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Original Article

Effects of ultrasound-guided erector spinae plane block on the immune function and postoperative recovery of patients undergoing radical mastectomy

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Background: To explore the effects of ultrasound-guided erector spinae plane (ESP) block on the immune function and postoperative recovery of patients undergoing radical mastectomy.

Methods: One hundred and four patients with breast cancer were randomly divided into the observation group and control group, with 52 cases in each group. The control group underwent induction of routine general anesthesia and thoracic paravertebral block, while the observation group underwent ultrasound-guided ESP block combined with general anesthesia. The recovery of autonomous respiration, eye opening, extubation time, postoperative eating, first anal exhaust, leaving bed and hospitalization time in both groups were statistically analyzed after surgery. The immune function indexes [CD4+, CD8+, interferon-γ (IFN-γ)] and the expression levels of serum neuropeptide Y (NPY), prostaglandin E2 (PGE2) and serotonin (5-HT) were compared between the two groups at 24 and 48 h before and after surgery. The visual analog scale (VAS) scores at rest and during exercise were recorded at 6, 12, 24, and 48 h after surgery.

Results: There was no significant difference in the recovery of autonomous respiration, eye opening, and extubation time between the two groups (P>0.05). However, postoperative eating, first anal exhaust, leaving bed, and hospitalization time in the observation group were shorter than those in the control group (P<0.05). At 24 and 48 h after surgery, compared with the control group, CD4+ and IFN-γ levels were increased significantly (P<0.05), CD8+ and levels of serum NPY, PGE2, 5-HT and the incidence of postoperative complications was decreased significantly in the observation group (P<0.05). VAS scores at rest and during exercise in the observation group were lower than those in the control group (P<0.05). At 5 and 10 min after intubation, the observation group had higher epinephrine (E) level and lower serum cortisol (Cor) level than the control group (P<0.05).

Conclusions: The analgesic effect of ultrasound-guided ESP block is significant after radical mastectomy. There are few adverse reactions and few effects on immune function, and it can promote the postoperative recovery of patients.

Keywords: Radical mastectomy; ultrasound guidance; erector spinae plane block (ESP block); analgesia; immune function; postoperative

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Introduction

In clinical practice, breast cancer patients are often treated with surgery (1,2), but this type of surgery is more traumatic and requires general anesthesia. Therefore, it is necessary to reduce hemodynamic fluctuations, stress responses during surgery and postoperative analgesia (3). Radical mastectomy for breast cancer results in a large wound area, and extensive nerves are involved in the operation area. Even after using a variety of analgesics, 50% of patients still have moderate or higher acute postoperative pain, which seriously affects early postoperative recovery (4). In the past, opioids such as morphine were usually used for postoperative analgesia, but the use of such drugs can induce nausea and vomiting or respiratory depression (5). Koga *et al.* (6) believe that regional block technology can effectively reduce the degree of postoperative pain in patients and reduce the frequency of opioid use. Erector spinae muscle plane block is an emerging nerve block method (7). It has been used in abdominal surgery, laparoscopic surgery, and spinal surgery (8). However, its application and effect in patients undergoing radical mastectomy is currently not well understood. In this study, ultrasound-guided erector spinae muscle plane block was applied to patients undergoing radical mastectomy, aiming to explore the effect of this method on patients' immune function and postoperative recovery. We present the following article in accordance with the STROBE reporting checklist (available at https://dx.doi.org/10.21037/gs-21-603).

Methods

General information

A total of 104 breast cancer patients who were admitted to our hospital from February 2019 to February 2021 were selected and randomly divided into the observation group and control group, with 52 cases in each group. The inclusion criteria were as follows: (I) the patients were diagnosed by pathological examination; (II) the first radical mastectomy for breast cancer was performed; (III) patients were classified as American Society of Anesthesiologists (ASA) grade I–II. The exclusion criteria were as follows: (I) the patient was addicted and resistant to opioids; (II) the patient had a history of allergies to the drugs and excipients involved in this study; (III) the patient had abnormal coagulation function. The observation group was 38–59 (48.36±5.23) years old, 28 cases were classified as ASA grade I, 24 cases were grade II, and the operation time was 74.91–115.35 (95.13±10.11) min. The average age of the control group was 39–59 (48.58±5.10) years old, 30 cases were classified as ASA grade I, 22 cases were grade II, and the operation time was 75.50–115.50 (95.50±10.00) min. The comparison of the above data between the two groups showed that they were balanced (P>0.05). This research was approved by the Sichuan Provincial People's Hospital, University of Electronic Science and Technology of China. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by ethics committee of Sichuan Provincial People's Hospital [Lunshen (Research) No.331-1, 2021] and informed consent was taken from all the patients.

Study methods

After the patients entered the operating room, the upper limb venous access on the opposite side of the operation was opened, and the patients were given fluids and 3 L/min mask oxygen. The observation group underwent ultrasound-guided erector spinae muscle plane block combined with general anesthesia. After disinfection, a high-frequency linear array probe was used for ultrasonic positioning (frequency 10–13 MHz), and the patient's fourth thoracic vertebra transverse process was explored. The probe was moved 2 cm to the fifth thoracic vertebra transverse process, and the needle was inserted in the plane to the fifth thoracic vertebra transverse process. Finally, 30 mL of 0.25% ropivacaine hydrochloride injection (Jiangsu Hengrui Pharmaceutical Co., Ltd., Lianyungang, China; Zhunzi H20060137) was injected. Control group: All patients were subjected to tracheal intubation general anesthesia combined with thoracic paravertebral nerve anesthesia after anesthesia induction. Before anesthesia induction, thoracic paravertebral nerve block was performed. The patients were taken in prone position, bowed back and low head. After routine disinfection, the T5 spinous process and paravertebral space (triangular area composed of transverse process, pleura and rib transverse process ligament) were determined under the guidance of ultrasound, and 1% lidocaine local anesthesia was injected. Ultrasound-guided needle, extraction of triangle gasless, blood, spinal cord injection 2.0 mL saline. After pleural compression, 0.4 mL/kg 0.5% ropivacaine was injected. General anesthesia: anesthesia induction included midazolam (Jiangsu Enhua Pharmaceutical Co., Ltd., Xuzhou, China; National Medicine Standard H10980026) 0.05–0.1 mg/kg, etomidate (Zhejiang Jiuxu Pharmaceutical

Table 1 Comparison of postoperative wakefulness between the two groups ($\bar{x}$ ± s, min)

Group	Spontaneous breathing recovery time	Light eye opening time	Extubation time
Observation group (n=52)	4.30±1.10	7.17±1.75	10.43±1.96
Control group (n=52)	4.58±1.23	6.99±1.50	10.20±1.45
t	1.224	0.563	0.680
P	0.224	0.575	0.498

Co., Ltd., Jinhua, China; National Medicine Standard H20083107) 0.2–0.3 mg/kg, sufentanil citrate (IDT Biologika GmbH, Dessau-Roslau, Germany; National Medicine Standard H20080426) 0.5 μg/kg, and rocuronium bromide (NV ORGANON, Oss, The Netherlands; National Medicine Standard JX20000288) 0.6 mg/kg. After 3 minutes of oxygen denitrification (100% oxygen), a visual laryngoscope was used to intubate the trachea, the balloon was inflated, the position of the tracheal tube was confirmed with a stethoscope, the dental pad was fixed, and the anesthesia machine was connected for mechanical ventilation. For maintenance of anesthesia, propofol and remifentanil hydrochloride were injected with a micro-pump to maintain anesthesia until the end of the suture, and intraoperatively, the muscle relaxant rocuronium 10 mg was administered as needed. After the two groups of patients recovered spontaneously, tracheal intubation was removed according to the indications for tracheal extubation. Postoperatively, intravenous analgesia and a patient-controlled analgesia pump were used for analgesia, which included dezocine (Yangzijiang Pharmaceutical Group Co., Ltd., Taizhou, China; National Medicine Zhunzi H20080329) 0.2–0.3 mg/kg + sufentanil citrate 1.5–2.0 μg/kg + tropisetron (Hainan Lingkang Pharmaceutical Co., Ltd., Haikou, China; Chinese Medicine Zhunzi H20060288) 10 mg + 0.9% sodium chloride injection added to 100 mL. The background dose was 1.5 mL/h, the single dose was 1.5 mL, and the lock time was 15 min.

Evaluation indicators

Recovery of spontaneous breathing, time to light eye opening, and extubation time were recorded in the two groups after the operation. Fasting venous blood (4 mL) was drawn from patients before and after (24 and 48 h) the operation. The levels of CD4+, CD8+, and interferon-γ (IFN-γ) were measured in venous blood. The levels of CD4+ and CD8+ were detected by flow cytometry. The levels of IFN-γ were detected by enzyme-linked immunosorbent assay (ELISA). The visual analog scale (VAS) pain scores of patients at rest and during exercise at 6, 12, 24, and 48 h after the operation were recorded. Peripheral venous blood was collected before and after (24 and 48 h) the operation, and the supernatant was collected by centrifugation. Radioimmunoassay was used to detect the expression levels of neuropeptide Y (NPY), prostaglandin E2 (PGE2), and serotonin (5-HT). Before induction and 5 min, 10 min after intubation, 2.0 mL peripheral venous blood was extracted, and the expression levels of serum epinephrine (E) and cortisol (Cor) were detected by high performance liquid chromatography. Postoperative food intake, first anal exhaust, getting out of bed, and hospital stay times were recorded in the two groups. The incidence of postoperative complications was also recorded.

Statistical processing

SPSS 23.0 software was used for statistical analysis. The measurement data was expressed as $\bar{x}$ ± s, the *t*-test was performed for comparisons between the two groups, and repeated measures analysis of variance was performed at different time points. The count data was expressed as percentages, the χ^2 test was performed, and the test level was α=0.05.

Results

Comparison of postoperative wakefulness between the two groups

There were no significant differences in the times of spontaneous breathing recovery, light eye opening, and extubation between the two groups (*Table 1*, P>0.05).

Comparison of the levels of various indicators of immune function between the two groups

The levels of CD4+, CD8+, and IFN-γ at 24 and 48 h after the operation in the two groups were significantly different (*Table 2*, P<0.05). The levels of CD4+ and IFN-γ at 24 and

Table 2 Comparison of the levels of various indicators of immune function between the two groups ($\bar{x} \pm s$)

Group	CD4+ (%)			CD8+ (%)			IFN-γ (pg/mL)		
	Preoperative	Postoperative 24 h	Postoperative 48 h	Preoperative	Postoperative 24 h	Postoperative 48 h	Preoperative	Postoperative 24 h	Postoperative 48 h
Observation group (n=52)	32.41±2.40	25.75±1.33*	21.32±0.98*	25.10±1.45	20.78±1.33*	19.82±0.76*	395.48±15.63	498.36±17.15*	485.85±15.12*
Control group (n=52)	32.52±2.29	23.74±1.11	20.78±1.23	25.33±1.21	22.98±1.05	21.63±1.20	394.96±15.81	478.26±18.80	441.23±15.09
Between groups		F=51.000, P=0.000			F=108.96, P=0.000			F=113.928, P=0.000	
Time		F=50.000, P=0.000			F=47.756, P=0.000			F=868.714, P=0.000	
Between groups-time		F=50.000, P=0.000			F=21.731, P=0.000			F=35.192, P=0.000	

Compared with the control group, *P<0.05. IFN-γ, interferon-γ.

48 h after the operation in the observation group were higher than those in the control group (P<0.05), while the level of CD8+ was lower than the control group (P<0.05).

Comparison of VAS scores between the two groups

The VAS scores of the two groups at rest and during exercise increased first and then decreased 6–48 h after the operation. There were statistical differences between the two groups at each time point (*Table 3*, P<0.05). The VAS scores of the observation group at each time point at rest and during exercise were lower than those of the control group (P<0.05).

Comparison of NPY, PGE2, and 5-HT levels between the two groups

The levels of serum NPY, PGE2, and 5-HT 24 h after the operation were increased compared with before the operation, while the levels of serum NPY, PGE2, and 5-HT 48 h after the operation were decreased compared with 24 h after the operation. There were statistical differences between the two groups at each time point (*Table 4*, P<0.05). Moreover, the above-mentioned index levels in the observation group were lower than those in the control group 24 and 48 h after the operation (P<0.05).

Comparison of recovery between the two groups

The recovery indicators of the observation group were better than those of the control group (*Table 5*, P<0.05).

Comparison of complications between the two groups

In the observation group, there were 2 cases of nausea and vomiting and 1 case of skin pruritus, with an incidence of 5.77%. In the control group, there were 6 cases of nausea and vomiting and 5 cases of skin pruritus, and the incidence was 21.15%. The incidence of complications in the observation group was significantly lower than the control group (χ^2=4.044, P=0.04<0.05).

Comparison of stress levels between the two groups of patients

After intubation 5 and 10 min, serum E decreased first and then increased, at each time point and between groups were statistically significant (P<0.05), and the observation

Table 3 Comparison of VAS scores between the two groups ($\bar{x}$ ± s, min)

Group	At rest				During exercise			
	Postoperative 6 h	Postoperative 12 h	Postoperative 24 h	Postoperative 48 h	Postoperative 6 h	Postoperative 12 h	Postoperative 24 h	Postoperative 48 h
Observation group (n=52)	1.65±0.62	1.80±0.51*	2.20±0.91*	2.00±0.80*	2.10±0.63	3.20±0.52*	3.81±0.82*	2.75±0.74*
Control group (n=52)	3.62±1.10	3.51±1.00	3.63±1.11	3.55±0.82	3.22±1.13	5.10±1.10	4.98±1.26	4.65±1.18
Between groups	F=51.00, P=0.000				F=419.299, P=0.000			
Time	F=49.00, P=0.000				F=49.274, P=0.000			
Between groups-time	F=49.00, P=0.000				F=7.507, P=0.000			

Compared with the control group, *P<0.05. VAS, visual analog scale.

Table 4 Comparison of NPY, PGE2, and 5-HT levels between the two groups ($\bar{x}$ ± s)

Group	NPY (ρ/μg)			PGE2 (ρ/μg)			5-HT (ρ/μg)		
	Preoperative	Postoperative 24 h	Postoperative 48 h	Preoperative	Postoperative 24 h	Postoperative 48 h	Preoperative	Postoperative 24 h	Postoperative 48 h
Observation group (n=52)	118.25±12.36	151.17±16.33*	132.00±13.65*	255.45±29.18	317.26±27.18*	281.00±27.31*	167.09±16.58	225.39±24.16*	190.36±22.18*
Control group (n=52)	117.98±12.45	160.32±18.15	135.45±13.59	255.82±29.00	328.69±27.82	290.30±27.55	166.96±16.82	236.34±22.98	198.32±21.48
Between groups	F=24.190, P=0.000			F=8.4310, P=0.005			F=9.829, P=0.003		
Time	F=89.556, P=0.000			F=98.088, P=0.000			F=128.254, P=0.000		
Between groups-time	F=4.624, P=0.036			F=6.027, P=0.018			F=5.321, P=0.023		

Compared with the control group, *P<0.05. NPY, neuropeptide Y; PGE2, prostaglandin E2; 5-HT, serotonin.

Table 5 Comparison of recovery between the two groups ($\bar{x}$ ± s, d)

Group	Eating time	First anal exhaust time	Leaving bed time	Hospital stay
Observation group (n=52)	4.39±1.16	1.71±0.61	2.34±0.82	6.06±1.81
Control group (n=52)	5.26±1.27	2.28±0.83	3.26±1.01	7.23±1.56
t	3.647	3.990	5.099	3.531
P	0.000	0.000	0.000	0.001

Table 6 Comparison of stress level between two groups ($\bar{x}$ ± s)

Group	E (ng/mL)			Cor (ng/mL)		
	Before induction	5 min after intubation	10 min after intubation	Before induction	5 min after intubation	10 min after intubation
Observation group (n=52)	120.36±8.12	90.36±7.13	95.11±4.30	160.36±27.35	170.69±24.77	167.40±21.99
Control group (n=52)	121.90±6.53	86.55±4.09	90.30±5.17	159.00±30.46	185.36±11.25	181.01±10.95
Between groups	F=1,153.761, P<0.001			F=12.481, P<0.001		
Time	F=9.570, P<0.001			F=19.358, P<0.001		
Between groups-time	F=54.303, P<0.001			F=4.152, P<0.001		

E, epinephrine; Cor, cortisol.

group after intubation 5 and 10 min serum E levels were higher than the control group (P<0.05). At 5 and 10 min after intubation, the level of Cor first increased and then decreased, and there was significant difference in each time point and between groups (P<0.05). At 5 and 10 min after intubation, the level of Cor in the observation group was lower than that in the control group (P<0.05, *Table 6*).

Discussion

Erector spinae muscle plane block is widely used in clinical practice, such as thoracic surgery, radical gastrectomy for gastric cancer and other diseases, and has significant effects. Patients undergoing radical mastectomy may have moderate to severe acute pain after surgery. If not treated in time, some patients will develop chronic pain, which seriously affects postoperative recovery. The use of epidural and paravertebral nerve block can reduce postoperative pain in breast cancer patients, but these methods have certain risks in the operation. The use of opioid-based intravenous patient-controlled analgesia can relieve acute postoperative pain, but such drugs can also cause postoperative complications. In 2016, Forero *et al.* (9) first injected local anesthetics into the deep surface of the T5 transverse erector spinae to treat chronic chest wall pain, thus the erector spinae muscle plane block got its name. It is reported in the literature that if the T7–T9 transverse process is blocked by erector spinae muscle plane block, it can provide good postoperative analgesia for hernia repair (10) and bariatric surgery (11).

Breast cancer recurrence and metastasis are the main causes of related deaths in these patients (12). Studies have confirmed that the impaired immune system of patients can induce malignant cells to evade host immune surveillance, which is closely related to tumor metastasis and recurrence during the perioperative period (13). At present, surgery is the first-line treatment for breast cancer, but anesthesia and surgery can inhibit the patient's immune function, thereby affecting tumor metastasis and the patient's prognosis (14). Cellular immunity is the main form of anti-tumor immunity (15). Among them, CD4+ cells can regulate or assist other lymphocytes to exert immune regulation (16). The count of CD8+ in the peripheral blood is positively correlated with the good prognosis of the tumor (17). In this study, the levels of CD4+, CD8+, and IFN-γ in the observation group at 24 and 48 h after surgery were better than those in the control group, suggesting that ultrasound-guided erector spinae muscle plane block has less impact on the patient's immune function. Ultrasound-guided erector spinae

muscle plane block can effectively alleviate intraoperative pain. At the same time, the VAS scores of the observation group at various points during rest and exercise were lower than those of the control group, indicating that the postoperative analgesia effect is good. Good analgesia can reduce the body's immunosuppressive responses during the perioperative period, and has a certain protective effect on the patient's immune function. This is because peripheral nerve tissue can block the transmission of noxious stimulus signals, thereby alleviating postoperative pain. The anatomical structure of the triangle area of thoracic paravertebral nerve anesthesia is complex, and the operation is readable. It is easy to penetrate the pleura and blood vessels, and the body is damaged. The erector spinae muscle plane block is to inject anesthetics into the rib angles and spinous process grooves on both sides of the back spine. The position is superficial, the anatomical structure is simple, the operation is simple, and it is not easy to damage other surrounding tissues. Under the guidance of ultrasound, the operation accuracy can be improved. Secondly, the drug entered the transverse process, erector spinae muscle, through penetration into the surrounding connective tissue, paravertebral space block nerve impulse. However, due to the dose-effect of anesthetics, a certain diffusion volume is needed. A large number of anesthetics may spread to the lumbar plexus, resulting in temporary motor dysfunction, muscle weakness and other complications.

Erector spinae muscle plane block can block the thoracic nerve, the long thoracic nerve, and the thoracic dorsal nerve, among others, and can reduce the perioperative stress and pain response of breast cancer patients. As pain mediators, the levels of NPY, PGE2, and 5-HT can reflect the severity of pain in patients. When NPY is expressed in large quantities, it will participate in pain nerve transmission (18). High expression of PGE2 will reduce the pain threshold of patients and increase their subjective pain (19). 5-HT can centrally transmission pain signals through the cerebral cortex to produce pain (20). In this study, serum NPY, PGE2, and 5-HT levels in the observation group were lower than those in the control group at 24 and 48 h after surgery, suggesting that ultrasound-guided erector spinae muscle plane block can reduce the secretion of postoperative pain mediators in patients undergoing radical mastectomy. The use of ultrasound-guided erector spinae muscle plane block can improve the accuracy of the positioning of the transverse process, the erector spinae, and surrounding anatomical structures. At the same time, it has a prominent effect on the display of peripheral nerves and blood vessels. In addition, there are no important blood vessels and nerves in the anatomical position of the transverse process. In summary, blocking this position during anesthesia can prevent nerve damage and block failure. Studies have found that patients with breast diseases undergoing the erector spinae muscle plane block technique have basically no adverse reactions such as nausea, vomiting, and respiratory depression, among others (21). In this study, the incidence of postoperative complications in the observation group was 5.77%. This was lower than 21.15% in the control group, which is consistent with the above-mentioned findings of other researchers. In addition, the eating, first anal exhaust, getting out of bed, and hospitalization times were shorter in the observation group compared with the control group, reflecting the better analgesic effect after ultrasound-guided erector spinae muscle plane block and highlighting the beneficial effect on carrying out postoperative rehabilitation activities as soon as possible. Patients' postoperative awakeness, immune function, VAS score, recovery, stress level and other aspects were evaluated to explore more comprehensively. But at the same time. Due to the limitations of this study, the sample size is small, and the results may have certain errors. In future research, it will further improve the research program, increase the sample size and improve the scientificity of the results.

In summary, ultrasound-guided erector spinae muscle plane block is effective for postoperative analgesia after radical mastectomy for breast cancer, and has less impact on the patient's immune function. It is beneficial to the patient's postoperative recovery and has mild adverse reactions.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://dx.doi.org/10.21037/gs-21-603

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by ethics committee of Sichuan Provincial People's Hospital [Lunshen (Research) No. 331-1, 2021] and informed consent was taken from all the patients.

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