Maternal Respiratory Arrests, Severe Hypotension, and Fetal Distress after Administration of Intrathecal, Sufentanil, and Bupivacaine after Intravenous Fentanyl

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There have been several reports of respiratory depression occurring in association with combined spinal epidural (CSE) analgesic techniques.1–3 Intravenous fentanyl has been commonly administered in our institution to laboring women who either do not desire epidural analgesia or request analgesia before placement of an epidural catheter. The use of intrathecal sufentanil (ITS) plus low dose bupivacaine in CSE techniques for labor analgesia has become popular, although the use of CSE analgesia techniques may increase the risk of respiratory depression if administered after intravenous opioids have been previously given. We report one case of maternal respiratory arrest and one case of maternal respiratory arrest and severe hypotension, both accompanied by fetal distress, in two parturients who received ITS and bupivacaine after intravenous fentanyl.

Case Reports

Case 1

A 19-year-old primigravida (weight, 75 kg; height, 150 cm) at 40 weeks gestation was admitted in labor. She had no significant medical history and had routine prenatal care. On admission, her cervix was dilated to 8 cm with a vertex presentation. Fetal heart rate was 130–140 beats/min. Delivery without epidural analgesia was planned.

The patient received intravenous fentanyl, 100 μg, on admission and again at 0.75 and 2 h after admission. Three hours after admission, the cervical examination was unchanged; fetal heart rate was 140–150 beats/min with good beat-to-beat variability. Arrest of the active phase of labor was diagnosed, and a Pitocin infusion was started. Three and one half hours after admission, because of worsening pain, consultation with anesthesiologists was sought for labor analgesia. At that time, the patient was awake, cooperative, alert, with stable vital signs, and extremely uncomfortable. Aspiration prophylaxis was not given to the patient. After evaluation and informed consent, a CSE technique was performed at the L3–L4 interspace using an 18-gauge Tuohy epidural needle and a 20-gauge Gertic-Marx spinal needle. After confirming the presence of free-flowing cerebrospinal fluid in the spinal needle, 10 μg of sufentanil and 2.5 mg of bupivacaine in 2 cc of saline was injected intrathecally. A 20-gauge epidural catheter was then introduced 4 cm into the epidural space.

The patient was placed in the supine position with left uterine displacement and became pain-free within 3 min of intrathecal injection. The anesthesiologist left the nurse to observe the patient and stepped into the hallway to fill out paperwork and consult on the care of other patients. Five minutes after injection, the nurse noticed that the patient was becoming difficult to arouse. The anesthesiologist was immediately called back into the room. A pulse oximeter was placed and read 54%. The patient developed apnea, cyanosis, and loss of consciousness during the next 2 min. Maternal heart rate was 45 beats/min: blood pressure was 108/47 mmHg; fetal heart rate was 60 beats/min. The anesthesiologist began positive pressure ventilation with bag, mask, and 100% oxygen while cricoid pressure was applied. With assisted ventilation, maternal heart rate was 88 beats/min; blood pressure was 134/71 mmHg; SaO2 was 97%; fetal heart rate was 109 beats/min. Intravenous naloxone, 0.4 mg, was administered approximately 2 min after positive pressure ventilation was initiated. Approximately 2 min after naloxone administration, the patient regained consciousness and spontaneous ventilation. Maternal heart rate was 91 beats/min; respirations were 10–12/min: blood pressure was 136/71 mmHg; SaO2 was 98%; fetal heart rate was 130 beats/min. The patient remained pain-free. A naloxone infusion, 80 μg/h, was begun to prevent recurrence of respiratory depression. Two hours after intrathecal drug injection, the epidural catheter was removed, and a continuous infusion of bupivacaine, 0.0625% at 10 cc/h, was initiated without incident. The patient delivered 9 h after...
admission, via vacuum extraction, a healthy boy, with APGAR scores of 9 and 9, at 1 and 5 min, respectively.

Case 2

A 22-yr-old primigravida (weight, 60 kg; height, 155 cm) at 40 weeks gestation was admitted in labor. On examination, her cervix was dilated to 6 cm with a vertex presentation. Fetal heart rate was 130 beats/min with good variability. She received two doses (130 min apart) of intravenous fentanyl, 50 μg, with the last dose being 2 h before consultation anesthesia services. After evaluation and informed consent, a CSE technique was performed at L3–L4; 10 μg of sufentanil with 2.5 mg bupivacaine in 2 cc of saline was injected intrathecally. A 20-gauge epidural catheter was inserted 4 cm into the epidural space. During the placement of the CSE, the patient was sitting up, awake, cooperative, and alert. Her blood pressure was 110/60 mmHg; pulse was 80 beats/min; respirations were 20/min. Approximately 10 min after injection of intrathecal sufentanil and bupivacaine, the patient became unresponsive, apneic, bradycardic, and cyanotic over approximately 1 min. Maternal heart rate was 40 beats/min; fetal heart rate was 60 beats/min. The anesthesiologist immediately began positive pressure ventilation with bag, mask, and 100% oxygen. Preparations to intubate were being made when a maternal pulse was not palpable. Approximately 10 chest compressions were delivered to the patient, simultaneously with intravenous naloxone, 0.4 mg. The patient’s pulse then became palpable. The SaO2, reading quickly rose from 50% to 95%, and the patient rapidly regained consciousness and spontaneous ventilation. As a precaution, she was placed on a naloxone infusion to prevent further episodes of respiratory depression. Two hours after intrathecal drug injection, the epidural catheter was tested, and a continuous infusion of bupivacaine, 0.0625% at 10 cc/h was initiated without incident. She went on to spontaneously deliver approximately 4 h later, an infant boy, with APGAR scores of 9 and 9 at 1 and 5 min, respectively.

Discussion

We report two cases of severe maternal respiratory and circulatory complications, and fetal distress occurring after the administration of intrathecal sufentanil and bupivacaine. Notably, the injections of intrathecal opioids were preceded by intravenous injections of fentanyl. Because these incidents occurred shortly after the administration of intrathecal sufentanil and were readily reversed with intravenous naloxone, opioid-induced respiratory depression most likely caused these events. At least three possible mechanisms may have caused the respiratory depression and arrest that these patients experienced.

First, the administration of intrathecal sufentanil alone may have caused these incidents, although to date, there exists just one case report of respiratory depression after only ITS administration. The adverse effects were minor in that only low SaO2 readings (89%) were found, and the hypoxemia was easily reversed with supplemental oxygen. We are not aware of any cases of single injections of intrathecal sufentanil alone causing the severe respiratory and hemodynamic derangements that we report.

Second, an interaction may have occurred between intravenous opioids and intrathecal opioids to cause profound respiratory depression. Although the clinical effects produced by intravenous opioids may no longer be apparent, residual blood opioid levels and subclinical opioid effects may persist. Such residual effects may predispose patients to greater respiratory depression after ITS administration. Baker and Sarna have reported a case where a second intrathecal dose of sufentanil, 3 h, 40 min after the first, resulted in complete apnea, loss of consciousness, cyanosis, and fetal distress. Based on Hansdottir’s data, they suggested that the incident was a result of residual plasma sufentanil levels from the first intrathecal sufentanil dose interacting with the second intrathecal dose. Gustafsson’s retrospective review of more than 9000 patients who received extradural narcotics notes that 19 of the 22 cases of respiratory depression involved the use of additional narcotics. Although Gustafsson’s report dealt primarily with extradural narcotics, we suspect that intrathecal opioids may have similar interactions with intravenous opioids. Our case reports question the possibility that subtherapeutic plasma concentrations of fentanyl may interact with ITS in a similar fashion. Unfortunately, plasma blood concentrations of fentanyl were not measured in either of these patients. However, using a STANPUMP pharmacokinetic simulation (Scott’s, Hug’s, and Shafer’s parameters), it was possible to estimate that for case 1 and case 2, the plasma and effect site concentrations of fentanyl at the time of these incidents were 0.45–0.6 ng/ml and 0.15–0.2 ng/ml, respectively. In nonpregnant, human volunteers, plasma fentanyl concentrations of 1.5 ng/ml provide analgesia. The severity of our cases, coupled with the lack of reported clinical evidence that intrathecal sufentanil alone could have caused these incidents, lead us to believe that previous administration of intravenous fentanyl may have increased the respiratory depression associated with administration of intrathecal sufentanil and bupivacaine. In addition, these incidents prompted our Labor and Delivery Ward practitioners to change to nalbuphine for labor analgesia instead of fentanyl. To date, there have been no further incidents of respiratory depression in association with intrathecal sufentanil and

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bupivacaine alone or after systemic analgesia with intravenous nalbuphine.

Our cases also suggest the addition of small doses of bupivacaine to ITS as a third potential cause of respiratory depression. Only recently has combined intrathecal sufentanil and bupivacaine been reported to be superior to ITS alone in relieving labor pain. Greenhalgh has recently reported a case of respiratory arrest in a parturient after intrathecal injection of the same amounts of sufentanil and bupivacaine that we used. Intravenous opioids were not reported to be administered before the intrathecal injection. It is possible that even small doses of intrathecal bupivacaine may somehow interact with intrathecal sufentanil and result in more respiratory depression compared with intrathecal sufentanil alone.

Perhaps any additional analgesia, whatever the agent or method of administration, could predispose patients to similar episodes of respiratory depression when associated with intrathecal sufentanil and bupivacaine. Finally, we can only speculate as to the role that the physiologic and hormonal changes of pregnancy and labor may also have played in producing respiratory and hemodynamic depression.

In summary, two cases of respiratory arrest and severe hypotension in laboring patients who received intrathecal sufentanil and bupivacaine after intravenous fentanyl are reported. We would like to caution others that the risk of significant respiratory depression may be greater when intrathecal sufentanil is combined with small doses of bupivacaine or when it is preceded by intravenous fentanyl.

References