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A Randomized Study of Combined Spinal–Epidural Analgesia versus *Intravenous Meperidine during Labor*

Impact on Cesarean Delivery Rate

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Background: **Combined spinal–epidural (CSE) analgesia produces rapid-onset pain relief and allows ambulation in early labor. Epidural local anesthetics may contribute to an increase in operative deliveries by decreasing perineal sensation and causing motor weakness. Operative delivery rates might be reduced with CSE, by avoiding or delaying administration of local anesthetics. This study compares the operative delivery rates associated with a CSE technique and those associated with intravenous meperidine for labor analgesia.**

Methods: **Healthy parturients at full term were assigned randomly to receive CSE or intravenous meperidine analgesia. The CSE group received 10 μg intrathecal sufentanil, followed by epidural bupivacaine and fentanyl at their next request for analgesia. Parturients receiving intravenous meperidine had 50 mg on demand (maximum, 200 mg in 4 h). Labor and delivery outcomes in both groups were recorded and compared.**

Results: **An intent-to-treat analysis of 1,223 women indicated that CSE does not increase the rate of cesarean delivery for dystocia in nulliparous and parous women (CSE, 3.5% *vs.* intravenous meperidine, 4; P = not significant) or in nulliparous women alone (CSE, 7% *vs.* intravenous meperidine, 8%; P = not significant). Profound fetal bradycardia that necessitated emergency cesarean delivery within 1 h of the time the mother received sufentanil occurred in 8 of 400 parturients (compared with 0 of 352 who received meperidine; $P < 0.01$). However, the method of fetal monitoring differed between the two groups. Despite this, neonatal outcomes were similar overall.**

Conclusions: **Combined spinal–epidural analgesia during labor does not increase the cesarean delivery rate for dystocia in healthy parturient patients at full term, regardless of parity. However, an unexpected increase in the number of cesarean deliveries for profound fetal bradycardia after intrathecal sufentanil was observed. Further investigation is warranted. (Key words: Intrathecal sufentanil; labor analgesia; operative delivery.)**

THERE has been considerable controversy in the past few years regarding the effect of epidural analgesia on the outcome of labor.[1,2] Results of two randomized studies suggest that labor epidural analgesia is associated with an increased incidence of cesarean deliveries for dystocia in nulliparous women[3] and an increase in forceps deliveries in all parturients.[4] However, a more recent study, which compared epidural analgesia with intravenous patient-controlled analgesia during labor, showed no difference in the incidence of cesarean deliveries between groups.[5]

Combined spinal–epidural (CSE) analgesia with intrathecal sufentanil is a technique that offers the potential to minimize the effects of epidural analgesia during labor on the cesarean birth rate. This technique necessitates smaller doses of local anesthetics, which theoretically could reduce motor block, a factor thought to interfere with the progress of labor. The benefits of intrathecal sufentanil include rapid onset of pain relief and the ability to ambulate, if desired, in early labor.[6–8] In parous parturients, there is the potential to avoid local anesthetic use in the second stage of labor, although most women require intrathecal or epidural local anesthetic supplements for satisfactory second-stage labor analgesia.

The primary goal of this study was to compare the effects of CSE and those of intravenous meperidine on

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the rate of cesarean delivery in laboring women with normal full-term pregnancies.

Materials and Methods

After receiving permission from the Institutional Review Board of the University of Texas Southwestern Medical Center in Dallas, healthy parturient patients in spontaneous labor were offered the chance to participate in this randomized investigation. We chose to recruit nulliparous and parous women to better reflect the effect of the CSE technique on our practice. However, all women with a pregnancy complication, cervical dilatation >5 cm on admission, or other than a singleton, cephalic gestation were excluded. Labor was diagnosed as the presence of regular uterine contractions and at least 3-cm cervical dilatation. Between August 1, 1994 and February 28, 1995, all women eligible for the study were told about it in the obstetric triage area by a nurse practitioner who was not otherwise involved in their labor management. After providing informed consent, the parturient patients were randomly assigned to one of two groups. The randomization was computer generated in groups of 100, and the allocation was secured in a numbered and sealed envelope. One group of women would receive CSE at their first request for pain relief. The women in the other group would receive intravenous meperidine at their first request for analgesia.

Those women allocated to the CSE arm received an intravenous bolus dose of 500 ml Ringer's lactate and were placed in either a sitting or a left lateral position. A 17-gauge Tuohy needle was inserted into the epidural space at the L2-3 or L3-4 interspace. A long (12.7 cm) 25-gauge Whitacre spinal needle was passed through the indwelling epidural needle into the subarachnoid space. After clear cerebrospinal fluid was aspirated, 10 μg sufentanil in 2 ml preservative-free saline was injected. This was followed by removal of the spinal needle and insertion of an epidural catheter in a cephalad direction. When the catheter was in place, the epidural needle was removed and the catheter was secured. The parturient patient was placed in the supine position as soon as possible, with left uterine placement. The time from injection of sufentanil until the next request for analgesia was documented. When the analgesia produced by sufentanil had dissipated, 0.25% bupivacaine in 3- to 5-ml increments was injected into the epidural catheter to achieve a bilateral T10–T8 sensory level. This was followed by an epidural infusion of 0.125% bupivacaine and 2 μg/ml fentanyl at 8–10 ml/h. The infusion was maintained until delivery, but the rate was halved at the start of the second stage of labor. If there was no progress in the second stage of labor, the infusion was discontinued but the patient was administered epidural increments of fentanyl, 0.125% bupivacaine, or both for breakthrough discomfort if necessary.

Women in the other group received an initial dose of 50 mg meperidine and 25 mg promethazine hydrochloride injected intravenously. This was followed by 50 mg intravenous meperidine on request, every hour, to a maximum of 200 mg in 4 h.

All CSE patients completed a preanalgesia pain score using a 10-cm visual analog scale. This was repeated 15 and 30 min after the sufentanil injection and hourly thereafter. The time to the first painless contraction also was documented. After delivery, compliant patients in both groups were interviewed to determine overall satisfaction with labor analgesia. This was evaluated using a five-point descriptive scale of excellent, very good, good, fair, and poor.

Side effects from intrathecal sufentanil were assessed and included sensory level (assessed hourly as dermatomal level of block using ice); pruritus (assessed as mild, not needing treatment; moderate (needing one treatment with diphenhydramine); or severe (needing more than one treatment with diphenhydramine); motor block using an hourly Bromage score; and development of hypotension. Maternal blood pressure was measured every 5 min for the first 30 min after injection of sufentanil and then hourly. If the patient became hypotensive (systolic blood pressure < 100 mmHg or > 25% decrease from baseline [*i.e.*, at admission]), intravenous ephedrine in 5- to 10-mg increments was administered as necessary, and a 200- to 500-ml intravenous bolus of Ringer's lactate was given. In the event of fetal bradycardia, the patient was turned into a full lateral position, oxygen was administered by face mask, and ephedrine was administered.

All patients were treated by a nurse-midwife and obstetric resident using standardized written protocols[4] and were supervised by an attending obstetrician. Procedures recorded in these protocols dictated the intrapartum management of nulliparous and parous women both. Routine intrapartum management of all women included intravenous fluid administration and periodic auscultation with Doppler or continuous electronic fetal heart rate (FHR) surveillance. Women who received CSE had 30 min of continuous FHR monitoring, which was discontinued after that time if there was no evidence of

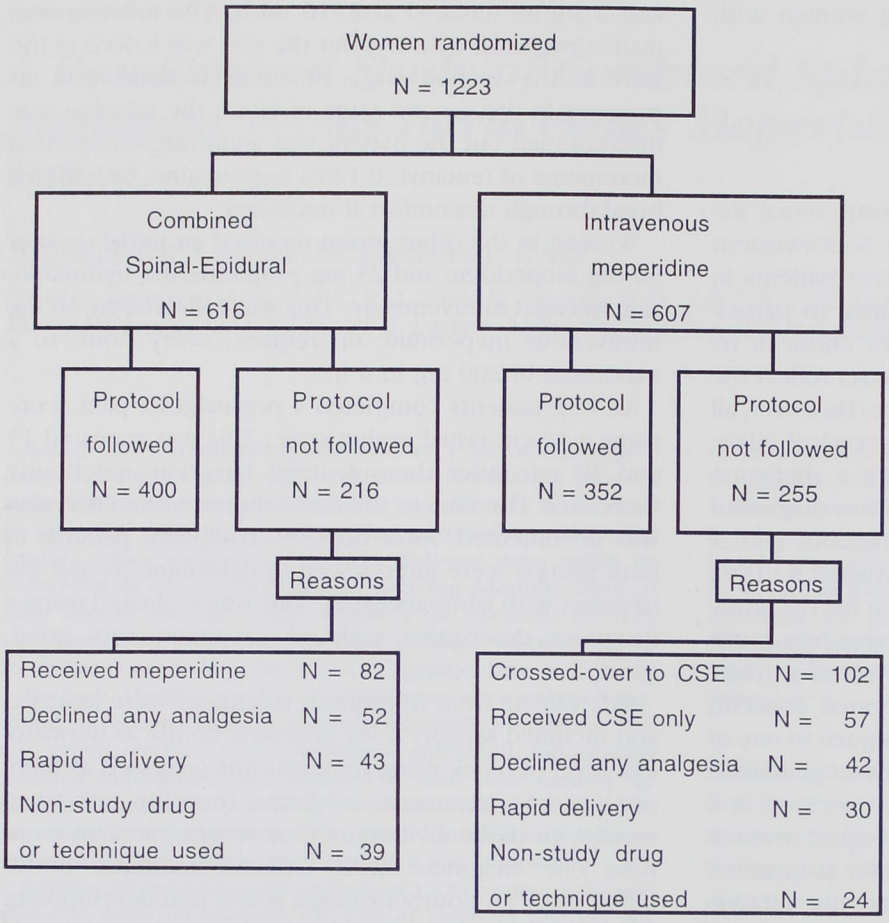

Fig. 1. Distribution of women randomly assigned to receive combined spinal–epidural analgesia or intravenous meperidine analgesia.

a nonreassuring FHR pattern. Internal electronic FHR monitoring was used in women in either group who had meconium-stained amniotic fluid, known FHR decelerations, or inadequate progress of labor. Labor management at Parkland Hospital encourages amniotomy in active labor when the fetal head is applied to the cervix. Pelvic examinations were performed approximately every 2 h to evaluate progress of labor. Cervical change less than 1 cm/h coincidental with a hypotonic contraction pattern, which was measured using an intrauterine pressure catheter, necessitated augmentation of labor with oxytocin. Briefly, oxytocin administration started at 6 mU/min and was increased by 6 mU/min at 40-min intervals to a maximum of 42 mU/min. Uterine activity of 200–250 Montevideo units for 2–4 h was considered adequate. Dystocia was diagnosed when adequate uterine activity did not result in progressive cervical dilatation or descent of the fetal head.

Elective forceps were not permitted, and no arbitrary limits were placed on the duration of the second stage of labor. Indications for low forceps delivery were limited to inadequate voluntary pushing or FHR abnormalities. Cesarean delivery was performed for dystocia or a nonreassuring FHR pattern. Umbilical artery blood samples were collected at all births from a doubly clamped cord segment to measure *p*H and oxygen and carbon dioxide pressures.

A previous power analysis was performed using a one-tailed test to show a 5% difference in the cesarean delivery rate between groups. Assuming an 8% cesarean delivery rate and using a power of 80% with a probability value ≤ 0.05, we estimated that at least 920 women would be needed for this study. The outcome data from all patients were analyzed on an intent-to-treat basis using chi-squared analysis and Fisher's exact test. Then data from those patients who complied with the randomization allocation were compared using chi-squared analysis and the Student's *t* test.

Results

Figure 1 summarizes the results of randomization. A total of 1,223 women were enrolled; 616 were assigned

Table 1. Maternal Demographic Characteristics Analyzed by Intent to Treat

Characteristic	CSE (N = 616)	Meperidine (N = 607)	Significance
Race			
Hispanic	360 (59%)	366 (60%)	NS
Black	180 (29%)	177 (29%)	NS
White	64 (10%)	54 (9%)	NS
Other	12 (2%)	10 (2%)	NS
Age (yr)	21.7 ± 4.9	22.4 ± 4.9	NS
Height (cm)	156 ± 8	156 ± 7.75	NS
Weight (kg)	74 ± 14	75 ± 15	NS
Nulliparous	336 (54.5%)	314 (51.7%)	NS

Data are N (%) or mean ± standard deviation.

CSE = combined spinal–epidural; NS = not significant.

to receive CSE and 607 were assigned to receive meperidine. Of the 616 women allocated to receive CSE, 400 (65%) complied with the protocol. Approximately 58% (n = 352) of those randomized to receive meperidine were protocol compliant. The major reasons for noncompliance are described in figure 1. Of note, 17% of the women randomized to receive meperidine had inadequate pain relief from at least one dose and were then administered CSE analgesia (these were deemed crossovers). As shown in table 1, there were no significant differences in the demographics of the study groups.

Although the cervical dilatation at first analgesia was equivalent in both study groups (table 2), the duration of labor after analgesia was significantly ($P = 0.0001$) prolonged by 1 h in women allocated to receive CSE.

Table 2. Labor Characteristics Analyzed by Intent to Treat

Labor Progress	CSE (N = 616)	Meperidine (N = 607)	Significance
Cervical dilatation at:			
Time of admission	4.0 (3.0, 5.0)	4.0 (3.25, 5.0)	NS
Time of first analgesia [cm (median + 1st and 3rd quartiles)]	5.0 (4.0, 6.0)	5.0 (4.0, 6.0)	NS
First analgesia to delivery interval (h)	5.0 ± 3.3	4.0 ± 3.1	0.0001
Second stage of labor (min)	48 ± 50	31 ± 34	0.0001
Second stage > 2 h	61 (10%)	24 (4%)	0.0002
Oxytocin augmentation	159 (26%)	141 (23%)	NS
Preanalgesia	27 (4.5%)	44 (7%)	NS
Postanalgesia	132 (21.5%)	97 (16%)	0.01

Unless otherwise stated, data are represented as N, percentage, or mean ± standard deviation.

CSE = combined spinal–epidural; NS = not significant.

Table 3. Mode of Delivery Analyzed by Intent to Treat

Delivery	CSE (N = 616) (%)	Meperidine (N = 607) (%)	Significance
Spontaneous	526 (86)	539 (89)	NS
Outlet forceps	10 (1.5)	10 (1.5)	NS
Low forceps	41 (6.5)	24 (4)	0.036
Forceps indication			
Failure to progress	16 (2.5)	14 (2.2)	NS
Nonreassuring FHR	35 (5.5)	20 (3.3)	0.045
Cesarean delivery	39 (6)	34 (5.5)	NS
Dystocia	23 (3.5)	25 (4.0)	NS
Nonreassuring FHR strip	16 (2.5)	9 (1.5)	NS
Profound fetal bradycardia within 60 min of initial administration of analgesic	9 (1.5)	0	<0.005

CSE = combined spinal–epidural; FHR = fetal heart rate; NS = not significant.

When outcome data were analyzed using the intent-to-treat approach (table 3), there was no difference seen in the rate of cesarean births (CSE, 6% *vs.* intravenous meperidine, 5.5%; 95% confidence interval [CI] for difference in rates: −1.92 to 3.38; $P = 0.34$). The rate of cesarean delivery for dystocia was not different between the groups (CSE, 3.5% *vs.* intravenous meperidine, 4%; 95% CI: −2.56 to 1.79; $P = 0.42$), and the number of cesarean deliveries performed for nonreassuring fetal heart tracings were also the same (CSE, 2.5% *vs.* intravenous meperidine, 1.5%; 95% CI: −0.47 to 2.7; $P = 0.12$). When a separate intent-to-treat analysis of outcomes in nulliparous women was performed, the cesarean delivery rate for dystocia did not differ between the groups (table 4). This finding was also shown in protocol-compliant nulliparous patients (table 5).

An emergency cesarean section for profound fetal bradycardia was performed in 9 of 616 patients assigned to receive CSE (compared with 0 of 607 in the meperidine group). This fetal bradycardia occurred within 60 min of the initiation of analgesia and was defined as a FHR ≤60 beats/min and lasting ≥60 s. All but one case occurred in protocol-compliant parturients, and 90% of cases occurred within 30 min of receiving intrathecal sufentanil (table 6). None of these cases responded to conservative measures (lateral position, oxygen administration, intravenous ephedrine), and none were associated with maternal hypotension.

In protocol-compliant patients, intrapartum FHR decelerations after intrathecal sufentanil administration were detected in 18% of cases (compared with 21% in those who received meperidine; P = not significant). Of those

Table 4. Important Outcomes in Nulliparous Women Analyzed by Intent to Treat

	CSE (n = 336)	Meperidine (n = 314)	Significance (*P*)
First analgesia to delivery interval (h)	6.0 ± 3.4	4.9 ± 3.2	<0.0002
Second stage of labor (min)	64 ± 54	43 ± 38	<0.0002
Second stage >2 h	54 (16%)	19 (6%)	<0.0008
Oxytocin augmentation	141 (42%)	97 (31%)	<0.015
Spontaneous vaginal delivery	229 (77%)	230 (80%)	NS
Forceps delivery			
Low	28 (10%)	22 (9%)	NS
Outlet	9 (3%)	10 (4%)	NS
Cesarean delivery	30 (10%)	25 (9%)	NS
Indication for cesarean			
Dystocia	21 (7%)	24 (8%)	NS
Nonreassuring fetal heart rate	9 (3%)	1 (0.3%)	<0.016
Neonatal birth weight > 4,000 g	17 (6.8%)	6 (2.4%)	<0.02

CSE = combined spinal–epidural; NS = not significant.

18% of cases, 50% resolved spontaneously, 39% responded to conservative treatment, and 11% required cesarean delivery for persistent profound fetal bradycardia. Two patients who required emergency cesarean delivery within 1 h of intrathecal sufentanil had evidence of severe FHR decelerations before they received sufentanil. Their outcomes were not included in our results from nine patients.

Immediate neonatal outcomes were similar between the groups, in terms of umbilical artery blood gases and Apgar scores (table 7). In protocol-compliant patients, more neonates in the meperidine arm required resuscitation with naloxone (14 of 352 [4%] compared with 0 of 400; $P < 0.005$). This finding was not seen when the groups were compared by intention to treat. There were no neonatal deaths, and no infants had seizures within 24 h of birth. Among the nine infants delivered by emergency cesarean section for severe bradycardia within 1 h of intrathecal sufentanil administration, umbilical artery blood *p*H was more than 7.20 in two infants, less than 7.10 in five infants, and less than 7.00 in the others. Umbilical artery carbon dioxide pressure was more than 80 mmHg in six of the nine infants (table 6).

We also compared protocol-compliant women (table 8) and found that those who received CSE were more likely to be nulliparous (63% *vs.* 50%; $P = 0.001$). As might be expected, they had longer-duration labors associated with maternal pyrexia more than 38°C and oxytocin augmentation. The cesarean section rate for dystocia was not significantly different among the protocol-compliant women, despite the larger numbers of nulliparous women in that group. An increase in all other types of operative delivery was seen more frequently after CSE when the analysis included all patients (table 8). However, when data from nulliparous women were analyzed, no difference in the forceps rates between protocol-compliant groups was observed (table 5).

The characteristics of labor analgesia obtained with intrathecal sufentanil were analyzed. The onset of analgesia was rapid, with a time to first painless contraction of 6 ± 6 min (SD) and duration of action of 2.5 ± 1.0 h (SD). The median sensory level obtained 15 and 30 min after injection of the sufentanil was T6 (range, T12–T2). The median visual analog score score for preanalgesia pain was 10 (range, 2–10) and 0 (range, 0–10) at 15 and 30 min after injection, respectively. Maternal hypotension that necessitated treatment with ephedrine occurred in 14% of women after intrathecal sufentanil. Pruritus necessitating treatment with Benadryl (Parke-Davis, Morris Plains, NJ) was seen in 17% of patients after sufentanil administration. Nausea was not a significant problem after intrathecal sufentanil, reported by only 2.4% of women, and no patient had significant motor block as measured using a Bromage scale.

The duration of the epidural component of CSE was 4.5 ± 2.9 h (SD) for nulliparous women and 2.2 ± 1.7 h (SD) for parous women. The cumulative doses of bupivacaine and fentanyl used were 72 ± 45 mg (SD) and 150 ± 110 μg (SD), respectively, in nulliparous women and 45 ± 29 mg (SD) and 97 ± 75 μg (SD), respectively, in parous women. Intrathecal sufentanil provided adequate analgesia as a sole agent in 20% of nulliparous women and in 45% of parous women before delivery.

Table 5. Operative Delivery Rates in Protocol Compliant Nulliparous Women

	CSE (n = 252) (%)	Meperidine (n = 175) (%)	Significance (*P*)
Forceps delivery			
Low	25 (10)	11 (6)	NS
Outlet	9 (4)	4 (2)	NS
Cesarean delivery	27 (11)	8 (5)	<0.023
Indications for cesarean			
Dystocia	18 (7)	7 (4)	NS
Nonreassuring fetal heart rate	9 (4)	1 (1)	<0.05

CSE = combined spinal–epidural; NS = not significant.

Table 6. Details of the Nine Neonates Born by Emergency Cesarean Section within 1 h of Administration of Intrathecal Sufentanil

Patient Study No.	Parity	Analgesia to Delivery Interval (min)	Gestational Age (wk)	Birth Weight (g)	Ua *p*H	Ua P_{CO_2}	Apgar Scores at 1 and 5 min
16	Nulliparous	48	39	2,615	7.03	94	6 and 8
167	Parous	33	39	3,715	6.94	117	5 and 8
509*	Nulliparous	48	39	3,290	7.23	59	9 and 9
712	Nulliparous	30	38	2,525	7.07	65	9 and 9
887	Nulliparous	24	41	4,261	7.08	84	8 and 9
924	Nulliparous	45	40	2,766	7.00	83	9 and 9
998	Nulliparous	23	41	2,875	6.96	97	8 and 9
1082	Nulliparous	34	39	2,870	7.21	60	8 and 9
1118	Parous	20	39	3,150	7.04	93	6 and 7

* Protocol noncompliant (other eight patients were all protocol compliant).

Figure 2 shows overall patient satisfaction, using a 5-point descriptive scale, in protocol-compliant women according to their type of analgesia. It shows superior analgesia with CSE, in that more women rated their analgesia as poor or fair if they received meperidine, and more women rated their analgesia as excellent if they received CSE.

Discussion

The primary finding of this study is that CSE analgesia during labor has no effect on the overall rate of cesarean delivery, or the rate of cesarean delivery for dystocia, compared with intravenous meperidine. However, we observed an unexpected number of emergency cesarean deliveries for profound fetal bradycardia within 1 h of intrathecal sufentanil dosing. This severe fetal bradycardia did not resolve despite the use of conservative measures such as supplemental oxygen administration, lateral maternal positioning, intravenous ephedrine (even in the absence of maternal hypotension), and fetal scalp stimulation. Other significant associations with CSE analgesia in this study included prolongation of the first and second stages of labor and more frequent use of oxytocin augmentation of labor.

Table 7. Neonatal Outcomes

Outcome	CSE (N = 616)	Meperidine (N = 607)	Significance
Birth weight			
Mean ± SD (g)	3,322 ± 442	3,329 ± 436	NS
>4,000 g	29 (4.7%)	23 (3.8%)	NS
Apgar Score			
<7 at 1 min	19 (3.1%)	23 (3.8%)	NS
<7 at 5 min	0	1 (0.2%)	NS
Umbilical artery blood			
*p*H <7.20	77 (12.5%)	82 (13.5%)	NS
P_{CO_2} > 60	46 (7.5%)	39 (6.4%)	NS

CSE = combined spinal–epidural; NS = not significant.
Data are N (%) or mean ± standard deviation.

How do we explain the presence of severe fetal bradycardia after intrathecal sufentanil? A recent report indicated that intrathecal opioids can be associated with uterine hyperstimulation[9]; however, we did not consistently monitor for it. Some of the severe bradycardias observed may have been caused by reduced placental perfusion secondary to uterine tetany. Had uterine hyperstimulation been actively sought, a resolution of the bradycardia may have occurred after uterine relaxation provided by subcutaneous terbutaline or intravenous (or sublingual) nitroglycerin. Despite the fact that our protocol did not call for this therapy, it is unlikely that severe uterine tetany would have been missed. However, less severe degrees of uterine hypertonus might have been unrecognized. Another possibility is that persistent severe FHR decelerations could occur as a result of direct vagotonic effects of sufentanil on the fetal heart. Sufentanil is highly lipid soluble, and plasma levels are detectable within 39 min of a 15-μg intrathecal sufentanil injection.[10] In turn, sufentanil can enter the fetal circulation by placental transfer, which occurs more readily in the presence of fetal acidemia.[11] A more plausible explanation for fetal bradycardia after sufentanil administration is uteroplacental hypoperfusion secondary to the decrease in blood pressure, which has been observed in this and other studies.[12,13] In our study, however, not one case of severe fetal bradycardia was associated with maternal hypotension, although it is possible that relative visceral hypotension was present. Hypotension associated with CSE may also be a result of an excessively high sensory block from intrathecal sufentanil,[12] although the presence of a sympathectomy after intrathecal sufentanil has been disputed by some inves-

Table 8. Important Outcomes in Protocol Compliant Women

Outcome	CSE (N = 400) (%)	Meperidinea (N = 352) (%)	Significance (*P*)
Nulliparous	252 (63)	175 (50)	<0.005
Maternal fever >38°C	88 (22)	11 (3)	<0.005
Oxytocin augmentation	128 (32)	62 (18)	<0.0005
Preanalgesia	20 (5)	23 (6.5)	NS
Postanalgesia	108 (27)	39 (11)	<0.0005
Analgesia to delivery interval (min ± SD)	298 ± 199	177 ± 131	<0.005
Low forceps delivery	30 (8)	11 (3)	<0.005
Outlet forceps delivery	9 (2)	4 (1)	<0.005
Cesarean delivery	29 (7)	10 (3)	<0.005
Dystocia	17 (5)	8 (2)	NS
Nonreassuring FHR	12 (3)	2 (1)	0.02
Profound fetal bradycardia within 1 h of initial analgesia	8 (2)	0	<0.01

CSE = combined spinal–epidural; NS = not significant.

tigators.[14] Accidental migration of the epidural catheter into the subarachnoid space[13] or a sudden decrease in circulating catecholamine levels with the rapid onset of analgesia are other potential causes of hypotension associated with CSE. To put our findings into perspective, we must note that others have found the incidence of hemodynamic effects[15] and the risk of FHR changes[16] after intrathecal sufentanil in parturient patients to be no different than that of epidural bupivacaine. In addition, one retrospective study concluded that CSE with subarachnoid sufentanil does not increase the incidence of emergency cesarean section.[17]

Similar to our results, Cohen *et al.*[18] also observed a 15% incidence of FHR decelerations when intrathecal sufentanil was used. In contrast to our study, their investigation involved a smaller sample size, and there were no cases of emergency cesarean delivery for persistent fetal distress after sufentanil was administered. The validity of this finding in our study is questionable because not all meperidine recipients were monitored continuously for FHR in the first 30 min after administration of analgesia. Indeed, internal FHR monitors were used at some point in labor in 70% of women who received CSE, but only in 45% of women who received meperidine. However, neonatal outcomes were not different between groups, and it is unlikely that severe fetal distress would be missed by intermittent auscultation of the FHR.

The concern will be raised that these cases of severe fetal bradycardia may have resolved with a more conservative approach, but the blood gases of seven of nine of the neonates indicated that they were significantly compromised for some reason, and expedient delivery was a wise course of action. The important finding of FHR abnormalities associated with intrathecal sufentanil emphasizes the need for vigilance when this technique is used, with appropriate protocols in place to ensure the availability of trained personnel to address a potential emergency.

Other side effects of intrathecal sufentanil include the common opioid-related symptoms of pruritus and nausea[19] and, less commonly, severe respiratory depression.[20] The incidence of pruritus in this study was 48%, although treatment was necessary in only 17% of patients. Nausea was less of a problem, with an incidence of 2.4%. There were no cases of respiratory arrest in this study. Some of these issues might be resolved if less intrathecal sufentanil was administered. A dose of 10 μg is commonly used, and one dose-response study defined an effective dose of 8.9 μg in 95% of women for intrathecal sufentanil in parturient patients, with no difference in the side-effect profile between 2.5 μg and 15 μg.[21]

Our study followed a previous investigation at Parkland Hospital in which the commonly used technique of epidural infusion during labor was compared with on-demand intravenous meperidine.[4] In that study, the cesarean delivery rate for dystocia was greater in protocol-compliant women who received epidural analgesia. However, similar to the study that we re-

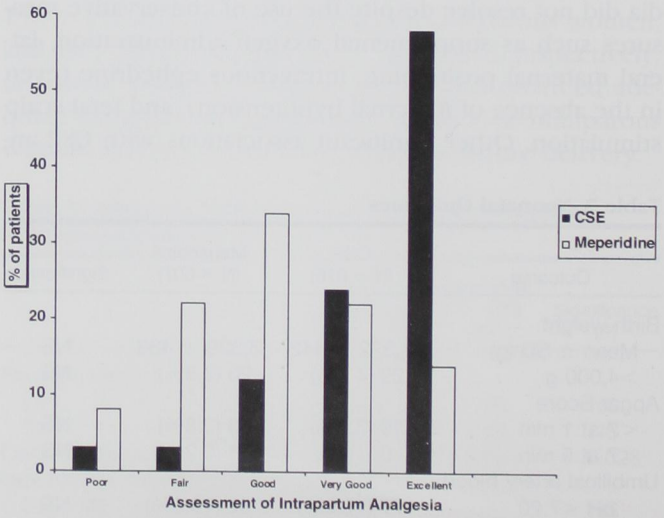

Fig. 2. Overall satisfaction with labor analgesia in protocol-compliant patients. Patients were asked within 12–24 h of delivery of a neonate how they rated overall satisfaction with pain relief during labor ($P < 0.0001$).

ported here, approximately one third of those recruited were not protocol compliant, and many crossed over from the meperidine arm because it provided inadequate analgesia. In this regard, we believe that analysis of data by intention to treat helps to overcome the problem of protocol failures and describes the real effect of offering CSE to our patients. The cesarean section rate for dystocia between compliant patients who received epidural analgesia in our first study[4] and those who received CSE in this study was identical (5%). The same finding was reported by Nageotte *et al.*[22] in a randomized study that compared CSE with epidural analgesia. Delaying the administration and reducing the dose of epidural local anesthetics therefore seems to confer no advantage in terms of cesarean delivery rates for dystocia. This may result from the finding that the reduction in dose of bupivacaine and fentanyl is small, in that bupivacaine use in the epidural infusion study[4] was 77 ± 46 mg compared with 63 ± 43 mg (mean ± SD) in this study. Fentanyl use was 150 ± 92 μg in the former study[4] compared with 124 ± 106 μg in this study.

Another randomized study from Parkland Hospital that compared intravenous meperidine, using patient-controlled analgesia, with an epidural infusion technique during labor had minimal crossovers, and no differences were detected in the cesarean delivery rates among protocol-compliant patients.[5] To date, this is the strongest evidence that epidural analgesia during labor does not cause an increase in the rate of cesarean delivery. Before that study[5] there was not one report that proved a cause-and-effect relation between epidural analgesia and an increase in the cesarean delivery rate. Evidence concerning the effect of epidural analgesia on the cesarean section rate has been confusing and different conclusions have been reached.[23] The current study and that of Sharma *et al.*[5] help to clarify this issue by showing that neither CSE nor epidural analgesia influences the cesarean section rate in low-risk parturients.

We conclude, during the conditions of the current study, that CSE analgesia during labor has no effect on the overall cesarean delivery rate or on the cesarean delivery rate for dystocia. The finding of an increase in cesarean delivery rate for profound fetal bradycardia within 1 h of administering sufentanil was unexpected. Some may challenge this observation because electronic FHR monitoring was performed less frequently in those who received meperidine. We contend, however, that the fetal bradycardias observed were severe enough to probably be detected by intermittent auscultation.

Intrathecal sufentanil provides excellent rapid onset analgesia in the first stage of labor, but its use can be associated with clinically significant side effects that necessitate prompt treatment. We recommend that, in addition to monitoring maternal blood pressure and ventilatory status after intrathecal sufentanil, FHR should be monitored continuously for at least 1 h after the injection.

References

1. Chestnut DH: Epidural analgesia and the incidence of cesarean section: Time for another close look. ANESTHESIOLOGY 1997; 87:472–6

2. Porreco RP, Thorp JA: The cesarean birth epidemic: Trends, causes, and solutions. Am J Obstet Gynecol 1996; 175:369–74

3. Thorp JA, Hu DH, Albin RM, McNitt J, Meyer BA, Cohen GR, Yeast JD: The effect of intrapartum epidural analgesia on nulliparous labor: A randomized, controlled, prospective trial. Am J Obstet Gynecol 1993; 169:851–8

4. Ramin SM, Gambling DR, Lucas MJ, Sharma SK, Sidawi JE, Leveno KJ: Randomized trial of epidural versus intravenous analgesia during labor. Obstet Gynecol 1995; 86:783–9

5. Sharma SK, Sidawi JE, Ramin SM, Lucas MJ, Leveno KJ, Cunningham FG: Cesarean delivery: A randomized trial of epidural versus patient-controlled meperidine analgesia during labor. ANESTHESIOLOGY 1997; 87:487–94

6. Collis RE, Baxandall ML, Srikantharajah ID, Edge G, Kadim MY, Morgan BM: Combined spinal epidural analgesia with ability to walk throughout labour. Lancet 1993; 341:767–8

7. Collis RE, Baxandall ML, Srikantharajah ID, Edge G, Kadim MY, Morgan BML Combined spinal epidural (CSE) analgesia: Technique, management, and outcome of 300 mothers. Int J Obstet Anesth 1994; 3:75–81

8. Norris MC, Grieco WM, Borkowski M, Leighton BL, Arkoosh VA, Huffnagle HJ, Huffnagle S: Complications of labor analgesia: Epidural versus combined spinal epidural techniques. Anesth Analg 1994; 79: 529–37

9. Herbstman CH, Zaidan JT, O'Neil L, Newman LM: Fetal bradycardia and uterine hypertonicity after intrathecal fentanyl in laboring women (abstract). ANESTHESIOLOGY 1997; 87:A873

10. Hansdottir V, Hedner T, Woestenborghs R, Nordberg G: The CSF and plasma pharmacokinetics of sufentanil after intrathecal administration. ANESTHESIOLOGY 1991; 74:264–9

11. Johnson RF, Herman N, Arney TL, Johnson HV, Paschall RL, Downing JW: The placental transfer of sufentanil: Effects of fetal pH, protein binding, and sufentanil concentration. Anesth Analg 1997; 84:1262–8

12. Hamilton CL, Cohen SE: High sensory block after intrathecal sufentanil for labor analgesia. ANESTHESIOLOGY 1995; 83:1118–21

13. Robbins PM, Fernando R, Lim GH: Accidental intrathecal insertion of an extradural catheter during combined spinal-extradural anaesthesia for caesarean section. Br J Anaesth 1995; 75:355–7

14. Riley ET, Walker D, Hamilton CL, Cohen SE: Intrathecal sufentanil for labor analgesia does not cause a sympathectomy. ANESTHESIOLOGY 1997; 87:874–8

15. Pham LH, Camann WR, Smith MP, Datta S, Bader AM: Hemodynamic effects of intrathecal sufentanil compared with epidural

bupivacaine in laboring parturients. J Clin Anesth 1996; 8:497–501

16. Neilsen PE, Erickson JR, Abouleish EI, Perriatt S, Sheppard C: Fetal heart rate changes after intrathecal sufentanil or epidural bupivacaine for labor analgesia: Incidence and clinical significance. Anesth Analg 1996; 83:742–6

17. Albright GA, Forster RM: Does combined spinal-epidural analgesia with subarachnoid sufentanil increase the incidence of emergency cesarean delivery? Reg Anesth 1997; 22:400–5

18. Cohen SE, Cherry CM, Holbrook RH Jr, El-sayed YY, Gibson RN, Jaffe RA: Intrathecal sufentanil for labor analgesia—sensory changes, side effects, and fetal heart rate changes. Anesth Analg 1993; 77:1155–60

19. Camann WR, Minzter BH, Denney RA, Datta S: Intrathecal sufentanil for labor analgesia: Effects of added epinephrine. ANESTHESIOLOGY 1993; 78:870–4

20. Hays RL, Palmer CM: Respiratory depression after intrathecal sufentanil during labor. ANESTHESIOLOGY 1994; 81:511–2

21. Herman NL, Calicott R, Van Decar TK, Conlin G, Tilton J: Determination of the dose-response relationship for intrathecal sufentanil in laboring patients. Anesth Analg 1997; 84:1256–61

22. Nageotte MP, Larson D, Rumney PJ, Sidhu M, Hollenbach K: Epidural analgesia compared with combined spinal-epidural analgesia during labor in nulliparous women. N Engl J Med 1997; 337:1715–9

23. Miller AC: The effects of epidural analgesia on uterine activity and labor. Int J Obstet Anesth 1997; 6:2–18