Epidural Fentanyl Produces Labor Analgesia by a Spinal Mechanism

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Background: The purpose of this study was to determine if epidural fentanyl produces analgesia in laboring patients by a primary spinal or supraspinal action.

Methods: Fifty-four parturients were randomized to receive epidural 0.125% bupivacaine plus one of three treatments: epidural saline—intravenous saline, epidural fentanyl (20 μg/h)—intravenous saline, or epidural saline—intravenous fentanyl (20 μg/h). The study treatments were administered by continuous infusion, whereas epidural bupivacaine use was patient controlled.

Results: Epidural bupivacaine use was significantly reduced by epidural (11.5 ± 4.6 mL/h) but not by intravenous fentanyl (15.9 ± 4.5 mL/h) compared with saline control (16 ± 5.9 mL/h). Analgesia characteristics and side effects were similar among groups.

Conclusions: Low-dose epidural infusions of fentanyl produce labor analgesia by a primary spinal action. (Key words: Opioid; pain relief; patient-controlled epidural analgesia.)

LABOR analgesia is often provided by the epidural administration of local anesthetic and opioid solutions. An opioid is combined with a local anesthetic in an attempt to reduce local anesthetic requirements and side effects, including systemic toxicity, hypotension, and motor blockade. Less leg weakness is desirable because motor block potentially prolongs second-stage labor and may increase the incidence of instrument-assisted delivery

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Materials and Methods

After institutional review board approval and informed written consent were obtained, 54 parturients classified as American Society of Anesthesiologists phys-
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Table 1. Patient Demographics and Analgesia Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Saline Placebo</th>
<th>Fentanyl iv</th>
<th>Epidural Fentanyl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>16</td>
<td>14</td>
<td>17</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>26 ± 5</td>
<td>24 ± 5</td>
<td>25 ± 6</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>163 ± 7</td>
<td>163 ± 9</td>
<td>163 ± 6</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>79 ± 14</td>
<td>76 ± 9</td>
<td>80 ± 12</td>
</tr>
<tr>
<td>Nulliparous (%)</td>
<td>100</td>
<td>93</td>
<td>81</td>
</tr>
<tr>
<td>Duration (min)*</td>
<td>201 ± 114</td>
<td>210 ± 102</td>
<td>252 ± 108</td>
</tr>
<tr>
<td>Sensory levels†</td>
<td>T8 (T6, T9)</td>
<td>T8 (T8, T10)</td>
<td>T6 (T5, T9)</td>
</tr>
<tr>
<td>Initial VAS pain (cm)</td>
<td>7.8 ± 1.7</td>
<td>8.4 ± 2.2</td>
<td>7.8 ± 2.1</td>
</tr>
<tr>
<td>Postanalgesia VAS pain (cm)</td>
<td>0.8 ± 0.9</td>
<td>0.6 ± 0.9</td>
<td>0.7 ± 0.9</td>
</tr>
</tbody>
</table>

Data are mean ± SD unless otherwise indicated. No significant differences exist between groups.
* Duration from epidural placement until complete cervical dilatation.
† Mean (25th, 75th percentile) pinprick sensory levels throughout labor.

...erating within 1 h of epidural insertion were excluded from data analysis.

All statistical analyses were performed using Sigmapstat (version 2.0, SPSS Inc., Chicago, IL). Unless otherwise indicated, data are presented as means ± SD. Bupivacaine requirements were analyzed using one-way analysis of variance. Side effects were analyzed using chi-squared and Fisher's exact tests as appropriate. Visual analog scores were analyzed using one-way analysis of variance on the change from baseline. Adjustments for multiple comparisons were made when appropriate. Probability values <0.05 were considered significant. Group size was determined by power analysis (β = 0.8) to detect a 25% reduction in epidural bupivacaine use from either epidural or intravenous fentanyl compared with the saline-only treatment group.

Results

Fifty-four patients were randomized and 47 completed the study. Seven patients were excluded: Three delivered within 1 h of epidural catheter placement and four experienced inadequate analgesia after epidural catheter placement and lidocaine administration.

Demographic variables, parity, duration of epidural analgesia, sensory levels to pinprick, and visual analog scores for pain were similar among groups (table 1). Similarly, side effects including hypotension, pruritus, nausea, and motor block were similar among the groups (table 2). Overall epidural bupivacaine use was significantly reduced by epidural but not by intravenous fen-
Epidural fentanyl produces labor analgesia by a spinal mechanism

Table 2. Side Effects (%)

<table>
<thead>
<tr>
<th></th>
<th>Saline Placebo</th>
<th>Fentanyl iv</th>
<th>Epidural Fentanyl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension (&gt;20%)</td>
<td>19</td>
<td>36</td>
<td>29</td>
</tr>
<tr>
<td>Pruritus</td>
<td>13</td>
<td>14</td>
<td>12</td>
</tr>
<tr>
<td>Nausea</td>
<td>31</td>
<td>14</td>
<td>6</td>
</tr>
<tr>
<td>Motor block*</td>
<td>0</td>
<td>19</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>56</td>
<td>64</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>25</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

No significant differences exist between groups.

* Motor block: 0 = straight leg raise; 1 = lifts knees; 2 = moves feet; 3 = no leg movement.

Table 3. PCEA Bupivacaine 0.125% Use

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>Usage (ml/h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saline placebo</td>
<td>16</td>
<td>16.0 ± 5.9</td>
</tr>
<tr>
<td>Fentanyl* iv</td>
<td>14</td>
<td>15.9 ± 4.5</td>
</tr>
<tr>
<td>Epidural fentanyl*</td>
<td>17</td>
<td>11.5 ± 4.6†</td>
</tr>
</tbody>
</table>

Data are mean ± SD.

* Fentanyl 20 µg/h was administered by continuous infusion at 12 ml/h.
† Significant difference versus saline and iv groups (P < 0.05).

Epidural fentanyl significantly reduced the number of PCEA patient demands and PCEA doses delivered (P = 0.035). Patients administered epidural fentanyl made 8 ± 6 (mean ± SD) PCEA demands, and 5 ± 4 doses were delivered throughout labor compared with 14 ± 7 requested, 9 ± 4 delivered doses with intravenous fentanyl, and 13 ± 8 requested, 8 ± 5 delivered doses placebo. There were no differences in PCEA characteristics between the intravenous fentanyl and placebo groups.

Discussion

The principal finding of this study is that fentanyl infused epidurally significantly reduces epidural bupivacaine use during labor, whereas fentanyl infused intravenously does not. This reduction in bupivacaine use most likely represents the spinal effect of epidural fentanyl. If epidural fentanyl produces labor analgesia by systemic absorption and a supraspinal effect, similar reductions in bupivacaine use would be expected from fentanyl administered intravenously. In contrast, bupivacaine use was similar between intravenous fentanyl and the saline control.

Our findings are in contrast to those of studies comparing postoperative analgesia from intravenous and epidural infusions of fentanyl[13-21] and may represent differences in study populations and study design. These postoperative pain studies used infusions of plain epidural or intravenous fentanyl, whereas our patients received a combination of fentanyl and bupivacaine. Because opioids and local anesthetics interact synergistically, [22-23] lower doses of fentanyl are required to produce analgesia when combined with bupivacaine than when administered alone. Typically, patients require 50-150 µg/h fentanyl to relieve postoperative pain, whereas labor analgesia is enhanced by 15-25 µg/h fentanyl when combined with epidural bupivacaine. [3-8] The higher doses of fentanyl infused to treat postoperative pain may mask the spinal effects of epidural fentanyl. In addition, pain during the early stages of labor is distinct from pain during the later stages of labor and postoperative pain, because the former is transmitted primarily by visceral afferents and the later types of pain are transmitted primarily by somatic afferents. [24-26] Opioids, including fentanyl, are much more effective in the treatment of early labor pain. [27-29] In many studies, epidural fentanyl is administered through a lumbar epidural catheter, even though analge-
sia is sought in a thoracic dermatome. Evidence suggests that spinal analgesia from bolus fentanyl administered epidurally is segmental in nature. Analgesia restricted to the dermatomes of the lower extremity was observed in volunteers when bolus fentanyl was administered through lumbar epidural catheters. Furthermore, pharmacokinetic studies in patients with chronic pain given bolus lumbar epidural fentanyl demonstrate cerebrospinal fluid concentrations of fentanyl 10 times greater in the lumbar cerebrospinal fluid than in cervical cerebrospinal fluid. Although the extent of segmental analgesia from low-dose lumbar epidural fentanyl infusions is unknown, it is likely to include the T10–L1 segments, which lie near the site of lumbar epidural catheter placement at which afferents relaying labor pain enter the spinal cord.

Although other studies use patient-controlled analgesia, our study differed in that while patients controlled the epidural administration of bupivacaine, fentanyl infusions were constant. This study design allows for a better delineation of the analgesic properties of a fixed dose of fentanyl, especially when comparing one route of administration with another. Had fentanyl been combined with epidural bupivacaine, epidural fentanyl doses would have varied with PCEA use, whereas intravenous fentanyl doses would remain constant and unaffected by PCEA use, making comparisons between groups difficult. Furthermore, higher doses of epidural fentanyl potentially favor systemic reabsorption and supraspinal analgesia, as observed with the treatment of postoperative pain.

In this study, epidural fentanyl reduced epidural bupivacaine requirements by 28% compared with either intravenous fentanyl or a saline placebo. This finding corresponds closely to a recent report estimating a 31% reduction in epidural bupivacaine use with the coadministration of epidural 2 μg/ml fentanyl.

Several limitations of this study must be noted. Only one dose of epidural fentanyl was administered to labor patients receiving PCEA bupivacaine. Thus our results may not be applicable to varying doses of epidural fentanyl, fentanyl administered alone, or to different patient populations. In addition, fentanyl was administered for an average of 4 h in our study. It is possible that the spinal effects of fentanyl diminish over time and that, as more fentanyl is administered, supraspinal analgesia may predominate. And, finally, although epidural bupivacaine use was reduced with epidural fentanyl, no significant reductions in side effects, including motor block, were associated with the decreased bupivacaine use. This probably reflects study design because we had insufficient power to test for differences in side effects. The initial power analysis was designed only to test for predicted reductions in bupivacaine use. Nevertheless, patients given epidural fentanyl did appear to have less motor block than did patients in the other two groups (table 2), although the difference was not significant. A larger study would be required to test for differences in motor block and side effects from the administration of epidural fentanyl.

In conclusion, low-dose epidural fentanyl infusions reduce epidural bupivacaine use and enhance labor analgesia primarily by a spinal, rather than a supraspinal, effect.

References


7. Chestnut DH, Owen CL, Bates JSN, Otsman LG, Chiow WW, Geiger MW. Continuous infusion epidural analgesia during labor: A randomized, double-blind comparison of 0.0625% bupivacaine 0.0002% fentanyl versus 0.125% bupivacaine. Anesthesiology 1988; 68:754-9


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