Subarachnoid Meperidine (Pethidine) Causes Significant Nausea and Vomiting during Labor


Background: The combined spinal–epidural (CSE) technique using bupivacaine–fentanyl has become an established method of pain control during parturition. One limitation is the relatively short duration of effective analgesia produced by bupivacaine–fentanyl. In contrast, subarachnoid meperidine has been shown to provide a long duration of anesthesia in nonobstetric patients. Therefore, the authors tested the hypothesis that subarachnoid meperidine produces a significant increase in the duration of analgesia compared with bupivacaine–fentanyl.

Methods: Based on a power analysis of preliminary data, the authors intended to recruit 90 patients for the study, randomized to three groups: 2.5 mg bupivacaine–25 μg fentanyl, 15 mg meperidine, or 25 mg meperidine. However, after enrolling 34 patients, the study was discontinued because of a significant increase in nausea or vomiting in the study patients.

Results: Nausea or vomiting was substantially increased in both meperidine groups compared with the bupivacaine–fentanyl group: 16 with nausea or vomiting in the meperidine groups (n = 21), compared with 1 in the bupivacaine–fentanyl group (n = 11), P = 0.0011. The mean duration of analgesia provided by 25 mg meperidine was 126 ± 51 min, compared with 98 ± 29 min for bupivacaine–fentanyl and 90 ± 67 min for 15 mg meperidine. These data were not significant (P = 0.27).

Conclusions: Although intrathecal meperidine could potentially prolong subarachnoid analgesia during labor, its use was associated with a significant incidence of nausea or vomiting. These data do not support the use of subarachnoid meperidine in doses of 15 or 25 mg for labor analgesia. (Key words: Labor analgesia; spinal anesthesia.)

The combined spinal–epidural (CSE) technique is used in many institutions to provide labor analgesia. CSE anesthesia can offer advantages versus epidural analgesia alone, including rapid onset of analgesia and reduced motor block, resulting in greater ambulation.1,2 A major limitation of the CSE technique is that the duration of analgesia provided by the spinal dose is only approximately 60–90 min.3

Meperidine is a synthetic opioid of intermediate lipid with opioid and local anesthetic properties.4–5 It has been used extensively in spinal anesthesia for urologic and orthopedic procedures6–7 and is used intramuscularly for labor analgesia in doses up to 100 mg.8,9 Studies of its use in labor via the subarachnoid route have been limited to a dose of 10 mg or dosing by continuous infusion by microcatheter.10–12 These studies indicate the drug to be effective during labor; however, the dose used conferred no advantage in duration or quality of analgesia compared with bupivacaine–fentanyl.

Therefore, we evaluated the effects of meperidine (15 or 25 mg) used during early labor on duration of analgesia provided by a single subarachnoid dose. In addition, we compared meperidine with our standard CSE technique of bupivacaine–fentanyl.

Materials and Methods

The Institutional Review Board at Duke University Medical Center approved all portions of the study de-
MEPERIDINE CSE IN LABOR

sign. Initially, a pilot study was performed in which six patients received meperidine (three at 15 mg, three at 25 mg) as part of a CSE technique. Subsequent power analysis indicated that 30 patients in each group ([1] bupivacaine 2.5 mg + fentanyl 25 µg, [2] meperidine 15 mg, or [3] meperidine 25 mg) would be necessary to provide 80% power to detect a 50% prolongation of analgesia. Healthy (American Society of Anesthesiologists physical status I or II) nulliparous women with singleton vertex pregnancies, cervical dilation less than or equal to 6 cm, and in spontaneous labor were eligible for enrollment in the study. Exclusion criteria included the following: preterm labor, cervical dilation greater than 6 cm; hypertension; bleeding diathesis; asthma or anticipated difficult intubation. After obtaining written informed consent, patients were randomized to one of the three arms of the study. To ensure a double-blind protocol, coded syringes were prepared by the research pharmacy.

Baseline vital signs were recorded before administration of the CSE anesthetic (blood pressure, heart rate, and fetal heart rate), whereas fluid loading occurred before commencement of the CSE anesthetic. In addition, pain visual analog scores (VAS), grade of motor block (Bromage scale), nausea or vomiting, and itching were noted before CSE anesthetic administration. These measurements were continued at 3, 5, 6, 9, 12, 15, 18, 21, and 30 min after subarachnoid drug administration. Specifically, nausea and vomiting were noted by asking parturients about nausea at each of the time points. Nausea was not graded, but emetic episodes were counted. APGAR scores at 1 and 5 min were also recorded.

Duration of analgesia, our primary end point, was defined as time from administration of subarachnoid drug until request for additional pain relief by the parturient. Effective spinal administration of the drug was confirmed by a rapid and sustained reduction in visual analog pain scores. Subsequent labor analgesia was provided by activation of the epidural catheter at the request of the parturient.

Statistical Analysis

Statistical analysis was performed using SAS Institute software (Cary, NC). Significant differences in duration of drug effect were tested by use of Kruskal–Wallis analysis when comparing three drugs and by use of the two-sample Wilcoxon rank sum test when comparing two drugs. Categorical data were analyzed with use of a two-sided Fisher exact test. All statistical tests were two-tailed and, because three comparisons were made, the critical α was set at P = 0.017. To preserve power to test main end points, the majority of measurements was not tested for statistical difference between treatment groups. Data are presented as the mean ± SD for continuous data or median (range) for ordinal or categorical data.

Results

The study was discontinued after enrollment of 34 patients after concern among investigators, patients, and nurses about the high incidence of nausea or vomiting evidenced in participating parturients. As a result, the study was unblinded and data analyzed. Two subjects were withdrawn from the study after intravenous butorphanol was administered in the time between informed consent and CSE placement. As a result, 32 patients were enrolled for analysis. Patient characteristics were similar between groups.

Nausea or vomiting were significantly increased in both of the meperidine groups, compared with the bupivacaine–fentanyl group: 16 of 21 with nausea or vomiting in the meperidine group, compared with 1 of 11 in the bupivacaine–fentanyl group, P = 0.0011, table 1. Itch was present in all groups of patients: 8 of 11 with itch in the bupivacaine–fentanyl group, compared with 6 of 21 in the meperidine groups. Duration of analgesia was 126 ± 51 min in the 25-mg meperidine group, compared with 90 ± 67 min in the 15-mg meperidine group and 98 ± 29 min in the bupivacaine–fentanyl

Table 1. Summary of Principle Data

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Bup/Fent (n = 11)</th>
<th>Mep 15 (n = 10)</th>
<th>Mep 25 (n = 11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of analgesia (min)</td>
<td>98 ± 29</td>
<td>90 ± 67</td>
<td>126 ± 51</td>
</tr>
<tr>
<td>N/V</td>
<td>1/11</td>
<td>9/10*</td>
<td>8/11*</td>
</tr>
<tr>
<td>Itch</td>
<td>9/11</td>
<td>3/10</td>
<td>3/11</td>
</tr>
<tr>
<td>Time to delivery (min)</td>
<td>268 ± 164</td>
<td>320 ± 208</td>
<td>339 ± 227</td>
</tr>
<tr>
<td>Motor block at 30 min (Bromage scale)†</td>
<td>0 (0–1)</td>
<td>0 (0–1)</td>
<td>0 (0–1)</td>
</tr>
<tr>
<td>VAS pain score at 15 min</td>
<td>0.2 ± 0.2</td>
<td>1.8 ± 0.53</td>
<td>0.4 ± 1</td>
</tr>
<tr>
<td>Appgar score at 1 min†</td>
<td>8 (7–9)</td>
<td>8 (7–9)</td>
<td>8 (7–9)</td>
</tr>
<tr>
<td>Appgar score at 5 min†</td>
<td>9 (8–9)</td>
<td>9 (8–9)</td>
<td>9 (8–9)</td>
</tr>
</tbody>
</table>

Time expressed in minutes. Data expressed as mean ± SD for continuous data.

* P = 0.0011.
† Data expressed as median (range) for ordinary data.

Bup/Fent = bupivacaine/fentanyl; Mep = meperidine; N/V = nausea/vomiting; VAS = Visual Analog Scale.
group. This difference was not statistically significant ($P = 0.15$).

Systolic blood pressure (baseline range, 129 ± 13–133 ± 14 mmHg) decreased in all groups, with a nadir of 110 ± 14 mmHg in the 15-mg meperidine group, 118 ± 13 mmHg in the 25-mg meperidine group, and 121 ± 12 mmHg in the bupivacaine–fentanyl group. The decrease was not significant (fig. 1). In addition, three patients in each of the meperidine groups required intervention with use of ephedrine bolus because of a greater than 20% decrease in systolic blood pressure, whereas no patients in the bupivacaine–fentanyl group required such intervention. There was no difference between groups with respect to motor block or Apgar scores.

**Discussion**

The first large scale report of the use of meperidine in labor (intramuscular) was published in 1947. However, there is a paucity of studies that relate the use of subarachnoid meperidine in labor. Previous studies that investigated subarachnoid meperidine (10 mg bolus) have not shown any significant advantages in duration or

---

**Fig. 1.** (A) Graph of systolic blood pressure *versus* time in minutes after subarachnoid drug administration. Legend as below. Data are expressed as mean ± SD. (B) Graph of diastolic blood pressure *versus* time in minutes after subarachnoid drug administration. Data are expressed as mean ± SD.
quality of analgesia versus conventional subarachnoid drugs in labor.\textsuperscript{10,11} However, much larger doses have been safely administered in nonobstetric practice.\textsuperscript{6,7} In addition, the dose of meperidine used via subarachnoid route for elective cesarean section has been reported to be as high as 1 mg/kg.\textsuperscript{14,15}

The study was primarily designed to evaluate the effects of different doses of meperidine, primarily on duration of labor analgesia. In addition, we evaluated potential side effects: nausea or vomiting and hypotension. As a result of these side effects, our study was discontinued prematurely. Reports to the investigators from patients and staff indicated that the frequency of nausea or vomiting was occurring at much higher rates in those patients enrolled in the study than in those parturients on the ward. The study was suspended, and subsequent analysis indicated that greater than 75% of the patients in each of the meperidine groups reported nausea or vomiting, compared with 9% in the bupivacaine–fentanyl group. Therefore we discontinued the study prematurely because of ethical considerations.

Two previous studies evaluated the effect of subarachnoid meperidine (10 mg) during labor\textsuperscript{10,11} but, although they have reported higher incidence of nausea or vomiting in the meperidine groups compared with the bupivacaine–fentanyl group, they did not discuss this as clinically significant. In the nonobstetric population, nausea or vomiting after subarachnoid meperidine has been reported between 0 and 55%.\textsuperscript{6,7,14} In our study, the incidence of nausea or vomiting was extremely high and, in most cases, occurred as emetic episodes.

Duration of time to request of subsequent analgesia was not significantly different among groups, though this came as no surprise because of our pilot data, which indicated that a sample size of 90 was necessary for 80% power to detect a difference in duration of effective analgesia. However, the data suggest a trend toward prolongation of effective analgesia in the 25-mg meperidine group (table 1). Nevertheless, any benefit from prolongation of analgesia would have to be balanced against meperidine side-effect profile.

In conclusion, we demonstrated that subarachnoid meperidine, in doses of 15 or 25 mg, induces significant nausea or vomiting during labor. Therefore, we suggest that subarachnoid meperidine should not be administered for labor analgesia.

The authors thank Emily Heath and Mary Carnell for their tireless secretarial assistance.

References