Anesthesiology
67:991–992, 1987

Profound Central Nervous System Depression from Epidural Fentanyl for Extracorporeal Shock Wave Lithotripsy

DOUGLAS G. WELLS, F.F.A.R.A.C.S.,* GERALD DAVIES, F.F.A.R.C.S.I.†

Epidural narcotics are being increasingly used to relieve chronic, postoperative, and labor pain. We describe a case in which the epidural administration of fentanyl, 100 μg, resulted in profound CNS depression during extracorporeal shock wave lithotripsy.

CASE REPORT

An obese, 112-kg, 61-yr-old ASA III male was scheduled to undergo extracorporeal shock wave lithotripsy (ESWL) to fragment a urinary calculus. The patient was 175 cm tall. He was currently receiving propranolol 80 mg, bid, and hydrochlorothiazide 50 mg daily for hypertension and ischemic heart disease. For the past 12 months, he had been receiving glibazide, 5 mg daily, because of the onset of type II diabetes. An uneventful ESWL had been performed 3 months earlier under general anesthesia using thiopental 450 mg, fentanyl 125 μg iv, inhalation of 70% nitrous oxide, and isoflurane 0.4% with paralysis induced by iv atracurium. Preoperative hematologic and biochemical tests were normal. An ECG showed sinus rhythm at 70 bpm with nonspecific ST changes in V_4 and V_5. Arterial blood pressure (BP) was 165/95 mmHg. No premedication was given. The patient received no narcotics prior to ESWL.

On arrival in the ESWL center, a peripheral intravenous catheter was inserted and ECG and BP monitoring commenced. Midazolam, 2.0 mg, was given iv at this time. With the patient in the sitting position, an epidural catheter was inserted at the L1–2 interspace. The catheter was passed 5 cm in a cephalad direction. The patient was then placed in the supine position and, following a negative aspiration test for cerebrospinal fluid (CSF) and blood, 3 cc bupivicaine 0.5% with epinephrine 1:200,000 was injected. Three minutes later, fentanyl, 100 μg, mixed with 5 ml normal saline was administered *via* the catheter. After a further 15 min, a zone of hypoalgesia was present between T4 and L2, where hypoalgesia is defined by a change in the intensity of pin prick sensation to maximal and is quite distinct from an anesthetic level. No motor block was present, and the patient positioned himself in the gantry. The respiratory rate was 14 breaths/minute. Heart rate and BP were stable at 70 bpm and 150/85 mmHg, respectively. ESWL commenced and, over the following 20 min, 1000 shocks were delivered. While in the water bath, the patient received a further 2.5 mg of midazolam iv. Although sedated, he remained cooperative during the procedure and arrived in the recovery room 40 min following the administration of the epidural fentanyl. BP and heart rate were stable at the previous levels. Good motor function was present in the legs, and the patient was alert and jovial. His respiratory rate was 12 breaths/min. Nalbuphine 2.5 mg was given iv upon arrival in recovery to counter pruritis, which we have found occurs with variable intensity in around 50% of patients receiving this anesthetic technique.

Fifteen minutes later, the patient volunteered that he felt drowsy. After a further 15 min, he had sudden projectile vomiting. Although his heart rate and BP remained stable, he began to perspire profusely on the face and trunk. At that time, the patient was sitting upright in bed holding an emesis bowl. He was capable of bilateral straight leg raising on command, and hypoalgesia had extended to the face to the level between the maxillary and mandibular divisions of the trigeminal nerve. Droperidol, 1 mg, was given because of this vomiting. It was now 70 min since the administration of fentanyl.

Over the following 30 min, he became increasingly drowsy to the point where he was no longer responsive to verbal command. His respiratory rate fell to 6 breaths/min in the presence of pinpoint pupils. The patient was unable to maintain his own airway in the absence of jaw support. Naloxone 0.6 mg iv and 0.2 mg sc were administered, after which his pupils increased in size slightly, he became responsive to verbal stimuli, and he was able to maintain his own airway. His respiratory rate increased to 8 breaths/min. Nevertheless, he remained extremely drowsy, and an infusion of naloxone was commenced at 0.2 mg/hour iv. A blood glucose level at this time was 325 mg%. The patient breathed 3 l/min O_2 *via* an intra-nasal cannula and was monitored with a pulse oximeter which showed 96% saturation.

After 20 min, the naloxone infusion was discontinued in order to more precisely ascertain the cause of his problem. Over the next 30 min, his conscious state deteriorated and his airway again obstructed without jaw support. His arterial saturation decreased to 93% whenever his airway was allowed to obstruct. His respiratory rate remained at 8 breaths/min. It was now 150 min since the administration of fentanyl. The patient did, however, respond to verbal encouragement to awaken and breathe deeply.

Over the next 90 min, the patient's condition improved in the absence of further naloxone administration. He suffered no further nausea, vomiting, or diaphoresis. He was discharged from recovery 7 h after the administration of the epidural fentanyl. At this time, his respiratory rate was 12 breaths/min, and pulse oximetry consistently read 97% while breathing room air. There were no residual signs of spinal opioid activity, such as sedation, pruritis, hypoalgesia, or urinary retention.

DISCUSSION

Respiratory depression, usually involving morphine, is the most feared complication of epidural narcotics. Its relative hydrophilicity results in slower efflux from the spinal cord and CSF resulting in greater migration to the brain.[1] Most cases of respiratory depression with morphine occur 4–6 h following its administration.[2] Maximum respiratory depression occurs 6–10 h after

* Staff Anaesthetist, Royal Melbourne Hospital.
† Assistant Professor, University of Iowa College of Medicine.

Received from the Department of Anaesthesia, Royal Melbourne Hospital, Melbourne, Australia; and the Department of Anesthesia, University of Iowa College of Medicine, Iowa City, Iowa. Accepted for publication June 22, 1987.

Address reprint requests to Dr. Davies: Department of Anesthesia, University of Iowa College of Medicine, Iowa City, Iowa 52242.

Key words: Anesthetics: fentanyl; narcotic. Anesthetic techniques: epidural; regional. Complications: central nervous system depression.

10 mg epidural morphine in volunteers with significant depression still present at 16 h.[3] In a series of over 1000 patients given epidural morphine, Stenseth *et al.*[4] found the incidence of respiratory depression to be 0.9%. The incidence of nausea and vomiting was 34%.

The extreme degree of CNS depression described here has not previously been reported with the use of epidural fentanyl in the dose of 100 μg. Drowsiness in the absence of respiratory depression has been reported with 100-μg and 200-μg doses, and is suggestive of a central narcotic effect.[5–7] Lam *et al.*[8] were unable to demonstrate any change in resting ventilation, end-tidal P_{CO_2}, and the ventilatory response to added CO_2 after epidural fentanyl 100 μg. Only with doses as high as 5 μg/kg has respiratory depression, as measured by changes in respiratory rate and P_{CO_2}, been demonstrated.[9]

The possibility of subdural or subarachnoid administration of fentanyl must be seriously considered. We would have expected a greater intensity of sympathetic, sensory, and motor blockade arising from the 0.5% bupivicaine had the catheter been in either of these positions. This patient experienced hypoalgesia to the T4 dermatome. This was detectable as a loss of sensory discrimination between pain and light touch. The quality and spread of the sensory blockade was similar to that observed in over 70 patients receiving the same epidural regimen. There were no detectable cardiovascular changes, and retention of motor function enabled the patient to position himself both on and off the gantry. It is highly unlikely, therefore, that the bupivicaine was subarachnoid or even subdural. Since the fentanyl was injected 3 min later through the same catheter with no change in patient position, we believe that this was also given epidurally.

Although a total of 5 mg of midazolam was given before commencement of ESWL, the patient was alert and jovial on arrival in the recovery room. At this time, nalbuphine 2.5 mg iv was given prophylactically. Nalbuphine acts as an opiate agonist/antagonist, and has been shown to reverse respiratory depression and sedation caused by fentanyl.[10] Its use in the treatment of pruritis and nausea following epidural hydromorphone has previously been described.[11] Droperidol 1 mg was given after projectile vomiting. In retrospect, this, along with the extension of hypoalgesia to the face, was a sign of the presence of narcotic in the CSF of the fourth ventricle. Vomiting would have been more appropriately treated at that time with naloxone. The combination of midazolam, nalbuphine, and droperidol was unlikely to produce the range and intensity of symptoms in a man of this size, but would certainly potentiate the effects of rostral migration of fentanyl.

Hypoalgesia extending to trigeminal nerve distribution is an unusual finding after epidural fentanyl, whereas it is almost invariable after epidural morphine.[3] Detection of ascending hypoalgesia, which tracks the rostral spread of opiate, is an important clinical sign, and could alert the clinician to the potential of respiratory depression. The careful mapping of the upper level of hypoalgesia after epidural narcotics has certainly become a routine in our practice. The extent of spread of fentanyl in the spinal cord, as gauged by hypoalgesic levels, may be affected by many variables, including dose and volume of dilution. Although speculative, it is possible that rostral migration of fentanyl could be augmented by obesity or ESWL shock waves.

The early onset of CNS depression, coupled with its relatively short duration, suggests caution is required for the first 1–2 h immediately after the injection of epidural fentanyl. A more delayed respiratory depression has never been described with this drug.

In summary, we have described a progression of CNS symptoms occurring after ESWL believed due to the administration of epidural fentanyl. A relatively large dose of naloxone resulted in an improvement in mental state and respiratory rate. Discontinuation of a naloxone infusion resulted in further deterioration in mental state.

References

1. Max M, Inturrisi CE, Grabrinski P, Kaiko RF, Foley KM: Epidural opiates; Plasma and cerebrospinal fluid (CSF) pharmacokinetics of morphine, methadone and beta-endorphin. Pain 1(suppl):S122, 1981
2. Morgan M: Epidural and intrathecal opioids. Anaesth Intensive Care 15:60–67, 1987
3. Camporesi EM, Nielsen CH, Bromage PR, Durrant PAC: Ventilatory CO_2 sensitivity after intravenous and epidural morphine in volunteers. Anesth Analg 62:633–640, 1983
4. Stenseth R, Sellevold O, Breivik H: Epidural morphine for postoperative pain: Experience with 1085 patients. Acta Anaesthesiol Scand 29:148–156, 1985
5. Rutter DV, Skewes DG, Morgan M: Extradural opioids for postoperative analgesia. A double-blind comparison of pethidine, fentanyl and morphine. Br J Anaesth 53:915–920, 1981
6. Naulty JS, Johnson M, Burger GA, Datta S, Weiss JB, Mornvon J: Epidural fentanyl for post cesarian delivery pain management. ANESTHESIOLOGY 58:A415, 1983
7. Lomessy A, Viale JP, Motin J: Analgesie post-operatoie au fentanyl par voie peridurale. Ann Anesthesiol Fr 22:17–21, 1981
8. Lam AM, Knill RL, Thompson WR, Clement JL, Varkey GP, Spoerel WE: Epidural fentanyl does not cause delayed respiratory depression. Can Anaesth Soc J 30:S78–S79, 1983
9. Pierrot M, Blaise M, Dupuy A, Hugon S, Cupa M: Peridural analgesia with higher doses of fentanyl: Failure of the method for early postoperative kinesitherapy in knee surgery. Can Anaesth Soc J 29:587–592, 1982
10. Latasch L, Probst S, Dudziak R: Reversal by nalbuphine of respiratory depression caused by fentanyl. Anesth Analg 63:814–816, 1984
11. Henderson SK, Cohen H: Nalbuphine augmentation of analgesia and reversal of side effects following epidural hydromorphone. ANESTHESIOLOGY 65:216–217, 1986