A Comparison of Epidural Ropivacaine Infusion Alone and in Combination with 1, 2, and 4 μg/mL Fentanyl for Seventy-Two Hours of Postoperative Analgesia After Major Abdominal Surgery

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Our aim in this prospective, randomized, double-blinded study was to compare the analgesic effectiveness and side effects of epidural infusions with ropivacaine 2 mg/mL alone (Group R; n = 60) and in combination with fentanyl 1 μg/mL (R1F; n = 59), 2 μg/mL (R2F; n = 62), and 4 μg/mL (R4F; n = 63) for up to 72 h after major abdominal surgery. Effective epidural neural blockade was established before surgery; postoperatively, the infusion rate was titrated to a maximum of 14 mL/h for analgesia. No additional analgesics other than acetaminophen were permitted during the infusion. The median of individual visual analog scale score with coughing were <20 mm for all groups (0 = no pain, 100 = worst pain) and was significantly lower (P < 0.01) for Group R4F at rest and with coughing (compared with Group R). Infusions were discontinued due to inability to control pain in significantly fewer patients in Group R4F (16%) than the other groups (34% to 39%; P < 0.01). For all groups, >90% of patients had no detectable motor block after 24 h. Hypotension, nausea, and pruritus were more common with the larger dose of fentanyl. We conclude that, after major abdominal surgery, an epidural infusion of ropivacaine 2 mg/mL with fentanyl 4 μg/mL provided significantly more effective pain relief over a 3-day period than ropivacaine alone or ropivacaine with lower concentrations of fentanyl. Implications: Postoperative epidural analgesic infusions are widely used, but there is little information regarding optimal strengths of opioid with local anesthetic. In this blinded, prospective study, we compared four different epidural infusion solutions for efficacy and side effects over a clinically useful postoperative period and conclude that an epidural infusion of ropivacaine 2 mg/mL with fentanyl 4 μg/mL was most effective.

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Epidual analgesia is often considered the most effective technique for providing pain relief after major abdominal surgery (1–3). Epidural infusions usually comprise a local anesthetic, an opioid, or, more commonly, a combination of the two, to minimize individual doses and to reduce unwanted side effects (4–6). Fentanyl is often used in such combinations, and the optimal concentration seems to lie in the range of 1–5 μg/mL (7). Ropivacaine, a less toxic homolog of bupivacaine, causes less motor block than bupivacaine when given by epidural infusion (8). This suggests that continuous postoperative epidural ropivacaine infusion may permit better patient mobility while providing a greater margin of safety compared with bupivacaine. The optimal concentration of ropivacaine may be 2 mg/mL.
ropivacaine when used alone for epidural analgesia is 2 mg/mL (2,9,10). Epidural ropivacaine has not been evaluated in combination with an opioid for postoperative analgesia, and few randomized studies have examined the effectiveness of epidural infusions for >24 h (11). This prospective, randomized, double-blinded trial was designed to investigate the effectiveness and safety of an epidural ropivacaine infusion (2 mg/mL), alone or admixed with fentanyl in concentrations of 1, 2, or 4 μg/mL, for pain management over 72 h after major abdominal surgery.

**Methods**

After appropriate institutional human research ethics committee approval and written, informed patient consent, 259 patients were enrolled into the study at 12 centers in Australia and New Zealand, with 244 of these receiving postoperative epidural infusions. Eligible patients were those scheduled for elective major abdominal surgery, aged 18–80 yr, ASA physical status I–III, weighing 50–110 kg who were suitable for 72 h of postoperative epidural infusion. Exclusions included abdominothoracic surgery, transverse lower abdominal incisions, and extraperitoneal procedures.

This study was double-blinded, and patients were block randomized on admission to the hospital for their surgery to receive one of four postoperative epidural infusion solutions: ropivacaine 2 mg/mL (Group R), ropivacaine 2 mg/mL and fentanyl 1 μg/mL (Group R1F), ropivacaine 2 mg/mL and fentanyl 2 μg/mL (Group R2F), or ropivacaine 2 mg/mL and fentanyl 4 μg/mL (Group R4F).

Patients received a nonanalgesic premedication 1 h before arrival in the anesthetic room, where an IV infusion was established and a 19-gauge or 20-gauge epidural catheter was inserted 3 to 5 cm through a 16- or 18-gauge Tuohy needle into the thoracic epidural space. The spinal level of epidural insertion was appropriate to the dermatome covering the midpoint of the planned surgical incision. A 3-mL test dose of 1.5% lidocaine with epinephrine 5 μg/mL was injected through the catheter. If no intrathecal or intravascular injection was evident 5 min later, a dose of 5–15 mL of 7.5 mg/mL ropivacaine was given incrementally over 5 min. Sensory block (to cold) covering the area of the proposed incision was confirmed before surgery. An additional 5-mL dose of ropivacaine 7.5 mg/mL could be given if an adequate block was not demonstrated by 30 min. Relaxant general anesthesia was then induced using the anesthesiologist’s choice of drugs for induction and maintenance (excluding propofol), and IV opioid supplementation was restricted to fentanyl. Within 1 h of induction, the epidural infusion with the blinded solution was commenced at 8 mL/h.

Time zero for the postoperative infusion was the time of patient arrival in the postanesthesia care unit (PACU). The infusion was continued at 8 mL/h, but the rate could then be increased by 2 mL/h every 30 min (with a 4-mL bolus of the infusion solution) or decreased as required to treat wound pain or problems associated with excessive block. All patients received acetaminophen 1 g every 6 h either orally, via a nasogastric tube, or rectally. No other analgesics, including nonsteroidal antiinflammatory drugs (NSAIDs), were administered during the infusion of the study drug. If analgesia was inadequate with the infusion rate at 14 mL/h and the patient had received two additional 4-mL bolus doses at least 30 min apart, the case was considered an “efficacy failure,” and alternate analgesia was provided.

During the infusion period, assessments were made every 4 h for heart rate, blood pressure, temperature, pain at rest and on coughing, quality of analgesia, sensory block (to cold), and motor block. Every 2 h, respiratory rate and sedation (sedation score: 5 = Sleep during night, 1 = awake and fully alert, 2 = awake but drowsy, 3 = sleeping but easily aroused, 4 = sleeping but difficult to arouse, 5 = unresponsive to verbal or tactile stimulation) were assessed. Between 10:00 pm and 8:00 am, the 4-h assessments were reduced to at least one measurement of heart rate, blood pressure, and temperature. Pain was measured using a visual analog scale (VAS) (0 = no pain, 100 mm = worst pain imaginable). Motor block was measured using the modified Bromage scale (12) (0 = no motor block, 1 = inability to raise extended leg, 2 = inability to flex knee, 3 = inability to flex ankle). Twice daily mobilization (walking bed to chair) was encouraged, and the VAS score was recorded or, if the patient was unable, the reason for inability to do so. All other aspects of care were left to the patients’ own clinicians.

The duration of surgery and length of stay in the PACU were recorded, as were need for admission to the intensive care unit (ICU) and time from start of surgery until hospital discharge. Specific daily patient questioning included quality of analgesia (1 = poor, 2 = fair, 3 = good, 4 = excellent), the presence of pruritus or nausea, and the time to passage of first flatus as an index of recovery of bowel function. All adverse events were also recorded.

Blood was collected before surgery and after the infusion was complete for analysis of urea, electrolytes, liver function tests, hemoglobin and white cell count.

Study data were entered into a central database which was checked, validated, and locked before the code was broken. Data presented for analysis are for those patients who continued study therapy (epidural infusion) in the PACU after surgery. It was estimated that four groups of 50 patients would enable a difference in infusion rates of 20% to be detected with a power of 0.8 and a type 1 error of 0.05. Analysis was
performed using SAS Ver 6.12 (SAS Institute, Cary, NC) and StatView 4.5 (Abacus Concepts, Palo Alto, CA). For continuous, normally distributed data, comparisons were made between the groups using analysis of variance or pairwise t-tests. Nonparametric tests used were Kruskal-Wallis, Wilcoxon, or Fisher’s exact tests as appropriate. Contingency table analysis ($\chi^2$) and survival curves were also constructed. When pairwise comparisons were performed, Bonferroni’s correction (for the six intergroup comparisons) was used (i.e., significant $P \leq 0.008$). For repeated assessments of pain, the area under the curve divided by the total infusion time was determined (AUCM) for each individual. Values are expressed as mean ± SE or median (interquartile range).

## Results

Of the 259 patients enrolled, 15 were not eligible for analysis because they did not receive an epidural infusion of the study solution beyond the intraoperative period (operation changed, epidural unable to be placed, patient withdrawal). The analysis was performed on the remaining 244 patients, whose demographics are shown in Table 1 which shows no significant differences between groups. The types of surgical procedures were evenly spread across the groups, with the most common being colorectal surgery (41%); laparotomy for small bowel, stomach, biliary, or splenic surgery (22%); and major gynecologic and urological procedures (19%).

The mean of each patient’s mean infusion rate was not significantly different among groups (Table 2), although fewer patients in the groups that received more fentanyl (R2F and R4F) reached the protocol-set maximal infusion rate (14 mL/h). The number of “top-ups” (bolus doses with rate increases) was not significantly different. The mean duration of epidural infusion was significantly longer in Group R4F compared with Group R. Discontinuation of infusion before 72 h was due to technical reasons (protocol violation, catheter displacement, pump failure) in 22 (9%) patients. Efficacy failure (see Methods) accounted for the remainder of premature discontinuations (31.6% of patients). Significantly fewer patients in Group R4F had efficacy failure than that in any of the other groups (Group R 38%, R1F 39%, R2F 34%, R4F 16%; $P < 0.01$ $\chi^2$) (Table 2). The survival graph for patients (excluding technical discontinuations) is shown in Figure 1. The survival (i.e., nondiscontinuation due to efficacy failure) was significantly greater for Group R4F ($P = 0.017$ Mantel-Cox test).

The VAS pain scores at rest, as expressed by AUCM, were low overall (all groups’ median AUCM <10 mm) and significantly lower for Group R4F than for Group R or R1F (AUCM median: R 8.8, R1F 6.4 [$P < 0.008$ versus R4F] R2F 7.2, R4F 4.0). With coughing, group median VAS scores were all <20 mm and were significantly lower for Group R4F than for Group R (AUCM median: R 18.3 [$P < 0.008$ versus R4F] R1F 18.5, R2F 16.7, R4F 11.5. The spread of values is plotted in Figure 2. The quality of analgesia was rated as “good” or “excellent” by >80% of all patients on Day 1, >90% on Day 2, and >88% on Day 3.

The median level of catheter insertion was T9-10 for all groups. The modal values are listed in Table 1. The dermatome spread of sensory block was similar in all groups for patients who continued to receive an infusion. The median upper level was T5-6, and the lower level was L1-3 by 72 h.

The degree of motor block, as assessed by the Bromage scale, was very low overall and was not significantly different among the groups. No motor block was detectable in >80% of patients within 8 h of infusion and in >90% by 24 h.

Ambulation was achieved by 56% of patients on Day 1, 88% on Day 2, and 97% on Day 3 with no significant differences among groups. However, patients whose infusions were discontinued were no longer assessed for their ability to ambulate; therefore, these data reflect only those patients with continuing infusions. Mean VAS scores on ambulation for each group were all <25 mm (median <13 mm). The most common specific reasons for inability to ambulate during the study were dizziness (18%), nausea (14%), tiredness or drowsiness (14%), pain (12%), motor block (10%), and postural hypotension (8%). These reasons were not significantly different among groups ($\chi^2$ tests).

The mean time until passage of flatus was shorter in the ropivacaine alone group (49 ± 6 h), but not significantly so (R1F 51 ± 5 h, R2F 62 ± 6 h, R4F 55 ± 5 h). The duration of hospital stay after surgery was independent of study group (Table 2), although the median values were lower in Group R.

Hypotension (low blood pressure requiring specific treatment) was most common during the first 24 h of the postoperative infusion and was most frequent in the R4F group (Group R 32%, R1F 31%, R2F 34%, R4F

### Table 1. Group Demographic Data

<table>
<thead>
<tr>
<th></th>
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<th>R1F</th>
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<th>R4F</th>
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<tbody>
<tr>
<td>$n$</td>
<td>60</td>
<td>59</td>
<td>62</td>
<td>63</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>59 ± 2</td>
<td>59 ± 2</td>
<td>57 ± 2</td>
<td>58 ± 2</td>
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<tr>
<td>Height (cm)</td>
<td>168 ± 1</td>
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<tr>
<td>Weight (kg)</td>
<td>74 ± 2</td>
<td>76 ± 2</td>
<td>72 ± 2</td>
<td>73 ± 2</td>
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<tr>
<td>Gender (M/F)</td>
<td>28:32</td>
<td>38:21</td>
<td>25:37</td>
<td>31:32</td>
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<td>Epidural level (mode)</td>
<td>T10–11</td>
<td>T10–11</td>
<td>T8–9</td>
<td>T9–10</td>
</tr>
<tr>
<td>Surgery duration (min)</td>
<td>132 ± 10</td>
<td>156 ± 10</td>
<td>144 ± 11</td>
<td>156 ± 11</td>
</tr>
</tbody>
</table>

Values are mean ± SEM. R = ropivacaine alone, R1F = ropivacaine plus fentanyl 1.0 μg/mL, R2F = ropivacaine plus fentanyl 2.0 μg/mL, R4F = ropivacaine plus fentanyl 4.0 μg/mL.
No episodes were rated as severe, and most were of short duration. After the first 24 h, the incidence of hypotension was 13% overall and was similar in all groups.

Nausea levels were not significantly different among groups, although there was a trend toward increasing frequency of nausea in Groups R2F and R4F by Day 3 (Table 3). Significantly more patients in Groups R2F and R4F received antiemetics on Day 3. Vomiting occurred in similar numbers of patients in all groups. The presence of a nasogastric tube (43% of patients overall) had no significant effect on the incidence of nausea.

Pruritus was significantly more common in the patients receiving the larger doses of epidural fentanyl on Days 1, 2, and 3 (Table 3). There was a trend toward an increasing incidence of pruritus with fentanyl dose. Symptoms peaked between 24 and 48 h, with promethazine being given more commonly in Groups R2F and R4F (Promethazine use for Day 1: Group R one patient, R1F two patients, R2F five patients, R4F five patients). Only one patient (in Group R4F) rated pruritus as severe.

The median or respiratory rate over time was similar among groups during the postoperative infusion. No patient had a recorded respiratory rate <8 during

Table 2. Infusion Variables

<table>
<thead>
<tr>
<th></th>
<th>R</th>
<th>R1F</th>
<th>R2F</th>
<th>R4F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean rate (mL/h)</td>
<td>11 ± 0.3</td>
<td>11 ± 0.2</td>
<td>10 ± 0.3</td>
<td>10 ± 0.3</td>
<td></td>
</tr>
<tr>
<td>Maximal rate</td>
<td>47 (78)</td>
<td>44 (75)</td>
<td>33 (53)**†</td>
<td>36 (57)**†</td>
<td>0.004</td>
</tr>
<tr>
<td>“Top-ups” per 24 h of infusion</td>
<td>4.0 ± 0.9</td>
<td>3.6 ± 0.9</td>
<td>3.0 ± 0.6</td>
<td>1.7 ± 0.2</td>
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</tr>
<tr>
<td>Infusion duration (h)</td>
<td>50.0 ± 3.2</td>
<td>52.9 ± 3.1</td>
<td>53.3 ± 3.0</td>
<td>63.3 ± 2.2*</td>
<td>0.008</td>
</tr>
</tbody>
</table>

Discontinuations

<table>
<thead>
<tr>
<th></th>
<th>R</th>
<th>R1F</th>
<th>R2F</th>
<th>R4F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technical</td>
<td>8 (13)</td>
<td>2 (3)</td>
<td>6 (10)</td>
<td>6 (10)</td>
<td></td>
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<tr>
<td>Efficacy failure</td>
<td>23 (38)</td>
<td>23 (39)</td>
<td>21 (34)</td>
<td>10 (16)**†‡</td>
<td>0.01</td>
</tr>
<tr>
<td>Duration of hospital stay (days)</td>
<td>8.0 (6.8–11.1)</td>
<td>8.4 (7.2–10.1)</td>
<td>10.0 (7.1–12.9)</td>
<td>9.9 (7.0–12.1)</td>
<td></td>
</tr>
</tbody>
</table>

Values are mean ± SEM, n (%), or median (interquartile range).

R = ropivacaine alone, R1F = ropivacaine plus fentanyl 1 µg/mL, R2F = ropivacaine plus fentanyl 2 µg/mL, R4F = ropivacaine plus fentanyl 4 µg/mL.

* P < 0.05 compared with R.

† P < 0.05 compared with R1F.

‡ P < 0.05 compared with R2F.

Figure 1. Kaplan-Meyer survival plot up to 72 h (not including data for patients excluded because of technical failures, protocol violations, or non-pain-related adverse events). Ropi = ropivacaine, fent = fentanyl.
postoperative infusion. Six cases of respiratory rates of 8 or 9 breaths/min were recorded (three in Group R1F, one in Group R2F, two in Group R4F). One patient in Group R4F developed respiratory failure and was reintubated within 1 h of extubation after a 7-h surgical procedure that had been associated with massive blood loss.

Sedation of moderate to severe degrees (levels 4 and 5) was uncommon (7%) and occurred in similar numbers in all groups during infusion (four cases in Group R, one in Group R1F, seven in Group R2F, and five in Group R4F). All of these patients were observed further or treated by infusion reduction, and none required naloxone. Most episodes occurred within 10 h of arrival in the PACU. One patient in Group R4F became confused and agitated after 62 h of infusion and had the infusion ceased (although blinding had not been broken).

A number of patients were admitted to an ICU postoperatively (Group R 0, R1F 2, R2F 5, and R4F 6) for surgical or medical reasons unrelated to the study infusion. A possible association with study therapy was present in one patient in Group R4F who developed respiratory failure in the PACU and was reintubated and ventilated (see above).

Excessive block occurred in two patients. A C2 sensory block developed in one patient after the initial dose of epidural ropivacaine (8 mL of 7.5 mg/mL solution at T9-10), which had regressed by arrival in PACU. The second case of excessive block was evident on arrival in the PACU after an initial dose of 5 mL of 7.5 mg/mL ropivacaine and 1.75 h of infusion with R4F at 8 mL/h during surgery. The high block resolved within 30 min of ceasing the infusion. Both patients continued 72 h of infusion without further incident.

In a population undergoing major abdominal surgery (such as this), complications of the surgery or preexisting medical conditions increase the chance of serious adverse events. These were similarly distributed among the groups (18% of patients in Group R, 21% R1F, 20% R2F, and 24% R4F). The three serious
Table 3. Pruritus and Nausea Incidence by Direct Questioning and Antiemetic Use

<table>
<thead>
<tr>
<th></th>
<th>R</th>
<th>R1F</th>
<th>R2F</th>
<th>R4F</th>
<th>P(χ²)</th>
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<td>Pruritus</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Day 1</td>
<td>19</td>
<td>33</td>
<td>40</td>
<td>45</td>
<td>0.04*</td>
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<tr>
<td>Day 2</td>
<td>24</td>
<td>31</td>
<td>53</td>
<td>49</td>
<td>0.02*</td>
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<tr>
<td>Day 3</td>
<td>17</td>
<td>24</td>
<td>39</td>
<td>47</td>
<td>0.02*</td>
</tr>
<tr>
<td>Nausea</td>
<td></td>
<td></td>
<td></td>
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<td>Day 1</td>
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</tr>
<tr>
<td>Day 2</td>
<td>56</td>
<td>42</td>
<td>58</td>
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<td>Day 3</td>
<td>33</td>
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<td>Days 0 and 1</td>
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<td>47</td>
<td>63</td>
<td>60</td>
<td></td>
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<tr>
<td>Day 2</td>
<td>35</td>
<td>37</td>
<td>51</td>
<td>58</td>
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</tr>
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<td>Day 3</td>
<td>21</td>
<td>12</td>
<td>49</td>
<td>52</td>
<td>&lt;0.001</td>
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</table>

Values are expressed as percentages.
R = ropivacaine alone, R1F = ropivacaine plus fentanyl 1 µg/mL, R2F = ropivacaine plus 2 µg/mL fentanyl, R4F = ropivacaine plus 4 µg/mL fentanyl.
* P = 0.02 for R versus R2F and R4F (Fisher’s exact test).

adverse events assessed as possibly related to the study drug(s) are mentioned above. In all other cases, a causal relationship was considered unlikely, including the five patients who died within 3 wk of surgery. There were no clinically relevant differences among the groups with respect to biochemical or hematological variables.

Discussion

Epidural infusions of ropivacaine combined with fentanyl 4 µg/mL provided good analgesia for up to 72 h after major abdominal surgery in patients receiving acetaminophen. Epidural infusions of ropivacaine plain or combined with lower concentrations of fentanyl resulted in a higher rate of inability to maintain the infusion for 72 h due to efficacy failure, but they were still effective in most patients.

The quality of pain relief was measured in three ways. First, VAS scores (0–100 mm) were used with the patients at rest, during coughing, and after limited ambulation. The group median VAS scores, even with coughing, were <20 mm at all times but <12 mm for Group R4F, which suggests better pain relief in this group. Consistent with this, the VAS scores with ambulation were lowest in Group R4F, although the other fentanyl-containing infusions also resulted in (nonsignificantly) lower VAS scores than Group R.

A second measure of pain relief was patient-rated quality of pain management. There was little difference among groups, with quality ratings of “good” or “excellent” given by approximately 80% of patients on Day 1 and by >90% for all groups after Day 2.

The third measure of quality of pain relief was the ability of the epidural infusion to provide pain relief for the full 72 h. Allowing for technical or protocol-based failures (9% overall), there were significantly fewer patients in Group R4F (16%) compared with all the others (34%–39%) who had to have their infusion discontinued because of efficacy failure, i.e., inability to control pain. There are a number of possible explanations for this. The simplest is that systemic absorption of the epidural fentanyl provided analgesia to areas not covered by the spread within the epidural space. If this were the only explanation, then Groups R1F and R2F should also have experienced some benefit. Another explanation is that the presence of epidural opioid is synergistic with the local anesthetic (13), so that areas with small-dose local anesthetic will still exceed the analgesic threshold. This effect would also compensate for infusions that may have been “patchy” or unilateral. Although all catheters were placed at a spinal level considered to be the midpoint of the incision, considerable variability in catheter direction and local anesthetic spread has been documented (14,15). Group R4F also required fewer interventions in the form of top-ups than the other groups. If infusion rates >14 mL/h had been allowed or if bolus doses had been larger, then efficacy failures in the other groups could have been reduced. The use of analgesics other than acetaminophen (e.g., NSAIDs) may also have reduced the efficacy failure rate in all groups. Epidural infusions of bupivacaine with fentanyl have been reported to have an efficacy failure rate of 7.6% (7), which may be consistent with R4F rate of 16% if the limitations in bolus doses, infusion rates, and NSAID use are considered. The maximal allowed rate of 14 mL/h would have contributed to the fact that mean infusion rates did not differ substantially among groups.

One possible explanation for more effective analgesia in Group R4F compared with Groups R2F and R1F is that, because of the lipophilic nature of fentanyl a large proportion of a given dose is absorbed by the epidural vasculature and fat before reaching the spinal cord. It may be that direct spinal cord effects are only achieved by using doses of fentanyl similar to those received by the patients in Group R4F.

Side effects limit the effectiveness of many analgesic therapies, with motor block being a major concern with local anesthetics. The incidence of motor block was very low in all groups, as might be expected from using a small dose of ropivacaine at a thoracic spinal level. Motor block was responsible for only 10% of occasions on which a patient was unable to ambulate. Although hypotension might be attributable to the local anesthetic, the incidence was highest in patients in Group R4F in the first 24 h (R4F 52% compared with 31%–34%). One possible explanation for this effect is that the combination of ropivacaine and fentanyl provided a more profound sympathetic blockade by the synergistic spinal effects as mentioned above, which more readily manifested hypotension in hypovolemic...
patients. Alternatively, better analgesia may simply have removed the pressor effect of pain.

Opioid-related side effects were predictably more common in Group R2F and R4F patients, with pruritus and nausea being most frequently reported. Pruritus was generally mild and occurred in up to 50% of patients. It was dose-related to the fentanyl component (Table 2) but was not responsible for discontinuation of therapy in any patients. Nausea after abdominal surgery is common, and there was no difference among groups on Day 1, with an incidence of 60%–80%. By Day 3, however, more patients in Groups R2F and R4F experienced nausea, and significantly more required antiemetics, which may represent a dose-related opioid effect. Nausea was also responsible for 14% of the occasions on which patients were unable to ambulate. Our data suggest that, although procedure-related factors are major triggers for nausea, avoiding opioids may reduce the incidence of nausea (from approximately 50% to 30% in this surgical population). Delayed return of bowel function is often attributed to opioids, but the highly variable rate of recovery in our patients resulted in no difference being detected.

Respiratory rate did not differ among the groups, and no patient developed severe respiratory depression during their infusion. Nonetheless, all six patients who had respiratory rates <10 breaths/min received epidural fentanyl, which suggests an opioid-related effect. The incidence of moderate to severe sedation was similar in all groups, with one patient in R4F having the infusion ceased because of confusion. Likewise, although dizziness (in the absence of hypotension) was reported as the most common specific reason for failure to ambulate, this symptom was not obviously related to the presence of epidural fentanyl.

A major factor in the cost of patient care is the duration of hospital stay. The median duration of hospital stay after surgery was shorter in Groups R and R1F, although not significantly so. The explanation for a possible difference is unclear. Although opioid side effects were more frequent in the large-dose fentanyl groups, these were not of such severity as to delay discharge a day or more, and the improved quality of analgesia in these groups would not be expected to be detrimental to recovery.

A limitation of this study is the lack of a group receiving epidural fentanyl alone. Some previous studies have demonstrated a significant improvement in the quality of postoperative epidural analgesia by the addition of bupivacaine to fentanyl 10 μg/mL (4,5,16), whereas others have reported no such benefit (17,18). A deficiency in a number of the earlier studies that found little or no benefit from the addition of a local anesthetic was the assessment of pain scores only at rest. Although opioids can provide reasonable pain relief at rest, they are often unable to provide adequate analgesia during mobilization (19). In our study, pain was assessed at rest, with coughing, and with mobilization. The benefit of epidural co-administration of fentanyl and ropivacaine is further supported by the evidence in animal models for synergistic antinociceptive effects between local anesthetics and opioids at a spinal level (13,20).

Had fentanyl been the prime determinant of analgesia, a larger difference in pain scores or outright efficacy failures would be expected among Groups R, R1F, and R2F than was observed. The infusion rates should also have been substantially higher in the lower concentration fentanyl groups, whereas the actual differences in infusion rates were small. We were unable to demonstrate any local anesthetic-sparing effect of fentanyl; however, the protocol limitation of the maximal infusion rate to 14 mL/h may have prevented patients being titrated to receive equal doses of opioid.

In conclusion, after major abdominal surgery, an epidural infusion of ropivacaine 2 mg/mL 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 4 μg/mL to the ropivacaine, and significantly more patients continued to have effective analgesia to 72 h. Side effects of hypotension, nausea, and pruritus were more common when fentanyl was added.

References
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