Ultrasound-guided transversus abdominis plane block using ropivacaine and dexmedetomidine in patients undergoing caesarian sections to relieve post-operative analgesia: A randomized controlled clinical trial

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Abstract. Dexmedetomidine, which is a highly selective α2 adrenoreceptor agonist, enhances the analgesic efficacy and prolongs the analgesic duration when administered in combination with local anesthetics. The current study aimed to evaluate the effects of dexmedetomidine combined with ropivacaine in ultrasound-guided transversus abdominis plane (TAP) block on post-operative analgesia following cesarean section (CS). A total of 70 patients scheduled for CS were divided randomly into 2 groups: The ropivacaine (R) group, in which patients were administered bilateral 20 ml 0.3% ropivacaine and 2 ml 0.9% normal saline, and the dexmedetomidine (RD) group, in which patients were administered bilateral 20 ml 0.3% ropivacaine and 2 ml dexmedetomidine (0.5 µg/kg). The primary outcome was pain-free duration, and secondary outcomes included heart rate (HR) and mean blood pressure (MBP) measurements, visual analogue scale (VAS) pain scores, number of patients who required rescue analgesic, time to first request for analgesia and patient satisfaction. There was no significant difference in HR and MBP between the two groups at 1 h post-surgery (P>0.05). However, VAS pain scores decreased at 6 and 8 h post-surgery [2 (1-2) vs. 0 (0-1), respectively; P<0.05], pain-free duration was prolonged (5.91±1.08 vs. 9.62±1.46 h; P<0.05), the number of patients who required rescue analgesic was reduced (19 vs. 9; P<0.05), the time to first request for analgesia was prolonged (7.10±1.21 vs. 11.60±2.11 h; P<0.05) and patient satisfaction was improved [3.5 (3-4) vs. 4 (4-5); P<0.05] in the RD group compared with the R group. Furthermore, no bradycardia or hypotension was observed. In conclusion, the results of the present study demonstrated that adding 0.5 µg/kg dexmedetomidine to 0.3% ropivacaine used in TAP block in patients undergoing CS prolonged pain-free duration, decreased VAS pain scores, reduced the number of patients who required rescue analgesic, prolonged the time to first request for analgesia and improved the patient satisfaction without serious side effects.

Introduction

Cesarean section (CS) is one of the most common surgical procedures in China (1). The abdominal wall incision and soft tissue dissection associated with this procedure may result in moderate to severe post-operative pain, which adversely affects early ambulation and breastfeeding (2). Successful post-operative pain management following CS is crucial in order to facilitate early ambulation, shorten the recovery period and provide optimum maternal-neonatal bonding for patients (3).

Epidural analgesia and patient-controlled intravenous analgesia (PCIA) are commonly used for pain management following CS. However, these methods have certain disadvantages. For instance, epidural analgesia is often associated with lower extremity numbness and weakness, which delays early ambulation and increases the risk of thrombotic incidents (4). Furthermore, since opioids are the main drugs used in PCIA, there are concerns surrounding opiate-related complications, including sedation, nausea, vomiting, pruritus, respiratory depression and urinary retention (5). Additionally, side effects of opioids on the newborn via breast milk is another concern (6).

The transversus abdominis plane (TAP) block is a regional technique for analgesia, which provides satisfactory
post-operative pain relief and reduces certain side effects associated with the use of opioids or epidural block (7,8). Previous trials have demonstrated the efficacy of TAP block in providing post-operative analgesia following abdominal surgery (9,10). However, a limitation of TAP block is its relatively short duration of analgesia due to the short duration of action of local anesthetics used in this technique. To resolve this issue, various adjuvants such as fentanyl, dexamethasone and clonidine have been used in combination with local anesthetics (11-13).

Dexmedetomidine is a potent and selective adrenergic α2 agonist, and numerous previous clinical trials have demonstrated that dexmedetomidine may enhance analgesic efficacy and prolong the analgesic duration when administered in combination with local anesthetics (14-16). However, no study has been performed on the effect of dexmedetomidine combined with ropivacaine in TAP block for post-CS pain management. The aim of the current study was to evaluate the efficacy of dexmedetomidine as an adjuvant to ropivacaine for TAP block in patients undergoing CS.

Materials and methods

Patients. The current study was approved by the Ethics Committee of the First People's Hospital of Lianyungang (February 2018 to February 2019). A total of 70 patients (age, 18-40 years) with an American Society of Anesthesiologists (ASA) score of I-II who were scheduled for CS under spinal anesthesia were enrolled (17). Informed written consent was obtained from all patients. Patients with a body mass index of >30 kg/m² prior to conception, a history of allergy to any local anesthetics and/or any known contraindications for neuraxial anesthesia were excluded.

Of the 70 patients who were enrolled in the current study, 8 did not meet the inclusion criteria and 2 refused to participate. Therefore, 30 patients were randomized into the R and RD group using a computer-generated sequence of random numbers. The details of the series, which were generated by a statistician who did not participate in this study, were hidden in sealed envelopes. The numbered envelope was opened and the numbers were hidden in sealed envelopes. The numbered envelope was opened and the card inside determined into which group the patient would be placed after the patient had entered the surgery room prior to the induction of anesthesia.

Anesthesia procedure. None of the patients were pre-medicated. After entering the surgery room, routine electrocardiogram, pulse oxygen saturation, non-invasive blood pressure (BP) and heart rate (HR) were monitored. A 20-gauge cannula was inserted into the dorsum of the patient's hand and Ringer's lactate was infused at a rate of 4-6 ml/min.

Following aseptic preparation, patients were placed in the left lateral decubitus position and the skin where the spinal anesthesia was performed (the L3-4 interspace) was infiltrated with 2% lidocaine. Spinal anesthesia was performed using a 25-gauge spinal needle via a middle approach at the level of the L3-4 interspace. After confirming the free flow of cerebrospinal fluid, 10 mg 0.5% hyperbaric bupivacaine was injected intrathecally over 20-30 sec. Following the induction of anesthesia, patients were immediately moved to a supine position with a 15° left lateral tilt to avoid aortocaval compression. All patients received supplemental oxygen at the rate of 5 l/min via a face mask.

Surgical incision was performed when the sensory block level T6 or higher was achieved. Hypotension (systolic BP <20% of baseline or an absolute value <90 mmHg) was treated with 4-8 µg intravenous norepinephrine, and bradycardia (HR <50 bpm) was treated with 0.5 mg intravenous atropine. The same surgical team performed the surgeries on all patients.

TAP block procedure. Following surgery, bilateral ultrasound-guided TAP block was performed. The procedure was performed under aseptic conditions. A linear high frequency ultrasound probe was placed transversely on the anterolateral abdominal wall between the iliac crest and the costal margin. Under ultrasound guidance, the three layers of muscles (external oblique, internal oblique and transversus abdominis) were identified. A 22-gauge 100 mm uniplex nanoline needle (Pajunk GmbH) was introduced medially in the plane of the ultrasound beam until its tip was between internal oblique and transverse abdominal muscles. Following negative aspiration, 20 ml 0.3% ropivacaine and 2 ml normal saline was administered on each side of the TAP block for the R group, and 20 ml 0.3% ropivacaine with 2 ml dexmedetomidine (0.5 µg/kg) was administered on each side of the TAP block for the RD group. Following the procedure, patients were transferred to the post-anesthesia care unit (PACU).

Statistical analysis. Sample size calculations were based on a previous pilot study (Qian et al, unpublished data). Furthermore, the sample size was calculated according to the pain-free duration. A mean pain-free duration value of 6.1 h and standard deviation 1.6 h in 10 patients who received TAP block with ropivacaine was calculated; a total of 27 patients were required for each group to detect significant differences between groups of 20% with α=0.05 two-tailed and β=0.1. This number was raised to 35, and a total of 70 patients were enrolled to take into account potential drop-outs in both groups, allowing a predicted 15% drop-out rate in both groups.

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Statistical analyses were performed using SPSS software (version 16.0; SPSS, Inc.). Continuous numerical data are expressed as mean ± standard deviation or median and interquartile range. Categorical data are expressed as frequencies or percentages. Normally distributed numerical data between groups were analyzed using the Student’s t-test, skewed data between groups were analyzed using the Mann-Whitney U-test, and categorical variables were analyzed using Fisher’s exact test or Pearson’s χ² test as applicable. All tests were two-tailed. P<0.05 was considered to indicate a statistically significant difference.

Results

There were no significant differences in the demographic characteristics of the patients and surgery duration between the two groups (P>0.05; Table I).

Heart rate was compared between groups R and RD at the observed time-points (79.0±8.3 vs. 78.0±8.8, 77.2±8.1 vs. 76.9±7.2, 75.4±7.3 vs. 74.6±7.5, 74.4±7.1 vs. 73.9±7.6, 73.7±7.7 vs. 71.3±7.8, 72.2±8.2 vs. 70.8±8.0, respectively; P>0.05; Fig. 1). Additionally, mean blood pressure was similar between groups at the same time-points (90.7±8.0 vs. 87.9±7.7, 88.1±8.4 vs. 86.2±7.5, 86.9±7.8 vs. 84.2±7.2, 87.0±7.9 vs. 86.0±7.6, 88.3±8.1 vs. 86.3±8.2; P>0.05; Fig. 2). No patients developed hypotension or bradycardia in either group during this time period.

Post-operative VAS pain scores were significantly lower the RD group at 6 and 8 h compared with those in the R group. However, there was no significant difference in scores between groups at 2, 4, 10, 12 and 24 h (Table II).

Compared with the R group, the pain-free duration and first request for analgesia were significantly prolonged in the RD group (Table III). The number of patients who required rescue analgesia was also significantly lower in the RD group compared with that in the R group (Table III). Additionally, patient satisfaction scores were significantly higher in the RD group compared with the R group during the initial 48 h post-surgery (Table III).

Discussion

In the current prospective study of patients undergoing CS, the results demonstrated that the addition of 0.5 µg/kg dexmedetomidine to 0.3% ropivacaine used in TAP block prolonged pain-free duration and time to first request for analgesia, reduced the number of patients who required rescue analgesic and improved patient satisfaction without serious side effects.

Ultrasound-guided TAP block affects the T9 to L1 nerve roots and is recommended to be used in lower abdominal surgery (21). It has also been introduced as an effective component of multimodal analgesia following CS (9,22).
ropivacaine was used as the local anesthetic for TAP block as it has higher safety margin and lower levels of cardiac toxicity compared with bupivacaine (23). Previous studies have demonstrated that 0.25-0.5% ropivacaine for TAP block is valid (24,25). Therefore, 0.3% ropivacaine was used for TAP block in the current study. However, the relatively short duration of analgesia is still a major limitation of this technique. Recently, adjuvants used in conjunction with local anesthetics in order to prolong analgesia duration have become a focus of interest in the field of peripheral nerve block (26).

Dexmedetomidine, which is a highly selective a2 adreno-receptor agonist, is an ideal adjuvant to local anesthetics in numerous regional blocks. Hetta et al (27) reported that epidural infusion of dexmedetomidine combined with bupivacaine reduced morphine consumption delayed the time to first analgesic supplementation and decreased pain intensity in patients undergoing major abdominal cancer surgery and epidural blocks. Ganesh and Krishnamurthy (28) reported that dexmedetomidine combined with bupivacaine administered intrathecally exhibited a faster onset of motor and sensory block and prolonged the duration of anesthesia in patients undergoing spinal block. Mangal et al (15) demonstrated that the addition 1 µg/kg dexmedetomidine to 0.75% ropivacaine in supraclavicular brachial plexus block prolonged the duration of sensory and motor block. Furthermore, Mohta et al (29) reported that paravertebral block using 1 µg/kg dexmedetomidine combined with 0.5% bupivacaine provided longer duration of anesthesia with decreased post-operative opioid consumption and lower incidence of nausea and vomiting compared with bupivacaine alone. Aksu et al (30) demonstrated that addition of dexmedetomidine to bupivacaine in TAP block decreased post-operative pain scores and morphine consumption, and increased patient satisfaction in patients undergoing lower abdominal surgery. Thus, all of these previous studies demonstrated that dexmedetomidine may enhance analgesic efficacy and prolong the analgesic duration of local anesthetics when administered in combination with local anesthetics.

In the current study, the results indicated that when compared with 0.3% ropivacaine alone, adding 0.5 µg/kg dexmedetomidine to 0.3% ropivacaine in TAP block prolonged pain-free duration, decreased post-operation VAS pain scores at 6 and 8 h post-surgery, reduced the number of patients who required rescue analgesic, prolonged the time to first request for analgesic and improved patient satisfaction without serious side effects. These results were consistent with a previous study by Ramya et al (31), which concluded that the addition of dexmedetomidine to bupivacaine in TAP block prolonged the time to first request of rescue analgesia and reduced the total dose of opioid requirement in the first 24 h post-CS. However, Ding et al (32) reported that adding dexmedetomidine did not significantly improve the quality or duration of TAP block. Different does and concentrations of ropivacaine and dexmedetomidine and analgesics used post-surgery may explain these differences in the results.

Bradycardia and hypotension are the most common side effects of dexmedetomidine when administered intravenously (33). Therefore, HR and MBP were continuously monitored, and the results were recorded every 10 min until the patients left the PACU. The results demonstrated a slight decrease in HR and MBP in the two groups, which was not significantly different between the groups. In addition, none of the patients exhibited bradycardia and/or hypotension during their time in the PACU.

A meta-analysis revealed that dexmedetomidine combined with ropivacaine in brachial plexus block had a better analgesic effect compared with ropivacaine alone. Meanwhile, there was no difference in the incidence of bradycardia and hypotension (34). Mangal et al (15) reported that two patients exhibited bradycardia (HR <60 bpm) in the dexmedetomidine (1.0 µg/kg) group when dexmedetomidine was used as an adjuvant to ropivacaine for supraclavicular brachial plexus. The differences in the definition of bradycardia (HR <50 bpm) and concentration of dexmedetomidine (0.5 µg/kg) in the current study may explain the difference in results.

The current study had certain limitations. First, the present randomized controlled double-blinded trial was conducted at a single center. Further clinical trials are required at multiple centers in order to generalize the results. Second, whether the action of dexmedetomidine was related to systemic absorption or pure local effect was not fully elucidated. Further research is necessary to determine the plasma levels of dexmedetomidine. Third, the onset of action of the TAP block was not assessed precisely as the effect of the spinal block may not have worn off when the TAP block was performed. Further studies concerning patients accepting general anesthesia rather than spinal anesthesia may resolve this issue.

In conclusion, the results of the current study demonstrated that the addition 0.5 µg/kg dexmedetomidine to 0.3% ropivacaine used in TAP block in patients undergoing CS prolonged

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**Table III. Comparison of post-operative variables between groups R and RD.**

<table>
<thead>
<tr>
<th>Post-operative variable</th>
<th>Group R (n=30)</th>
<th>Group RD (n=30)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain-free duration, h</td>
<td>5.91±1.08</td>
<td>9.62±1.46</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No. of patients who required rescue analgesic</td>
<td>19</td>
<td>9</td>
<td>0.010*</td>
</tr>
<tr>
<td>Time to first request for analgesia, h</td>
<td>7.10±1.21</td>
<td>11.60±2.11</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Patient satisfaction score</td>
<td>3.5 (3-4)</td>
<td>4 (4-5)</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

*P<0.05. Data are expressed as mean ± standard deviation, patient of number or median (interquartile range). R, ropivacaine; RD, ropivacaine with dexmedetomidine.
pain-free duration, decreased VAS pain scores, reduced the number of patients who required rescue analgesia, prolonged the time of first request for analgesia and improved patient satisfaction without serious side effects.

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors’ contributions
HQ and QZ designed the study, performed the transversus abdominis plane blocks and wrote the first draft of the manuscript. PZ, XZ, LT and JF collected the clinical data. YW and ZZ analyzed the data and interpreted the results. HL designed the study and revised the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate
The current study was approved by the Ethics Committee of the First People's Hospital of Lianyungang. Informed written consent was obtained from all patients. The current study was approved by the Ethics Committee. A prospective, randomized controlled trial. Am J Surg 215: 498-501, 2018.

Patient consent for publication
Not applicable.

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

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