Clinical Reports

Respiratory arrest following intrathecal injection of sufentanil and bupivacaine in a parturient

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Purpose: To present a case of respiratory arrest following the use of intrathecal sufentanil and bupivacaine for combined spinal-epidural anaesthesia in a healthy labouring parturient.

Clinical Features: A 20-yr-old term parturient received 10 µg sufentanil and 2.5 mg bupivacaine intrathecally as part of a combined spinal-epidural technique for labour analgesia. She had received no previous analgesics. Twenty-three minutes after the intrathecal injection she became unresponsive and suffered a respiratory arrest. Resuscitation included manual bag/mask ventilation with oxygen and intravenous naloxone.

Conclusion: Respiratory arrest is a rare but potentially life-threatening complication associated with the use of intrathecal opioids for labour analgesia. Vigilance in post-procedure patient monitoring is imperative.

Objectif : Présenter un cas d'arrêt respiratoire suivant l'emploi de sufentanil et de bupivacaine intrathécaux pour l'anesthésie rachidienne-péridurale combinée pendant le travail d'une parturiente en bonne santé.

Aspects cliniques : On a utilisé 10 µg de sufentanil et 2,5 mg de bupivacaine intrathécaux pour l'analgésie rachidienne-péridurale combinée pendant le travail d'une parturiente de 20 ans. Elle n'avait reçu aucun analgésique avant. Vingt-trois minutes après l'injection intrathécale, il y a une perte de sensibilité et la patiente a subi un arrêt respiratoire. La réanimation a été manuelle par ventilation avec masque et ballon avec de l'oxygène et par injection intraveineuse de naloxone.

Conclusion : L'arrêt respiratoire est une complication rare mais potentiellement dangereuse associée à l'usage des opioïdes intrathécaux pour l'analgésie pendant le travail obstétrical. La vigilance est de rigueur pendant le monitoring du patient consécutif à l'analgésie.

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THE combined spinal epidural (CSE) technique has been gaining popularity as a means of relieving pain in labouring parturients. Reduced drug dosage, minimal motor and sympathetic blockade with highly selective sensory blockade, and rapid onset of analgesia make CSE an attractive alternative to epidural in the obstetric patient.¹ However, there have been cases of maternal respiratory depression and/or arrest with the use of intrathecal opioids in labour.²⁻⁷ In most of these, the patient had received previous parenteral opioids or a larger dose of sufentanil than did our patient. We report a case of respiratory arrest after initiation of a CSE in a labouring parturient who had not been exposed to opioids.

Case report

A healthy 20 yr old term G4 P 1 A2 patient was admitted to hospital in active labour. On vaginal examination her cervix was 4 cm dilated. She was 168 cm tall and weighed 88 kg. Her past medical history was non-contributory. Her current pregnancy was unremarkable except for early hyperemesis gravidarum. She had no drug allergies and was taking no regular medications. She denied taking any drugs before admission.

The patient requested analgesia within 30 min of arrival at hospital and agreed to CSE. A 16-gauge intravenous cannula was inserted and 500 ml Ringer's Lactate were given as a bolus. The patient was placed in the sitting position. Using aseptic technique, the patient's lumbar spine was prepared and draped, and the skin was infiltrated with lidocaine 2%. A 17 gauge 3½" Tuohy epidural needle was inserted at the L₃₋₄ interspace. The epidural space was entered easily on the first attempt using the loss of resistance to air technique. A 25 gauge 4 11/16" Whitacre disposable spinal needle was then inserted through the epidural needle and into the subarachnoid space. Clear cerebrospinal fluid (CSF) flowed freely from the spinal needle. Sufentanil 50 µg diluted in 10 ml preservative-free normal saline was prepared. Two millilitres of this solution (10 µg) were mixed with 2.5 mg bupivacaine 0.25% in a volume of 3 ml and were injected intrathecally. Clear CSF was gently aspirated at the beginning, midway, and at near completion of the injection verifying correct positioning of the needle. After removal of the spinal needle, an epidural catheter was easily threaded through the Tuohy needle and was taped in place approximately 5 cm into the epidural space. No blood or CSF was aspirated from the catheter.

Once the catheter had been taped in place, the patient was positioned on her back with left uterine displacement. After five minutes, she was pain-free and had only mild tingling and slight heaviness in her legs. The epidural catheter was then tested with 2.5 ml

lidocaine 2%. There were no signs or symptoms of intravascular or intrathecal injection. The patient's blood pressure was stable throughout.

Approximately 15 min after the intrathecal injection, the patient complained of mild pruritus and, five minutes later, stated she felt sleepy although she was alert and responsive. Twenty-three minutes after the intrathecal injection the patient became unresponsive and apneic. There had been continuous verbal contact with the patient by her caregivers until immediately before her respiratory arrest. Her blood pressure was 130 mmHg systolic with a heart rate of approximately 60 bpm. The fetal heart rate was 86 bpm. Within one minute the patient was given oxygen 100% and her lungs were ventilated manually. Naloxone 0.4 mg *iv* was given three minutes after the respiratory arrest with prompt return of consciousness and respiratory efforts by the patient. The fetal heart rate at that time was 132 bpm. We were first able to measure the patient's oxygen saturation five minutes into the resuscitation when it was 99% and it remained at that level.

The patient remained awake but quite drowsy which prompted additional doses of naloxone 0.4 mg *iv* at 7 and 13 min from initiation of resuscitation. A naloxone infusion of 500 µg·hr⁻¹ was started shortly after the third dose. On regaining consciousness, the patient denied having any pain, and was able to move all four limbs to command.

One hundred and five minutes after the intrathecal injection, the patient started to develop pain with her contractions. A total of 8 ml bupivacaine 0.25% given in 2 ml aliquots over 10 min was injected through the epidural catheter with good effect. An infusion of bupivacaine 0.125% with epinephrine, 1:600 000 was started at 8 ml·hr⁻¹. No opioids were given via the epidural catheter. The epidural infusion was discontinued after 115 min, and 60 min later vacuum delivery of a live male infant was performed. Apgar scores were 8 at one minute and 9 at five minutes. The naloxone infusion was discontinued shortly before delivery. The remaining hospital stay for the mother and her baby were uneventful.

The remaining eight ml of diluted sufentanil were sent to Janssen-Ortho medical laboratories for analysis. The concentration was reported to be 5.5 µg·ml⁻¹. Since undiluted sufentanil from that batch was found to have a concentration (undiluted) of 49.1 µg·ml⁻¹, we concluded that an overdose did not occur.

Discussion

The physicochemical properties of opioids determine their rate of absorption and also their movement within the CSF. The rostral spread of opioid within the subarachnoid space may result in respiratory depres-

sion if the opioids gain access to the respiratory centres on the ventral surface of the medulla. Hydrophilic opioids (e.g., morphine) travel freely and may move a great distance within the subarachnoid space before diffusing into the lipid tissue of the spinal cord. The more lipid-soluble agents (e.g., fentanyl, sufentanil) penetrate tissues rapidly, which both limits the amount of opioid that moves cephalad and hastens the clearance of drug from the CSF.^{8,9} Rapid tissue penetration, combined with enhanced potency may account for the rare cases of respiratory arrest. Despite this, only six other cases of respiratory depression/arrest with intrathecal sufentanil have been reported.²⁻⁶

We report the second case of respiratory arrest and fetal bradycardia in an opioid-free patient receiving 10 µg intrathecal sufentanil. We verified the intrathecal sufentanil dose by laboratory investigation. Therefore, we are certain that accidental overdose did not occur. It is unlikely that the volume of diluent was a factor in causing respiratory depression in this case because in volumes of up to 10 ml, oxygen saturation and respiratory rate, have remained normal.¹⁰ In addition, it is unlikely that the hypobaric mixture was responsible for the respiratory depression since saline is a standard diluent. When dextrose is used, making the solution hyperbaric, labour analgesia is unreliable.¹¹ The direction of the needle bevel at the time of injection does not influence the spread of sufentanil.¹¹ Other factors that may influence the spread of drug in the subarachnoid space such as site of injection, speed of injection and spinal column length have not been reported to influence the spread of sufentanil. We are unable to identify any factors present in this patient that may have predisposed her to respiratory arrest.

Greenhalgh² reported a similar case. A healthy, obese 19 yr old G2 P1 patient with no history of drug use and a negative urine drug screen received CSE with 10 µg sufentanil and 2.5 mg bupivacaine intrathecally. Nineteen minutes after injection, the patient was unrousable, apneic, and hypotensive with fetal bradycardia. The patient was resuscitated and regained consciousness after naloxone was administered. This patient required additional naloxone for increasing somnolence and remained drowsy for the duration of her labour. Greenhalgh did not analyse the sufentanil solution and, hence, did not verify the administered dose of sufentanil.

The remaining cases of respiratory depression/arrest occurred after larger sufentanil doses or in patients who had previously received parenteral opioids. Lu *et al.*³ reported two cases of respiratory arrest occurring shortly after administration of intrathecal 10 µg sufentanil with 2.5 mg bupivacaine. The first patient became apneic five minutes after CSE, and had received 100 µg

fentanyl *iv* 1.5, 2.75, and 3.5 hr before the procedure. The second patient became apneic 10 min after CSE, and had received two doses of 50 µg fentanyl *iv* with the last dose two hours before the procedure. Both of these cases were successfully treated with naloxone. Hays⁴ described respiratory depression in a labouring patient 20-30 min after 15 µg sufentanil intrathecally. This patient had not received previous analgesics, and was treated successfully with verbal stimulation and oxygen. Ferouz⁵ reported a respiratory arrest four minutes after injecting 10 µg sufentanil intrathecally into a labouring woman who had received one dose of 50 mg meperidine *iv* 150 min before the CSE. The trachea was intubated, her lungs ventilated and an emergency Caesarean delivery was performed for fetal bradycardia. The patient remained normotensive throughout the procedure. The mother and baby had an uneventful remaining hospital stay.

Intrathecal sufentanil has been used thousands of times, without incident, to provide analgesia to labouring parturients.^{12,13} Although infrequent, severe respiratory depression and/or respiratory arrest is a potential complication of the CSE technique using 10 µg sufentanil with bupivacaine 2.5 mg intrathecally and can occur without a history of previous opioid administration. The fact that our patient's arrest occurred 23 min after the intrathecal injection demonstrates the importance of continuous vigilance for at least 30 min after the procedure. One author (BL) has participated in the resuscitation of three patients who became apneic after intrathecal sufentanil. In all three cases, the patients were alert while caregivers spoke to them, but lost consciousness shortly after the verbal stimulation ceased. This may account for the variability in the timing of respiratory depression/arrest reported in the literature after intrathecal sufentanil injection.

The timing of CSE complications may be different from those associated with epidural injection, and can occur relatively late, after the attending anaesthetist has left the patient's room. These patients should be closely monitored, and personnel and equipment be available for resuscitation even if the patient has no identifiable risk factors for respiratory depression. In particular, naloxone must be close at hand if one is administering intrathecal sufentanil. Careful assessment of the potential benefits as well as the potential risks must be considered before performing a CSE procedure.

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