Comparison of rhomboid intercostal nerve block, erector spinae plane block, and serratus plane block on analgesia for modified radical mastectomy: A prospective, randomized, controlled trial

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Abstract

Background and objectives Breast cancer is one of the most common malignant tumors in women. Herein, we compared the analgesic efficacy of ultrasound-guided rhomboid intercostal nerve block , erector spinae plane block and serratus plane block after modified radical mastectomy of unilateral breast cancer. Methods: A total of 90 patients who underwent modified radical mastectomy for unilateral breast cancer were selected. patients were randomly allocated into three groups receiving ultrasound-guided serratus plane block, erector spinae plane block, and the rhomboid intercostal block group. All groups received 20 mL 0.5% ropivacaine. Within 24 hours after operation, the patient received intravenous injection of tramadol 1-2 mg/kg to relieve pain in the surgical ward. Results: The dosage of tramadol 24-hours postoperatively in the rhomboid intercostal block and erector spinae plane block groups was significantly lower than that in serratus plane block group ($P < 0.001$). There was no statistical difference in tramadol consumption between the erector spinae plane block and rhomboid intercostal block groups within 24 hours ($P = 0.676$). The numerical rating scale scores in the erector spinae plane block and rhomboid intercostal block groups at 0.5, 1, 3, 6, 12, 18, and 24 hours postoperatively once patients were active were significantly lower than in the serratus plane block group ($P < 0.05$ for all comparisons); however, The numerical rating scale scores between rhomboid intercostal block and erector spinae plane block groups did not differ significatively within 24 hours after surgery when patients were active. Conclusions: Ultrasound-guided rhomboid intercostal block and erector spinae plane block can reduce the dosage of tramadol and NRS score compared with serratus plane block after modified radical mastectomy.

1. Introduction

Breast cancer is one of the most common malignant tumors in women [1]. Postoperative pain is a significant concern following modified radical mastectomy (MRM) [2]. Excision of the pectoralis major fascia and extension of the pectoralis muscles to improve surgical access are likely causes of perioperative myofascial pain [3]. Moreover, drain placement may contribute to pain experienced during the postoperative period. In addition to branches of the intercostal nerves, the pectoral, thoracodorsal and long thoracic nerves may also be involved in perioperative pain following radical mastectomy with axillary involvement [2]. Therefore, many different kinds of analgesic techniques have been proposed, including intercostal block, local anesthetic infiltration, erector spinae plane block (ESP), paravertebral block, serratus plane block (SAB block) and rhomboid intercostal block (RIB) block to relieve acute postoperative pain [3-7]. it is still not clear which one is superior to others. The effects of regional block technology needs to be compared by further researches.

Ultrasound-guided erector spinae plane (US-ESP) block is a fascial nerve block technique described for the first time by Forero et al [8]. US-ESP can provide effective postoperative analgesia for patients undergoing modified radical mastectomy [3]. Serratus plane block (SAB) is a new analgesic technique proposed by Blanco

et al [9], and provides a good postoperative analgesic effect in patients undergoing MRM [7, 10]. Ultrasound-guided rhomboid intercostal block (US-RIB) is a new fascial block technique discovered by Elsharkawy et al.[11] in 2016. Recently, some clinical studies have reported that RIB can effectively reduce postoperative pain in patients with breast cancer after MRM. However, the comparison of postoperative analgesic effects of RIB, SAB and ESP block on patients undergoing MRM has not been reported. In the current research, we compared the analgesic effects of these three kinds of nerve block after MRM for the first time.

This prospective randomized controlled trial was performed to analyze the postoperative analgesic efects of ultrasound-guided RIB, ESP and SAB block after MRM. The primary hypothesis of this study is that the ultrasound-guided RIB block and ESP block reduced postoperative tramadol consumption and pain scores more efectively than the SAB block in the frst 24 h after MRM.

2. Material and methods

2.1 Patient enrollment and study design

After obtaining approval from the Ethics Committee of the Affiliated Hospital of Jiaxing University ((Identifier: LS2020-307). The study protocol was registered in the Chinese Clinical Trial Registry (ChiCTR2000038376). The Chinese Clinical Trial Registration date is September 21, 2020 (21/09/2020), and the date of patient enrollment is September 23, 2020 (23/09/2020). This experimental study obtained the consent of all the participants and signed a written informed consent form. The age of the patient is between 18 and 80 years old, with American Society of Anesthesiologists (ASA) grade 1-2, and preparing to undergo modified radical mastectomy in our hospital. The exclusion criteria included patients with shock or coma, abnormal blood coagulation, infection in the planned block area, severe nerve injury on the side of the limb; patients with history of chronic pain and taking analgesic; patients with psychiatric diseases; patents on radiotherapy and/or chemotherapy; patients allergic to local anesthetics (e.g. lidocaine and ropivacaine) and to general anesthetics; patients and/or their families that refused surgical anesthesia; Previous history of breast surgery or other chest surgery; body mass index (BMI) [?]35 kg/m^2.

2.2 Anesthesia application

The patient was admitted to the operating room for pulse oxygen saturation, electrocardiogram and non-invasive blood pressure monitoring. Following placement of a 20-gage intravenous line, all patients received 14 $mL*kg^{-1}*h^{-1}$isotonic Lactic acid Ringer's solution intravenously (i.v.). Anesthesia induction: midazolam (0.05 mg/kg body weight), sufentanil (0.5μg/kg), propofol (2 mg/kg) and cis atracurium (0.15 mg/kg) were injected intravenously 3-5 minutes after denitrification and oxygenation. A single-lumen endotracheal catheter was used to complete ventilation. The ventilator ventilation mode is volume control mode, and the patient's end-expiratory carbon dioxide level is maintained at 35-40 mmHg throughout the anesthesia process.

During the anesthesia maintenance phase, 2% sevoflurane mixed with 60% oxygen, remifentanil (0.5 μg/kg/min) and propofol (100 μg/kg/min) were continuously pumped. Cisatracurium (0.15 mg/kg) was given every hour during the operation. If the non-invasive blood pressure is more than 20% of the base value, remifentanil (0.1–1.0 μg/kg/min) is added intravenously. If the blood pressure is more than 20% lower than the baseline, give a rapid intravenous drip of saline 250mL or ephedrine 0.1 mg/kg. If the heart rate decreased to less than 50 bpm, atropine (0.5 mg/kg) was administered. At the end of the modified radical mastectomy (MRM) procedure, neostigmine (0.05mg/kg) and atropine (0.02mg/kg) can reverse the muscle relaxation effect of cisatracurium. After the operation, the patient is transferred to the postoperative recovery room, and the endotracheal tube can be extubated after being evaluated by the anesthesiologist.

2.3 Patient grouping and randomization

Patients undergoing modified radical mastectomy were randomly divided into three groups. The patients were randomly allocated into three groups based on a computerized randomization table created by a researcher who was not involved in the study. The researchers randomly assigned an ID card to each registered

patient, each of which was sealed in an opaque envelope[3]. The nerve block technique was performed by another anesthesiologist who was completely unaware of the patient's ID. None of the patients knew the specific grouping. a blind anesthesiologist(AIU), used the patient's ID, to collect data In the breast surgery ward. Surgeons, attending anesthesiologists, outcome evaluators and data analysts do not know the specific grouping.

2.4 Application of block intervention

In the SAB group, an anesthetist with experience in interfascial blocks performed the ultrasound (US)-guided technique using a linear probe (6–12 MHz), a US device (LOGIQ e US system, Deutschland GmbH & Co. KG, Solingen, Germany), and a 21G x 80-mm echogenic needle. The patient is in supine position with 90-degree arm abduction, the US probe was positioned in a sagittal plane at the midaxillary line. There is a fascia plane between the fourth and fifth ribs in the middle axillary region, which is located between the serratus anterior muscle and the external intercostal muscle[9]. When the needle reached the fascia plane of the anterior serratus muscle and the external intercostal muscle, 20 mL 0.5% ropivacaine was given. ·

In the ESP group, The patient was in a lateral position. The T4 spinous process was determined, and the transducer was placed about 2-3 cm away from the midline in the longitudinal direction to identify the hyperechoic line of the transverse process and its related sound shadow. After determining the trapezius muscle, rhomboid major muscle and vertical spinal muscle group on the superficial surface of the transverse process. The tip of the needle (a 21G x 80-mm block needle) moves forward until it is located in the deep interfascial plane of the erector spinalis muscle group and above the transverse process. 0.5% ropivacaine 20mL was injected into the interfascial plane between the rhomboid major muscle and the erector spine muscle. Under the guidance of ultrasound, the local anesthetic spread to the depths of the erector spinae muscle in the mode of longitudinal fascia [12].

In the RIB group, The patient was placed in a lateral position with the affected breast at the top. Extend the ipsilateral arm to the same level of the ipsilateral chest and breast, and move the scapula outward. On the oblique sagittal plane, a high frequency (6-12 mhz) linear ultrasound probe was placed on the medial edge of the scapula. The US landmarks, trapezius muscle, rhomboid muscle, intercostal muscles, pleura, and lung were identified. Under aseptic condition, insert a 21G x 80m nerve block needle into the plan of the US probe at T5 to T6 levels. 0.5% ropivacaine 20mL was injected into the interfascial plane between the rhomboid major muscle and the intercostal muscle. Under the ultrasonic probe, the diffusion of ropivacaine in the fascia between the rhomboid muscle and the intercostal muscle can be visualized. Then the patient was positioned in supine position. All nerve blocks are performed by the same anesthesiologist, who has experienced with SAB, ESP and RIB block in more than 30 patients prior to nerve block.

2.5 Analgesia protocol, evaluation of pain, and sensorial block

Another blinded anesthesiologist (AIU) conducted pain assessments at 0.5 h postoperatively using the 11-point Numerical Rating Scale (NRS), which ranges from '0' (meaning 'no pain') to'10' (meaning 'worst pain imaginable'). Within 24 hours after operation, the patient received intravenous injection of tramadol 1-2 mg/kg to relieve pain in the surgical ward until the NRS pain score was [?]3 in accordance with hospital policy. The patients were sent to the surgical ward at the end of the 0.5 h. In the surgical ward, patients were assessed again 0.5, 1, 3, 6, 12, 18, and 24 hours postoperatively. If the postoperative NRS was greater than 3 points, tramadol 1–2 mg/kg was administered i.v., and then pain was evaluated after 30 minutes.

2.6 Outcome measures

The primary outcome measures were to compare the effects of US-RIB, ESP, and SAB on postoperative tramadol consumption of patients, and postoperative pain scores of the patients undergoing unilateral MRM surgery. The secondary outcome measures were the dose of remifentanil and propofol, time of the first pain, the satisfaction score of patients (1–10, where 10 was the highest). In addition to these measures, postoperative nausea and vomiting (PONV, which were rated on a four-point verbal scale: none=no nausea,

mild=nausea but no vomiting, moderate=vomiting one attack, severe=vomiting>one attack) and block-related complications such as pneumothorax, bleeding, allergy, local anesthetic toxicity were also recorded.

2.7 Sample size

The sample size of the study was calculated using the PASS 15 based on a pilot study with 10 patients in each group. The mean tramadol consumption was 281.50 +- 14.53 mg in the SAB group and 256 +- 36.57 mg in the RIB group. Assuming an α error = 0.01 (two tailed) with a power of 0.90, at least 27 participants were needed per group. With consideration of potential patient drop-out, we decided to include 30 patients in each group.

2.8 Statistical analysis

Statistical analyses were performed using SPSS v25.0 (IBM, Armonk, NY, USA). The shapes of the distributions of the variables in this study were assessed by using the Shapiro-Wilk test, whether the observation is normal or skewed. In cases where the test results have indicated that the data were normally distributed, then data were detailed with mean ± standard deviation (SD). The continuous data which yielded the non-parametric dispersion was detailed with median and IQR and analyzed with the Mann-Whitney U test to observe the group-wise differences. One-way ANOVA was used to compare the differences of outcome parameters (age, BMI, procedure duration, duration of anesthesia, dose of remifentanil and propofol, recovery time, NRS score, NRS dynamic score, time of first pain, total tramadol consumption (mg) in 24 h, satisfaction score) among groups (group SAB vs group ESP vs RIB). Pairwise comparison of one-way ANOVA was made using post hoc analysis and the Student-Newman-Keuls Q-test. The prevalence of nausea, vomiting, and limb paresthesia is presented as a percentage, and differences among groups were evaluated using the chi-square test. The corrected P-value was obtained directly, and the cutoff value was 0.05.

3. Results

A total of 110 patients were selected to meet the criteria for inclusion in this study, 20 patients were excluded, of which 4 patients did not meet the inclusion criteria, 12 patients refused to participate in this study, and 4 patients did not enter the experimental group for other reasons. Ninety patients were equally allocated to the study groups. Ultimately, the data of ninety patients were analyzed. The consort diagram is shown Fig. 1. Table 1 describes the demographic characteristics of the three groups of patients.

The dosage of tramadol consumption at 24 hours after the surgical procedure in the ESP group and RIB group was significantly lower than that in the SAB group ($P < 0.001$) (Fig. 2C). There was no statistical difference in tramadol consumption between the ESP and RIB groups within 24 hours ($P = 0.676$) (Fig. 2C). Similarly, the postoperative NRS score in the ESP and RIB groups 0.5, 1, 3,6,12, 18 and 24 hour after surgery when patients were active was significantly lower than that in the SAB group ($P < 0.05$ for all comparisons) (Fig. 3B). However, there was no significant difference in postoperative pain scores at 0.5, 1, 3, 6, 12, 18, and 24 hours after operation across the three groups (Fig.3A). There was no statistical difference in the postoperative NRS score between groups ESP and RIB within 24 hours after surgery when patients were active (Fig. 3AB).

The total number of complaints about pain, the time of first pain , and the satisfaction scores in groups ESP and RIB were significantly shorter than those in group SAB ($P < 0.05$ for all comparisons) (Fig. 2AB, Fig. 3D), There was no significant difference in the time of first pain ($P = 0.543$) (Fig. 2B), total number of complaints about pain, and satisfaction scores ($P = 0.697$) between the ESP and RIB groups (Fig. 2AD).

There was no significant difference in the dosage of propofol ($P = 0.912$ for all comparisons) and remifentanil ($P = 0.954$ for all comparisons) among the three groups (Table 2), and there was no significant difference in recovery time ($P = 0.201$ for all comparisons), age ($P = 0.439$ for all comparisons), or BMI ($P = 0.104$ for all comparisons) across the three groups (Tables 1, 2). No significant differences in the duration of the surgical procedure ($P = 0.436$ for all comparisons) or duration of anesthesia ($P = 0.606$ for all comparisons) were observed across the three groups (Table 2). There was no significant difference in the incidence of nausea (P

= 0.894 for all comparisons) and vomiting ($P = 0.770$ for all comparisons) among the SAB, ESP, and RIB groups (Table 3).

4. Discussion

This is the first randomized, double-blind clinical trial to compare the analgesic effects of SAB, ESP, and RIB block after MRM. We demonstrated that the patients who received RIB block and SPB block before operation had lower tramadol dosage and dynamic NRS score within 24 hours after operation, indicating that RIB block and SPB block had better analgesic effect than SAB. At the same time, RIB block and SPB block had longer first pain time and less times of complaining pain after single injection than SAB block. However, there was no difference in intraoperative anesthetic consumption, incidence of adverse reactions and patient satisfaction among SAB block, SPB block and RIB block. In addition, we found that SAB block, SPB block and RIB block were less effective in relieving axillary pain.

Blanco et al reported for the first time that SAB block has a blocking effect on the intercostal nerve of T_2˜T_9 and can provide chest wall and axillary regional anesthesia [9]. Previous studies have reported the effects of SAB blockers and placebos on opioid consumption in patients with breast cancer after modified radical mastectomy [13, 14]. Recently, Yao et al. [14]reported that pre-operative administration of SAB with ropivacaine improved the quality of recovery, postoperative analgesia, and patient satisfaction following breast cancer surgery, However, Fu jii et al.[15] found that compared to SAB block, the PECS-2 block reduced chronic pain six months after MRM. Their findings were similar to our results. In this study, we found that in patients receiving the SAB block for MRM compared with the ESP and RIB block, the dosage of tramadol was higher, the postoperative analgesic effect was worse, and the nerve block time was shorter.

ESP block is a kind of new plane block, which provides analgesia for thoracic and abdominal segmental innervation according to the level of spinal cord injection[8]. After horizontal injection of T4 transverse process, the local anesthetic spread to multiple segments of the cranial tail.The local anesthetic diffused forward through the costal transverse foramen and into the paraspinal space of the thoracic vertebrae. The US-ESP block could block the ventral and dorsal branches of the spinal nerve, as well as the communicating branches of the spinal nerve [16]. Gürkan et al.[17] reported that ESP block has a good analgesic effect after modified radical mastectomy for unilateral breast cancer. Recently, Finnerty et al.[12] found that compared with SAP, ESP had higher recovery quality, and better analgesic effects within 24 hours after minimally invasive thoracotomy. Their findings are similar to those of the present study, which found for the first time that during MRM, the application of ESP block resulted in lower tramadol consumption, lower postoperative pain score, longer duration to first pain, fewer complaints of pain, and higher postoperative patient satisfaction than those achieved using SAB block.

RIB block is a novel interfascial plane block technique described by Elsharkawy et al [18]. Following the injection of local anesthetic into the interfascial plane between the rhomboid major and intercostal muscles, the block provides analgesia between the T2 and T9 dermatomes [18]. In addition, RIB has the advantage of being an easily applicable technique and the injection site is distant from the surgical area. Recently, Altıparmak et al[3]. reported that RIB block promoted enhanced recovery and decreased opioid consumption need after mastectomy. Tulgar et al. [19] applied RIB block to an 82-year-old woman who required MRM, and 40 mL local anesthetic (LA) (20 mL bupivacaine, 0.25 mL 2% lidocaine, and 20 mL saline) were injected to the rhomboid muscle and the fifth costal fascia. Ultrasonography demonstrated the spread of LA between the second and seventh ribs, under the rhomboid muscle. The total anesthesia time was 75 min. In this study, we also found that RIB block can provide good postoperative analgesia for patients undergoing MRM. In addition, we found for the first time that ESP block and RIB block resulted in better postoperative analgesic effect than the SAB block for MRM. Both the RIB and ESP blocks had similar analgesic effects after MRM.

Our study also has some limitations. First of all, we give the patient nerve block after general anesthesia, so we can't evaluate the scope of anesthesia very well. Secondly, patients who undergo nerve block may also have back injection pain, which is likely to let patients know what kind of nerve block they are performing, which makes it impossible for the experiment to be a double-blind trial. However, there were only four such

patients; thus, it was unlikely to have affected the results of the study. Third, we did not monitor the depth of anesthesia during the maintenance of general anesthesia, which may have affected the anesthetic dosage or influenced the patient's intraoperative knowledge. Nonetheless, in this experiment, we used sevoflurane to prevent intraoperative awareness and none of patients reported any intraoperative knowledge during the postoperative return visits.

Conclusions:

Ultrasound-guided rhomboid intercostal block and erector spinae plane block can reduce the dosage of tramadol and NRS score compared with serratus plane block after modified radical mastectomy.

CRediT authorship contribution statement

Wei Deng: Conceptualization, Methodology, Writing - review & editing, Funding acquisition, Formal analysis, Visualization,Writing - original draft, Investigation, Resources, Project administration. Fen Liu: Conceptualization, Validation, Writing - review & editing, Supervision, Formal analysis, Funding acquisition. Chen-Wei Jiang: Formal analysis, Visualization. Qinghe Zhou:Formal analysis, Visualization,Writing - original draft, Investigation, Resources, Project administration

Declaration of competing interest

The author reports no conflicts of interest in this work.

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Data sharing statement

The authors intend to share individual anonymized participant data, and all the data are published in the China Clinical Trial Registration Center. No additional unpublished data are available. You can log in to the China Clinical Trial Registration Center to share our data. When the article is published, it can be used permanently.

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Tables

Table 1. Basic characteristics of patients in the three groups ((±s, n=30))

	SAB	**ESP**	**RIB**	P
Age (years)	52.10±11.50	54.73±13.60	56.06±11.15	0.439
BMI(kg/m^2)	23.52±3.12	23.40±3.05	23.71±4.03	0.104
Procedure duration (min)	100.96±29.30	97±21.77	104.8±17.33	0.436
Duration of anesthesia (min)	113.3±30.59	109.36±21.91	112.75±24.20	0.606
ASA class I /II	12 /18	13/17	14/16	0.271

Statistical tests: Pairwise comparisons of groups analyzed by one-way ANOVA were made using *post hoc*

analyses and the Student–Newman–Keuls Q -test.

Table 2. Intraoperative anesthetic dosage and recovery time in the three groups ((±s, n=30))

	SAB	**ESP**	**RIB**	**F**	P
Ρεμιφεντανιλ (μγ)	315±94.31	311±80.61	309.33±80.61	0.047	0.954
Propofol (mg)	195±51.57	192.66±39.21	190.66±20.16	0.092	0.912
Recovery time (min)	13.56±1.07	13.26±1.11	13.06±1.04	1.635	0.201

Statistical tests: Pairwise comparisons of groups analyzed by one-way ANOVA were made using *post hoc* analyses and the Student–Newman–Keuls Q -test as well as the chi-square test.

Table 3. Prevalence of adverse events in the three groups ((±s, n=30))

	SAB	**ESP**	**RIB**	χ^2	P
Nausea (n/%)	4 (13.33%)	3 (10%)	3 (10%)	0.225	0.894
Vomiting (n/%)	2 (6.67%)	1 (3.33%)	1 (3.33%)	0.523	0.770
block-related complications (n/%)	0	0	0	–	–

Statistical test: Chi-square test.

Figure legend

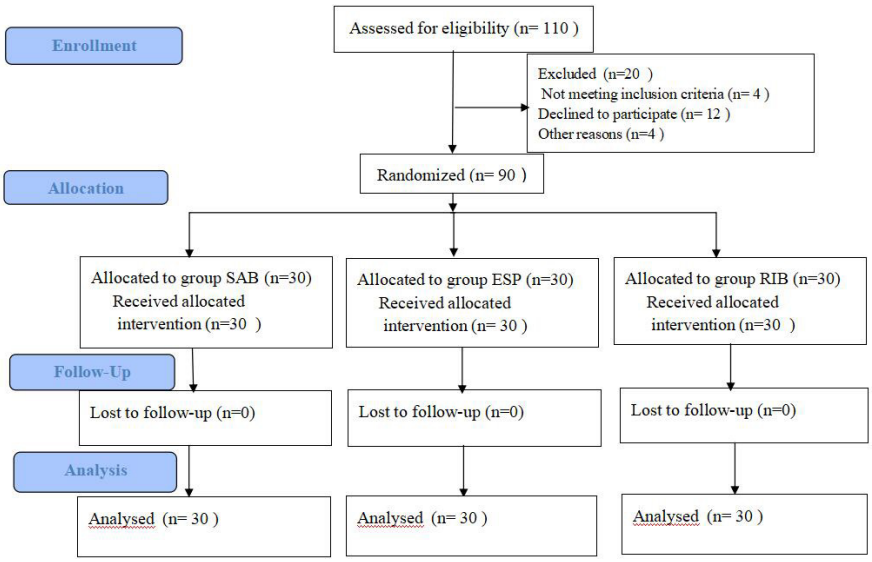
Figure 1. Consort diagram for the study.

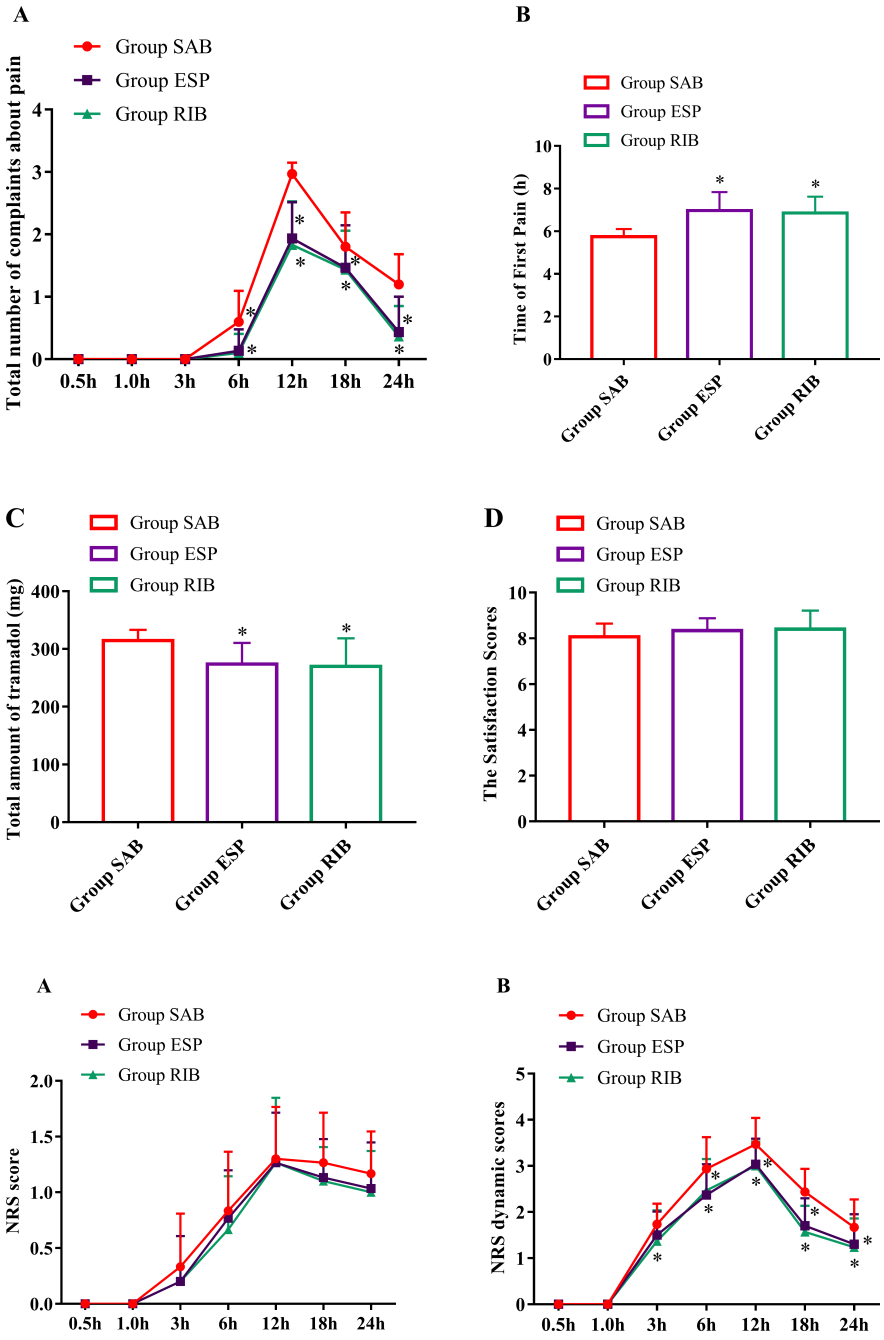
Figure 2 (A) Total number of complaints during 0.5, 1, 3, 6, 12, 18 and 24 h. (B)Time that pain was first felt after surgery. (C) Total tramadol consumption (mg) in 24 h. (D) Satisfaction score in the three groups 24 h after surgery.

*P<0.05 compared with SAB *group* ,#P<0.05 compared with *ESP group*.

Figure 3. NRS score at different times after surgery in the three groups. (A) NRS score when patients were at rest. (B) NRS score when patients were active.

*P<0.05 compared with SAB *group* ,#P<0.05 compared with *ESP group*.





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