Epidural Fentanyl for Postcesarean Delivery Pain Management

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The injection of narcotics into the epidural space produces analgesia by the action of these drugs on opiate receptors in the spinal cord. However, the drug (morphine) that was initially employed for epidural analgesia had a low lipid solubility and a long latency before analgesia is adequate and has proven to be of limited utility in acutely painful situations (e.g., labor pain, trauma pain). Also, epidural injection of morphine and its congeners has caused many undesirable side effects. Pruritus is the most common and may be severe. Nausea, vomiting, urinary retention, and delayed respiratory depression also have been reported and may be especially troublesome and dangerous because morphine has been demonstrated to have an extremely long duration of action, 12–24 h or longer.

Fentanyl is a highly lipid-soluble narcotic agonist with a relatively short duration of action when used iv in small doses, and in vitro penetrates samples of dura mater more rapidly than any other narcotic. To evaluate its suitability for epidural use and the dosages required in the parturient, we undertook a double-blind, randomized dose-response study of fentanyl in patients following cesarean delivery.

METHODS AND MATERIALS

The protocol was approved by the Committee for the Protection of Human Subjects from Research Risks of the Brigham and Women’s Hospital, and written informed consent was obtained from the patients before their entry into the study. Thirty ASA Class I patients scheduled for elective repeat cesarean delivery were enrolled in the study. Before operation, a large-bore iv catheter was inserted in a peripheral arm vein and patients received 1,500 ml of lactated Ringer’s solution before induction of anesthesia. An epidural catheter was inserted at the third lumbar interspace, and sensory anesthesia to the fourth thoracic dermatome was achieved using incremental doses of 0.75% bupivacaine. (At the time of the research study, 0.75% bupivacaine was approved by the FDA for use in obstetric epidural anesthesia. This approval subsequently has been withdrawn.) The parturients were positioned on the operating room table with the pelvis tilted 15 degrees to the left, using a wedge under the right hip.

After the birth of the baby and exteriorization of the uterus, the level of sensory block was determined by pinprick, and motor blockade was assessed at the feet, knees, and hips using Bromage’s criteria. Patients were asked to rate their pain at that time on a 10-cm linear analog pain scale, and baseline arterial blood pressure, heart rate and respiratory rate were noted. The patients (five patients in each group) were randomly assigned to receive an injection of 0, 12.5, 25, 50, 70 or 100 μg of fentanyl citrate, dissolved in normal saline to a total volume of 10 ml, through the epidural catheter. These doses have been shown to be nonneurotoxic in humans. The amount of fentanyl injected was not known by the anesthesiologists who performed the injection or evaluated the patient’s response. After the injection, the level of sensory block, motor block, and pain intensity was evaluated at 3, 6, 9, and 30 min, and then at 30-min intervals for at least 6 h. The duration of sensory anesthesia was defined as the time elapsed from the injection to when the patient had no detectable sensory blockade, as determined by pinprick. The duration of motor block was defined as the time elapsed from injection to when the patient was just able to elevate her knees. The duration of analgesia was defined as the time elapsed from the injection to when the patient experienced any pain, i.e., a pain score greater than 0 on the linear analog scale. Side effects such as pruritus, nausea, or somnolence were scored as: 0 = absent; 1 = mild, requiring no treatment; or 2 = severe, requiring treatment. Arterial blood pressure, heart rate, and respiratory rate (determined by a nurse–observer counting respirations) were also recorded as the same time intervals.

The patients stayed in the postanesthetic recovery room
FIG. 1. The percentage of patients reporting a pain score of 0 at 0, 3, 6, and 9 min following the injection of increasing doses and epidural fentanyl. See “Results” section for details.

for at least 6 h following the injection of the study group. They were instructed to ask for parenteral narcotics (morphine, meperidine, or hydromorphone) when they began to experience pain and throughout the postpartum period. The time interval to first systemic narcotic administration and the total dosage and timing of parenteral narcotics in the first 24 hours postpartum were recorded. Patients were informed that, should any side effects develop, immediate treatment would be available, should it be necessary. Since all patients had experienced at least one previous cesarean delivery, they were also queried as to how the amount of pain they experienced postoperatively with the experimental drug compared with their previous postoperative experience.

Numeric data were evaluated for statistical significance using analysis of variance. Nonparametric data were evaluated for significance using chi-square analysis.

RESULTS

Patient Variables. There were no differences in patient height, weight, parity, or dose of local anesthetic in any of the dosage groups. There were five patients in each dosage group, for a total of 30 patients.

Onset. As can be seen from figure 1, most of the patients experienced some mild pain (e.g., a pain score > 0), pain following birth of the baby and exteriorization of the uterus, despite a T₄ sensory level of anesthesia, with a mean pain scale of 3.7 ± 1.2 before injection of the study drug. The onset of pain relief with epidural of fentanyl was rapid and depended on dosage (fig. 1), with doses of 50 μg of fentanyl producing pain scores of 0 in all patients (N = 6) within 9 min (mean 7.2 min), and doses of 100 μg providing complete analgesia in approximately 3–6 min (mean = 3.4 min). Doses of 12.5 μg did not provide noticeable pain relief, while two of the patients in the 25–μg dose group had no demonstrable pain relief and received iv narcotics.

Sensory and Motor Blockade. No significant prolongation of sensory blockade was observed in any of the dose groups. No prolongation of motor block was seen with any of the fentanyl doses employed in the study. A significant (P < 0.01) decrease in the number of patients reporting intraoperative pain following the epidural injection of fentanyl was observed in patients who received 50 μg or greater of fentanyl (fig. 2).

Duration. Figure 3 shows the duration of complete analgesia (i.e., a score on the linear analog of pain of 0) found with the various fentanyl doses. Fentanyl, 25 μg, provided a mean duration of analgesia of approximately

FIG. 2. Number of patients who experienced intraoperative pain following injection of varying doses of epidural fentanyl. *P < 0.1 compared with control.
3 h. Higher doses of fentanyl (50, 75, 100 µg) produced an increase in the mean duration of complete analgesia of approximately 1.5 h. In the 25-µg group, two patients had no apparent prolongation of analgesia, whereas all patients who received 50 µg or more of fentanyl had prolonged analgesia. The minimum dose that provided reliable postcesarean delivery analgesia was 50 µg. Higher doses produced no significant increase in duration.

**Side Effects.** The incidence of side effects is recorded in table 1. Pruritus was noted in 10 of the 30 patients and was localized to the face and upper chest. The pruritus was of short duration (usually less than 15 min) and of minimal severity, with no patients requesting treatment for the itching. One patient had a transient erythematous rash on her upper chest, which resolved within 10 min. Interestingly, two control (i.e., patients who received no epidural fentanyl) patients described pruritus following the injection.

Nausea was noted in two patients, but no cases of vomiting occurred following the injection. Three patients (including one control) reported a mild sense of drowsiness, which occurred about 1 h following the injection and lasted approximately 1 h. These patients were all easily arousable and required no treatment. The only patient who reported pruritus, nausea, and drowsiness received no fentanyl.

The incidence of postoperative urinary retention could not be evaluated until after 12–18 h postpartum because all patients had indwelling urinary catheters, so the incidence of this side effect in the immediate postoperative period cannot be assessed from these results, but there were no differences between any of the dosage groups after urinary catheter removal.

**Twenty-four-Hour Postoperative Narcotic Dose.** The total cumulative dose and times of parenteral narcotic received by our patients in the postdelivery period was recorded. The patients in the study received a combination of narcotic analgesics in the postdelivery period on a prn schedule. The drugs used were morphine, meperidine, and hydromorphone. No attempt was made to influence the obstetrician’s choice of narcotic. To allow comparison of patients, all narcotic analgesic drugs were converted to “morphine equivalents,” using the following equivalencies: 100 mg meperidine = 10 mg morphine sulfate; 3 mg hydromorphone = 10 mg morphine sulfate.

The results are shown in figure 4. No statistically significant reduction of 24-h narcotic dosage was seen with 0, 12.5, 25, 50, or 75 µg doses of fentanyl. A statistically significant (P < 0.05) reduction was observed with 100 µg of epidural fentanyl for 24 h. Statistically significant decreases were observed for doses of 50 µg for 8 h and for 75 µg for 16 h.
Subjective Response. One of the patients who received no epidural fentanyl, one who received 12.5 μg, and three who received 25 μg of epidural fentanyl reported less pain than with her previous cesarean delivery. All of the 15 patients who received 50 μg or greater reported less pain than previously, a significant change from control ($P < 0.01$).

DISCUSSION

We have investigated the dose–response of epidural fentanyl in the postpartum period. The minimum reliably effective dose of epidural fentanyl in our patients was 50 μg of fentanyl citrate added to 9 ml of preservative-free normal saline solution in patients who received 0.75% bupivacaine for cesarean delivery. Higher doses did not produce longer or more profound analgesia, merely a more rapid onset of analgesia. The onset of action of epidural fentanyl was rapid, as had been predicted by in vitro studies.\(^5\) We also observed that injection of more than 50 μg epidural fentanyl immediately following delivery of the infant rapidly relieve the discomfort that we frequently note intraoperatively during intraabdominal manipulations (e.g., extraperitoneal uterine closure, abdominal exploration, manipulation of fallopian tubes, and peritoneal closure) during cesarean delivery, despite high thoracic levels of anesthesia.

The duration of analgesia produced by epidural injection of fentanyl in adequate doses ranged from 3 to 7 h, with the use of our strict criteria of a pain score of 0. Our tabulation of postoperative narcotic doses in these patients suggests that a reduction in postoperative pain is observable for 24 h, because patients who received epidural fentanyl in the largest dosage (100 μg) received significantly less parenteral narcotics during the observation period than patients receiving placebo. Smaller doses of epidural fentanyl (50, 75 μg) produced decreases in narcotic doses for shorter periods of time. All of our patients had previous cesarean deliveries, and all those who received greater than 50 μg of fentanyl found the postoperative period to be better than their recollections of their previous experience.

Narcotic analgesics have been used to produce postoperative analgesia in surgical and obstetric patients,\(^8,9\) but several factors have limited the application of these drugs to everyday clinical practice: first, the unavailability of human dose–response data, and, second, the potential for serious side effects such as pruritus, nausea, vomiting, urinary retention, and respiratory depression, occurring at unpredictable times, often many hours after the injection of drug.\(^10\)

Delayed respiratory depression is the most troublesome of these side effects and appears to be largely responsible for the reluctance of anaesthesiologists to use intrathecal or epidural narcotics. This phenomenon is thought to be due to transport of drug in cerebrospinal fluid from the lumbar region to the fourth intracranial ventricle, with consequent depression of medullary respiratory centers. The incidence of delayed respiratory depression appears to be greatest with poorly lipid-soluble narcotic drugs, such as morphine.\(^4\) Bromage\(^3\) suggested that lipid-soluble, highly protein bound narcotic analgesics might be less likely to exhibit this phenomenon, and this appears to be true of fentanyl. The side effects we observed with epidural fentanyl were all mild and required no treatment. They were also of extremely short duration—no patient had pruritus for more than 15 min. None of the patients had a respiratory rate develop of less than 12 per min in our controlled study, and in more than 700 subsequent
administration of postpartum epidural fentanyl in routine use, we have observed no cases of respiratory depression.

Because of the short, predictable nature of the effects produced by epidural fentanyl, we have found that the analgesia produced by 50 µg of epidural fentanyl is useful in postcesarean patients. The commercial preparation of fentanyl is preservative free, thus obviating the needs for special formulations, as is found with morphine. If a longer duration of action is required, repeat injections of 50 µg of fentanyl, after the initial analgesia disappears, will provide further analgesia.

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Tracheal Rupture Following the Insertion of a Disposable Double-lumen Endotracheal Tube

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Fortunately, tracheobronchial rupture following tracheal intubation is a rare complication. Single-lumen, endobronchial, and double-lumen endotracheal tubes can cause serious airway injury.1–5 Nondisposable red rubber and disposable polyvinylchloride (PVC) single-lumen tubes have been implicated in tracheobronchial lacerations. In contrast, nondisposable red rubber tubes have been responsible for all double-lumen endotracheal tube injuries.6,4 No airway injuries have been reported with the recently introduced disposable PVC double-lumen tubes.

Risk factors associated with tracheobronchial rupture include inexperienced endoscopists, intubating stylists, multiple vigorous attempts at intubation, tracheal abnormalities, overdistension of tracheal or bronchial cuffs with high pressure, low-volume cuffs, and old age.5–6 We recently anesthetized a patient, in whom none of these factors were present, who sustained a tracheal rupture following an "atraumatic" endotracheal intubation with a disposable, left-sided double-lumen tube.

REPORT OF A CASE

A 59-year-old woman, 1.6 m in height, weighing 65 kg, who had squamous cell carcinoma of the lung was admitted for right middle and right lower lobectomies. Significant medical history included a left-sided cerebrovascular accident without sequelae in 1950 and a total abdominal hysterectomy and bilateral salpingo-oophorectomy for endometrial carcinoma in 1976. There was no preoperative history of medications, including steroids. Preoperative laboratory studies, including complete blood count, serum electrolytes, and electrocardiogram were normal. A right, lower-middle lobe, 5-cm nodule was seen on a chest roentgenogram. Pulmonary function studies revealed a forced vital capacity of 4.50 l and a FEV1, if 1.96 l.

Prenedication consisted of diazepam, 10 mg orally. Two peripheral iv catheters and a left radial arterial catheter were inserted. Anesthesia was induced with diazepam, 10 mg iv, followed by thiopental, 250 mg, and succinylcholine, 80 mg iv. A left-sided 39 French O.D. BronchoCath® National Catheter Corporation endobronchial tube with stylet then was inserted into the trachea. Immediately after the tip of the tube passed the vocal cords, its insertion was stopped and the stylet removed. The tube then was rotated 90 degrees counterclockwise and advanced without resistance until 27.0 cm (at the lips), where mild resistance was encountered. The resistance experienced was felt to be the normal resistance of the left mainstem bronchus and carina as the tube advanced into position. The tracheal cuff was inflated to "minimal occlusion" with 5.0 ml air, and 2.0 ml air injected into the bronchial cuff. Initial auscultation of the chest revealed breath sounds on the right, with absent breath sounds on the left, while both lumens were