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OBSTETRICS

Intrathecal morphine reduces breakthrough pain during labour epidural analgesia

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Background. When using the combined spinal-epidural (CSE) technique for labour analgesia, parturients often experience breakthrough pain after the spinal medication has receded. We tested the hypothesis that a small dose of intrathecal morphine would reduce breakthrough pain.

Methods. This was a randomized, double-blind, placebo-controlled trial. Subjects were randomized to receive either 100 μg of morphine (MS) or placebo (PLCB) with the spinal injection of bupivacaine and fentanyl. Assessments included need for supplementation during labour analgesia, use of pain medications for 24 h after delivery, and side-effects. The primary endpoint was the rate of breakthrough pain.

Results. Sixty subjects were enrolled, 55 subjects completed the trial. The MS group had a significantly lower rate of breakthrough pain than the PLCB group [0.6 (0.6) *vs* 1.1 (0.8) episodes per patient; $P<0.01$], and longer time to first episode of breakthrough pain (300 *vs* 180 min; $P=0.03$). The MS group used 75% less opioid medications during the subsequent 24 h, but had a 17% incidence of nausea.

Conclusions. The addition of small dose of morphine to the spinal component of the CSE technique improved the effectiveness of epidural labour analgesia and reduced the need for pain medications over 24 h, but resulted in a small increase in nausea.

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The combined spinal-epidural (CSE) technique has gained popularity as a method of providing labour analgesia due to the rapid onset of effective pain relief, preservation of motor function, and minimal side-effects. The intrathecal medications provide rapid onset of pain relief with a limited duration, whereas the slower epidural medications maintain prolonged analgesia. Some clinicians believe that the pain relief provided by epidural medications is not as consistent and effective as that provided by the spinal injection. This leads to an increase in requests for supplemental medications. To improve the effectiveness of pain control with the CSE technique, several investigators have sought to prolong the duration of analgesia provided by spinal medications. One such method is to initiate the epidural infusion immediately after spinal injection.[1 2] Alternatively, investigators have studied the use of intrathecal medications with a longer duration of action. Yeh and colleagues[3] found that morphine 150 μg added to a fentanyl-bupivacaine spinal injection prolonged the duration of labour analgesia; however, this increased duration was noted to be associated with significant side effects. Previously, we found that morphine 125 μg, when added to a spinal injection of bupivacaine 2 mg and fentanyl 12.5 μg, did not prolong the duration of the spinal component of analgesia, but appeared to improve the effectiveness of subsequent epidural analgesia.[4] Women who received intrathecal morphine had a 40% decrease in breakthrough pain. One criticism of that study was that we did not standardize the treatment of breakthrough pain after the initiation of epidural analgesia. In this present study, using a strict protocol for

breakthrough pain, we hypothesized that a small dose of intrathecal morphine would improve the quality of subsequent epidural analgesia.

Materials and methods

This placebo-controlled, double-blinded, randomized trial was approved by the hospital committee on clinical investigations. After written informed consent, 60 healthy parturients of mixed parity who requested neuraxial analgesia were randomized via a computer-generated list to receive a small dose of morphine or placebo during their CSE placement. The randomized assignments were maintained in opaque envelopes and opened by an independent investigator who prepared the medication; neither the patient nor assessor knew the randomization group. Inclusion criteria consisted of active labour with a term, singleton foetus in a vertex position. Women who had received analgesics within 4 h and those with chronic pain, pre-gestational diabetes, morbid obesity, or foetal abnormalities were excluded. A midline CSE was placed at the L3–4 or L4–5 interspace with the subject in the sitting position using the needle-through-needle technique. Spinal injection consisted of 12.5 μg (0.25 ml) of fentanyl with 2 mg (0.8 ml) of bupivacaine through a 24 g Sprotte needle. The morphine group (MS) received an additional 100 μg (0.2 ml) of morphine, whereas the placebo group (PLCB) received an equal volume of normal saline, for a final volume of 1.25 ml. After successful spinal injection, a three-holed epidural catheter was placed via a 17 g Tuohy needle. Immediately after successful placement, a test dose of lidocaine 1%, 3 ml with 1:200000 epinephrine was given through the epidural catheter. Promptly after confirming negative intrathecal and i.v. injection, the epidural catheter was infused with a standard epidural solution (bupivacaine 0.04%, fentanyl 1.7 μg ml^{-1}, and 1:600000 epinephrine) at a rate of 15 ml h^{-1}.

Patient assessments before spinal injection included vital signs, pain score, and cervical dilation. After spinal injection, vital signs, pain score, sensory block to cold and pinprick, motor blockade, and side-effects were evaluated at 5, 10, and 15 min. Successful spinal analgesia was defined as the relief of labour pain within the first 15 min. Failed spinal injection would constitute removal from further study. All pain scores were evaluated using a numeric pain score (NPS) of 0 to 10, with 0 being 'No pain' and 10 representing 'Worst possible pain'. Motor block was assessed using the modified Bromage scale described by Breen and colleagues.[5] Zero was defined as no movement, and five was defined as no weakness on hip flexion. Although parturient activity was not restricted after spinal injection, we did not test for success of deep knee bending. Evaluation of side-effects included direct questioning at each interval for pruritus, nausea, and sedation rated on a four-point scale: none, mild, moderate, or severe.

An episode of breakthrough pain during labour analgesia was defined as subjective discomfort due to pain or pressure increasing during a contraction, and which was successfully treated with supplemental medications. Patients were assessed during each episode of breakthrough pain for technical causes of the epidural failure, such as catheter dislodgement or migration. The treatment of each episode of breakthrough pain was by strict protocol as follows.

- The initial treatment of breakthrough pain consisted of epidural injection of bupivacaine 0.125%, 8 ml and fentanyl 100 μg (final solution was bupivacaine 10 mg and fentanyl 100 μg in 10 ml).
- Fifteen minutes after supplementation, the subject was assessed and, if needed, an additional 10 ml of bupivacaine 0.125% would be administered.
- A final reassessment was performed after an additional 15 min, and a final 10 ml of bupivacaine 0.125% would be given if the patient was still uncomfortable.
- Failure of adequate pain relief after completion of this sequence, or other evidence such as complete loss of anaesthetic level, would result in a replacement of the epidural catheter and elimination from further study.

Recurrent breakthrough pain was defined as three or more episodes of breakthrough pain and was treated by increasing the background infusion. The following protocol was used to determine the amount of background epidural infusion medication.

- On the third episode of breakthrough pain, the concentration of the background epidural infusion was increased to bupivacaine 0.08%, fentanyl 3.33 μg ml^{-1}, and 1:600000 epinephrine at 15 ml h^{-1}.
- On the sixth episode of breakthrough pain, the concentration of the background epidural infusion was increased to bupivacaine 0.125% and fentanyl 3.33 μg ml^{-1} at 15 cc h^{-1}.

24 h follow-up

Subjects underwent evaluation of pain and side-effects every 4 h for 24 h after delivery. Subjects who delivered by Caesarean were eliminated from analysis due to the large requirements for pain medications after Caesarean delivery. Pain medications were prescribed by a standard protocol: 800 mg Ibuprofen initially, followed by oxycodone (5 mg)-acetaminophen (325 mg), one to two tablets every 4 h, as needed. Moderate or severe side-effects were treated by standing orders of medications as follows.

For pruritis: naloxone 40–80 μg, every 5 min, as needed up to 3 boluses, and naloxone 200 μg h^{-1}, continuous infusion for persistent pruritis.

For nausea: dolasetron 12.5 mg, every 8 h, as needed, and metoclopromide 10 mg, every 6 h, as needed.