Effects of Epidural Low Concentration Ropivacaine with Fentanyl on Sympathetic Block in Labor Analgesia: A Randomized Controlled Trial

Yu-Ling Yeh¹,², Shou-Zen Fan³,⁴, Yi Chang¹,², Kuo-Ching Wang¹,²,*

ABSTRACT

Objective: Epidural low concentration local anesthetics combined with opioids are widely used in labor analgesia. However, whether epidural low concentration local anesthetics decrease the degree of sympathetic block is not clear. Methods: Forty nulliparous parturients admitted for spontaneous vaginal delivery were enrolled and randomly assigned into group A and B. Epidural labor analgesia was initiated with 15 ml 0.07 % ropivacaine with 50 µg fentanyl for group A parturients and 15 ml of 0.25 % ropivacaine for group B parturients followed by a 12 ml/hr infusion of 0.07% ropivacaine plus 2 µg/ml fentanyl. Skin temperature and skin blood flow of the hand and foot were measured before and 30 minutes after the beginning of epidural analgesia by the temperature probe and laser-Doppler flowmetry. Results: Skin temperature of the foot increased more in group B parturients 30 min after epidural analgesia than group A parturients (Group A: +0.5 ± 1.3 °C; Group B: +3.5 ± 2.4 °C; p < 0.001). Skin blood flow of the foot also significantly increased in group B parturients (Group A: +9 ± 62%; Group B: +195 ± 318%; p = 0.01). On the contrary, skin temperature and blood flow of the hand slightly decreased in group B parturients but slightly increased in group A parturients (p = 0.01 and 0.09, respectively). Conclusions: Epidural 15 ml 0.07% ropivacaine plus 50µg fentanyl for labor analgesia produced less sympathetic block and also provided good quality of analgesia at the beginning of labor.

Keywords: epidural analgesia, obstetrical analgesia, sympathetic block, Laser-Doppler flowmetry, skin temperature, local anesthetics

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INTRODUCTION

Labor pain has been considered as one of the most intolerable pains and can have negative impacts on the mother and fetus [1]. For pain relief of vaginal delivery, epidural analgesia remains a very effective pain-relieving method with the benefits of lower pain scores, high satisfaction and least adverse effects on maternal and fetal physiological functions [2].

Ropivacaine is a widely used long-acting local anesthetic for epidural labor analgesia [3, 4]. Ropivacaine is found to have less cardiotoxic properties and produces lower incidence of motor block than its homologue, bupivacaine [5, 6]. The motor function preservation property of epidural ropivacaine can help to facilitate maternal ambulation, promote uterine contraction, hasten fetal head descent, and increase maternal satisfaction [7, 8]. On the other hand, fentanyl, a high-potency lipid-soluble opioid, is a suitable agent for epidural supplementary and can decrease the dosage of local anesthetics without a decline of analgesic effects [9, 10]. Because of the efficacy and safety, epidural regimens consist of ropivacaine and fentanyl are now very popular for labor analgesia [2,11-13].

Epidural local anesthetics may impede parturients’ muscle power of lower limbs, pelvic floor and abdomen. Previous studies showed maternal motor blockade produced by epidural labor analgesia can prolong the second stage of labor and increase the incidence of instrumental vaginal delivery [14, 15]. In addition, higher concentration of local anesthetics for epidural labor analgesia produces greater degree of motor block [16, 17]. On the contrary, several randomized controlled trials pointed out the utilization of low concentration local anesthetics (usually defined as bupivacaine <0.1% or ropivacaine <0.17%) plus opioids for epidural analgesia can decrease motor-blockade-associated adverse effects and also maintain adequate analgesia [16, 17]. Therefore, there is a trend of using low concentration epidural local anesthetics with opioids in current clinical practice [17].

Human preganglionic sympathetic nerve fibers, originating from the thoracolumbar segments of the spinal cord, can also be blocked by epidural local anesthetics [18]. The intensity and extent of sympathetic blockade produced by epidural labor analgesia depends on the dose, concentration, volume and injection sites of local anesthetics [19]. The venodilation effects produced by sympathetic block increase venous capacitance, result in peripheral blood pooling, develop maternal hypotension and may deteriorate uterine blood flow in parturients [20, 21]. Because the thin or unmyelinated neural fibers for pain and sympathetic transmissions were found to be more sensitive to local anesthetics in comparison with the large myelinated fibers [22-25], whether the low concentration epidural local anesthetics used in epidural labor analgesia also decrease the degree of sympathetic blockade is not clear. Till the recent, the experimental and clinical data regarding the sympathetic block effects of low concentration epidural local anesthetics are scarce [26].

It is difficult to measure the sympathetic activity directly and there are no standardized criteria to define the strength of sympathetic action [27]. Many investigators had studied sympathetic blocking effects by indirect methods focusing on the functional changes of effector organs [26, 28, 29]. For spinal or epidural anesthesia/analgesia, measur-
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The change of skin temperature and cutaneous blood flow are two commonly used methods to determine the sympathetic activity [30, 31]. By measuring skin temperature and cutaneous blood flow of hands and feet with temperature probes and laser-Doppler flowmetry, the aim of our study was to evaluate the difference of sympathetic blocks produced by epidural 15 ml 0.07% ropivacaine plus 50 µg fentanyl and 15 ml 0.25% ropivacaine used in labor analgesia.

MATERIALS AND METHODS

After institutional review approval (number: BE-2-24) of Shin-Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan, this double-blind, randomized controlled trial was conducted. Forty nulliparous parturients, classified as the American society of anesthesiologists (ASA) physical status classification I or II, who presented in spontaneous labor or were scheduled for elective induction of labor were enrolled. Study inclusion criteria were 36-42 weeks’ gestation, singleton pregnancy in the vertex position, a normal fetal heart rate pattern, requesting epidural analgesia, and 2-5 cm cervical opening at the time of epidural catheter insertion. The exclusion criteria were body weight > 90 kg, age > 45 yr, failed epidural catheterization, inadvertent epidural puncture, smoking history, previous administration of opioids or vasoactive agents, the presence of pregnancy-induced hypertension and diabetes mellitus, preeclampsia and eclampsia, a contraindication to epidural analgesia, and an allergic history to ropivacaine or fentanyl.

Following request for epidural analgesia, each woman received at least 500 ml of compound lactate solution before initiation of epidural analgesia. Room temperature was kept at 22-26°C. Before the procedure, the baseline heart rate, blood pressure, tympanic temperature, skin temperature and skin blood flow of the hand and foot were all documented. Heart rate and noninvasive blood pressure measurements were performed under lateral position. Each patient completed baseline assessments of pain using a 100-mm visual analog scale (VAS: the value of 0 representing no pain; the value of 100 representing the worst possible pain) and finished lower limb muscle power tests with the modified Bromage score (Grade 1: complete block, unable to move feet or knees; Grade 2: almost complete block, able to move feet only; Grade 3: partial block, just able to move knee; Grade 4: detectable weakness of hip flexion; Grade 5: no detectable weakness of hip flexion while supine with full flexion of knees). Patients were asked to relate any symptoms of nausea, vomiting and shivering during laboring. All of observations and measurements were performed by staff members blinded to the parturients’ study allocations. During the whole course of labor, all parturients were monitored with a fetal heart beat monitor.

The epidural spaces were identified by a loss-of-resistance technique with air utilizing 16-gauge epidural needles at the interspaces of the 4-5th lumbar spines under lateral position. A multiport epidural catheter was inserted about 5 cm deep into the epidural space. Aspiration was attempted from the epidural catheter in an effort to detect the intravascular or intrathecal placement of the catheters. Patients with any signs of accidental dural puncture or intravascular catheter placement will be excluded from this study.

Forty patients were randomly assigned into two groups: group A and group B. Each group has
20 patients. Epidural labor analgesia was initiated with a bolus of 15 ml 0.07% ropivacaine with 50 µg fentanyl for parturients of group A or 15 ml 0.25% ropivacaine without fentanyl for parturients of group B. The 15 ml epidural solution was fractionated into 3 top-up doses (5 ml each time) under careful observations of any signs of spinal block. Epidural loading dose was followed by an infusion of a solution mixture of 0.07% ropivacaine with 2 µg/ml fentanyl at a rate of 12 ml/hr. If a patient did not experience adequate analgesia (defined as VAS > 40) 30 min after the initial loading dose, 8 ml of 0.25% ropivacaine was planned to be given epidurally after completion of data collection. If this rescue dose failed, 5 ml of 2% epidural lidocaine was then administered. If both of the rescue doses failed, we will exclude the parturient from the study. During the entire course of labor analgesia, parturients’ blood pressure was monitored every 5 minutes. Any reduction of mean blood pressure over 20% of the baseline value was promptly treated with repeated doses of 8 mg intravenous ephedrine.

Thirty minutes after the loading of epidural solutions, following data were collected: heart rate; blood pressure; tympanic temperature; skin temperature of hand and foot; skin blood flow of hand and foot; VAS score; blocking level of temperature sensation (using cold spirit); motor power of lower limbs (using the modified Bromage scale); presence of shivering, nausea and vomiting.

**Procedures of Skin Blood Flow Measurement**

The parturients were kept at the lateral position. According to the topography, the blood flow measurements were proceeded during the period of uterine relaxation with a laser flow meter (LASER-FLO BMP, Vasamedics®, Minnesota, USA). The skin flowmetry probe (P-430 Right Angle Probe, Vasamedics®) was attached to the nondependent limb of parturients with adhesive tapes. The probe attaching sites were at the dorsum of hand (for data collection before analgesia), the dorsum of foot (for data collection before analgesia and 30 min after analgesia), and then the dorsum of hand (for data collection 30 min after analgesia) in sequence. The skin blood flow values were the means values of the 30 seconds’ recording and were expressed as ml/min/100g tissue. The changed ratios of skin blood flow before and after epidural analgesia were calculated.

**Method of Skin Temperature Recording**

Skin temperature was measured at the same time of skin blood flow measurements with a temperature probe (21078A Skin Probe, HP Co., USA). The temperature probe was attached to the skin area nearby the attaching sites of the flowmetry probe over the dorsum of hand and foot.

**Statistical Analysis**

Assuming the mean skin blood flow change of foot before and after epidural labor analgesia in group A is 20% (SD 100%) and the change in group B is 200% (SD 200%) with an α at 0.05 and a β at 0.9, it was determined that 17 patients would be required per group to detect this difference between the two groups. To allow for parturients who might not complete the study, we enrolled 20 patients in each group.

Data were presented as mean ± standard deviation, or median (range). All parametric data were compared with the Student t test. Categorical variables were analyzed using the Fisher’s exact test.
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Non-normally distributed variables including VAS scores, and thoracic blocking level were compared using the Mann-Whitney U-test. A value of \( p < 0.05 \) was considered to be statistically significant.

**RESULTS**

Among the 40 enrolled patients in this study, no patient was excluded due to technique failure, dural puncture, intravascular catheter implantation, inadequate pain relief, or incomplete data collection. Maternal demographic characteristics were similar between the two groups with respect to age, weight, height, gestational age, ASA classification, oxytocin usage, and opening of the cervix before epidural insertion (Table 1).

Before epidural labor analgesia, the median VAS score of Group A was 73 with a range of 58-100; the median VAS score of Group B was 75 with a range of 60-100 (\( p = 0.37 \)). Thirty minutes after epidural analgesia, the median VAS score of Group A was 10 with a range of 0-35; the median VAS score of Group B was 15 with a range of 0-40 (\( p = 0.74 \)). There were no significant differences in VAS scores before and after epidural analgesia between the two groups (Table 2). The median blocking levels of temperature sensation of two groups were both at the 6th thoracic dermatome (\( p = 0.90 \)). There were 4 parturients in group A and 8 parturients in group B suffering from shivering (\( p = 0.66 \)) (Table 2). There were no patients receiving epidural rescue doses for VAS scores higher than 40 or receiving intravenous ephedrine to correct hypotension. There were no parturients suffering from nausea or vomiting during the study periods (Table 2). But there were 8 parturients in group B found with detectable weakness of lower limbs (modified Bromage scale grade 4). However, no women in group A had lower limbs weakness (\( p < 0.01 \)) (Table 2).

The temperature data are shown in Table 3. Before epidural labor analgesia, parturients of both groups had similar baseline values of tympanic temperature, hand skin temperature and foot skin temperature (Table 3). Thirty minutes after epidural analgesia, skin temperature of the foot increased more and became higher in group B parturients than group A parturients (foot temperature after analgesia: Group A: 29.1 ± 3.2 °C; Group B: 32.7 ± 2.6 °C; \( p < 0.001 \); foot temperature difference: Group A: +0.5 ± 1.3 °C; Group B: +3.5 ± 2.4 °C; \( p < 0.001 \)). On the contrary, skin temperature of the hand slightly increased in group A parturients but slightly decreased in group B parturients after epidural analgesia (hand temperature difference: Group A: +0.6 ± 1.4 °C; Group B: -0.6 ± 1.4 °C; \( p = 0.01 \)) (Table 3). After epidural analgesia, tympanic temperature was significantly lower in group B parturients than group A parturients (Group A 37.1 ± 0.5 °C; Group B 36.8 ± 0.5 °C; \( p = 0.04 \)). However, the change of tympanic temperature before and after epidural analgesia was both small in the two groups (Group A +0.2 ± 0.3 °C; Group B +0.0 ± 0.4 °C; \( p = 0.08 \)).

Table 4 shows the skin blood flow values and their changes before and after epidural labor analgesia. The change of skin blood flow is similar to the change of skin temperature in both groups. Skin blood flow of the foot markedly increased in group B parturients thirty minutes after epidural analgesia when compared with the group A parturients (Group A: 962%; Group B: 195 ± 318%; \( p = 0.01 \)). Skin blood
flow of the hand decreased in group B parturients after epidural analgesia but increased in group A parturients (Group A: 41.7 ± 193%; Group B: -20.8 ± 52.5%; p = 0.09).

Hemodynamic data are shown in Table 5. The group B parturients had higher baseline heart rate than group A parturients before epidural analgesia (Group A: 75.2 ± 10.2 bpm; Group B: 86.2 ± 17.3 bpm, p = 0.02). But the heart rates of two groups after epidural analgesia were similar (Table 5). The mean systolic blood pressure and the change of systolic blood pressure were similar between the two groups either before or after epidural analgesia, (Table 5). However, group B parturients had slightly higher baseline diastolic blood pressure than that of group A parturients before analgesia (Group A: 70± 11 mmHg; Group B: 77 ± 12 mmHg, p = 0.06). Although the mean diastolic blood pressures of two groups were similar after epidural analgesia (Group A: 66 ± 8 mmHg; Group B: 66 ± 13 mmHg, p = 0.94), the mean diastolic blood pressure of group B parturients decreased more that of group A parturients. (Group A: -4 ± 9 mmHg; Group B: -10 ± 12 mmHg, p = 0.05) (Table 5).

Table 1. Baseline demographic and obstetric characteristics of parturients

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>31.1 ± 4.3</td>
<td>29.7 ± 4.5</td>
<td>0.75</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>67.9 ± 7.3</td>
<td>72.2 ± 7.2</td>
<td>0.07</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>160.1 ± 4.25</td>
<td>160.9 ± 5.6</td>
<td>0.61</td>
</tr>
<tr>
<td>Gestational age (week)</td>
<td>39.3 ± 1.0</td>
<td>39.7 ± 1.0</td>
<td>0.17</td>
</tr>
<tr>
<td>Opening of the cervix (cm)</td>
<td>2.8 ± 0.9</td>
<td>2.6 ± 0.8</td>
<td>0.57</td>
</tr>
<tr>
<td>ASA I/II (No. of cases)</td>
<td>17/3</td>
<td>19/1</td>
<td>0.60</td>
</tr>
<tr>
<td>Use of oxytocin (No. of cases)</td>
<td>12</td>
<td>13</td>
<td>0.74</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± SD or number of cases as appropriate.
ASA: American society of anesthesiologists physical status classification

Table 2. Analgesic and other characteristics of epidural labor analgesia of the two study groups

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAS score before epidural analgesia</td>
<td>73 (58-100)</td>
<td>75 (60-100)</td>
<td>0.37</td>
</tr>
<tr>
<td>VAS score after epidural analgesia</td>
<td>10 (0-35)</td>
<td>15 (0-40)</td>
<td>0.74</td>
</tr>
<tr>
<td>Blocking level of temperature sensation (thoracic dermatome)</td>
<td>T6 (T4-T10)</td>
<td>T6 (T4-T11)</td>
<td>0.90</td>
</tr>
<tr>
<td>Ephedrine usage</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Receiving rescue dose</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Nausea or vomiting</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Shivering</td>
<td>4</td>
<td>2</td>
<td>0.66</td>
</tr>
<tr>
<td>Muscle power (modified Bromage scale Grade 4/Grade 5)</td>
<td>0/20</td>
<td>8/12</td>
<td>&lt;0.01*</td>
</tr>
</tbody>
</table>

Results are expressed a median (range) or number of cases as appropriate.
VAS: visual analog scale; NA: non-available; *, p<0.05
## Table 3. Tympanic and skin temperature of parturients before and 30 minutes after the initiation of epidural labor analgesia

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tympanic temperature before epidural analgesia</td>
<td>37.0 ± 0.4</td>
<td>36.8 ± 0.5</td>
<td>0.39</td>
</tr>
<tr>
<td>Tympanic temperature after epidural analgesia</td>
<td>37.1 ± 0.5</td>
<td>36.8 ± 0.5</td>
<td>0.04*</td>
</tr>
<tr>
<td>Tympanic temperature difference</td>
<td>0.2 ± 0.3</td>
<td>0.0 ± 0.4</td>
<td>0.08</td>
</tr>
<tr>
<td>Hand skin temperature before epidural analgesia</td>
<td>31.3 ± 2.2</td>
<td>31.6 ± 1.2</td>
<td>0.52</td>
</tr>
<tr>
<td>Hand skin temperature after epidural analgesia</td>
<td>31.8 ± 2.1</td>
<td>31.0 ± 1.8</td>
<td>0.20</td>
</tr>
<tr>
<td>Hand skin temperature difference</td>
<td>0.6 ± 1.4</td>
<td>-0.6 ± 1.4</td>
<td>0.01*</td>
</tr>
<tr>
<td>Foot skin temperature before epidural analgesia</td>
<td>28.6 ± 2.7</td>
<td>29.2 ± 2.0</td>
<td>0.41</td>
</tr>
<tr>
<td>Foot skin temperature after epidural analgesia</td>
<td>29.1 ± 3.2</td>
<td>32.7 ± 2.6</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Foot skin temperature difference</td>
<td>0.5 ± 1.3</td>
<td>3.5 ± 2.4</td>
<td>&lt; 0.001*</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± SD °C.

*: p<0.05

## Table 4. Hand and foot skin blood flow of parturients before and 30 minutes after the initiation of epidural labor analgesia

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hand SBF before epidural analgesia (ml/min/100g tissue)</td>
<td>4.1 ± 3.0</td>
<td>4.4 ± 2.8</td>
<td>0.78</td>
</tr>
<tr>
<td>Hand SBF after epidural analgesia (ml/min/100g tissue)</td>
<td>4.1 ± 2.1</td>
<td>3.4 ± 2.3</td>
<td>0.32</td>
</tr>
<tr>
<td>Change of hand SBF (%)</td>
<td>+56 ± 173</td>
<td>-15 ± 48</td>
<td>0.09</td>
</tr>
<tr>
<td>Foot SBF before epidural analgesia (ml/min/100g tissue)</td>
<td>2.3 ± 1.6</td>
<td>1.9 ± 0.9</td>
<td>0.06</td>
</tr>
<tr>
<td>Foot SBF after epidural analgesia (ml/min/100g tissue)</td>
<td>2.4 ± 2.4</td>
<td>6.4 ± 9.1</td>
<td>0.07</td>
</tr>
<tr>
<td>Change of foot SBF (%)</td>
<td>+9 ± 62</td>
<td>+195 ± 318</td>
<td>0.01*</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± SD.

SBF: skin blood flow; *: p<0.05

## Table 5. Parturient heart rate and blood pressure before and 30 minutes after the initiation of epidural labor analgesia

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR before epidural analgesia (bpm)</td>
<td>75.2 ± 10.2</td>
<td>86.2 ± 17.3</td>
<td>0.02*</td>
</tr>
<tr>
<td>HR after epidural analgesia (bpm)</td>
<td>76.1 ± 15.9</td>
<td>78.1 ± 14.1</td>
<td>0.68</td>
</tr>
<tr>
<td>HR difference (bpm)</td>
<td>0.9 ± 16.2</td>
<td>-8.2 ± 23.1</td>
<td>0.16</td>
</tr>
<tr>
<td>SBP before epidural analgesia (mmHg)</td>
<td>125 ± 16</td>
<td>128 ± 14</td>
<td>0.61</td>
</tr>
<tr>
<td>SBP after epidural analgesia (mmHg)</td>
<td>112 ± 11</td>
<td>112 ± 15</td>
<td>0.94</td>
</tr>
<tr>
<td>SBP difference (mmHg)</td>
<td>-13 ± 10</td>
<td>-16 ± 12</td>
<td>0.43</td>
</tr>
<tr>
<td>DBP before epidural analgesia (mmHg)</td>
<td>70 ± 11</td>
<td>77 ± 12</td>
<td>0.06</td>
</tr>
<tr>
<td>DBP after epidural analgesia (mmHg)</td>
<td>66 ± 8</td>
<td>66 ± 13</td>
<td>0.94</td>
</tr>
<tr>
<td>DBP difference (mmHg)</td>
<td>-4 ± 9</td>
<td>-10 ± 12</td>
<td>0.05*</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± SD.

HR: heart rate; SBP: systolic blood pressure; DBP: diastolic blood pressure; *: p<0.05
DISCUSSION

Our results showed that 0.07% 15ml ropivacaine combined with 50 µg fentanyl produced little sympathetic blocking effects supported by the evidences of tiny change of foot skin temperature and foot skin blood flow after lumbar epidural analgesia. This epidural regimen of 0.07% ropivacaine combined with fentanyl also had negligible motor blocking effects that are similar to the results of previous studies [10, 32]. In contrast, lumbar epidural 15ml 0.25% ropivacaine had significant sympathetic blocking effects and markedly increased foot skin temperature and foot skin blood flow. In addition, our study found epidural 0.25% ropivacaine frequently induced muscle weakness in lower limbs.

Lumbar epidural high concentration local anesthetics dilate the blood vessels of lower body. Previous literatures showed the vasodilatation of lower body can decrease blood pressure, induce baroreceptor reflex and cause compensatory increased sympathetic activity in the unanesthetized regions [26, 33, 34]. In our study, the hand skin temperature and cutaneous blood flow in group B were slightly decreased after analgesia. These results suggest the sympathetic blocking effects of epidural 15 ml 0.25% ropivacaine produced mild compensatory vessel constriction over the upper extremities. But, on the contrary, the hand skin temperature and skin blood flow did not decrease but increase in group A parturients. This evidence showed there were no reflex vasoconstriction induced by 15 ml 0.07% epidural ropivacaine plus fentanyl. The slightly increased hand skin temperature and skin blood flow in group A are possible to be caused by the generally decreased sympathetic tone after the elimination of labor pain.

Although our results showed there were significantly different degrees of sympathetic block between the two groups, however, parturients of both groups had similar hemodynamic parameters such as heart rate, systolic and diastolic blood pressure after labor analgesia. The lack of difference in hemodynamic data between the two groups after analgesia may be caused by multiple factors, such as compensatory vessel constriction in unanesthetized area (group B parturients), limited extent of sympathetic block, prehydration before epidural analgesia, or small sample size of our study, etc. This result consisted with the meta-analysis by Sultan P et al. The meta-analysis showed there are no differences in the incidences of maternal hypotension whatever the epidural labor analgesia utilizing low- or high-concentration local anesthetics [17]. In contrast to frequent hypotension events produced by spinal/epidural anesthesia employed for operation, the incidence of hypotension in epidural labor analgesia was usually low and it was seldom severe enough to require medical treatments [17, 35]. In our study, the parturients of both groups had acceptable blood pressure during the study course and did not receive ephedrine to correct their blood pressure.

Because the direct access of sympathetic activity is invasive and technically difficult, our study applied indirect methods focusing on the sympathetic-related changes of skin blood flow and temperature. However, indirect methods are subject to many confounders. For pregnant women near term, the huge uterus may compress the descending aorta and inferior vena cava. Parturients develop signs of aortocaval compression easily when they assume the supine position [36]. Aor-
tocaval compression reduces venous return and the arterial blood flow to lower body. This makes the blood supply of lower extremities unstable and produced marked disturbance on skin blood flow measurements. For this reason, we collected all the blood flow data at a lateral position during the non-contracting period of uterus to minimize the effects of aortocaval compression. We also recorded the heart rate and blood pressure at the same condition.

In the aspect of skin temperature measurement, the major confounders are body temperature, room temperature and patients’ clothing. The mean tympanic temperature of group B after epidural analgesia was significantly lower than that of group A (Table 3). Because group B parturients had higher degrees of sympathetic block, the lower body temperature in group B can be caused by a core-to-peripheral redistribution of internal heat induced by vasodilatation [37]. However, the tympanic temperature of group B kept the same before and after epidural analgesia (tympanic temperature change +0.0 ± 0.4 °C). This may be able to explain the fact that the group B parturients did not suffer from higher incidence of shivering than group A. In this study, we kept the room temperature at the range of 22-26 °C. But, for the parturients’ convenience and comfort, we didn’t standardize the parturients’ clothing and covering.

Because labor pain stimulates sympathetic activity greatly, it is important to keep similar pain intensity between the two groups to minimize the interference of labor pain. In this study, we added 50μg fentanyl to the regimen of 15 ml 0.07% epidural ropivacaine to make its analgesic effects equivalent to that of epidural 0.25% ropivacaine. However, literatures showed fentanyl can have some effects on autonomic system, thermoregulation and vascular tone. In the canine model of coronary artery occlusion, intravenous fentanyl was demonstrated to increase vagal drive [38]. Previous study of labor analgesia by Tsai F.F. et al revealed 4 μg/mL epidural fentanyl induced more extensive segmental sensory block when added to 10 ml 0.0625% epidural bupivacaine compared to bupivacaine alone [10]. In the study of rats, fentanyl was found to have potency to produce hyperthermia [39]. Brookes Z.L. et al revealed that fentanyl can constrict the arterioles and significantly change the microcirculation of rat skeletal muscle in vivo [40]. On the contrary, fentanyl was found to be able to attenuate artery contractions or cause vasodilation by a dose-dependent manner in the porcine and canine experiments [41, 42]. Since the effects of epidural fentanyl on autonomic nerve system, body temperature and organ circulation are still unknown, the solely sympathetic blocking effects of epidural 0.07% ropivacaine are remained to be elucidated.

Epidural fentanyl generates its analgesic and adverse effects via both spinal and systemic mechanisms [43]. Epidural fentanyl used for labor analgesia, just like other opioids, elicits several side effects such as nausea/vomiting, pruritus, maternal sedation, respiratory depression, low neonatal Apgar score, etc. [44, 45]. The severity of adverse side effects produced by epidural opioids is dose-dependent and correlates with their concentrations in the cerebrospinal fluid [46]. Among these adverse effects, pruritus is frequently observed in the treated patients [45]. The symptoms of pruritus in parturients are generally mild and seldom severe enough to warrant management [47]. Because our study focusing on the sympathetic blocking effects of local anesthetic was not designed to investigate the side effects of epidural fentanyl, we did not specifically ask about and recorded the pres-
ence of pruritus. However, during the study periods, there were no parturients complained and asked for specific treatment for pruritus. Also, during the study course, no parturients in group A or B suffered from nausea or vomiting. The low incidences of pruritus and nausea/vomiting in our study may be due to the short observation time (only the first thirty minutes after the initiation of epidural loading doses). Because investigating the fentanyl-associated side effects is beyond the scope of this article, our study did not include the maternal sedation score and the neonatal Apgar score.

Although our study showed that the 15 ml 0.07% epidural ropivacaine with 50 µg fentanyl produced less sympathetic block than 15 ml 0.25% epidural ropivacaine, however, this study has several limitations. First, in our study, we omitted the epidural test dose. Generally, an epidural test dose contains 45-60 mg lidocaine or an equivalent dose of bupivacaine with epinephrine used to prevent the unintentional intrathecal and intravascular injection of epidural anesthetic agents [48]. However, unlike the high-volume high-concentration local anesthetics utilized in epidural anesthesia for surgery, malinjection of low concentration local anesthetics for epidural labor analgesia rarely cause a serious threat [49]. Also, epidural test dose is found not completely effective in the obstetric patients [50]. Therefore, there is no consensus about the usage of epidural test dose in labor analgesia and some anesthesiologists suggested abandoning the standard test dose [49]. In our study, we fractionated the epidural loading solution into 3 top-up doses and consider the therapeutic dose as the test dose itself [50]. However, the standard epidural test dose can have nerve blocking effects by its own. Previous report of Valley et al revealed that 50mg lidocaine in epidural test dose markedly increased the skin perfusion and inspiratory gasp vasoconstrictive response of lower limbs [51]. The studies of Calimaran et al and Cohen et al showed the test dose of 45 mg lidocaine for epidural or spinal-epidural labor analgesia produces motor block and interferes with the parturients’ ambulation [52, 53]. For that reason, when the epidural test dose was added to the regimens, the degrees of sympathetic block may be altered.

The second limitation of our study is that we did not record the skin blood flow and skin temperature till the end of labor. Previous studies showed that the minimum effective epidural local anesthetic concentrations increase as labor progresses [54]. This means higher concentrations of epidural local anesthetics may be required to achieve satisfactory analgesia at the later stage of labor. Also, the parturients who received low concentration epidural local anesthetics for labor analgesia may need more frequent rescue boluses of high concentration local anesthetics to release their breakthrough pain [55]. With the addition of high concentration epidural local anesthetic rescue boluses, the degree of sympathetic block may be increased. Therefore, the sympathetic sparing effects of low concentration epidural local anesthetics are possible to be lost at the end of labor.

In addition, the level of sympathetic block was not measured in our study. Although, we used the same volume of lumbar epidural solution, we do not know whether the cephalad and caudal extents of sympathetic block produced by the two epidural regimens are the same or not. Since the sympathetic block may cranially exceed the sensory block by two or more dermatomes in epidural analgesia and the cardiac sympathetic nerves originate from C1 down to T7 [26], it is possible that cardiac
sympathetic block can be induced by our epidural regimens. In addition, the level of sympathetic block can also be influenced by different concentrations of local anesthetics [26]. Therefore, the extents of sympathetic block of parturients in two groups may be different and their influence on the cardiac activity cannot be excluded.

**CONCLUSION**

In conclusion, our preliminary study showed that 15 ml 0.07% epidural ropivacaine plus 50μg fentanyl for labor analgesia produced less sympathetic block than 15 ml 0.25% epidural ropivacaine and the two regimens both can provide good quality of analgesia at the beginning of labor. However, more studies are necessary to test the sympathetic blocking effects of other commonly used epidural/combined spinal-epidural regimens during the entire course of labor. In addition, the association of sympathetic block with the incidences of adverse side effects, maternal hemodynamic stability, and maternal or fetal short/long-term outcomes is required to be further investigated.

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中文摘要

目的:硬膜外低濃度局部麻醉劑結合鴉片類藥物廣泛被使用於自然生產的止痛上。然而硬膜外低濃度局部麻醉劑是否可以降低交感神經阻斷，目前仍不清楚。方法:本研究選取 40 位自然生產的初產婦，將這些病人隨機平分為 A、B 兩組。A 組的產婦給予 15 ml 含有 50µg 吡喃尼的 0.07% 羅派卡因；B 組中的產婦則給予 15 ml 0.25% 羅派卡因。接著經由硬膜外導管每小時給予 12 ml 含有 2 µg/ml 吡喃尼的 0.07% 羅派卡因。在硬膜外給藥前以及給藥三十分鐘後，我們使用皮膚溫度探頭與雷射都卜勒血流計測量了兩組產婦手、腳的皮膚溫度與血流。結果: B 組產婦腳的皮膚溫度在硬膜外止痛三十分鐘後與 A 組產婦比較起來明顯上升 (A 組: +0.5 ± 1.3 °C；B 組: +3.5 ± 2.4 °C；p < 0.001)。B 組產婦腳的皮膚血流在止痛後也明顯增加 (A 組: +9 ± 62%；B 組: +195 ± 318%；p = 0.01)。相對的，B 組產婦的手的皮膚溫度與血流是下降的，而 A 組產婦的手的皮膚溫度與血流則略有上升 (p 值分別為 0.01 與 0.09)。結論: 我們的研究顯示 15 ml 硬膜外 0.07% 羅派卡因加上 50µg 吡喃尼使用於自然生產，可以減少交感神經阻斷，並在生產初期提供良好的止痛作用。