Clinical Study Protocol

Program name: Comparison of the analgesic efficacy of the combination of transversus abdominis plane block and rectus sheath block in relation to erector spinae plane block after patients undergoing laparoscopic liver resection surgery

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1.Research background

According to the 2022 guidelines for perioperative care for liver surgery, implementing Enhanced Recovery After Surgery(ERAS) in liver surgery may improve postoperative outcomes. Compared with open hepatectomy, laparoscopic hepatectomy has the advantages of less postoperative hospitalization time and lower complication rates, which is recommended in well-trained teams and clinically appropriate situations[1]. Postoperative pain after laparoscopic liver resection is composed of multiple factors, including somatic and visceral pain,which is caused by abdominal distension, laparoscopic port position and abdominal wall wounds[2]. The peak pain of postlaparoscopic surgery mainly occurs in the first 24 hours[3], it is particularly significant to find an appropriate way to relieve pain.

Epidural analgesia has been the gold standard for perioperative pain control, but it is associated with longer hospitalization time and increased hospital costs and a higher incidence of urinary tract infections. Additionally, its use is limited by an increasing number of drugs that interfere with blood coagulation function[4,5]. Regional anesthesia is an important component of multimodal analgesia, which can reduce the dosage of opioids after surgery, thereby reducing the occurrence of adverse reactions and it is helpful for postoperative recovery. Transversus abdominis plane block (TAPB) and Rectus sheath blocks (RSB) are widely used in abdominal surgery. TAPB blocks the sensory nerves of the anterolateral abdominal wall (T6-L1), and a Meta-analysis has shown that it is effective as epidural analgesia while having fewer episodes of hypotension[6]. Bilateral rectus sheath blocks (RSB) was originally introduced to loosen the abdominal wall during surgery by blocking the terminal branches of the 9th, 10th and 11th intercostal nerves between the internal oblique and transversus abdominis muscles. It has now been shown to reduce opioid use and alleviate postoperative pain[7], but if the needle tip too deep during RSB, it will has the risk of puncture the abdominal organs. The limitation of both TAPB and RSB lied in their ability to provide somatic analgesia only without visceral analgesia.

Some studies have applied Erector spinae plane block (ESPB) in abdominal surgery where it can act on both the ventral and dorsal branches of spinal nerves, further enhancing visceral analgesia by blocking sympathetic nerve. Altiparmak et al[8] compared ultrasound-guided ESPB with oblique subcostal TAPB for postoperative pain relief in patients undergoing laparoscopic cholecystectomy, and proved that ESPB could reduce tramadol consumption and pain score more effectively. Kamel et

al. [9] concluded that bilateral ESPB provides longer duration of postoperative analgesia and less morphine consumption than TAPB in patients undergoing open abdominal total hysterectomy. In open hepatectomy, ESPB has been proved to have better analgesic properties than oblique subcostal TAPB, specifically manifests in lower postoperative pain scores, longer time to first need for morphine, and less morphine consumption[10]. The analgesic effect of ESPB has been demonstrated after abdominal surgery.

The analgesic and postoperative recovery effects of ESPB have not been compared with TAPB combined with RSB in patients undergoing laparoscopic hepatectomy.

2. Study Purpose

Comparing the postoperative analgesic and recovery effect of TAPB combined with RSB and ESPB in patients undergoing laparoscopic hepatectomy.

3. Study design

3.1 Study types

single-center, prospective, randomized, double-blind, controlled study

3.2 Random grouping

Patients were randomly divided into two groups according to computer generate random number table: TAPB combined with RSB group (control group) and ESPB group (experimental group). Group assignment information was stored in a sealed opaque envelope and stored and distributed by a specific person.

3.3 Double-blind

All patients included in the study were required to sign informed consent. Before anesthesia induction, the experimental group received ESPB while the control group was given TAPB combined with RSB. The abdominal incision and puncture points due to the block were covered with sterile dressings in both experimental and control groups after surgery. The anesthesiologist who performed the nerve block carries out the corresponding nerve block according to the groups in the envelope. Anesthesiologists responsible for anesthesia management, surgeons, and those conducting postoperative follow-up visits were unaware of the group situations.

4. Selection and withdrawal of subjects

4.1 Inclusion criteria

1)ASA grades I-II

2)age 18~70 years old

3)BMI 19～28 kg/m2

4)patients undergoing elective laparoscopic partial liver resection

4.2 Exclusive criteria:

1) The nerve block cannot be performed, such as skin infection at the puncture site

2) Daily using the opioid analgesics or have a history of opioid abuse

3) Allergy or a history of drug allergy to any of the drugs used in the study

4) Patients have cognitive impairment, mental or neurological diseases, motor or sensory deficits

5) Coagulation disorders

6) Severe lung, heart, liver, or kidney dysfunction

7) Participating in other clinical trials within 3 months before being included in this study

5. Sample estimation

The sample size was calculated based on previous literature[2], requiring 27 patients per group to achieve a two-sided 0.05 significance level and 90% power of the test. A sample size of 60 was required to set a dropout rate of 10%.

6. Research process

The experiment was carried out in Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology. For patient who were going to undergo laparoscopic partial hepatectomy, anesthesiologists went to the ward one day before surgery for preoperative evaluation, signed the informed consent form, and screened the subjects according to the inclusion and exclusion criteria. In according with the random results, the patients were randomly divided into ESPB group (experimental group) and TAPB&RSB group (control group). The patients were instructed to use analgesic pump and visual analogue scale (VAS). (Visual analogue scale (VAS): a 100 mm transverse line with 0mm at one end of the line indicates no pain, 100mm at the other end indicates severe pain and the middle part shows different levels of pain.)

1) All patients were routinely fasted before surgery, and no preoperative medication was given.

2) After entering the operation room, the patients in the experimental group and the control group took the sitting position, and the VAS scores of the patients in the resting state and the cough state were recorded. The subjects were scored preoperatively using the QoR-15 patient questionnaire (see supplementary).

3) Electrocardiogram, blood pressure, pulse, and blood oxygen saturation were monitored. After local anesthesia, ultrasound-guided internal jugular vein catheterization was performed, which could monitor central venous pressure(CVP) and record preoperative CVP after connecting the transducer.

4) The experimental group received ultrasound-guided ESPB, and bilateral ESPB was performed at T7 segment with 20ml 0.375% ropivacaine on each side.While the control group receives ultrasound-guided TAPB combined with RSB, which was performed under the costal margin with 10ml 0.375% ropivacaine for bilateral TAPB and 10ml 0.375% ropivacaine for bilateral RSB.

5) Anesthesia was induced with methylprednisolone 5mg, dexamethasone 5mg, penehyclidine hydrochloride 0.5 mg and palonosetron 0.25 mg, sufentanil 0.5μg·kg-1, etomidate 0.15-0.20 mg·kg-1 and cisatracurium 0.20mg·kg-1.

6) Tracheal intubation was performed after 5 minutes of mask oxygen inhalation; Ultrasound guided radial artery puncture catheterization was preformed to monitor ambulatory blood pressure.

7) Maintenance of anesthesia should use 1-2% sevoflurane inhalation, dexmedetomidine 0.5ug·kg^{-1}min^{-1} and fentanyl 0.1 -0.2ug·kg^{-1}·min^{-1}, and maintain blood pressure at baseline values of plus or minus 20%. In volume controlled ventilation mode, tidal volume was 6ml/kg, airway pressure was maintained within 25cmH2O, and end-tidal CO2 is maintained 35-45 mmHg. CVP values were recorded at 5, 10, 15, and 30min after nerve block. ECG, HR, BP, SpO2, CVP, PetCO2, BIS value, temperature, liquid intake and output are monitored during operation. Arterial blood gas analysis was used to correct acid-base imbalance and electrolyte imbalance.

8) Analgesic coherence: 30 minutes before the end of surgery, sufentanil 5ug was injected intravenously.

9) The patient was sent to PACU for observation for one hour after awake extubation, and then connected to an analgesic pump: sufentanil 15ug, nojan 15mg, palonosetron 0.3mg, 0.9% normal saline added to 150ml. The background infusion

rate was set according to the weight <50 kg at 1ml/h, 1.5ml/h for 50-60 kg and >70 kg at 2ml/h with a single compression dose of 2ml and a lockout time of 10min. According to the needs of patients, the analgesic pump could be pressed by themselves for analgesia. If pain cannot relieve (VAS&gt>4 at rest), the remedial analgesia with a single dose of 2mg oxycodone can be used. At 1 hour after the end of surgery, recording the VAS scores of patients in resting and coughing states and the dose of analgesic pump. Asking patients if they had any adverse reactions, such as nausea, vomiting, pruritus, dizziness, headache, respiratory depression, etc.

10) After returning to the ward, patients could press the analgesic pump by themselves for additional analgesia. Lack of pain relief (VAS&gt at rest; 4 points) or, at the patient's request, rescue analgesia with a single dose of diclofenac sodium suppository. The dosage of analgesic pump, times of rescue analgesia, VAS scores in the resting and coughing and adverse reactions were recorded at 2h, 4h, 8h and 24h after operation. The QoR-15 patient questionnaire was used to evaluate the postoperative recovery at 24 hours after surgery.

7. Possible risks and preventive measures

7.1 Adverse event

The investigators should faithfully fill in the adverse event recording form, record the time, severity, duration, measures taken and outcomes of adverse events. Explaining the criteria for the severity of adverse events, judging the relationship between adverse events and the trial drug was the 5-level classification standard (definitely related, possibly related, possibly unrelated, unrelated, and could not be determined). All adverse events should be traced until resolved properly or the patient's condition is stable.

Precautions for adverse events:

① Ultrasound-guided nerve block can visualize the puncture needle tips, effectively and greatly reduce the risk of local anesthetic poisoning and puncture injury.

② Local anesthetic poisoning: strict control the dose of drug, strict intraoperative monitoring. Once local anesthetic poisoning presents, it should be treated immediately according to the treatment procedure of local anesthetic poisoning, such as electrocardiogram monitoring, respiratory tract management, volume control, sedation and anticonvulsion, and the use of corresponding vasoactive drugs.

③ Puncture injury: Performing carefully and discreetly under visualization of ultrasound to ensure that tissue damage is minimized. Once present, surgery may intervene depending on severity.

Doctor will closely monitor your condition to ensure your health, and will truthfully tell you any changes in the course of the study and any newly identified adverse effects.

If you are harmed or have anything unexpected circumstances because of participating in this study, whether it is related to the intervention or not, your doctor will make a judgment and take medical action.

Physicians will try their best to prevent and treat possible harm as a result of this study. If an adverse event occurs during a clinical trial, a committee of medical experts will determine whether it is related to the intervention. Finally, according to the provisions of "Good Clinical Practice" in China, the sponsor will provide the cost of treatment and corresponding economic compensation for trial-related injuries.

7.2 Serious adverse event

Serious adverse events are defined as an adverse event leading to one of the following consequences: death, extension of hospitalization time, disability, fatal reaction or teratogenicity. Any serious adverse events occurring during the clinical trials must be reported within 24 hours to the principal investigator of the Department of Anesthesiology of Tongji Hospital and the Ethics Committee of the Drug Clinical Research Base of Tongji Hospital.

7.3 Safety monitoring

The data and safety management committee consists of anesthesiologists. The committee will conduct the interim analysis when half of the patients have been enrolled. If the interim analysis shows an extremely higher rate of death or significantly more complications in the trial group, the trial will stop.

8.Data collection and statistical analysis

8.1 Data collection

Main observation indicator: consumption of morphine within 24 hours after surgery

Secondary observation indicators

1) Morphine consumption at 1h, 2h, 4h and 8h after surgery

2) Number of rescue analgesia at 1h, 2h, 4h, 8h and 24 hours after surgery

3) VAS scores in resting and coughing at 1h, 2h, 4h, 8h and 24h after surgery

4) CVP values at 5, 10, 15 and 30min after nerve block

5) QoR-15 patient questionnaire scores before and 24h after surgery

6) Postoperative liver function (the percentage increase of AST and ALT compare with preoperative), postoperative complications and discharge time

8.2 Statistical analysis

The Shapiroe Wilk test was used to determine the normality of data distribution for measurement data. Measurement data with normal distribution were expressed as mean ± standard deviation, and measurement data with non-normal distribution were expressed as median (interquartile range, IQR). Measurement data were compared between groups by t test or Mann-Whitney U test according to whether the data were normal distribution, and VAS scores were compared by repeated measures analysis of variance. Count data were expressed as frequency (%), and compared between groups by using chi-square test or Fisher exact test.The value of P less than 0.05 was considered statistical significance.

References

Uncategorized References

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