Efficacy of ultrasound-guided rectus sheath block, butorphanol for single-incision laparoscopic cholecystectomy: A prospective, randomized, clinical trial

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Abstract

Background: Whether rectus sheath block (RSB) combined with butorphanol can relieve incision pain and visceral pain in patients undergoing single-incision laparoscopic cholecystectomy (SILC) remains unknown. The goal of this study was to assess the efficacy of ultrasound-guided bilateral RSB, butorphanol on postoperative analgesia in patients undergoing SILC.

Methods: All 116 patients who met the criteria were randomly divided into four groups: (Ⅰ)(n=29) general anesthesia combined with patient controlled intravenous analgesia (PCIA) (sufentanil 100ug); (Ⅱ)(n=29) general anesthesia combined with PCIA (butorphanol 8mg); (Ⅲ)(n=29) ultrasound-guided RSB combined with PCIA (sufentanil 100ug). (Ⅳ)(n=29) RSB combined with PCIA (butorphanol 8mg). Outcomes included visual analog scale (VAS) scores of incisional and visceral pain at rest and cough at 2,6,12 and 24 h postoperatively, if a patient’s pain score≥3, then butorphanol 2mg was administered intravenously. the dose of butorphanol and opioids, the pressing numbers of PCIA, the length of hospital stay and the incidence of postoperative adverse events.

Results: Both rest and cough pain scores were lower during first 2,6 hours in group Ⅲ than groupⅠ, similarly, group Ⅳwas significantly lower than groupⅡ. GroupIneeded more butorphanol as rescue analgesic for pain relief than group Ⅲ, group Ⅳ was better than group Ⅱ. In the above pairwise comparisons, it was clear that group Ⅲ and group Ⅳ had lower VAS scores. VAS scores of visceral pain was lower in groupⅡ at 2, 6 and 12 h after surgery compared with the groupⅠ. In the both groups Ⅲ and Ⅳ, the group Ⅳ was also lower than groupⅢ. Overall, RSB combined with PCIA (butorphanol 8mg) is the best match.

Conclusions: Ultrasound-guided RSB combined with butorphanol can provide sufficient pain treatment after SILC. Trial registration: The study was registered prospectively with the Chinese Clinical Trial Registry(reg no.ChCTR1900020738), obtained ethics committee
Background

Cholecystolithiasis is a common and frequently-occurring disease. Laparoscopic cholecystectomy is the “gold standard” for cholecystolithiasis. Nevertheless, the progress of minimally invasive surgery is "open-laparoscopic-single incision-robot". As surgeons embrace the concept of less invasiveness, less pain, earlier recovery, shorter operation period, Compared with laparoscopic cholecystectomy, single-incision laparoscopic cholecystectomy (SILC) has outstanding cosmetic effect[1]. SILC is increasingly popular[2]. It is an undeniable fact that SILC can reduce pain[3], but postoperative pain which can arise from the incision site and visceral structures is still a major problem for patients to complain about.

At present, opioids are widely used in postoperative analgesia[4], as matters stand, it has been suggested that postoperative pain management is insufficient. On the one hand, they are associated with side effect such as somnolence, postoperative nausea and vomiting (PONV), constipation, uroschesis, pruritus and respiratory depression, resulting in delayed discharge[5-7]. On the other hand, even though opioid drugs are a primary choice for the management of patients experiencing severe visceral pain[8], they cannot produce adequate pain relief, furthermore, the occurrence of visceral pain after SILC also reduces patient satisfaction. To improve pain management after operation, multimodal analgesic regimens which include regional block and non-steroidal anti-inflammatory drugs (NSAIDS) is increasingly used. Schleich first used rectus sheath block (RSB) in 1899 to provide muscle relaxation and analgesia[9]. Formerly, RSB was not extensive used because its non-visualization lead to a high incidence of complication, for instance, neurologic injury, inadvertent peritoneal injury, visceral trauma, and block failure. Nevertheless, with the introduction of ultrasound into regional anesthesia practice, tissue planes, bowel and the spread of local anesthetics can be seen, which may decrease accidental puncture. it is mainly used for postoperative analgesia after abdominal operation. Studies have shown that 10ml of 0.5% ropivacaine is usually the right amount[10, 11]. Recently, More and more studies emphasize RSB clinical application value of pain relief about midline abdominal incision, laparoscopic and umbilical surgery[12]. Visceral pain is a complex disorder, which can be caused by mechanical traction, dilation, spasm, inflammation and chemical stimulation. Some studies suggest that butorphanol, a κ-agonist, produce profound visceral analgesia[13].

The efficacy of RSB has been reported for postoperative analgesia after SILC[14], but
this article no thoroughly studied postoperative pain about incision pain and visceral pain. Accordingly, we decided to assess the efficiency of ultrasound-guided RSB, butorphanol for incision pain and visceral pain in patients undergoing SILC.

Methods

Patients and study design

128 patients undergoing elective SILC were enrolled in this study from February 2019 to April 2019 at Affiliated Hospital of Nantong University. Inclusion criteria: between 18 and 59 years of age, men and women are not limited, American Society of Anesthesiology (ASA) score is I or II, Body Mass Index (BMI) is 18-30 kg/m². Patients with preexisting neuropathy, coagulopathy, local skin infection, hepatic, renal or cardiorespiratory failure, local anesthetic allergy, pregnancy, complications of gallstone with gallbladder perforation, diffuse peritonitis and acute pyogenic cholangitis were excluded.

The study was registered prospectively with the Chinese Clinical Trial Registry (ChiCTR1900020738), obtained ethics committee of Affiliated Hospital of Nantong University approval (approved number: 2018-K067), and written informed consent.

Randomization and blinding

All 116 patients, 64 males, 52 females, scheduled for elective single-incision laparoscopic cholecystectomy, were randomly divided into four groups by using a computer-generated random sequence concealed in consecutively numbered opaque sealed envelopes, which were opened on the morning of surgery. The anesthesiologist performed anesthesia and nerve block and postoperative assessors were blinded to grouping.

Anesthesia

116 patients were induced with intravenous midazolam 0.1mg/kg, propofol 2mg/kg, sufentanil 0.5ug/kg and cisatracurium 0.15mg/kg. Maintenance of anesthesia was performed with infusion of propofol 10mg/ml, 4mg/kg/h, remifentanil 50ug/ml, 0.2ug/kg/min. To ensure adequate depth of anesthesia, response entropy indexes were kept between 40 and 60 during the whole anesthesia period by adjusting the Infusion pump speed of sufentanil and propofol.

After systemic anesthesia, in the group III and IV, the probe was transversely placed at the lateral level of the umbilicus. Using in-plane technique, the needle was advanced until the posterior aspect of the rectus muscle is penetrated. No blood and no gas were drawn.
back, furthermore, A small volume of saline (around 2 ml) was initially injected to ensure that the needle tip was correctly positioned. At present, the needle located between the posterior rectus muscle and posterior sheath, 20 ml of 0.5% ropivacaine was injected bilaterally (Figure 1).

In particular, the group II and group IV received intravenous infusion of 1 mg butorphanol 30 minutes before the end of surgery. The group I and group III received intravenous infusion of 10 ug sufentanil 30 minutes before the end of surgery.

Vital signs such as blood pressure, heart rate, oxygen saturation electrocardiogram were recorded during the operation. Operation time, hemorrhage volume and the consumption of remifentanil and propofol were also taken notes.

PCIA with a bolus dose of 2 ug sufentanil, a lock-out interval of 15 minutes and the maximum dose of 2 ug/h was used for routine analgesia in the group I and group III. In the group II and group IV, all patients received butorphanol PCIA set at a background rate of 170 ug/h and a demand dose of 170 ug every 15 min as rescue analgesia for postoperative pain management. During a preoperative visit, patients were adequately informed about the concept of VAS and trained how to use PCIA.

All patients were operated by the same experienced anesthesiologist, who specialized in ultrasound-guided regional anesthesia, blinded to the grouping and did not participate in postoperative data collection.

Measurements
Primary outcomes: In both groups, a blinded investigator who was not involved in patient recruitment or anesthesia procedure recorded the incision and visceral pain using a 10-cm visual analog scale (0 cm = no pain; 10 cm = worst pain) at 2, 6, 12, and 24 hours after the operation. Postoperative nausea and vomiting (PONV), somnolence, constipation, uroshesis, pruritus, and respiratory depression were assessed by a blinded observer separately. 1 mg butorphanol was administered intravenously as rescue analgesia in patients with VAS ≥ 3. Secondary outcome: The blinded observer recorded the doses of butorphanol, opioids, and pressing times of PCIA.

Statistical analyses
Statistical analysis was performed using IBM SPSS 21. Date in every group were expressed with mean±SD or frequency. Analysis of variance is used for measurement data groups, count data groups were analyzed using chi-square test. P < 0.05 was considered statistically significant. Sample size calculation was based on α = 0.05, β = 0.2, power = 80%, lost follow-up rate = 10%.
Results

Patients

The study flow diagram is presented in Figure 2. A total of 128 participants were recruited into the study, eleven of them were excluded from the study, including six patients due to be disqualified for complications of gallstone with gallbladder perforation during surgery, three patients due to BMI $\geq 30$ kg/m², two patients due to age $\geq 59$. Other patients are on schedule. Individual characteristics of patients are expressed in Table 1. There was no significant different in age, sex, BMI, and ASA score among the four groups ($P > 0.05$).

Table 1. Patient Characteristics

|                  | GroupⅠ (n=19) | GroupⅡ (n=19) | GroupⅢ (n=20) | GroupⅣ (n=20) | p-value |
|------------------|---------------|---------------|---------------|---------------|---------|
| Age, mean±SD, y  | 37.2±10.9     | 39.3±10.5     | 38.8±11.4     | 41.5±11.4     | 0.521   |
| Sex, no. male/no. female | 17/12        | 15/14        | 16/13        | 16/13        | 0.964   |
| BMI, mean±SD, kg/m² | 23.9±3.31   | 24.0±3.52     | 24.8±3.18     | 23.6±3.13     | 0.521   |
| ASAⅠ/Ⅱ, n       | 19/10        | 16/13        | 15/14        | 14/15        | 0.582   |

The four groups showed no statistically significant differences in patients’ characteristics.

BMI indicates body mass index; ASA, American Society of Anesthesiologists.

Postoperative pain

There were no significant differences in the time needed for the block procedure, quality of ultrasound images. At rest and cough, VAS of incisional pain was lower during first 2, 6 hours in the group Ⅲ than in the groupⅠ(2.41±1.05 vs 3.83±1.28, $P > 0.05$; 4.03±0.87 vs 4.97±1.38, $P > 0.05$; 1.93±1.00 vs 2.79±1.11, $P > 0.05$; 3.55±0.69 vs 4.28±1.07, $P > 0.05$). Similarly, the group Ⅳ was significantly lower than the groupⅡ(2.03±0.98 vs 3.90±1.29, $P > 0.05$; 3.83±1.00 vs 5.07±1.33, $P > 0.05$; 1.83±0.89 vs 2.76±0.99, $P > 0.05$; 3.41±0.91 vs 4.17±1.10, $P > 0.05$). In the above pairwise comparisons, it was clear that the group Ⅲ and Ⅳ had lower VAS scores. VAS scores of visceral pain was lower in group Ⅱ at 2, 6 and 12 h after surgery compared with the group(3.90±1.14 vs 5.21±1.12, $P > 0.05$; 3.69±0.93 vs 5.28±1.07, $P > 0.05$; 3.38±0.82 vs 4.55±1.33, $P > 0.05$). In the both groups Ⅲ and Ⅳ, the group Ⅳ was also lower than group Ⅲ (3.97±1.12 vs 4.97±1.38, $P > 0.05$; 3.90±1.14 vs 5.03±1.18, $P > 0.05$; 3.41±0.91 vs 4.00±0.96, $P > 0.05$). The group needed more butorphanol as rescue analgesic for pain relief than the group Ⅲ (5.57±0.81 vs 2.45±0.99, $P > 0.05$), similarly, the group Ⅳ was better than the groupⅡ(4.90±2.02 vs 5.17±1.07, $P > 0.05$). The patients who were applied to less opioids in the groupⅡand group Ⅳ experience less PONV. Overall, RSB combined with PCIA (butorphanol 8mg) is the best match.
Table 2 Visual analog scale scores at several time points.

| Time point | Group I (n=19) | Group II (n=20) | Group III (n=20) | Group IV (n=20) | p-value |
|------------|----------------|-----------------|------------------|-----------------|---------|
| At rest    |                |                 |                  |                 |         |
| 2h         | 3.83±1.28*     | 3.90±1.29       | 2.41±1.05        | 2.03±0.98       | P<0.05 |
| 6h         | 2.79±1.11**    | 2.76±0.99       | 1.93±1.00        | 1.83±0.89       | P<0.05 |
| 12h        | 2.38±1.05      | 2.10±1.14       | 2.14±1.09        | 1.93±0.92       | 0.450   |
| 24h        | 2.03±0.82      | 1.86±0.88       | 1.83±0.85        | 1.62±0.78       | 0.309   |
| At cough   |                |                 |                  |                 |         |
| 2h         | 4.97±1.38#     | 5.07±1.13       | 4.03±0.87        | 3.83±1.00       | P<0.05 |
| 6h         | 4.28±1.07##    | 4.17±1.10       | 3.55±0.69        | 3.41±0.91       | P<0.05 |
| 12h        | 4.14±1.25      | 3.83±1.07       | 3.52±0.74        | 3.45±0.91       | 0.124   |
| 24h        | 3.66±0.97      | 3.55±1.09       | 3.38±0.78        | 3.48±0.83       | 0.205   |
| Visceral pain |            |                 |                  |                 |         |
| 2h         | 5.21±1.21      | 3.90±1.14       | 4.97±1.38##**    | 3.97±1.12       | P<0.05 |
| 6h         | 5.28±1.07      | 3.69±0.93       | 5.03±1.18##**    | 3.90±1.14       | P<0.05 |
| 12h        | 4.55±1.33      | 3.38±0.82       | 4.00±0.96        | 3.41±0.91       | P<0.05 |
| 24h        | 2.72±0.88      | 2.55±0.74       | 2.66±0.86        | 2.28±0.80       | 0.176   |

*P<0.01 compared to group III, **P<0.05 compared to group III, #P<0.05 compared to group III, ##P<0.01 compared to group III, ### P<0.01 compared to group IV.

All data are expressed as mean±SD.

Table 3 Cumulative butorphanol and Opioids consumption

|                      | Group I (n=19) | Group II (n=19) | Group III (n=20) | Group IV (n=20) | p-value |
|----------------------|----------------|-----------------|------------------|-----------------|---------|
| Butorphanol consumption (mg) | 5.57±0.81*     | 5.17±1.07       | 2.45±0.99        | 4.90±2.02       | P<0.05 |
| Opioids consumption in PCIA (ug) | 84.8±11.0      | /               | 70.6±17.0        | /               | P<0.05 |

*P<0.01 compared to group III

Table 4 comparison of postoperative outcomes

|                      | Group I (n=19) | Group II (n=19) | Group III (n=20) | Group IV (n=20) | p-value |
|----------------------|----------------|-----------------|------------------|-----------------|---------|
| Duration of operation (min) | 59.4±11.3     | 61.4±10.8       | 62.2±9.86        | 61.7±11.0       | 0.785   |
| Bleeding amount (ml) | 16.8±5.42      | 14.2±5.54       | 13.9±4.66        | 15.1±5.15       | 0.138   |
| Length of stay (days) | 4.62±1.29      | 3.97±0.94       | 3.28±0.84        | 2.24±0.69       | P<0.05 |
| Pressing times of PCIA | 3.55±1.09      | 2.79±0.90       | 1.59±1.21        | 0.52±0.74       | P<0.05 |
| Frequency of analgesic request (n) | 2.45±0.99     | 1.45±0.91       | 1.17±0.80        | 0.38±0.56       | P<0.05 |

Date are expressed as mean±SD.
Table 5 adverse events during the first 24h after surgery.

|                      | Group I(n=29) | Group II(n=29) | Group III (n=29) | Group IV(n=29) | p-value |
|----------------------|--------------|---------------|------------------|----------------|--------|
| PONV                 | 21(72.4)     | 6(20.7)       | 13(44.8)         | 3(10.3)        | P<0.01 |
| constipation, uroschisis | 3(10.3)     | 1(3.4)        | 0(0.0)           | 0(0.0)         | 0.632  |
| somnolence           | 11(37.9)     | 8(27.6)       | 5(17.2)          | 3(10.3)        | 0.069  |
| pruritus pruritus    | 1(3.45)      | 0(0.0)        | 1(3.45)          | 0(0.0)         | 0.565  |
| Respiratory depression | 1(3.45)   | 0(0.0)        | 0(0.0)           | 0(0.0)         | 0.388  |

Values are the number of patients (%). PONV: post-operative nausea and vomiting.

Discussion

SILC has only a 2-cm incision into the umbilicus between the T7 and T11 intercostal nerves[15]. As far as RSB is concerned, RSB mainly blocks the sheath nerve plexus between rectus abdominis and posterior sheath of the rectus muscles which is dominated by ventral rami of the 6th to 11th intercostal nerves, providing analgesic technology for peritoneum, muscle and skin of incision of anterior abdominal wall[9]. In the PACU, we found that the range of sensory blockade was measured as a circular area with a radius of 5 cm centered on the umbilical. RSB covers all the nerves that innervate the umbilicus and provides preemptive analgesia and avoids central sensitization caused by nociceptive stimuli before surgery[16, 17]. According to our data, RSB for these patients resulted in low incisional pain scores at rest and on movement at 2, 6h after surgery. This showed that the incision pain in patients receiving RSB can relieve effectively. Butorphanol consumptions, pressing times of PCIA in group III was lower than that in the group I. There was no marked difference at 12, 24h after SILC among the three groups, this is perhaps because the efficacy of ropivacaine wears off after 12h. Theoretically, the RSB block should provide excellent analgesia to the abdominal wall, but unfortunately visceral pain is still evident in these groupland group III. By limiting postoperative opioid use in the groupIIand group IV, patients have fewer adverse biological reactions, it has been shown to have poor effect on the visceral pain.

Visceral pain are mainly transmitted by unmyelinated C fibers, which is a complex sensory experience caused by trauma and inflammation, generally described as a dull, diffuse, poorly localized[8]. Visceral pain is difficult to manage effectively, largely because visceral sensory mechanisms and factors that contribute to the pathogenesis of visceral
pain are poorly understood[18]. Visceral hyperalgesia and central sensitization have been suggested to be part of the pathophysiology[19]. At present, some studies have shown that the management of visceral pain can be achieved by activating κ-receptors[20, 21]. Opioids have been reported to have an effect on visceral pain but is little[8], that's the same as our data: VAS scores of visceral pain was lower in groupⅡat 2, 6 and 12 h after surgery compared with the groupⅠ. In the both groups Ⅲ and Ⅳ, the group Ⅳ was also lower than group Ⅲ. Butorphanol, a mixed agonist-antagonist opioid, induce analgesia by opioid pathways[13]. Some studies show that butorphanol relieve visceral pain by indirectly suppressing cyclooxygenase activity and thus preventing prostaglandin formation in response to injury[8, 16]. In addition, the main metabolite of butorphanol activates K-receptor, has dual effects of excitation and antagonism on u-receptor. In contrast to u-receptor agonist, such as sufentanil, Side effects caused by u-receptor such as respiratory depression, nausea and vomiting, prurits were alleviated and the incidence was low[13].

Compared with other methods, there is indicating the utility of RSB and butorphanol as part of multimodal postoperative pain treatment for SILC. It also facilitate earlier mobilization and discharge, follows the trend of enhanced recovery after surgery (ERAS). Analgesia Management has a far-reaching impact in perioperative Period. There are a number of limitations to this study. Firstly, this study unproven from a continuous infusion standpoint through the rectus sheath catheter placement, which studied whether it can provide longer analgesia after surgery. Secondly, RSB, as a postoperative analgesic method for SILC, we did not study the optimal volume and dose.

Conclusions

Our results suggest that ultrasound-guided RSB combined with butorphanol can relieve postoperative incision and visceral pain significantly in patients undergoing SILC. Adding adjuvants to prolong the duration of local anesthesia should be on the list for the in-depth study.

Abbreviations

RSB: rectus sheath block; SILC: single-incision laparoscopic cholecystectomy; PCIA: patient controlled intravenous analgesia; VAS: visual analog scale; PONV: postoperative nausea and vomiting; non-steroidal anti-inflammatory drugs(NSAIDS); ASA: American Society of Anesthesiology; BMI: Body Mass Index; ERAS: enhanced recovery after surgery
Declarations

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Authors’ contributions
HMF carried out the studies, and drafted the manuscript. CCZ performed the statistical analysis and helped to collect the data. XGX and YTG helped to revise the manuscript. All authors read and approved the final manuscript.

Availability of data and materials
All necessary data supporting our findings has been presented within the manuscript. The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate
This study was obtained ethics committee of Affiliated Hospital of Nantong University approval (approved number: 2018-K067), each patient provided a written informed consent.

Consent for publication
Not applicable

Competing interests
The authors declare that we have no competing interests.

Statement
The study adheres to CONSORT guidelines.

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Figures

Figure 1

ultrasound images (a) before and (b) after rectus sheath block RAM, rectus abdominal muscle, LA, local anesthetic
Supplementary Files

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Figure 2

Flow chart of the study