properly applied consistent with prudent patient care, and as suggested in the manufacturer's instructions. The probe should be placed so that no pressure or torque can be applied on the probe or finger. After application, the finger should be inspected for reduced blood flow due to positioning or the probe, since this will decrease the removal of the applied heat and increase the likelihood of a thermal burn. This observation is best done where the probe can be observed during our surgery. The quality of the pulsations should be monitored and the probe moved periodically to prevent prolonged local contact. This allows inspection for the onset of injury, and may prevent injury when long procedures are necessary.

The manufacturer, in this case, has notified the Food and Drug Administration of the potential failure of other such probes if similar damage occurs. They have placed a voluntary recall of these probes and redesigned the device to prevent a recurrence of the problem by limiting the total current that can enter the probe. They state that, during the period of shorting, the values of the heart rate and saturation would have been "frozen," similar to other error conditions, such as electrocautery. Therefore, the manufacturer has also altered the software control circuitry to detect circumstances that may indicate potential hazardous conditions in the probe, and indicate that to the user through the visual display.

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Epidural Anesthesia with Fentanyl and Lidocaine for Cesarean Section: Maternal Effects and Neonatal Outcome

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Epidural lidocaine is frequently used to provide anesthesia for cesarean delivery. Despite the high thoracic levels of sensory anesthesia obtained, some patients anesthetized with 2% lidocaine experience discomfort during surgery and require supplemental medication.[1]

Epidural fentanyl may augment anesthesia produced by local anesthetics by binding with spinal opiate receptors. This therapy has been reported to improve comfort when added to bupivacaine during labor and cesarean section.[2-7] After delivery of the neonate, the addition of epidural fentanyl to an epidural lidocaine anesthetic has been reported to improve maternal comfort during the latter part of cesarean surgery.[8] The present randomized, double-blind study was performed to determine the effects on maternal comfort of adding fentanyl to 2% lidocaine at the onset of epidural blockade, before surgery and neonatal delivery. Additionally, we evaluated the effects on the newborn of epidural fentanyl administration before delivery.

MATERIALS AND METHODS

Thirty healthy parturients undergoing non-emergent cesarean section were studied. Patients were excluded from this study if maternal systemic disease was present, systemic or epidural analgesia was administered during labor, or fetal distress was apparent. Approval from the Committee on Human Research at the University of California, San Francisco, and written informed consent from each patient were obtained. Patients were randomized to either a saline group or a fentanyl group. All patients were hydrated with at least 1500 ml crystalloid solution prior to epidural blockade, and left uterine displacement of at least 15° was maintained at all times. The epidural space at the second or third lumbar interspace was located by loss of resistance in all patients, and then distended with 5 ml of saline to facilitate passage of

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a catheter. Catheter location was tested in all patients with 3 ml of 2% lidocaine containing 15 μg epinephrine. Three minutes later, patients in the saline group received 8 ml of 2% lidocaine with 1:200,000 epinephrine mixed with 2 ml saline (n = 15), and patients in the fentanyl group received 8 ml of 2% lidocaine with 1:200,000 epinephrine mixed with 2 ml of a saline solution containing fentanyl, 1 μg/kg (n = 15). These 10-ml local anesthetic solutions containing either saline or saline with fentanyl were prepared by laboratory personnel who otherwise were not involved in the study, and administered in 5-ml doses with 30-s intervals between doses. Subsequently, incremental 3–5-ml doses of 2% lidocaine with 1:200,000 epinephrine, without fentanyl, were administered to achieve a T4 sensory block to pinprick in each patient. Supplemental 2% lidocaine with epinephrine (without fentanyl) was administered when sensory block receded by two or more dermatomes.

Intraoperative pain was treated with supplemental epidural 2% lidocaine with epinephrine. If relief was not obtained, intravenous analgesics and sedatives were administered. Other epidural local anesthetics or epidural opiates were withheld until completion of the study period, after peritoneal closure. All doses of supplemental intravenous analgesics and sedatives were recorded. The patients, anesthesiologists, and personnel collecting data were blind to the epidural medication administered. Patients were continuously observed for side effects, including nausea, vomiting, pruritus, sedation, hypotension, and clinical evidence of respiratory depression, including respiratory rates < 11 per minute. At the conclusion of the study period, patients were also questioned about the occurrence of these side effects. Hypotension, as defined by systolic blood pressure < 100 mmHg, was treated with head-down positioning, additional hydration, and intravenous ephedrine.

Surgical pain was measured with a four-point scale, by requesting subjects to rank their perception of pain as none, mild, moderate, or severe. Pain was measured at the time of skin incision, during bladder retraction, at neonatal delivery, during exteriorization and repair of the uterus, and during closure of the peritoneum.

Heparinized arterial and venous blood samples were obtained from a doubly clamped segment of umbilical cord, and maternal venous blood samples were drawn at neonatal delivery. Umbilical cord vessel blood-gas tensions were measured with a Corning® 158 blood gas analyzer. Maternal and umbilical blood samples were centrifuged and plasma removed for later fentanyl concentration determination. Plasma samples were stored at −20° C, until analyzed by radioimmunoassay for fentanyl content. Sensitivity of this assay was 0.1 ng/ml.[9]

TABLE 1. Maternal Clinical Characteristics*

	Saline (n = 15)	Fentanyl (n = 15)
Age (yrs)	30.0 ± 7.1	32.0 ± 3.6
Weight (kg)	73.9 ± 12.1	71.5 ± 10.3
Height (cm)	158 ± 5.3	159 ± 8.4
Lidocaine dose (ml)	25.6 ± 4.7	24.2 ± 4.3
Duration of anesthesia prior to delivery (min)	38.0 ± 8.0	37.0 ± 9.0

* Values are expressed as mean ± SD. No significant differences existed between groups.

The condition of the neonate was evaluated using Apgar scores at 1 and 5 min, and the Neurologic and Adaptive Capacity Scoring System (NACS)[10,11] at 0.25, 2, and 24 h of age. Measurements were made by examiners blinded to maternal treatment.

Categorical data were analyzed using the two-tailed Fisher exact test, or the Mann-Whitney unpaired rank sum test. Ratio data were analyzed using the unpaired Student's *t* test, and presented as mean ± SD. A *P* value of <0.05 was considered significant.

RESULTS

Maternal age, weight, height, duration of anesthesia prepartum, and the anesthetic dose required to achieve T4 sensory blockade did not differ significantly between groups (table 1). Two patients in the saline group and three patients in the fentanyl group underwent cesarean section after an active phase arrest of labor or failure to progress in the second stage, and the indication for surgical delivery in all others was elective.

The intensity of surgical pain was consistently less in patients given epidural fentanyl (fig. 1), but at no individual evaluation time was the difference in pain between groups statistically significant. Only one patient (7%) in the fentanyl group reported moderate or severe pain at any time during surgery, while eight patients (53%) in the saline group experienced moderate or severe pain at one or more times during surgery ($P < 0.02$). One patient in the saline group required an additional 10 ml of epidural lidocaine followed by general anesthesia before delivery of the infant. This patient did not have demonstrable, unblocked nerve roots below a T4 level, but complained of severe pain during visceral traction. Only this patient required supplemental lidocaine during the study period.

Five patients in the saline group received intravenous opiates for discomfort, although none before delivery of the infant. No patients in the fentanyl group received additional opiates ($P < 0.05$). The two groups did not differ significantly in administration of other sedatives, primarily benzodiazepines, either before or after delivery (fig. 2).

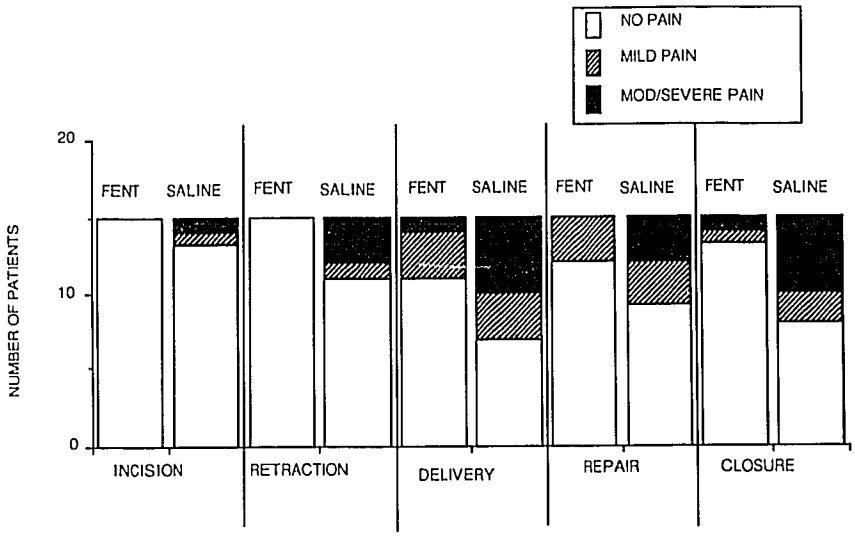

FIG. 1. The incidence of maternal pain at five times during surgery, divided into no pain, mild pain, or moderate and severe pain. Fentanyl and saline groups do not differ significantly at individual time points.

The condition of the neonate was not measurably affected by the presence of epidural fentanyl. One infant in the saline group received an Apgar score of 5 at 1 min after birth, following a surgically difficult extraction and prolonged uterine incision-to-delivery time of 240 s. This child had an Apgar score of 8 by 5 min of age. All other Apgar scores were ≥7 at 1 min of age, and ≥8 at 5 min. The NACS demonstrated no significant differences between the two groups in adaptive capacity, passive or active tone, primary reflexes, or general status of the infants. Table 2 reports the percentages of perfect scores in each category for the two groups. Two newborns in the fentanyl group required supplemental oxygen at the 2- and 24-h examination times. These neonates did not have evidence of respiratory depression, but were subsequently diagnosed with transient tachypnea of the newborn, which resolved by 2 days of age. Neurobehavioral evaluation of these infants was not performed, as it would have involved interruption of their supplemental oxygen therapy for several minutes. Umbilical cord plasma fentanyl concentrations in one of these infants were found to be below the level of accurate detection (0.1 ng/ml), while the cord specimen was inadequate for sampling in the second infant. Umbilical arterial and venous blood gas tensions and acid base values were measured in 29 neonates, and did not differ between groups.

Maternal and umbilical cord plasma fentanyl concentrations were measured in 13 of the 15 patients given epidural fentanyl, at a total dose of 72.6 ± 11.0 μg (mean ± SD). Plasma fentanyl concentrations in all umbilical artery samples were <0.1 ng/ml, below the limit of accuracy for this assay. Plasma fentanyl exceeded this value in only one umbilical venous sample, measuring 0.24 ng/ml, with a maternal venous level of 0.91 ng/ml. These concentrations were measured from samples obtained 38 min after maternal epidural fentanyl administration, and were the highest maternal and fetal plasma fentanyl concentrations measured. All other plasma concentrations were measured from samples

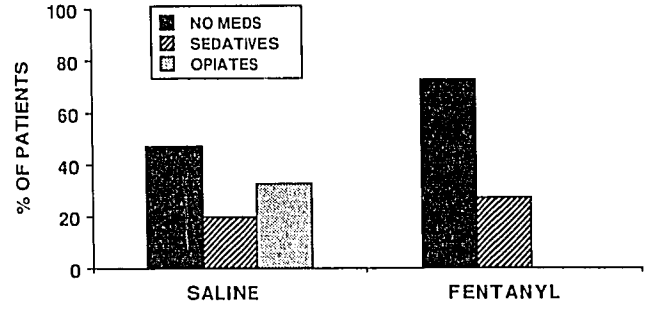

FIG. 2. The percentage of patients requiring supplemental parenteral opiates or sedatives during the study period. Single asterisk indicates a significant difference between the saline and fentanyl groups in the number of patients requiring opiates ($P < 0.05$).

TABLE 2. Percentages of Infants with Perfect Scores in Each Category of the Neurologic and Adaptive Capacity Score (NACS)*

	15 Min		2 h		24 h	
	Saline (n = 15)	Fentanyl (n = 15)	Saline (n = 15)	Fentanyl (n = 13)†	Saline (n = 15)	Fentanyl (n = 13)†
Adaptive capacity	6.7	20.0	13.3	23.0	20.0	38.4
Passive tone	73.4	80.0	66.7	84.6	66.7	84.6
Active tone	33.3	40.0	46.7	15.4	53.3	38.5
Primary reflexes	53.3	80.0	60.0	69.2	46.7	76.9
General assessment	86.7	86.7	86.7	100	80.0	100

* No significant differences between groups.
† Data from two infants were excluded.

obtained 40 ± 8.5 min (mean ± SD) after injection of fentanyl. Maternal venous plasma fentanyl concentrations did not correlate with the length of time between administration and delivery (r = 0.30).

There were no significant differences between groups in the incidence of nausea, vomiting, or hypotension (table 3). No patient had pruritus or clinical evidence of respiratory depression. Hypotension was noted and treated in 12 patients in the fentanyl group and 11 patients in the saline group. Two patients, one in each group, required a total dose of intravenous ephedrine of 25 mg, administered in divided doses, to restore systolic blood pressure to values greater than 100 mmHg. Umbilical blood gas tensions indicated a moderate respiratory acidosis in the neonates of these two patients. All other hypotensive episodes were quite responsive to small doses (5–20 mg) of intravenous ephedrine, and no evidence of neonatal acidosis resulted.

TABLE 3. Percentage of Patients with Side Effects after Receiving Epidural Lidocaine or Lidocaine with Fentanyl*

	Saline	Fentanyl
Nausea	33%	33%
Emesis	13%	20%
Pruritus	0%	0%
Hypotension	73%	80%
Respiratory Depression	0%	0%

* No significant differences between groups.

DISCUSSION

A 2% solution of epidural lidocaine with epinephrine usually provides adequate analgesia for cesarean section, although brief periods of maternal discomfort frequently occur.[1,12] This contrasts to a higher frequency of pain reported with epidural administration of 0.5% bupivacaine.[2,3] Before recommending the prepartum addition of other drugs, such as fentanyl, to improve an adequate but not perfect anesthetic, examination of additional benefits and potential side effects must be conducted.

This study demonstrates a significant decrease in moderate and severe pain during the duration of surgery from incision to peritoneal closure when 1 μg/kg fentanyl was added to 2% lidocaine for cesarean section. Further administration of supplemental intraoperative opiate medication was significantly reduced in the group of women receiving epidural fentanyl. Despite a trend, this decreased pain intensity was not statistically significant in the period of time before and during delivery of the infant. While not as striking as data reported for 0.5% bupivacaine,[2,3] our results indicate that fentanyl augments the analgesic effectiveness of 2% lidocaine. A larger study might demonstrate a significant improvement in maternal comfort in the immediate pre-delivery period of surgery.

No differences in condition of the neonate were demonstrable between groups in this study. Apgar scores, neurobehavioral examinations, and umbilical cord gases did not reflect drug-related depression in any infants. Large doses of maternal epidural lidocaine have been reported to cause subtle depression of motor function in the neonate;[13] however, the long-term significance is unknown. While some infants in our study had mild depression in adaptive capacity, passive tone, and active tone categories, these changes were not universal, and did not differ between groups. In addition, no infants required opiate antagonists, or exhibited respiratory depression.

The plasma fentanyl concentrations we obtained from maternal and umbilical cord blood samples were lower than those reported in other studies of epidural fentanyl for labor or cesarean delivery.[3,7,14] These differences may be explained by the use of lower fentanyl doses in the present study, and longer time intervals from epidural fentanyl administration to sampling. In the present study, epidural fentanyl doses administered were 1 μg/kg, 72.6 ± 11 mg (mean ± SD), and fentanyl concentrations were measured later, 40 ± 8.5 min (mean ± SD). Milon *et al.* administered epidural fentanyl, 1.70 ± 0.09 μg/kg (mean ± SEM), with 0.5% bupivacaine for cesarean delivery.[3] Following this dose, maternal venous fentanyl concentrations were highest 17.4 ± 1.9 min (mean ± SEM) after administration, with a mean level of 0.65 ± 0.09 ng/ml and a maximum level of 1.5 ng/ml. Umbilical artery plasma concentrations were reported at 0.21 ± 0.05 ng/ml (mean ± SEM), with a maximum of 0.8 ng/ml, with the interval from drug administration to delivery of the newborn not reported. Carrie *et al.* administered epidural fentanyl in doses of 150 and 200 μg for labor analgesia,[14] and measured maternal arterial plasma concentrations at 30 min, ranging from <0.1 to 1.1 ng/ml, with a median value of 0.30 ng/ml. Although drug administration-to-delivery time was not reported, umbilical arterial plasma concentrations ranged from <0.1 to 0.25 ng/ml, with a median value of 0.18 ng/ml. One neonate in this series had a plasma fentanyl concentration of 0.25 ng/ml and required ventilation and naloxone administration. Justins *et al.* administered epidural fentanyl, 80 μg, with bupivacaine for labor analgesia,[7] and obtained maximum maternal concentrations ranging from 0.116 to 1.55 ng/ml, with a mean of 1.01 ng/ml at 8.75 ± 1.83 min (mean ± SE). However, in the study by Justins *et al.*, fentanyl concentrations were measured at intervals < 20 min following drug administration.

We did not find a close correlation between fentanyl concentration and the drug-to-delivery interval. This may be explained by the considerable variation in interindividual pharmacokinetics, the low dose of fentanyl administered, and the small number of patients studied.

The correlation between blood fentanyl concentrations and neonatal respiratory depression is not exact. The concentrations measured by Milon *et al.*[3] and Carrie *et al.*[14] are below those usually associated with respiratory depression.[15,16] However, some investigators postulate extreme sensitivity of the neonate to respiratory effects.[17] Carrie *et al.*[14] reported one infant who may have had respiratory depression related to epidural fentanyl, and suggested that an arterial plasma concentration of 0.25 ng/ml may place infants at risk for this complication. In addition, the presence of fetal acidosis may predispose to entrapping fentanyl in the fetal circulation, resulting in higher fetal/neonatal plasma concentrations relative to maternal plasma concentrations, and greater risk of neonatal respiratory depression. This possibility was not examined in the present study of healthy patients without evidence of fetal distress. The absence of adverse neonatal effects and low plasma fentanyl concentrations measured in the present study suggest that small prepartum fentanyl doses may be more appropriate than the larger doses studied by other investigators for improving maternal comfort.

Following epidural administration, highly lipid soluble opioids, such as fentanyl, are thought to diffuse more rapidly from the CSF than hydrophilic opioids, such as morphine. As a consequence, cephalad migration of these opiates should be minimal, with fewer maternal side effects of nausea, vomiting, pruritus, and respiratory depression than with epidural morphine and other hydrophilic opioids. Few of these side effects were noted in this study. However, the duration of analgesia or late occurrence of side effects were not examined, since all patients received epidural morphine after the final measurements of pain intensity had been obtained during peritoneal closure. Also, subtle degrees of respiratory depression might have been overlooked in this series.

Previous workers[2] have noted a trend towards an increased incidence of hypotension in patients receiving epidural fentanyl. We found no difference in the incidence of hypotension between groups in this series. We have previously demonstrated the lack of cardiovascular effects of epidural morphine in sheep,¶ and have not noted this problem in a large clinical series.[18] However, hypotension occurred quite frequently in the present study, as has been reported in other elective cesarean populations.[19] We emphasize the need for generous hydration in the elective cesarean delivery population, and speculate that this incidence might have been lower if 30 ml/kg of intravenous crystalloid had been given before the onset of anesthesia.

In summary, for healthy parturients and fetuses, maternal epidural fentanyl administration at the onset of epidural anesthesia for elective cesarean section is safe, without significant maternal or fetal side effects. A 2% lidocaine solution containing 1:200,000 epinephrine and 1 μg/kg of fentanyl provides more effective maternal analgesia over the entire duration of surgery than a 2% lidocaine solution with epinephrine alone. While this study only demonstrates limited maternal analgesic benefit and does not demonstrate statistically significant improvement in maternal comfort in the pre-delivery period, this dose of epidural fentanyl can improve the quality of anesthesia for some patients. Alternatively, epidural fentanyl could be administered immediately after delivery, avoiding the possibility of as yet undetected neonatal side effects. However, the predelivery administration of fentanyl, or other lipid soluble opioids, may confer an analgesic benefit to the mother during the interval between skin incision through delivery. A larger study is suggested to compare the maternal analgesic benefit of epidural fentanyl administration before *versus* just after delivery.

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Psychogenic Cardiac Arrest during Extensive Sympathetic Blockade

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Extensive epidural or spinal blockade alters the balance between the sympathetic and parasympathetic nervous systems. When this occurs, situations that increase parasympathetic tone may be more likely to result in clinically significant vagal effects, such as bradycardia. A case is described in which a young athlete suffered emotionally induced asystole during an epidural blockade.

REPORT OF A CASE

A 75-kg, 30-yr-old male physician presented for arthroscopic examination of a knee that had been injured by chronic abuse during a wide variety of athletic endeavors. Past medical history was unremarkable. Physical examination revealed a well-developed young man, 180 cm tall, with an arterial blood pressure of 110/65 mmHg and a heart rate of 56 bpm that was felt to be due to a training effect.

After the patient's arrival in the operating room unpremedicated, an epidural block was administered at the third lumbar interspace, with injection through a Tuohy needle over an 8-min period using a careful test-dosing procedure. A combination of bupivacaine 0.5% (150 mg) and fentanyl 50 μg was employed, resulting in a sensory level at the third thoracic dermatome. No intraoperative sedation was employed, since the patient wished to view the procedure on a video monitor and discuss any pathologic condition with the surgeon.

The arthroscopy proceeded uneventfully with the patient and his wife (a resident in OB-GYN) observing the procedure. Approximately 35 min after skin incision, the surgeon began to discuss the severe pathology found, and the fact that reconstructive surgery could be attempted but would be unlikely to improve the poor prognosis. The patient was informed that absolute curtailment of athletic activity would be necessary to prevent further deterioration of the joint. At this point, in response to the surgeon's asking whether he should proceed with further surgery, the patient turned to his wife, expressed disappointment, asked her for her opinion, suddenly developed a bradycardia to a heart rate of 30 bpm from a prevailing rate between 70 and 80 bpm, became asystolic, and lost consciousness.

Following two precordial "thumps," intravenous administration of a total of 2 mg atropine in 1-mg aliquots over 1 min, controlled ventilation with a $F_{I_{O_2}}$ of 1.0 *via* a mask, and external cardiac compression, spontaneous cardiac rhythm (nodal tachycardia) and respiratory effort returned within 2 min. Consciousness was regained rapidly thereafter, and the surgical procedure was concluded without further event. Upon rechecking, the sensory level was found to be unchanged from that measured immediately before surgery began.

A 12-lead electrocardiogram performed in the recovery room showed no evidence of dysrhythmia or myocardial damage. The patient's memory of the event was of feeling very disheartened about the news given to him by the surgeon and then losing consciousness. After discharge from the hospital on the following day, cardiography was performed for a 24-h period by Holter® monitor. This revealed a

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