PROFOUND RESPIRATORY DEPRESSION AFTER EXTRADURAL FENTANYL

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SUMMARY
A case is described of profound respiratory depression occurring 100 min after the extradural administration of fentanyl 100 μg to a patient undergoing Caesarean section.

KEY WORDS

The administration of extradural fentanyl in addition to local anaesthetic is becoming popular during labour and operative delivery [1—5]. Fentanyl has a rapid, intense and relatively short duration of action [6,7] and is considered to improve the efficacy of extradural block. These features, together with its high lipid solubility, have made it the opioid of choice for obstetric extradural anaesthesia [2]. The lipophilicity of fentanyl allows rapid absorption into the spinal cord or extradural fat, so that little drug is available to cause respiratory depression by cephalad spread in the CSF [2, 8].

CASE REPORT
A 27-yr-old patient (para 1 + 0) presented for elective lower uterine segment Caesarean section (LUSCS). Her past medical history included an emergency LUSCS delivery 5 yr earlier, which was performed under extradural anaesthesia; on that occasion extradural analgesia had been established during labour and a total of 18 ml of 0.5% bupivacaine was administered over a 3-h period. She presented for LUSCS and received a further 17 ml of 0.5% bupivacaine incrementally. The block extended to T1 bilaterally. There were no adverse cardiovascular sequelae and delivery was uneventful, although i.v. diamorphine was required because of left flank discomfort during the procedure.

The current pregnancy had been uneventful, but the patient was scheduled for elective LUSCS because of the previous surgery and cephalo-pelvic disproportion. Preoperative examination was unremarkable, except for moderate obesity (weight 88.5 kg, height 1.55 m). She had given informed consent to take part in a controlled study on the effect of the addition of fentanyl on onset time of extradural analgesia with 0.5% bupivacaine. Routine prophylaxis against pulmonary acid aspiration syndrome, consisting of two doses of oral ranitidine 150 mg and sodium citrate 30 ml were administered. After the sodium citrate, she complained of nausea and vomited.

Whilst the extradural was being established the patient received Hartmann's solution 10 ml kg⁻¹. With the patient in the left lateral position, using loss of resistance to saline, the L2-3 extradural space was identified with a 16-gauge Tuohy needle. A lateral-eyed extradural catheter was inserted 4 cm in a cephalad direction and 0.5% bupivacaine 5 ml with fentanyl 25μg was injected as a test dose. The patient was returned to a left lateral tilt position. After 5 min, and with no evidence of intrathecal or intravascular administration, a further 0.5% bupivacaine 15 ml with fentanyl 75 μg was injected incrementally over 135 s.

The onset of sensory block (analgesia to 27-gauge short-bevelled needle) was recorded. Loss of sensation at T10 occurred after 5 min and at T6 after 10 min (left) and 15 min (right). Maximum block height was obtained at 30 min: C4 on the...
The block reached the sacral segments after 15 min. The patient could raise both legs at all times, although she admitted that both felt heavy. One episode of retching was followed by a decrease in systolic arterial pressure from 130 to 110 mm Hg and heart rate from 95 to 60 beat min⁻¹ so ephedrine 3 mg was administered i.v. prophylactically. Thereafter, arterial pressure and heart rate were unremarkable.

Surgery was commenced 35 min after completion of the injection. Before delivery, the mother received 60% oxygen by Ventimask. On delivery of a healthy child (Apgar score 9 at both 1 and 5 min), syntocinon 10 iu was administered i.v. The patient received two doses of metoclopramide 5 mg i.v. (45 and 55 min after extradural injection) for persistent nausea. With this exception, anaesthesia and surgery continued unremarkably, with the patient lying placidly, until 100 min after the initial injection of bupivacaine and fentanyl. At this point she complained again of nausea, and became unresponsive for a period of approximately 10 s. Heart rate was unchanged. Thereafter, she responded appropriately to mild physical and verbal stimulation, but her SaO₂ (measured with an Ohmeda Biox 3700 pulse oximeter) had decreased from 95% to 83% breathing air. On command, she took a deep breath and restored her saturation. She repeatedly became apnoeic, with decreases in saturation to between 85 and 90% and on each occasion she was instructed to take a breath. At this time the patient was awake, but drowsy. After 4 min, when it had become obvious that the apnoea was persistent, naloxone 0.4 mg i.v. and 0.4 mg i.m. were administered. Approximately 20 s later there was complete resolution of the apnoea with the patient alert, breathing spontaneously and maintaining SaO₂ greater than 95%. The extent of extradural block was checked, and found to have regressed to C6 (left) and T1 (right). Surgery was completed about 5 min later, and the patient transferred to the recovery room. Continuous monitoring of oxygen saturation for a period of 4 h did not detect any further episode of desaturation, and she was returned subsequently to the post-natal ward.

**DISCUSSION**

Since 1983, 0.75% bupivacaine has not been recommended for use in obstetric anaesthesia and many investigators have found that 0.5% bupivacaine provides less satisfactory extradural anaesthesia for Caesarean section [1, 4]. Investigators seeking to enhance the performance of the less concentrated solution, have found that the addition of opioids, particularly fentanyl, was beneficial and reported no respiratory depression [1, 4]. Other investigators, using non-obstetric patients, have reported mild depression, especially of the carbon dioxide response curve, with extradural but not i.m. fentanyl in the same dose [9]. Moreover, plasma concentrations of fentanyl were greater after administration by the i.m. route, despite the greater respiratory depression seen with the extradural route. Thus it seems that the main mechanism of respiratory depression after extradural fentanyl is cephalad spread in CSF. The respiratory depression demonstrated previously has been mild [9, 10], and it has been concluded that it is probably of little clinical significance [10].

The extradural anaesthetic described in this report was unremarkable, with the exception of a somewhat higher than normal sensory block (analgesia as opposed to anaesthesia). The pattern of onset and intensity of block were as expected with a mixture of bupivacaine and fentanyl [1]. Subdural administration would seem unlikely but, even if it had occurred, the implications of subsequent events would be unaltered. The late and sudden onset of apnoea (and transient unresponsiveness) was unexpected. Plasma concentrations of fentanyl following absorption from the extradural space tend to peak at 5–10 min when administered with plain bupivacaine [11]. Systemic absorption is therefore an unlikely explanation for the events described. The respiratory pattern was consistent with central opioid toxicity, and resolution with naloxone would appear to confirm the diagnosis.

Only one case of profound, life threatening, respiratory depression has been reported previously with extradural fentanyl [12]. In that case an obese (112 kg) ASA III man received fentanyl 100 μg through a catheter inserted at L1–2. In addition, he received other sedative agents (midazolam, nalbuphine and droperidol) systemically. At 70–100 min after injection, the patient became increasingly drowsy and unresponsive. The rate of ventilation decreased, and there was a tendency to airway obstruction. An infusion of naloxone was commenced with moderate response, and was discontinued after
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20 min. The respiratory pattern again deteriorated, although with verbal encouragement the patient would breathe. No further doses of naloxone were required, and he was eventually discharged from the recovery ward after 7 h.

Sensory block to C4 implies that the bupivacaine and fentanyl solution had spread as far as the cervical extradural space. Whilst fentanyl would have been taken up by fatty tissues, the small amount of drug remaining free within the CSF would not have far to diffuse to the fourth ventricle. Presumably, even a tiny amount of opioid in the vicinity of the respiratory centre has a profound effect.

The time (100 min) at which apnoea occurred is of particular concern. Surgery had started 35 min after the extradural injection as the study design required frequent assessments of sensory and motor block over 30 min. This patient was considered to be anaesthetized adequately for surgery after 15 min. It is conceivable, therefore that surgery could have been completed, and the patient returned to the ward before the onset of respiratory depression.

If fentanyl is administered extradurally, it is essential that the patient is observed continuously for an adequate period. This case report would suggest a minimum of 3 h after administration.

REFERENCES