducing respiratory pain. Furthermore, we observed the incidence of postoperative adverse reactions in the two groups, and found that the incidence was remarkably lower in the research group. This suggests that TNB combined with TTMPB is effective and safe. It also further demonstrates our above results that the combination has a better analgesic effect after radical mastectomy. According to previous data, TNB and TTMPB are easier to identify on ultrasound images, with shallower injection points and fewer side effects. Additionally, they can be operated in a horizontal position to reduce unnecessary movement [27]. The former can block the lateral cutaneous branch of intercostal nerve, anterior cutaneous branch, and long thoracic nerve, with a good blocking effect on the axillary region, so it is suitable for modified radical mastectomy, exploration of sentinel lymph node, and axillary lymph node dissection [28]. This is similar to our research results. Next, we observed the patients' inflammatory responses after operation, and found that the expression of the inflammatory cytokines was lower in the research group. Uncontrolled postoperative pain stimulates peripheral nociceptors, thus inducing injured cells to produce pain-causing factors and inflammatory mediators [29]. Therefore, the lower inflammatory cytokine levels in the research group further reveal that TNB combined with TTMPB can control the postoperative pain of the patients. Finally, we verified the postoperative stress responses in the two groups. The responses were better in the research group, further confirming our above conjecture. Therefore, we come to the conclusion that TNB combined with TTMPB has a better analgesic effect on patients with breast cancer after operation.

The purpose of this research is to explore effects of TNB combined with TTMPB on the analgesic effect, inflammatory responses, and stress responses in patients after radical mastectomy, but it still has shortcomings due to limited experimental conditions. For instance, *in vitro* experiments were not conducted to determine effects of different blocking methods on biological changes of modified radical mastectomy. In addition, the experimental results may have some contingency because of the limitations of the research subjects. Moreover, there are many analgesic methods for radical mastectomy, so we cannot determine whether other analgesic methods have different effects on the analgesia, inflammatory responses, and stress responses of patients with breast cancer after operation. Therefore, we will carry out more comprehensive experiments and analysis as soon as possible based on the above deficiencies, so as to obtain the best experimental results.

In summary, TNB combined with TTMPB has a better analgesic effect on patients with breast cancer after operation. The combination reduces the inflammatory responses and avoids the stress responses; which makes it worthy of clinical application and promotion.

Disclosure of conflict of interest

None.

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