ROPIVACAINE 0.1% WITH OR WITHOUT FENTANYL FOR EPIDURAL POSTOPERATIVE ANALGESIA: A RANDOMIZED, DOUBLE-BLIND COMPARISON

Wai-Keung Lee, Kwong-Leung Yu, Chao-Shun Tang, Lim-Shen Lee, Hsiao-Ti Fang, and Chung-Fai Au

Department of Anesthesiology, Kaohsiung Medical University, Kaohsiung, and Department of Anesthesia, Tainan Municipal Hospital, Tainan, Taiwan.

Epidural analgesia is often considered optimal postoperative analgesia for certain surgical procedures. Ropivacaine is a new local anesthetic that is less toxic than its homologue, bupivacaine. Epidural infusions usually comprise a local anesthetic, an opioid, or a combination of the two to improve analgesic efficacy and reduce unwanted side effects. All 210 patients undergoing lower abdominal or lower extremity surgery received epidural analgesia infusions at 7 mL/hour, 105 with 0.1% ropivacaine and 105 with 0.1% ropivacaine plus 1 µg/mL fentanyl. Pain score and side effects (hypotension, nausea, vomiting, pruritus, paresthesia, urinary retention and motor block) were measured at 0, 0.5, 1, 3, 6, 12, and 24 hours. There was no statistical difference in patient profile between the groups. Pain relief scores were similar in the two groups in the first hour after the drugs were given. However, pain relief was significantly better in the ropivacaine/fentanyl group after the first hour and this difference lasted for the remaining time. There was no significant difference in adverse events between the two groups during 24 hours of assessment. In conclusion, the quality of analgesia was significantly improved by the addition of fentanyl 1 µg/mL to ropivacaine.

Key Words: epidural analgesia, ropivacaine, fentanyl


Ropivacaine is a new local anesthetic for epidural analgesia. Epidural ropivacaine appears to be superior to its homologue bupivacaine because of decreased motor block potency [10], making it less toxic. The optimal concentration of ropivacaine when used alone for epidural analgesia is 2 mg/mL [2,11,12], but this often gives inadequate analgesia or excessive motor block [13,14]. If a combination of both local anesthetic and opioid is used with the addition of fentanyl [15], the optimal concentration of fentanyl seems to lie in the range of 1–5 µg/mL [16]. This combination can improve analgesia and allow the use of a 0.1% solution of epidural ropivacaine with a decreased risk of motor block [17]. Although the combination of epidural opioid with local anesthetics is known to provide superior analgesia in the postoperative period, epidural ropivacaine has not been evaluated in combination with low-dose opioid for...
postoperative analgesia. Therefore, we designed this randomized, double-blind study to evaluate the effect of the addition of opioid to ropivacaine for postoperative analgesia.

**Materials and Methods**

The study protocol was approved by the education and research committee in our hospital, and written informed consent was obtained from each patient. A total of 210 healthy patients were to receive epidural anesthesia for lower abdominal surgery or lower extremity surgery. Patients were randomly allocated into two groups. Exclusion criteria were as follows: American Society of Anesthesiologists physical status more than III, age less than 18 or more than 85 years, weight less than 50 kg or more than 110 kg, allergy to local anesthetics or opioid, or inability to understand the use of PCEA. Patients who were not considered suitable candidates for epidural anesthesia were also excluded. The pharmacist packaged and labeled drugs so that the study medications were indistinguishable and could only be identified by breaking the code.

All patients received standard epidural anesthetic. An epidural catheter was placed 4 cm into the epidural space at the L₂–L₃, L₃–L₄, or L₄–L₅ interspace depending on the site of the proposed surgical incision. After insertion and negative aspiration of blood or cerebrospinal fluid, an epidural test dose (3 mL of 2% lidocaine with 1:200,000 epinephrine) was injected through the catheter. After 5 minutes, if no intravascular or intrathecal injection was evident, a dose of 2–10 mL of 2% lidocaine with epinephrine was given incrementally over 5 minutes. Administration was stopped when the bilateral sensory block of definite dermatome was reached.

Before the surgical procedure, patients were randomized in a double-blind manner to receive ropivacaine without (Group R, 0.1% ropivacaine) or with fentanyl (Group RF, 0.1% ropivacaine plus 1 µg/mL fentanyl) for postoperative epidural analgesia. Time zero for postoperative infusion was the time of patient arrival in the post-anesthesia care unit. The epidural infusion was delivered at a loading dose of 8 mL followed by a continual dose of 7 mL/hour, with a 3 mL bolus on successful demand at a 40 minute lockout period.

Pain and sensory and motor block assessments were recorded immediately before initiation of epidural analgesia (time zero) and then at 30 minutes and 1, 3, 6, 12, and 24 hours after administration of the study solution. Pain was assessed using a visual analog scale (VAS; 0 = no pain to 10 = worst pain imaginable), sensory level was assessed using pinprick, and motor block was assessed using a modified Bromage scale (0 = no motor block, 1 = unable to raise extended leg but able to move knee and foot, 2 = unable to raise extended leg or knee but able to move foot, 3 = complete motor block of lower limb).

Patients with inadequate analgesia (VAS = 5) received a 4 mL bolus of study solution and a 2 mL/hour increment in the rate of continual infusion and were reassessed 15 minutes later. Hypotension, defined as a decrease in systolic blood pressure of more than 20% from baseline, was initially treated with intravenous (IV) fluids and IV boluses of 8 mg ephedrine as required. At each assessment time, patients were assessed for the presence of nausea, vomiting, pruritus, urinary retention, and paresthesia.

**Results**

Demographic characteristics were similar in the two groups (Table 1). There was no statistical difference in pain relief score in the two groups within the first hour of epidural analgesia. However, pain relief was much improved from 1 hour (Figure 1). With regard to the VAS, pain relief in Group R seemed to peak at about 3 during 24 hours, while it appeared to peak at around 4.5 in Group RF. Bolus demand was most frequent in Group R (74%, 78 patients; Figure 2). This showed that the 0.1% ropivacaine used in Group R was inadequate. There was no significant difference in the incidence of side effects between the two groups ($p > 0.05$; Table 2).

**Discussion**

A number of studies report superior pain control with epidural infusions of local anesthetics with or without opioids, compared to systemic opioids, after lower abdominal surgery [18–22]. The use of PCEA has become more popular and is safe and effective in hospital wards [4]. Some studies have found several benefits of PCEA over conventional epidural continuous infusion or bolus techniques, including better analgesia and superior patient satisfaction [4].

Ropivacaine is a relatively new local anesthetic that may have decreased potency for motor block in epidural use when compared on a mg/mg basis to bupivacaine [10,23]. Use of a 0.2% ropivacaine solution, with or without fentanyl,
provided effective pain relief in most major abdominal surgery with a very low degree of motor blockade [24]. Some previous studies on dose and concentration have determined that concentrations of ropivacaine of 0.05–0.1% are optimal for epidural analgesia when combined with fentanyl [17,25]. Low concentrations of local anesthetic are used for epidural analgesia in lower abdominal and lower extremity surgery to minimize motor block and lessen side effects.

Both basic research [26–30] and clinical studies evaluating postoperative pain [31] have demonstrated synergistic effects between local anesthetics and opioids. In spite of the widely held impression that the combination of epidural local anesthetics and opioids provides superior analgesia with less untoward effects than epidural local anesthetics alone, the mechanism of action of epidurally administered opioids remains unclear. Spinal opioids exert their analgesic effects by reducing neurotransmitter release at the presynaptic level and by hyperpolarizing the membrane of dorsal horn neurons at the postsynaptic level [32]. Epidural opioids have the advantage of producing analgesia without motor or sympathetic blockade. The mechanism of postoperative fentanyl analgesia after epidural administration is primarily systemic. However, there are also studies to suggest that a spinal effect may occur after epidural administration of fentanyl [33–36].

Therefore, in clinical practice, the objectives of co-administration of epidural opioids with subanesthetic concentrations of local anesthetics are important for three reasons: a reduction in the dose of both drugs (Figure 2) [17, 37], maintenance or enhancement of the degree of pain relief, and a reduction in the incidence of adverse effects produced by both opioids and/or local anesthetics [37].

Side effects limit the effectiveness of many analgesic therapies, and motor block is a major concern with local

Table 1. Demographic data

<table>
<thead>
<tr>
<th>Group</th>
<th>Group RF</th>
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<tbody>
<tr>
<td>Age (yr)</td>
<td>33 ± 2.83</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>57/48</td>
</tr>
<tr>
<td>ASA (I/II/III)</td>
<td>51/34/20</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>162 ± 5.66</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>67 ± 3.83</td>
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</table>

<table>
<thead>
<tr>
<th>Group R</th>
<th>Group RF</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>n (%)</td>
</tr>
</tbody>
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Values are expressed as mean ± standard deviation or number. Group R = 0.1% ropivacaine; Group RF = 0.1% ropivacaine + 1 µg/mL fentanyl; M = male; F = female; ASA = American Society of Anesthesiologists physical status grade.

Table 2. Side effects with ropivacaine (Group R) and ropivacaine/fentanyl (Group RF)

<table>
<thead>
<tr>
<th>Side effect</th>
<th>Group R</th>
<th>Group RF</th>
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<tbody>
<tr>
<td>Hypotension</td>
<td>0 (0)</td>
<td>2 (1.9)</td>
</tr>
<tr>
<td>Nausea</td>
<td>0 (0)</td>
<td>3 (2.9)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1 (1.0)</td>
<td>3 (2.9)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>0 (0)</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>2 (1.9)</td>
<td>3 (2.9)</td>
</tr>
<tr>
<td>Urinary retention</td>
<td>0 (0)</td>
<td>1 (1.0)</td>
</tr>
</tbody>
</table>

Figure 1. Visual analog scale (VAS) score for pain relief with epidural blockade with 0.1% ropivacaine (Group R) and 0.1% ropivacaine + 1 µg/mL fentanyl (Group RF). *p < 0.05.

Figure 2. Percentage additional dose (bolus demand) required by patients receiving 0.1% ropivacaine (Group R) and 0.1% ropivacaine + 1 µg/mL fentanyl (Group RF).
anesthetics. The incidence of motor block was very low in both groups, as might be expected from using a small dose of ropivacaine at a lumbar spinal level. The combination of ropivacaine and fentanyl provided more profound sympathetic blockade due to the synergistic spinal effects mentioned above, which more readily manifested hypotension in hypovolemic patients. Opioid-related side effects were predictably more common in Group RF patients, with pruritus and nausea being most frequently reported.

In conclusion, an epidural infusion of ropivacaine 0.1% with or without fentanyl provided effective pain relief in most patients, with a low degree of motor block. The quality of analgesia was, however, significantly improved by the addition of fentanyl 1 µg/mL. Side effects of hypotension, nausea, and pruritus were found with fentanyl, but were not statistically significant.

**References**


26. Tejwani GA, Rattan AK, McDonald JS. Role of spinal opioid


