SCIENTIFIC ARTICLE

Efficacy of ultrasound-guided erector spinae plane block for analgesia after laparoscopic cholecystectomy: a randomized controlled trial†∗

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Ultrasoundography

Abstract
Background and objectives: The primary aim of this study is to assess the effect of ultrasound-guided erector spinae block on postoperative opioid consumption after laparoscopic cholecystectomy. The secondary aims are to assess the effects of erector spinae plane block on intraoperative fentanyl need and postoperative pain scores.
Methods: Patients between 18–70 years old, ASA I-II were included in the study and randomly allocated into two groups. In Group ESP, patients received bilateral US-ESP with 40 ml of 0.25% bupivacaine at the level of T7, while in Group Control, they received bilateral US-ESP with 40 ml of saline before the induction of anesthesia. Then a standard general anesthesia procedure was conducted in both groups. NRS scores at the postoperative 15th, 30th, 60th minutes, 12th and 24th hours, intraoperative fentanyl need and total postoperative tramadol consumption were recorded.
Results: There were 21 patients in Group ESP and 20 patients in Group Control. Mean postoperative tramadol consumption was 100 ± 19.2 mg in Group ESP, while it was 143 ± 18.6 mg in Group Control (p < 0.001). The mean intraoperative fentanyl need was significantly lower in Group ESP (p = 0.022). NRS scores at the postoperative 15th, 30th min, 12th hour and 24th hour were significantly lower in ESP group (p < 0.05). According to repeated measures analysis, NRS score variation over time was significantly varied between two groups (F[1, 39] = 24.061, p < 0.0005).

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Introduction

The laparoscopic technique for cholecystectomy surgery has gained popularity in recent years. According to previous research, this approach reduced mortality rates and perioperative and surgical postoperative complications as compared with outcomes using the open technique. Although considered a minimally invasive procedure, Laparoscopic Cholecystectomy (LC) frequently results in moderate to severe immediate postoperative pain. In addition to predominant visceral pain, nearly half of all patients suffer from Shoulder Pain (SP) in the early postoperative period. The most likely reason is subdiaphragmatic irritation, which is transmitted by the phrenic nerve, causing referred pain in the C4 dermatome. Due to multiple sources of pain, multimodal analgesia approaches with opioids, paracetamol, dexamethasone, gabapentitnoids, local anesthetic infiltration to port sites, Transversus Abdominis Plane (TAP) block, and Oblique Subcostal Transversus Abdominis Plane (OSTAP) block have been used in the perioperative period following LC.

Ultrasound-Guided Erector Spinae Plane (US-ESP) block, described by Forero et al. in 2016, has gained popularity in the last 3 years. This new regional technique provides analgesia via its effects on the ventral rami and dorsal rami of the spinal nerves, depending on the level of the injection site. As the erector spinae fascia extends between the nuchal fascia cranially and sacrum caudally, the injected local anesthetic agent spreads over several levels. Previous studies reported that US-ESP provided effective analgesia after different types of surgeries. According to a randomized controlled trial, US-ESP seemed to be effective following abdominal surgery. However, there are insufficient studies in this area. Therefore, the primary aim of this study was to assess the effect of US-ESP block on postoperative opioid consumption after LC. The secondary aims were to assess the intraoperative fentanyl requirements and postoperative pain scores of the patients.
Methods

After obtaining institutional ethics committee approval, the study was conducted as a randomized, double-blinded, placebo-controlled trial in an academic university hospital in accordance with the principles outlined in the Declaration of Helsinki. Patients aged between 18 and 70 years with American Society of Anesthesiology physical status I and II who were scheduled for elective LC surgery were included in the study. Patients with coagulation disorders, known allergies to local anesthetics, infections at the injection site, advanced hepatic or renal failure, chronic opioid consumption, or morbid obesity (body mass index $\geq 35 \text{ kg.m}^{-2}$) were excluded from the study.

Ethics, consent and permissions

Written informed consent was obtained from each patient both for the block interventions and participation before enrolment. The study is registered in the Australian New Zealand Clinical Trials Registry (Trial Id: ACTRN12618001106224) on 03/07/2018. The first participant was enrolled on 06/07/2018.

Interventions

The enrolled patients were randomly allocated to two groups based on a computerized randomization table created by a researcher who was not involved in the study. There were two Operating Room (OR) anesthesiologists (BA and YK). For each randomized patient, the first anesthesiologist (BA) took a corresponding sealed envelope from a folder, which indicated the treatment assigned to the patient, and prepared the drug solutions for use in the study (0.25% bupivacaine or isotonic saline solution). The first anesthesiologist prepared the drug solutions in two identical 20 mL syringes and a 10 mL syringe of isotonic saline for hydro-dissection and then passed the labeled syringes to the second anesthesiologist (YK) who was blinded to the group allocations. In the OR, all the patients received standard monitoring, including electrocardiography, noninvasive blood pressure, peripheral oxygen saturation, and bi-spectral index monitoring (Datex-Ohmeda S/5 monitor M-BIS module, Helsinki, Finland). The first heart rate and Mean Arterial Pressure (MAP) values measured in the OR were recorded as baseline values. After the placement of a 22 gauge intravenous line, 15 mL/kg$^{-1}$ of isotonic saline infusion was started. All the patients received intravenous 0.05 mg.kg$^{-1}$ of midazolam for sedation. The patients were then placed in a sitting position.

In the first group (ESP group), the second anesthesiologist placed a high-frequency (6–12 mHz) linear ultrasound probe (Fujifilm Sonosite, Bothwell, USA) in a longitudinal orientation at the level of the T7 spinous process 3 cm laterally from the midline. The ultrasound landmarks, T7 transverse process, and overlying erector spinae muscle were identified. Under aseptic conditions, an 80 mm 21 gauge block needle (Stimuplex® B-Braun medical, Melsungen, Germany) was inserted in-plane at an angle of 30°–40° in a cranial-to-caudal direction until the tip contacted the T7 transverse process. After hydro-dissection with 2–3 mL of isotonic saline solution had confirmed the correct needle tip position, the anesthesiologist injected 20 mL of 0.25% bupivacaine deep into the erector spinae muscle. The same procedure was repeated using 20 mL of 0.25% bupivacaine solution at the contra lateral side. In the second group (control group), the patients received the same bilateral US-ESP block with a total of 40 mL of isotonic saline (20 mL for each side) to minimize the placebo effect. After the block interventions in both groups, the patients received 100% oxygen via a face mask. The anesthesiologists induced anesthesia with intravenous propofol (2–3 mg.kg$^{-1}$) and fentanyl (1 mcg.kg$^{-1}$), with the infusion continued until each patient’s BIS score decreased to 40–60. Intravenous (IV) rocuronium bromide 0.6 mg.kg$^{-1}$ was applied to perform endotracheal intubation. After intubation, all the patients received 4 mg of ondansetron, 8 mg of dexamethasone and 75 mg of dexketoprofen trometamol intravenously for postoperative nausea and analgesia. For the maintenance of anesthesia, 4–6% end-tidal seflurane was used in 3 L of an oxygen (40%) air (60%) mixture. The minimum alveolar concentration of seflurane (4–6%) was targeted to reach a BIS value of between 40 and 60. When the heart rate and MAP of the patients increased more than 20% from baseline values, IV fentanyl (0.5 mcg.kg$^{-1}$) was administered. The inhaled anesthetic agents were stopped by the end of skin closure, and IV atropine (0.1 mg.kg$^{-1}$) and neostigmine (0.5 mg.kg$^{-1}$) were applied to reverse the neuromuscular blockage.

After successful extubation, the patients were sent to the recovery room where they were monitored using the Modified Observer’s Assessment of Alertness/Sedation scale (OAA/S), with a 5 min interval for the assessment of the sedation level. When the OASS score of the patients increased to 5 (responded readily to name spoken in a normal tone/awake), they were assessed using the 11 point Numerical Rating Scale (NRS) by another anesthesiologist (MTK) who was blinded to the study groups. The patients were then sent to the surgical ward. Postoperative analgesia in the surgical ward was maintained with an IV Patient- Controlled Analgesia (PCA) device with the same settings for all the patients. The PCA device administered a bolus dose of 20 mg of tramadol, with a 15 minutes lock-time and no basal infusion in the postoperative first 24 hours. Each patient was assessed 15 and 30 min after surgery and 1, 2, and 24 hours later by the same blinded anesthesiologist (AIU), using the NRS for pain evaluation. When the NRS score was $\geq 4$, IV morphine (4 mg) was administered as rescue analgesic. The anesthesiologist used a 3 point scale ($0 = $none, 1 = mild and 2 = severe) to assess SP at the same time points. The severity of nausea was assessed by patients on a 4 point scale (none, mild, moderate, and severe). The incidence of severe nausea and vomiting was noted in the nurse care records. The following parameters were recorded in the first 24 hours: the NRS scores at each time point; intraoperative fentanyl requirements; intraoperative hemodynamic parameters; total postoperative tramadol consumption; rescue analgesic requirements; incidence of severe nausea, vomiting and SP; and complications related to ESP block.

Statistical analysis

We conducted the statistical analysis using the software Statistical Package for Social Science (SPSS, version 17 (SPSS Inc., Chicago, IL, USA). The sample size of the study was
calculated based on a pilot study, with 10 patients in each group. At least a 20% reduction in postoperative tramadol consumption 24 h post surgery was accepted as clinically significant. Mean tramadol consumption was 95 ± 17.79 mg in the ESP group and 128 ± 9.48 mg in the control group. Assuming an α error of 0.01, β error of 0.1, and power of 0.90, 15 participants were needed in each group. Considering possible drop-outs, we decided to include at least 20 patients per group.

Parametric parameters in the groups were compared using an independent samples t-test whereas nonparametric parameters were compared using the Mann-Whitney U test. A p-value of < 0.05 was accepted as statistically significant. A repeated measures analysis was used for the NRS scores and hemodynamic parameters. Normality checks were carried out on the residuals, which were approximately normally distributed. Mauchly’s test of sphericity indicated that the assumption of sphericity was violated: χ²(9) = 29.05, p < 0.0005 for the NRS scores; χ²(27) = 242.869, p < 0.0005 for heart rate; and χ²(27) = 164.524, p < 0.0005 for MAP values. Therefore, a Greenhouse-Geisser correction was used for all three analyses. The values were expressed as mean ± standard deviation, median, or percentages.

Results
Fifty patients were screened for the study. Of these, three patients were excluded due to uncontrolled hypertension, and one patient was excluded due to a body mass index ≥35 kg.m⁻². Thus, 46 patients (ESP group, n = 23; control group, n = 23) were enrolled in the randomized study (Fig. 1). Two patients in the ESP group and three patients in the control group were lost during follow-up due to mechanical failure of the PCA device. Consequently, 41 patients (ESP group, n = 21; and control group, n = 20) were included in the study. Patient-related variables, including sex, American Society of Anesthesiology class, mean weight, body mass index, and surgical times, are shown in Table 1. The groups were similar in terms of demographic variables.

There was a statistically significant difference in mean postoperative tramadol consumption in the ESP group and control group (100 ± 19.2 mg and 143 ± 18.6 mg, respectively; p < 0.001). The NRS scores 15 and 30 minutes post surgery were significantly lower in the ESP group (p < 0.001). The NRS scores of the two groups were similar 60 minutes post surgery. The NRS scores 12 and 24 hours post surgery were lower in the ESP group as compared with those in the control group (Table 2). According to the repeated measures analysis, the mean NRS scores differed significantly at the different time points, (F [2.925, 114.067] = 12.951, p < 0.0005). As a result, there was a significant difference in the NRS scores recorded at least two time points. Moreover, there were significant differences in the NRS scores of the two groups over time (F [1, 39] = 24.061, p < 0.0005) (Fig. 2).

The mean intraoperative fentanyl requirement was 83.1 ± 22 mcg in the ESP group and 109.25 ± 43.2 mcg in the control group. The difference was statistically significant, but the power was 70% (p = 0.022).

The intraoperative hemodynamic parameters of the two groups were similar throughout the surgery. However, there were significant differences in the heart rates of the patients at some time points (Table 3). According to the
repeated measures analysis, the mean heart rate scores differed significantly at the different time points ($F [2.565, 100.045] = 6.451, p < 0.005$). Moreover, variations in heart rates over time were significantly different in the two groups ($F [1, 39] = 6.493, p < 0.05$). However, the base multivariate results indicated that the time-points Wilks’ Lambda score analysis was not significant ($p = 0.179$). Therefore, we concluded that the between-group variations in heart rates were not statistically significant. The MAP values of the patients differed significantly at the different time points, ($F [3.86, 150.524] = 6.153, p < 0.005$). On the other hand, the variations in MAP values over time were not significantly different in the two groups (control and ESP) ($F [1, 39] = 2.726, p > 0.05$). Moreover, the base multivariate results indicated that the time-points Wilks’ Lambda score was not significant ($p = 0.362$). Therefore, we concluded that variations in the MAP values of the two groups were not statistically significant.

Three patients in the ESP group and 13 patients in the control group required morphine as rescue analgesic in the first 24 hours postoperatively ($p = 0.001$). None of the patients had severe complications, such as a hematoma, pneumothorax, or bleeding related to the block procedure. However, four (19%) patients in the ESP group and 4 (20%) patients in the control group had mild pain at the injection site of the ESP block ($p = 0.939$). At postoperative 1h, four patients had mild SP, and one patient had severe SP ($n = 5, 23.8\%$) in the ESP group. In the control group, six patients had mild SP and two patients had severe SP ($n = 8, 40\%$) in the control group ($p = 0.527$). None of the patients complained about SP at any other time points. None of the patients had severe nausea or vomiting in the first postoperative 24 hours.

**Discussion**

In the current study, US-ESP block significantly reduced postoperative tramadol consumption and NRS scores 15 and 30 minutes post surgery and, 12 and 24 hours post surgery. Moreover, the intraoperative fentanyl requirements and rescue analgesic consumption in the ESP group were significantly lower than those in the control group. Although the mean heart rate of the patients in the ESP group was lower than that in the control group, there was no significant between-group difference.

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### Table 1 Demographic variables of the patients among groups.

<table>
<thead>
<tr>
<th></th>
<th>Group ESP (n, %)</th>
<th>Group control (n, %)</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender M/F</td>
<td>11/10 (52%-48%)</td>
<td>9/11 (45%-55%)</td>
<td>0.636</td>
</tr>
<tr>
<td>ASA I/II</td>
<td>10/11 (48%-52%)</td>
<td>11/9 (55%-45%)</td>
<td>0.642</td>
</tr>
<tr>
<td>Age (years)</td>
<td>47.9 ± 9.8</td>
<td>45.9 ± 11.8</td>
<td>0.549</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>70.4 ± 9.4</td>
<td>72.3 ± 10</td>
<td>0.540</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>165.5 ± 7.9</td>
<td>164.6 ± 7.9</td>
<td>0.711</td>
</tr>
<tr>
<td>BMI (kg. m$^{-2}$)</td>
<td>25.6 ± 2.3</td>
<td>26.6 ± 2.5</td>
<td>0.222</td>
</tr>
<tr>
<td>Surgical time (minutes)</td>
<td>41.5 ± 5.2</td>
<td>44.1 ± 6.5</td>
<td>0.168</td>
</tr>
</tbody>
</table>

ASA, American Society of Anesthesiologist; BMI, body mass index.

### Table 2 Comparison of NRS scores at different time-points between groups.

<table>
<thead>
<tr>
<th>NRS</th>
<th>Group ESP median (min-max) Mean ± SD</th>
<th>Group control median (min-max) Mean ± SD</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>15th minute</td>
<td>1 (0, 3) 1.24 ± 0.89</td>
<td>3 (0, 5) 2.9 ± 1.16</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>30th minute</td>
<td>2 (0, 4) 2.0 ± 0.89</td>
<td>3 (2, 6) 3.25 ± 0.85</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>60th minute</td>
<td>2 (1, 5) 2.43 ± 1.03</td>
<td>3 (1, 6) 2.9 ± 1.16</td>
<td>0.272</td>
</tr>
<tr>
<td>12th hour</td>
<td>2 (0, 5) 2.3 ± 1.1</td>
<td>3 (2, 7) 3.15 ± 1.2</td>
<td>0.036</td>
</tr>
<tr>
<td>24th hour</td>
<td>1 (0, 2) 1.3 ± 0.57</td>
<td>2 (1, 3) 1.95 ± 0.76</td>
<td>0.011</td>
</tr>
</tbody>
</table>

NRS, numerical rating scale.
Acute pain following LC has different components: incisional pain from the trocar site, local visceral pain, parietal pain, and referred SP. Bisgaard et al. reported that parietal pain due to a skin incision contributed more to laparoscopic pain than did other components. Based on this report, recent studies evaluated the effect of OSTAP block for postoperative analgesia after LC. One study reported that TAP/OSTAP block provided analgesia for somatic pain and parietal pain of almost the entire anterior abdomen and effectively reduced postoperative pain. Visceral pain that occurs due to tissue trauma during gall bladder resection is generally accepted as the most predominant component after LC and TAP/OSTAP blocks are known to fail in effecting visceral nerves. Thus, an alternative approach to attenuating visceral pain as part of multimodal analgesia may be needed after LC.

US-ESP block is an easily performed anesthesia technique, which leads to the blockage of both visceral and somatic nerve fibers. Previous research described its use in both adult and pediatric patients for pain relief after LC. Tulgar et al. described multimodal analgesia protocols in three patients who had endoscopic retrograde cholangiopancreatography, followed by LC. They performed US-ESP block at the level of T8 with 10 mL of 0.5% bupivacaine 5 mL of 2% lidocaine and 5 mL of isotonic saline following anesthesia induction. They reported that the NRS scores of the patients were under 3/10 in an ambulatory surgical setting. They performed bilateral ESP block while the patients were awake and in a sitting position. They injected 20 mL of 5% ropivacaine at each side at the level of T7. Similar to the study by Hannig et al., we performed bilateral ESP blocks while the patients were in a sitting position. However, we injected a lower concentration of local anesthetic solution (20 mL of 0.25% bupivacaine) than that applied in the study by Hannig et al. and achieved a significant reduction in postoperative tramadol consumption. In a recent study, Tulgar et al. evaluated the effect of US-ESP block on postoperative pain scores and analgesic consumption after LC in a randomized controlled trial. In their study, they reported that they increased the bupivacaine concentration to 0.375% due to block failure and insufficient sensorial block. In our study, 0.25% bupivacaine at the same volume (20 mL) provided similar pain scores. Our findings were in accordance with those of Tulgar et al., who reported average NRS scores during movement 1.5–2.5 hours post surgery. In both studies, US-ESP block effectively reduced postoperative pain scores as compared with those in the control group. Oksar et al. evaluated the effects of TAP block, OSTAP block, and tramadol PCA on postoperative opioid consumption and pain scores after LC. They found a significant reduction in pain scores in the OSTAP block group. However, the average pain scores at all time points were higher than those found in the present study. Moreover, the average postoperative tramadol consumption of the two groups was similar at different time points. On the other hand, Tulgar et al. found a significant reduction in postoperative tramadol consumption after US-ESP block as compared with that in a control group.

Similar to the findings of Tulgar et al., in the present study, postoperative tramadol consumption and morphine requirements in the US-ESP group were significantly lower than those in the control group, with power of >90%. The risk of patchy blockade in ESP block is well known. However, in the present study, it appeared to be better than OSTAP block in reducing postoperative pain. The most probable reason for this finding is the ability of ESP block to affect both parietal and visceral pain. Aksu et al. described the cases of three pediatric patients who received ESP block and IV paracetamol (15 mg·kg⁻¹) for pain management after LC. They performed ESP blocks at the level of T7 with 0.5 mL·kg⁻¹ of 0.25% bupivacaine (maximum dose: 20 mL per each side) and found that none of the patients required rescue analgesia in the first postoperative 48 hours.

Some authors have suggested that a multimodal analgesic approach, including nonsteroid anti-inflammatory drugs and local anesthetic infiltration to the port sites, has similar effects to those of block interventions in terms of pain management after LC. Viseo et al. compared the effects of paravertebral block and local anesthetic injections at laparoscopic port sites in pediatric patients. They reported that although intraoperative fentanyl requirements were lower in the paravertebral group, there was no significant between-group difference in postoperative pain scores. Similarly, Dost et al. compared the analgesic efficacy of US TAP block, local anesthetic infiltration to the port sites, and iv tramadol (1 mg·kg⁻¹). The authors reported no difference in the postoperative pain scores of the groups, with a median score of ≥ 4 in all the groups at postoperative 1 hour. Although conventional pain management, such as paracetamol, local anesthetic infiltration to port sites
and dexamethasone, provides effective analgesia in the first postoperative 24 hours, plane blocks, such as ESP and OSTAR, may be useful, especially in the early postoperative period.

SP is a well-known complication following LC. Although the origin of referred pain after LC is not fully understood, the irritative effect of the insufflated gas is thought to result in the release of inflammatory mediators and cause referred pain to the shoulder. Prolonged SP has been attributed to excitation of the phrenic nerve during LC. In the study by Tulgar et al., 33.3% of patients had SP after LC. In the current study, 31.7% of patients had SP in the first 2 hours postoperatively. In both studies, there was no between-group difference in the incidence of SP. Tulgar et al. performed ESP block at the level of T9, whereas we performed the block at the level of T7. Both levels were presumably too low to affect the phrenic nerve.

The main strength of our study is the presence of a placebo group. We performed the block interventions in both groups in a double-blinded fashion during the study period. The main limitation of the study was the small sample size, which was insufficient to detect postoperative complications, such as postoperative nausea and vomiting. As we routinely administered IV ondansetron (4 mg) and dexamethasone (8 mg), none of the patients had severe nausea or vomiting in the postoperative period. Similarly, we did not calculate the sample size required to demonstrate a difference in intraoperative hemodynamic parameters of the two groups. In addition, the patients received IV tramadol for postoperative analgesia and ondansetron for nausea/vomiting prophylaxis as a part of routine practice in our clinic. A drug interaction between ondansetron and tramadol was reported in a previous meta-analysis. The authors reported that ondansetron reduced the effectiveness of tramadol, especially in the early postoperative hours. The use of morphine PCA could have provided more objective results in this study.

Conclusions

In the current study, bilateral US-ESP block with 40 mL of 0.25% bupivacaine reduced the postoperative opioid consumption, pain scores, and intraoperative fentanyl requirements of patients undergoing LC. Further studies are needed to determine the optimum dose, concentration, and block level.

Conflicts of interest

The authors declare no conflicts of interest.

References
