Study of ultrasound-guided ropivacaine combined with butorphanol continuous paravertebral block to prevent pain syndrome by evaluating ccl2 gene expression after radical mastectomy

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ABSTRACT

This study aimed to investigate the clinical effect of ultrasound-guided ropivacaine combined with butorphanol continuous paravertebral block in preventing postoperative pain syndrome of breast cancer. For this purpose, 100 women treated for breast cancer from April 2018 to July 2019 were enrolled as research objects. Surgical procedures included local sentinel lymph node biopsy, mastectomy, sentinel lymph node biopsy for mastectomy, modified radical mastectomy, and implantation. The selected patients were randomly divided into two groups: control group (routine operation anesthesia; n = 50) and observation group (ultrasound-guided thoracic paravertebral block before induction of ropivacaine+butorphanol anesthesia; n = 50). The Real-time PCR technique was performed to evaluate CCL2 gene expression. VAS scores were recorded during the postoperative period. Compared with the control group, the observation group had lower VAS scores at six h, 24h, and 48h (P<0.05). The pain effect of the observation group was less than that of the control group. The observation group had better analgesic effects after anesthesia. The observation group had a lower incidence of pain syndrome at the 6th, 8th, and 12th months (P<0.05), and the incidence of pain syndrome in the two groups decreased with the extension of time. The observation group had lower levels of related factors (P<0.05), and the observation group had lower traumatic stress responses. The protein expression of IL-6, IL-17, and CRP in the observation group was lower than that in the control group (P<0.05). The results of CCL2 gene expression also showed that gene expression in the control group increased significantly (P=0.0047). Since the expression of this gene is one of the factors that stimulate pain signals in the body, the method used in the present study was able to reduce the amount of pain significantly. Therefore, the combination of ropivacaine combined with butorphanol ultrasound-assisted paravertebral block can reduce the intensity of postoperative pain in patients with breast cancer surgery, decrease the incidence of pain syndrome, and increase pain tolerance.

Introduction

The thoracic paravertebral block is a technique of injecting local anesthetics near the thoracic vertebra. It is a useful adjunctive therapy for breast surgery, providing effective analgesia and reducing the need for deep general anesthesia (1). To what extent paraspinal block reduces the need for analgesic drugs remains unclear. Anesthetic and analgesic drugs can impair many immune functions, including neutrophils, macrophages, dendritic cells, T lymphocytes and NK cells, which may affect the prognosis after cancer surgery (2, 3). In animal models, local anesthesia and optimal postoperative analgesia can independently reduce the burden of metastasis in animals inoculated with breast cancer cells after surgery (4, 5). A small retrospective analysis of cancer patients showed that paravertebral analgesia reduced the risk of recurrence (6). A meta-analysis showed that regional anesthesia was associated with improved outcomes in patients with operable prostate cancer (7). The anatomy of the paravertebral space can be clearly defined in each patient using ultrasound (8). Real-time imaging can be used to guide needle entry, making it possible to improve the safety of this particular block technique (9). It was reported that ultrasound-guided paravertebral block was described using the transverse probe position and needle planar graph (10).

One of the most critical genetic indicators in pain prediction is the evaluation of pain-related genes expression (11). Many studies on different

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populations have shown that the CCL2 gene has a significant impact on the prevalence of pain (12-14). CCL2 (C-C Motif Chemokine Ligand 2) is a Protein-coding gene that activates during reperfusion lesions (damage caused by the return of blood flow to ischemic tissue), inflammation, and oxidative stress (15, 16). CCL2 gene expression is influenced by adenosine, an endogenous nucleoside, produced under stress and in interaction with G protein receptors, which helps regulate brain function (17). CCL2 has been reported to induce pain in patients by causing oxidative stress. Therefore, evaluating the expression of this gene is an influential factor in determining the amount of pain (18).

Hence, we reported a clinical study on the prevention of pain syndrome after radical mastectomy using ultrasound-guided ropivacaine combined with butorphanol continuous paravertebral block. We also evaluated the expression of the CCL2 gene to evaluate the efficiency of the present study.

Materials and methods
General Data

We included patients scheduled for elective unilateral mastectomy in a prospective, randomized, double-blind, parallel-group clinical trial. The study enrolled 100 women with breast cancer from April 2018 to July 2019. After obtaining the written informed consent of the participants, surgical procedures were performed including local sentinel lymph node biopsy, mastectomy, sentinel lymph node biopsy mastectomy, modified radical mastectomy, and implant implantation. The subjects were divided into two groups using the random number method: the control group (conventional surgical anesthesia; n =50), and the observation group (Ultrasound-guided thoracic paravertebral block before induction of anesthesia with ropivacaine and butorphanol;n = 50).

Inclusion criteria

Age 18-70 years old; the clinical symptoms and pathological examination were consistent with the diagnostic criteria of breast cancer. Informed consent was signed; No chemotherapy was administered.

Exclusion criteria

Age<18 or age>86; Grade IV or above according to the American College of Anesthesiologists; any contraindications to paravertebral block (e.g. clotting disease, infection, or history of allergy to local anesthetics).

Medical ethics

The research has been approved by the hospital ethics committee and the informed consent of all patients has been obtained.

Method
Randomization

The patients were randomly divided using the sequence generated by the Study Randomizer. The number was hidden in a sealed opaque envelope and drawn up by the anesthesiologist who arranged the use of the blocker to ensure that concealment was allocated. Surgeons, nurses, patients, relatives, and data collectors were unaware of the type of block being used.

Preoperative program

After ensuring venous access, standard routine monitoring of noninvasive blood pressure, pulse oximetry, and electrocardiogram was initiated. All patients were administrated with midazolam (1 mg) for anti-anxiety therapy before the blockade. All patients in the observation group and control group were in a sitting position from T1 to T5 before surgery. In both groups, a linear array ultrasound transducer probe (L12-3, Philips CX50) was used to scan the ipsilateral upper chest to identify and mark the transverse processes.

Ultrasonic technology

By placing the probe in the transverse plane, a suitable thoracic spinous process can be found. The transversal process can be located by moving the probe laterally. The probe should be slightly punctured or cranked to locate the intercostal space and avoid sound shadows from adjacent ribs. The transverse processes were visualized below the medial side, and the pleura was immersed below the lateral side (Figure 1). The medial intercostal membrane, adjacent to the superior transverse costal ligament, is often seen as a thin line of impenetrable rays extending from the transverse process, forming a wedge-shaped pouch representing the parathyroid space. A 22 facet needle (SonoPlex, Pajunk Medical

Systems, L.P., Norcross, GA) was pushed along the plane from the side of the ultrasound probe (Figure 2). When the needle was inserted into the intercostal intima, suction revealed no air or blood, and 15 to 20 mL of 0.5% bupivacaine and 1:400,000 epinephrine were deposited in an increment of 5 mL. The unilateral block was injected with 20 mL of local anesthetic, and bilateral operation was injected with 30 mL of anesthetics (15 mL on each side). The pleural depression is considered the endpoint of the operation, which can be clearly seen in each case (Figure 3). The patient's vital signs were continuously monitored during the placement of the block for at least 30 minutes thereafter. All patients underwent general anesthesia for their surgical procedure and were admitted to the hospital at least one night after surgery.
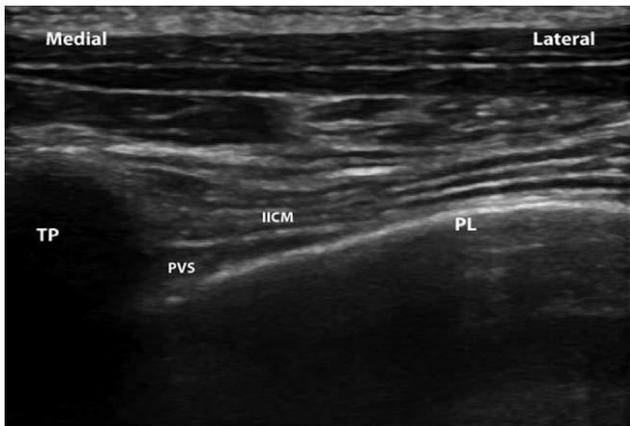
Figure 1. Ultrasonographic images of the paravertebral space between T3 and T4; Note: IICM = intercostal intima;PL = pleura; PVS = apex of paravertebral space; TP = transverse process
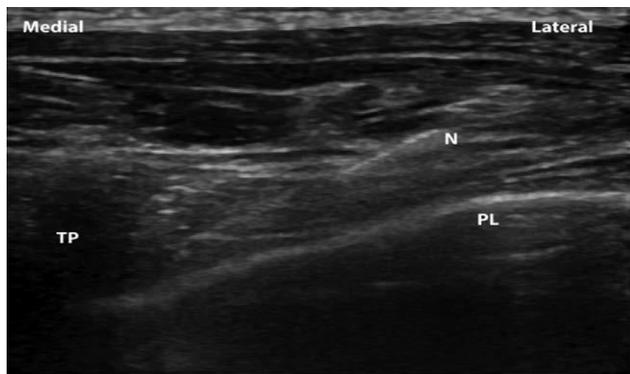
Figure 2. Ultrasound image of intra - surface needle entering the paravertebral space; Note: the tip can be seen on the back of the intercostal intima. N = pin stop; PL = pleura;TP = transverse process
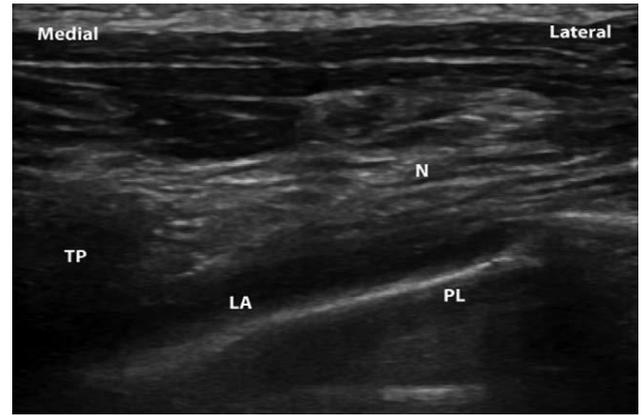
Figure 3. Ultrasonographic images of local anesthetics in the paravertebral cavity of the thoracic cavity.
Note: The indentation of the medial pleura can be observed below the needle. LA = local anesthetic; N = pin stop; PL = pleura;TP = transverse process.

Intraoperative program

The anesthesiologist providing intraoperative care understood the team assignments. The analgesic effect of the observation group was mainly based on paraviral block and maintained by target-controlled infusion of anesthetics. During anesthesia induction, 0.2% ropivacaine + butofenol (5mg4ml/h) was given to facilitate the insertion of the laryngeal mask airway. In the control group, 25 to 50mg of propofol was injected intravenously to induce general anesthesia. Propofol was administered by intravenous injection at a dose of 2.0-2.5mg/kg and injection rate of 4ml/10s to maintain anesthesia. For both groups, additional medications may be used if blood pressure or heart rate exceeds 20% of the preoperative value. Two different anesthesia regimens were selected as part of our study design. In either group, if one or more of the three predefined signs (a 20% increase in baseline heart rate or blood pressure, purposeful limb movements, or facial grimacing) are found on the incision, local pain medication infiltration will be performed to increase anesthesia level to 1.2MAC. Within 5 minutes, try to cut again. Underblocking is defined as the resuscitation of any of the last three predefined symptoms.

Postoperative program

At the end of the operation, all patients were transferred to the post-anesthesia care unit (PACU), where they were monitored. PACU paramedics without knowledge of patient assignment monitored the patient's symptoms including pain, postoperative

nausea and vomiting. During the postoperative period, the VAS score was recorded, and if the VAS score was greater than 4 or the patient had a special request, the patient was given 1 gm of acetaminophen (maximum 24 h dose of 4 gm). If VAS was greater than 6, or greater than the full dose of acetaminophen (4 gm within 24 hours), patients were intravenously injected with 75 mg of diclofenac. Oral analgesics were administrated according to the prescription within the first 24 hours after surgery.

Temperature pain threshold

Heat stimulation was transmitted to participants using the Medoc pathway pain and sensation assessment system with Medoc Main Station (version 6.3.6.18.1). The Pathway system uses thermal contact evoked potential (TEP) thermal electrodes to deliver thermal stimulation accurately and controllably. The circular contact area of the contact evoked potential thermal electrode was 573 mm^2 (with a diameter of 27 mm), which can produce temperatures ranging from 30°C to 55°C. A thermal pain threshold test was performed to determine the individual thermal pain threshold (i.e., they perceived the thermal stimulus as a pain point for the first time) on the dominant forearm front surface with a wrist crease of nearly 5 cm. Three experiments were carried out. The first test results were discarded for the sake of overall understanding, and the thermal pain threshold was calculated as the average of the last two tests. Discarding data from the first trial is consistent with effective methods used in recent studies. As has been done in many previous studies, this approach was far superior to the method of determining pain thresholds using a single trial. The current intensity started at 1 mW and increased by 0.01MW each time. The output power was gradually increased (up to 6 mA at most). Meanwhile, the patient's response was inquired and observed. The power value when the patient began to have a slight tingling sensation was the temperature pain perception threshold, which was tested for 3 times and averaged. The interval between tests was 60 seconds to minimize sensitivity.

Electrical pain threshold

Painmatcher was used to test the electrical pain threshold. The Painmatcher in 15 mA and 10 Hz single-phase square wave provided up to 13 k Ω

constant current, and the strength randomly increased in 4 μs–396μs. The measurement ranged from 0 to 99. We used only one of the three available metrics, which is the pain threshold. Subjects must press the electrode between the main thumb and index finger, withstand the pain up to the maximum strength, then the value will be displayed on an LCD display that is hidden from the subject. Three experiments were carried out to take the average.

VAS pain grade

Visual Analogue scale (VAS) pain scores were recorded every half hour during the first hour after surgery. 10 cm as a unit, record once every hour in the first hour, then once in the next two hours, and then once in the second hour until the 48th hour. Input data were VAS score and total application times of analgesics.

Post-operative nausea and vomiting

Postoperative nausea and vomiting is defined as any nausea or vomiting occurring in the first 24 hours after surgery. In the post-anesthetic care unit, patients were required to report nausea "this makes you uncomfortable" or vomiting in the form of a "yes/no" every four hours. The input data were postoperative nausea and vomiting that existed/did not exist in each patient.

Gene expression evaluations

The 5 ml of peripheral blood was prepared from two groups of control and observation before and after the operation. RNA purification kit (Takara Bio, Japan) was used for RNA extraction. Bioneer cDNA synthesis kit (South Korea) was used to produce cDNA. All steps were performed on ice under sterile conditions. After RNA extraction and cDNA synthesis, the PCR reaction was performed in a volume of 10μl. 5μl of Master Mix 2x (Sigma-Aldrich, USA), 3μl of water containing DEPC, and 0.5μl of primer were added to each tube. At this stage, the cDNA was melted on ice, and after short centrifugation, one microliter was added to each tube. Then, the initial denaturation stage was performed at 94°C for 4 minutes, the annealing stage was performed at 55°C for 20 seconds, and the extension stage was performed at 72°C for 20 seconds in 45 cycles. After preparing cDNA samples, the

microtubes were transferred to 4°C. The beta-actin gene was used as the reference gene to normalize the reaction. Primer design for CCL2 gene and β-actin were performed according to the sequence obtained from the Ensemble database by Oligo V.7.0 software. BLAST server was used to ensure the specificity of the primer connection (Table 1).

Table1. The sequence of primers used to amplify CCL2 and β-actin genes

Gene		Sequence	Product Length
CCL2	Forward	5'-CCAATAGGAAGATCTCAGTGC-3'	123 bp
	Reverse	5'-GTGGTTCAAGAGGAAAAGC-3'	
β-actin	Forward	5'-CATGTACGTTGCTATCCAGGC-3'	176 bp
	Reverse	5'-CTCCTTAATGTCACGCACGAT-3'	

Each PCR reaction was performed by SYBR Green dye in Corbett 5 Plex HRM (Australia) according to the manufacturer's instructions. To quantify the expression values of the desired gene, first, the light absorption coefficient data were converted into numerical data by Rotor-Gene 6000 series Virtual Mode software. Then we used the formula $2^{-\Delta\Delta CT}$ in Excel software, and considering the gene expression of the control group as number 1, the equality of CCL2 gene expression in the observation group was calculated.

Statistical analysis

SPSS 21 was used for data analysis. The normality of the data was tested by the Kolmogorov-Smirnov test and was expressed as an average (standard deviation) or median (interquartile spacing). If the variables were normally distributed, the students' t-test was used to compare the continuous variables, the chi-square test was used to compare the categorical variables, otherwise, the substitution test for non-parametric variables was used. The pain score was considered a continuous variable. The confidence interval was calculated and statistically significant differences were obtained.

Results and discussion
Comparison of General Data

In this study, 100 cases of breast cancer prevention surgery were involved in the study. The average age of the control group was 43.57 ± 4.265, the average BMI was 23.47 ± 1.88, the initial diagnosis time was 2.35 ± 0.45 months, and the I: II of ASA grade was 27:23. In the observation group, the average age was 44.19 ± 5.08, the average BMI was 24.08 ± 1.96, the initial diagnosis time was 2.75 ± 0.36 months, and the

I: II in ASA classification was 31:19. There was no difference in general data between the two groups (Table 2). A total of 100 patients who underwent surgical resection for breast cancer prevention in the hospital were involved in this study. The mean age of the patients in the control group was 43.57±4.265, the mean BMI23.47±1.88, the initial diagnosis time was 2.35±0.45 months, and the ASA classification I: II was 27:23. In the observation group, the mean age was 44.19±5.08, the mean BMI24.08±1.96, the initial diagnosis time was 2.75±0.36 months, and the ASA grading I: II was 31:19. There was no statistical difference in general information between the two groups as shown in Table 2.

Table 2. General information of clinical patients; Group (A), Age (B), BMI (C), Time of illness (month) (D), ASA (I : II) (E), Genetic disease history (n,%) (F)

A	B	C	D	E	F
Control group(n=50)	43.57±4.265	23.47±1.88	2.35±0.45	27:23	3(6.00%)
Observation group(n=50)	44.19±5.08	24.08±1.96	2.75±0.36	31:19	1(1.66%)
t / x^2	5.238	4.172	6.283	4.117	5.085
P value	0.254	0.337	0.286	0.176	0.587

Comparison of Postoperative VAS Scores

VAS scores between two groups were compared at 6h, 24h and 48h after surgery. It was found that the VAS scores in the observation group were lower at 6h, 24h and 48h than those in the control group (P<0.05). The pain effect in the observation group was lighter than that in the control group, and the analgesic effect after anesthesia was better in the observation group as show in Table 3.

Table 3. VAS scores at different postoperative times

Group	6h after operation	24h after operation	48h after operation	F value	P value
Control group(n=50)	4.48±1.25	3.65±1.08	2.58±0.62	19.526	0.012
Observation group(n=50)	3.62±114	2.72±0.74	1.59±0.37	12.781	0.025
T value	5.038	6.417	5.082	-	-
P value	0.014	0.025	0.033	-	-

Temperature Pain Threshold

There was no difference in temperature pain threshold between the two groups before operation (P>0.05), the temperature and pain perception threshold of the observation group was increased compared with the control group 24 and 48 hours after the operation (P<0.05), the temperature pain threshold of the observation group was stronger than that of the control group (P<0.05), as shown in Table 4.

Table4. Comparison of temperature pain threshold

Group	Before operation	24h after operation	48h after operation	F value	P value
Control group(n=50)	3.75±0.27	5.37±0.42	8.26±0.22	19.526	0.012
Observation group(n=50)	3.65±0.85	6.17±0.58	13.08±0.37	12.781	0.025
T value	5.038	6.471	5.008	-	-
P value	0.026	0.034	0.005	-	-

Electrical Pain Threshold

There was no difference in the threshold of electric pain between the two groups before operation (P>0.055); At 24 and 48 h postoperatively, the threshold of electric pain was higher in the observation group than in the control group (P<0.055); the electric pain threshold of the observation group was stronger than that of the control group (P<0.05), as shown in Table 5.

Table 5. Comparison of electric pain threshold

Group	Before operation	24h after operation	48h after operation	F value	P value
Control group(n=50)	0.42±0.18	0.96±0.17	1.87±0.13	13.547	0.012
Observation group(n=50)	0.45±0.12	1.53±0.12	2.45±0.28	12.156	0.007
T value	3.964	15.634	14.328	-	-
P value	0.458	0.027	0.001	-	-

Comparison of Postoperative Pain Syndrome

The patients in the two groups were followed up for one year, and the incidence of postoperative pain syndrome was calculated according to the case data. The results showed that the observation group had a lower incidence of pain syndromes at 6, 8, and 12 months after the operation than the control group (P<0.05), and the incidence of pain syndromes decreased in both groups with the extending of time (P<0.05), as shown in Table 6.

Table 6. Comparison of the incidence of postoperative pain syndrome

Group	T6 (%)	T8 (%)	T12 (%)	x^2 value	p value
Control group(n=50)	11(22.00%)	8(16.00%)	6(12.00%)	5.021	0.020
Observation group(n=50)	6(12.00%)	4(8.00%)	1(2.00%)	5.869	0.011
x^2 value	4.162	5.734	5.081	-	-
p value	0.026	0.014	0.008	-	-

Comparison of Levels of Traumatic Stress Factors

The levels of trauma factors, including serum adrenaline, norepinephrine, aldosterone and cortisol, were compared within 24 hours after surgery, and the levels of trauma factors were found to be lower in the observation group than in the control group (P<0.05), indicating the post-traumatic stress response in the observation group was lower, as shown in Table 7.

Table 7. Comparison of levels of trauma stress factors

Group	Epinephrine (mmol/L)	Methylepinephrine (mmol/L)	Aldosterone (pg/ml)	Cortisol (µg/L)
Control group(n=50)	0.87±0.18	1.35±0.26	78.64±12.59	368.45±45.09
Observation group(n=50)	0.54±0.12	0.83±0.14	49.37±8.66	267.34±29.87
t value	4.368	5.224	4.126	5.087
P value	0.017	0.025	0.034	0.026

Analysis of Inflammatory Response Molecular Protein Expression

Western blot analysis of postoperative serum inflammatory factors IL-6, IL-17 and C Reactive protein (CRP) protein expression in the two groups was carried out, and the results showed that the observation group had lower expression levels of IL-6, IL-17, CRP compared with the control group (P<0.05). The predominance diagram showed the average rating ratio (98.75% confidence interval, CI)

between the regional group and the general group for each major outcome. Parenthesis indicates that the two-sided CI estimated using self-weighting sampling was 98.75%. A combined hypothesis test of the three main outcomes showed that paravertebral analgesia was more effective than general anesthesia because all three CI were located in the dominant region as shown in Table 8 and Figure 4.
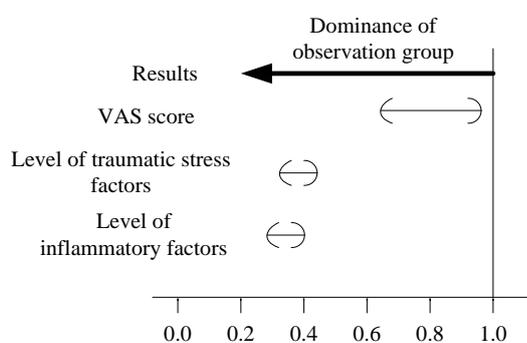
Figure 4. Average rating ratio (98.75%CI)

Table 8. Protein expression analysis of inflammatory factors

Group	IL-6	IL-17	CRP
Control group(n=50)	1.85±0.12	1.74±0.11	1.85±0.14
Observation group(n=50)	1.05±0.07	1.15±0.08	0.94±0.05
t value	5.028	6.355	4.152
P value	0.014	0.037	0.022

Gene expression Results

The results of this section showed that there was no significant difference between the two groups before operation in terms of CCL2 gene expression. But after the operation, gene expression in the control group increased significantly (P = 0.0047).
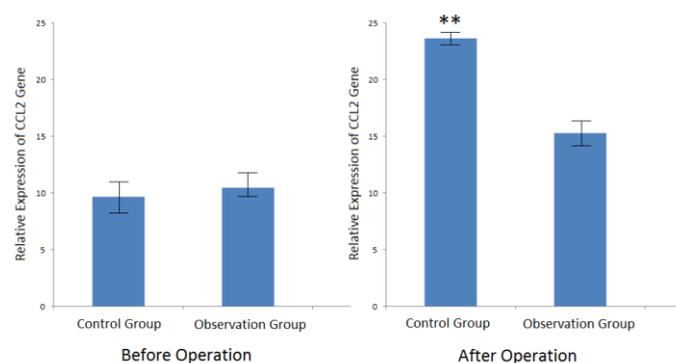
Figure 5. CCL2 gene expression in control and observation groups before and after the operation

Breast cancer is the second most common cancer in the world after lung cancer. Postoperative pain syndrome after mastectomy is one of the chronic postoperative pain diseases with neurological characteristics. Nearly 20-50% of breast cancer patients undergoing mastectomy may develop pain syndrome (19, 20). Paravertebral block has been used as a diagnostic, prognostic or therapeutic intervention for different pain syndromes (21). Surgical and anesthetic techniques have been shown to inhibit NK and functional T lymphocyte activity. Volatile anesthetics, such as sevoflurane, have been reported to impair NK and T cell functions, while acute and chronic administration of exogenous opioids can inhibit components of cellular and humoral immune responses, such as antibody production, NK cell activity, cytokine secretion, and the proliferative response and phagocytic activity of lymphocytes to mitogens (22). The overall incidence of pleural puncture in thoracic and para-lumbar vertebral block performed using nerve stimulation techniques is reported to be 0.8%, and the incidence of subsequent pneumothorax is 0.5% (23). In a small-sample study, the paravertebral block was used in 15 patients, of which 1 patient had an unexpected pleural puncture, which was suspected to be due to greater resistance loss of local anesthetic than normal loss (24). Our study did not show any suspicious pleural puncture or any patients with clinical symptoms of pneumothorax after placement of paravertebral block, which was mainly due to the use of improved safety using real-time needle visualization and ultrasound for pleural imaging.

In our healthcare system, the relatively high cost of patient pump control after surgery is not covered by basic health insurance, so we chose a novel multilayer technique that utilizes ultrasound combined with a traditional approach to paravertebral block. Real-time ultrasound guidance can be used to help identify paraviral spaces, guide needle placement and monitor the diffusion of local anesthetics (25). Using this technique, a clinician can perform a paravertebral block for 2 or 3 patients within 15 minutes, and the incidence of complications can be reduced because of the ability to view the pleura (26). In animal models, the optimal postoperative analgesia can independently reduce the metastatic burden of rats inoculated with breast cancer cells after surgery, so the most severe

pain within two hours after surgery is one of our main outcome indicators (27, 28). In this study, the analgesic effect of both groups was clinically satisfactory, but the observation group had lower VAS scores at 6h, 24h and 48h compared with the control group (P<0.05), The pain effect in the observation group was lighter than that in the control group, and the analgesic effect after anesthesia was better in the observation group. There was no difference in temperature pain threshold and electrical pain threshold between the two groups before operation (P>0.05), the temperature pain threshold and electrical pain threshold were increased in the observation group 24 and 48 hours after surgery compared with the control group (P<0.05), indicating the temperature and electrical pain thresholds of the observation group were stronger than those of the control group. The incidence of pain syndromes was lower in the observation group than in the control group at 6, 8, and 12 months after operation (P<0.05), and the incidence of pain syndrome decreased in both groups with the extension of time.

Hemodynamic instability or compromise, surgical stress response, poor postoperative pain control and delayed spontaneous respiratory recovery, many inflammatory mediators produced by white blood cells and endothelial cells can all cause pain, and such pain can be offset by endogenous opioids in peripheral termination of the nerve (29, 30). Inflammation occurs in the trauma area, leading to the activation of pain receptors (31, 32). Low immune function may affect the risk of postoperative infection, duration of wound healing, treatment response, and tumor cell proliferation (33) Paravertovertebral block can be considered a unilateral pleural epidural block, with virtually no clinical significance for hemodynamic effects in patients after mastectomy (34). Our study found that the levels of adrenaline, norepinephrine, aldosterone and cortisol in the observation group were lower than those in the control group (P<0.05), indicating the post-traumatic stress response in the observation group was low (35). Compared with control group, the protein expression of IL-6, IL-17 and CRP in the observation group were decreased (P<0.05) (36).

In confirmation of the results obtained from this study, the results of CCL2 gene expression also showed that ultrasound-guided ropivacaine combined with butorphanol continuous paravertebral block significantly prevented gene expression in the observation group after the operation (p = 0.0047)(Figure 5). Since the expression of this gene increases during inflammation and oxidative stress and is one of the factors that stimulate pain signals in the body (18), the method used in the present study was able to reduce the amount of pain significantly.

In summary, the combination of ropivacaine and butorphanol ultrasonic-assisted paravertebral block can reduce postoperative pain intensity, decrease the incidence of pain syndrome, and increase pain tolerance in patients undergoing breast cancer surgery (37). Further tests are needed to examine the role of ultrasound-assisted paravertebral block in other breast surgery (38-40).

Acknowledgement

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