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A Randomized, Double-masked, Multicenter Comparison of the Safety of Continuous Intrathecal Labor Analgesia Using a 28-Gauge Catheter versus *Continuous Epidural Labor Analgesia*

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Background: **Continuous intrathecal labor analgesia produces rapid analgesia or anesthesia and allows substantial flexibility in medication choice. The US Food and Drug Administration, in 1992, removed intrathecal microcatheters (27–32 gauge) from clinical use after reports of neurologic injury in nonobstetric patients. This study examined the safety and efficacy of a 28-gauge intrathecal catheter for labor analgesia in a prospective, randomized, multicenter trial.**

Methods: **Laboring patients were randomly assigned to continuous intrathecal analgesia with a 28-gauge catheter (n = 329) or continuous epidural analgesia with a 20-gauge catheter (n = 100), using bupivacaine and sufentanil. The primary outcome was the incidence of neurologic complications, as determined by masked neurologic examinations at 24 and 48 h postpartum, plus telephone follow-up at 7–10 and 30 days after delivery. The secondary outcomes included adequacy of labor analgesia, maternal satisfaction, and neonatal status.**

Results: **No patient had a permanent neurologic change. The continuous intrathecal analgesia patients had better early analgesia, less motor blockade, more pruritus, and higher maternal satisfaction with pain relief at 24 h postpartum. The intrathecal catheter was significantly more difficult to remove. There were no significant differences between the two groups in neonatal status, post–dural puncture headache, hemodynamic stability, or obstetric outcomes.**

Conclusions: **Providing intrathecal labor analgesia with sufentanil and bupivacaine *via* a 28-gauge catheter has an incidence of neurologic complication less than 1%, and produces better initial pain relief and higher maternal satisfaction, but is associated with more technical difficulties and catheter failures compared with epidural analgesia.**

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CONTINUOUS intrathecal labor analgesia was first described by Carpenter *et al.*[1] in 1951 using an infusion of procaine *via* a reusable vinyl catheter inserted through an 18-gauge Quincke spinal needle. The resulting analgesia was satisfactory, but the technique was limited by the inevitable headache associated with the large-gauge needle and catheter. During the late 1980s, the development of 28-gauge or smaller catheters that could pass through a 22-gauge needle stimulated a resurgence of interest in continuous intrathecal labor analgesia. In 1990, Benedetti and Tiengo[2] described repeated intrathecal injections of 0.25% bupivacaine *via* a 32-gauge spinal catheter producing satisfactory labor analgesia in 12 parturients. Other investigators described successful continuous intrathecal labor analgesia using combinations of both dilute local anesthetics and opioids given *via* a small-gauge catheter.[3–6]

In 1991, however, four cases of cauda equina syndrome (CES) associated with continuous intrathecal anesthesia in nonobstetric patients were reported to the US Food and Drug Administration (FDA).[7] Three of the four cases involved a 28-gauge catheter. After receiving reports of eleven cases, the FDA required the manufacturers of continuous intrathecal catheters, 27 gauge or smaller, to withdraw their products from the market.[8]

This prompted investigations to determine whether the CES was inherent to the use of an intrathecal catheter or the drugs injected through it. The drug in all 11 cases of reported CES with a 28-gauge catheter was 5% hyperbaric lidocaine in excess of 100 mg. A single case involved a 20-gauge catheter and hyperbaric tetracaine. Subsequent laboratory animal studies have demonstrated that nerves exposed to 5% hyperbaric lidocaine are permanently damaged.[9–11] It is likely that the slow flow rate through the 28-gauge catheter contributed to the pooling of hyperbaric, highly concentrated drug in the sacral area, resulting in neurologic injury.[12–14]

As the understanding of the relation between lidocaine, small-gauge catheters, and CES matured, investigators concluded that the catheters themselves were unlikely to be the direct cause of CES. A small-gauge catheter offers the greatest potential advantage to the obstetric population, where speed and flexibility are often essential and post–dural puncture headache (PDPH) frequently accompanies large-gauge dural puncture. Although practitioners may use an epidural catheter for continuous spinal analgesia after unintentional dural puncture, the overall PDPH rate has been reported to be as high as 50%.[15] Therefore, the FDA granted an Investigational Device Exemption in 1996 for a randomized, double-masked, multicenter study of labor analgesia and anesthesia designed to compare the safety of continuous spinal administration of sufentanil and bupivacaine, using a 28-gauge catheter, with continuous epidural administration, using a 20-gauge catheter. The primary null hypothesis of this study was that there would be no difference in the incidence of neurologic complications presenting during the postpartum period in women who received continuous intrathecal analgesia compared with those who received continuous epidural analgesia. The secondary null hypothesis was that there would be no difference between the two groups in failed or inadequate analgesia, maternal satisfaction, or neonatal outcome.

Materials and Methods

After institutional review board approval from each of the participating institutions (Albert Einstein College of Medicine, Bronx, New York; Jefferson Medical College, Philadelphia, Pennsylvania; Drexel University College of Medicine, Philadelphia, Pennsylvania; University of Arizona College of Medicine, Tucson, Arizona; University of Iowa College of Medicine, Iowa City, Iowa; University of Rochester School of Medicine and Dentistry, Rochester, New York; and University of Texas Southwestern Medical Center, Dallas, Texas), all parturients gave written informed consent to participate in this randomized, double-masked trial. Obstetric patients were recruited who met the following criteria: American Society of Anesthesiologists physical status I or II; age between 18 and 45 yr; and in spontaneous or induced labor with a healthy vertex fetus(es), at term of pregnancy. Exclusion criteria included patient refusal; inability to participate in the informed consent process; presence of preeclampsia, eclampsia, sepsis, coagulopathy, or neurologic problems involving the bladder, bowel, or lower extremities; history of back surgery; ongoing symptoms of disc disease; and drug or alcohol dependency. In addition, women whose obstetricians believed that they were at high risk for cesarean delivery were not enrolled. Any woman who had received intravenous opioid agonist/antagonist medication within the 60 min before catheter placement was not eligible to participate. Finally, all patients had to have a working telephone with no plans to change their current residence within 45 days of delivery. Women who met these criteria were approached about participating in the study while in early labor.

Experimental Protocol

Randomization. A computer-generated randomization list was produced with the goal of enrolling a total of 325 parturients in the continuous intrathecal (CIT) arm and 100 parturients in the continuous epidural (CEPI) arm of the trial. The randomization list was stratified by study location such that each site would enroll approximately the same number of participants. Treatment assignment was placed in a sealed envelope, numbered with a site-specific numbering system and delivered to each location by the national study coordinator. All principal investigators at each study location had used small-gauge spinal catheters before the product withdrawal from the market (see appendix for the complete list of spinal catheter study group members).

Data Collection. After obtaining written consent, demographic data, including maternal age, height, weight, gravidity, parity, and history of previous vaginal or cesarean deliveries, were recorded. All participants underwent a baseline focused lower extremity neurologic examination, including observation of gait (if possible), muscle strength, sensory assessment using pinprick of the L1–S4 dermatomes bilaterally, and patellar and Achilles deep tendon reflexes bilaterally. Patients were specifically questioned about their current bladder and bowel function. Any finding of significant neurologic abnormality precluded further participation by the parturient in the trial, and the patient was removed from the study at this point. If the baseline neurologic examination results were within normal limits, the investigator who was to insert the catheter opened the next numbered envelope and notified the hospital pharmacy of treatment allocation.

Drug Handling and Preparation. Neither sufentanil nor bupivacaine is approved specifically for continuous intrathecal use. Therefore, these medications were considered investigational for the purposes of this trial. All

medications were stored and prepared by the hospital pharmacy at each location with the exception of bupivacaine vials (0.25% and 0.5%) that were kept at patient care areas for additional bolus doses. Abbott Laboratories, Inc. (Chicago, IL) provided both generic sufentanil and bupivacaine through an agreement with the study sponsor. Upon notification of enrollment of a study participant, the first bolus of medication and infusion was prepared in a sterile fashion using preservative-free saline as diluent by the respective hospital pharmacy. All infusions were administered using the Abbott Laboratories Pain Manager Pump®.

Analgesic Protocol. At patient request for analgesia, the following baseline data were obtained from all participants by an investigator unaware of treatment allocation: maternal blood pressure, heart rate, respiratory rate, cervical dilation, modified Bromage motor blockade score (4 = no motor block, 3 = can flex leg at knee, 2 = can flex leg at ankle, 1 = complete motor blockade), and fetal heart rate. Visual analog scores for pain, nausea, and pruritus were obtained on 10-cm unmarked lines with, for example, "no pain" written on the left end and "worst pain" written on the right end. An investigator familiar with the technique placed all catheters or, at the discretion of the investigator, a fellow or senior resident placed the catheter under direct supervision. Doses for the initial injection and infusions of bupivacaine and sufentanil were based on the collective experience of the investigators with continuous epidural and intrathecal labor analgesia. After injection of the first dose of medication (time 0), the following data were obtained by a masked investigator every 5 min for the first 20 min, again at 30 and 60 min, and then hourly until delivery: maternal blood pressure, heart rate, and respiratory rate; fetal heart rate; and maternal visual analog scores for pain, nausea, and pruritus. Any systolic blood pressure below 100 mmHg occurring during the interval since the last evaluation was recorded, and the amount of any systemic vasopressor given was noted. Ephedrine or other vasopressor administration was at the discretion of the investigator. Any episode of fetal bradycardia, defined as a fetal heart rate less than 100 beats/min, occurring during the interval since the last evaluation was also recorded. In addition, the Bromage score was recorded at 60 min and at each subsequent 2-h interval until delivery.

Continuous Intrathecal Group. After sterile preparation and draping of the back, a 28-gauge single end-hole polyurethane catheter (Ballard Medical Products, Salt Lake City, UT, a division of Kimberly-Clark) was inserted 3–4 cm into the intrathecal space *via* a 22-gauge ramped Sprotte® needle (Rusch, a Teleflex Medical Company, Limerick, PA) at the L3–L4, L4–L5, or L2–L3 interspace using the paramedian approach. The paramedian approach was chosen whenever possible to aid subsequent removal of the catheter. After securing the catheter, the parturient was placed supine with head up approximately 45° and left uterine displacement. After the initial bolus of 5 μg sufentanil in 1 ml preservative-free saline, subsequent doses were based on the CIT algorithm (fig. 1). As a condition of the FDA approval of this study, only one medication, not a mixture, could be infused continuously in the CIT group. Sufentanil was chosen, rather than bupivacaine, to collect data that would support FDA approval of sufentanil for continuous intrathecal use. Patients without any evidence of intrathecal catheter location or who required more than the hourly allowed maximum dose of bupivacaine had their catheter removed and analgesia provided as clinically appropriate. Patients delivering by cesarean section were allowed to receive preservative-free morphine, 0.15–0.2 mg in 1 ml preservative-free saline, through the intrathecal catheter for postoperative pain relief at the discretion of the investigator. No other medications were given through the intrathecal catheter.

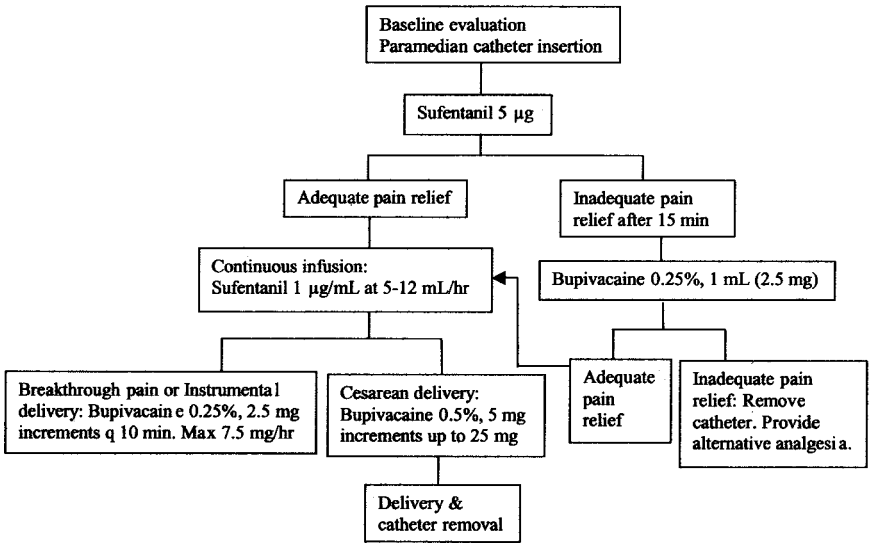

Fig. 1. Dosing algorithm for the continuous intrathecal group.

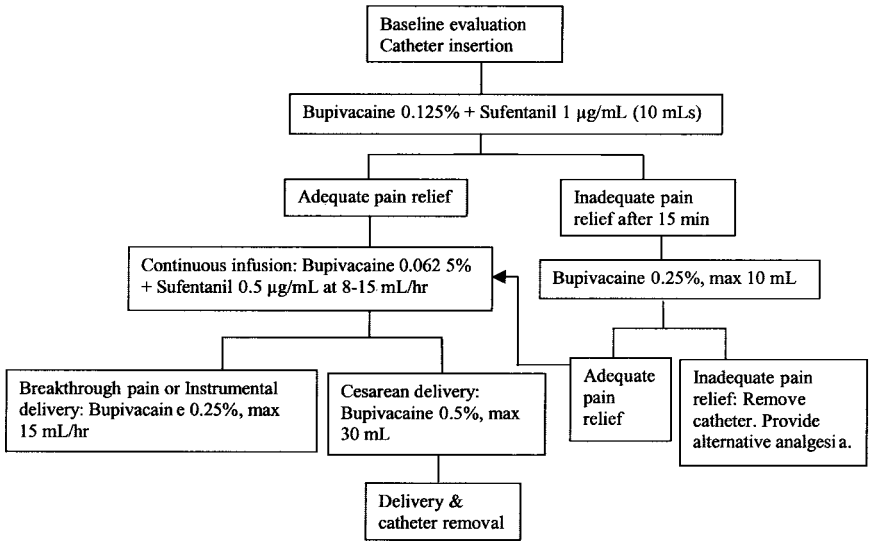

Fig. 2. Dosing algorithm for the continuous epidural group.

Continuous Epidural Group. After sterile preparation and draping of the back, a 20-gauge single end-hole nylon catheter (Ballard Medical Products) was inserted 3–5 cm into the epidural space *via* an 18-gauge Tuohy needle at the L3–L4, L4–L5, or L2–L3 interspace using the midline or paramedian approach. After securing the catheter, the parturient was placed supine with head up approximately 45° and left uterine displacement. After the initial 10-ml bolus, administered in divided doses of 0.125% bupivacaine with 1 μg/ml sufentanil, subsequent doses were based on the CEPI algorithm (fig. 2). A lidocaine with epinephrine test dose was not administered. Patients without any evidence of epidural catheter location or who required more than the hourly allowed maximum medication had their catheter removed and analgesia provided as clinically appropriate. Patients undergoing cesarean delivery were allowed to receive preservative-free morphine, 3–5 mg, through the epidural catheter for postoperative pain relief at the discretion of the investigator. Patients undergoing emergency cesarean delivery could receive 2% lidocaine with 1:200,000 epinephrine, up to 25 ml. No other medications were given through the epidural catheter.

Delivery and Postpartum. At delivery, the type of delivery was recorded, and if delivery was by cesarean section, the indication was noted as well as the ability of the catheter to function adequately for the surgery. The total dose of each medication given was recorded. Neonatal assessments included 1- and 5-min Apgar scores and neonatal weight. The nursery to which the neonate was admitted was recorded and, if not the normal newborn nursery, the team caring for the neonate was asked whether the disposition of the baby was impacted by maternal analgesia or anesthesia.

At the time of catheter removal, investigators were asked to rate the ease of removal of the catheter as easy, moderately difficult, or difficult and to record intact removal. For catheter removal, patients in the CIT group were placed in the lateral position to decrease axial loading[16,17] with the back flexed. If the investigator met resistance, the patient was asked to arch or extend her spine. The catheter was withdrawn. If resistance recurred, the patient was alternately asked to flex and extend her back until the catheter was fully removed. If these maneuvers did not result in the removal of the catheter, it was left in place until the patient was able to stand upright and fully flex and/or extend her back.

Postpartum, a masked investigator visited patients at 24 and 48 h, if still hospitalized. At these visits, the focused neurologic examination was repeated, and patients were asked about symptoms of headache and back pain. Participants were asked to rate their satisfaction with their pain relief as poor, fair, good, very good, or excellent. Women were also asked whether they would choose this method of pain control again for delivery. Each participant was contacted by telephone at 7–10 days after delivery and again at approximately 30 days after delivery. During these phone calls, patients were asked about any new neurologic symptoms, bladder or bowel problems, headache, or back pain that had developed since discharge. They were asked again whether they would choose this method of pain relief in the future. At the conclusion of the 30-day phone call, patients were told which type of catheter they received.

Sufentanil Pharmacokinetic Analysis

Sixteen patients who had agreed to participate in the main investigation and who were assigned to the CIT group were asked to participate in an additional substudy to assess maternal systemic levels and possible fetal transfer of sufentanil administered continuously by the intrathecal route. These patients signed a second consent form and agreed to have a second capped intravenous catheter placed for the purpose of blood sampling. Each of these participants had blood (5–10 ml) sampled at baseline (before medication injection); at 15,

30, 45, 60, 90, 180, 300, 480, and 720 min after injection (assuming the patient was still in labor); and at delivery. A sample was also obtained from the umbilical cord blood at delivery.

Plasma was separated from each sample by centrifuge and placed in a coded vial for storage at a minimum of −10°C. Samples were shipped on dry ice *via* overnight courier to National Medical Services Labs, Inc. (Willow Grove, PA), where sufentanil concentrations were determined by high-performance liquid chromatography with tandem mass spectrometry. D5-fentanyl was added as the internal standard to 1.0-ml aliquots of plasma. If less than 1.0 ml was available, testing was performed on dilution. The samples were diluted with water and buffered to pH 6.0 with a phosphate buffer and extracted by a solid phase procedure using Varian Bond Elute Certify® extraction columns (Varian, Inc., Palo Alto, CA). The final eluent (2% ammonium hydroxide in methanol) was evaporated and reconstituted with the high-performance liquid chromatography mobile phase. After high-performance liquid chromatography, separation samples were analyzed using a Waters Micro-Quattro LC tandem mass spectrometer (Waters Corporation, Seattle, WA) instrument with electrospray ionization. Two ion transitions were monitored for sufentanil and internal standard to assure that there were no interferences. Each analytical run was independently calibrated at concentrations of 0.1, 0.2, 1.0, 4.0, 10, and 40 ng sufentanil/ml. This method had a lower limit of quantitation of 0.1 ng/ml and intraassay coefficients of variation of 9.3 and 9.0 at 1.0 and 10 ng/ml, respectively, for sufentanil. The detection limit with this method was 0.05 ng/ml.

Sample Size Determination

A review of 32,718 epidural anesthetics (nonobstetric patients) resulted in a 0.1% incidence of transient neurologic deficits and a 0.02% incidence of permanent lesions.[18] Eleven known cases of cauda equina syndrome in an estimated worldwide 250,000 continuous spinal anesthesia procedures resulted in an estimated incidence of 0.004%. Because, given these rates, development of permanent neurologic lesions is rare for both procedures, the number of patients with the event follows a Poisson distribution.[19] Therefore, if no events are seen in a study, the upper limit of the 95% confidence interval (CI) for the possible incidence of such events is 3/n, where n is the number of patients studied.[20,21] To have sufficient statistical power to detect a greater than 1% incidence of neurologic complications related to intrathecal catheter use, 325 CIT patients were planned for enrollment. A greater than 1% incidence of neurologic complication would be unacceptable for clinical use. If, however, we assume that permanent neurologic deficits occur with the intrathecal catheter in the same rate as an epidural catheter, approximately 0.02%,[18] to detect one case of permanent deficit with an 80% power of detection using a two-tailed test would require approximately 8,000 observations of CIT labor analgesia. Therefore, after extensive discussion with the FDA about this issue, agreement was reached that demonstrating the incidence of permanent neurologic complication was less than 1% would support a premarket approval application for the 28-gauge catheter. A plan was developed for a slow reintroduction of the catheter to clinical use accompanied by postmarket surveillance of, at a minimum, the first 5,000 patients to receive the catheter.

Because the rare occurrence of permanent neurologic sequelae after epidural analgesia is established in the literature, enrollment of an equal number of epidural patients was not needed to determine a difference. The primary use of the epidural group of 100 patients was to make comparisons of efficacy measures, particularly of equivalence with respect to rate of failed or inadequate blocks and to degree of maternal satisfaction. Epidural blocks fail completely in approximately 4–5% of cases or are patchy or unilateral in approximately 12–15% of cases.[18,22,23] In a study of elderly patients undergoing lower extremity surgery, the failure rate of continuous spinal anesthesia was 1.7% as compared with 9% in the continuous epidural anesthesia group.[24] Differences of 10% in the failure and inadequate block rates for the two techniques was considered equivalent. With the sample sizes as given, and α set at 0.05 for a two-tailed test, the study had 85% or greater power to detect lack of equivalence for both complete failure and unilateral/patchy block. The incidence of PDPH was compared between the two groups. With the sample sizes as given and α set at 0.05 for a two-tailed test, the study had an 80% or greater power to detect a difference on the order of 10% *versus* 2% in PDPH.

Statistical Analysis

All analyses were based on the intention to treat. Chi-square tests (with continuity correction for small n values, as appropriate) were used to compare the groups on dichotomous and other nonnumeric variables. For numeric variables, the distribution was first assessed. Unpaired *t* tests were used if the data were normally distributed, and Mann–Whitney U tests were used if the data were nonnormal. For variables measured over time, the analysis consisted of comparisons between the groups at each time. In addition, to compare the pain scores over time, a Kaplan-Meier curve was used, with time until the first reported pain score less than 1 cm as the outcome. Ninety-five percent CIs were placed around all estimates of event rates.

Results

A total of 429 patients were enrolled in this trial (fig. 3). Of the 329 patients assigned to the CIT group, 7 did not

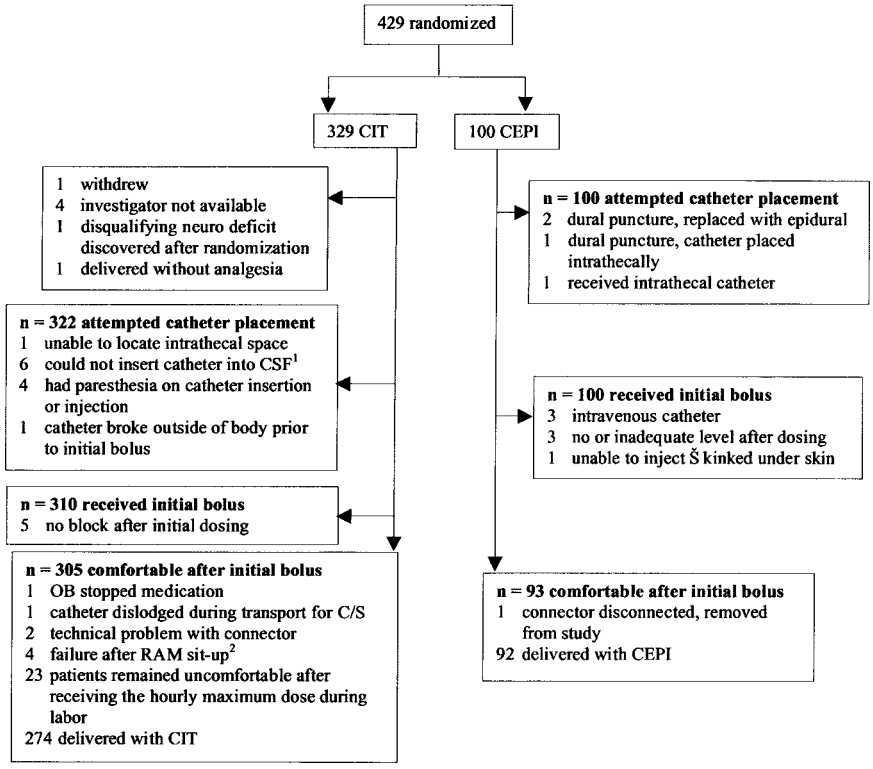

Fig. 3. Patient progress through trial. [1]In two of these patients, a manufacturing defect was noted with the stylet. This entire lot of catheters was replaced. [2]As a measure of motor strength, patients were asked to perform a modified sit-up. This test was discontinued when the catheter stopped working in four patients after they performed the test. CEPI = continuous epidural group; CIT = continuous intrathecal group; C/S = cesarean section; CSF = cerebrospinal fluid; OB = obstetrician; RAM = rectus abdominal muscle.

participate in the trial for a variety of reasons (fig. 3), leaving 322 participants who actually received CIT. To ensure the integrity of the database, all data were entered into two separate databases, which were then compared. Any discrepancies were corrected using the original data collection sheets. Two planned interim analyses were conducted when approximately one third (n = 138) and two thirds (n = 256), respectively, of the patients had completed the protocol. These analyses were requested by the FDA and served primarily to check for any significant trends between the groups in the occurrence of adverse events.

There were four enrollment protocol deviations. Two patients with Harrington rods (who received compassionate use approval from the FDA), one patient status post spinal fusion at L5–S1, and one patient status post a herniated disc in 1992 were allowed to participate in the study after neurologic evaluation found them to be stable. All four of these patients received an intrathecal catheter. There were two randomization protocol deviations. One patient who was assigned to the epidural group underwent successful placement of an intrathecal catheter. This patient was included in all CEPI statistical comparisons with the exception of the calculation comparing insertion failures between the two groups. A second epidural group patient experienced an inadvertent dural puncture and was managed as a continuous spinal. For the purpose of statistical analysis, this patient was placed in the epidural group.

Patients were demographically similar (table 1) Obstetric histories were also comparable (table 2). Oxytocin use during labor was similar, with 78% of women in both groups receiving oxytocin.

Technical Issues

There were technical issues that affected the successful placement and use of both catheters. Catheter insertion was not successful in 12 of 322 patients assigned to CIT *versus* 3 of 99 assigned to CEPI (3.7% *vs.* 3.0%; difference, 0.7%; 95% CI, −3.48% to 4.87%; $P = 0.986$). In the CIT group, investigators could not locate the intrathecal space in 1 patient. In 6 others, the space was located but investigators were unable to successfully insert the catheter. In 2 of these patients, a manufacturing defect causing the stylet to stick in the catheter was considered the cause of difficult insertion. The manufacturer replaced this lot of catheters. In the remaining 4 patients, the cause was not described. Four additional CIT patients experienced frank paresthesias either dur-

Table 1. Maternal Demographics

	Maternal Age, yr	Maternal Height, cm	Maternal Weight, kg	Cervical Dilation at Time 0, cm
CIT (n = 329)				
Mean (median)	28.97	163.8	81.41	(4)
SD (range)	5.57	8.1	14.75	(1–9)
CEPI (n = 100)				
Mean (median)	28.94	162.9	80.81	(4)
SD (range)	6.23	6.7	16.31	(1–9)

$P > 0.05$ between the two groups for each category.

CEPI = continuous epidural group; CIT = continuous intrathecal group.

Table 2. Obstetric History

	First Delivery, %	Second Delivery, %	Third or Greater Delivery, %	Previous Cesarean Delivery, %
CIT	23.7	27.4	48.9	9.9
CEPI	24.0	24.0	52.0	6.0

$P > 0.05$ between the two groups for each category.
CEPI = continuous epidural group; CIT = continuous intrathecal group.

ing insertion or with the first injection of drug. The catheter broke outside of the body before the initial dose in 1 CIT patient. These patients were considered failures, and participation in the efficacy portion of this trial ended for these 12 patients. All were followed up for safety outcomes.

Five of the remaining 310 CIT patients had no evidence of a block after the initial dosing. Three hundred five CIT patients were comfortable after the initial bolus (98%). Eight (2.6%) of these patients experienced technical challenges with the use of the catheter before delivery. Problems with the connector necessitated the removal of 2 patients during labor. In one the catheter became disconnected, and in another the connector seemed to occlude the catheter, preventing injection. Perceived difficulties with the connector led the sponsor to replace the original Tuohy-Borst style connector with a modified Tuohy-Borst connector (Medex, Dublin, OH) after approximately 5% of the patients had been enrolled. The replacement connector consisted of a softer rubber grommet with a longer contact surface area, reducing the likelihood of point occlusion of the catheter. Four other CIT patients who were initially comfortable experienced analgesic failure after performing a modified sit-up to assess abdominal muscle motor strength. This test was discontinued after the fourth patient experienced analgesic failure under the presumption that the sit-up may have caused the catheter to become dislodged. One catheter was found dislodged immediately after patient transport for cesarean delivery. One obstetrician discontinued a patient's intrathecal infusion without the consent of the study team. Twenty-three patients became uncomfortable despite receiving the maximum hourly dose of bupivacaine. None of these patients had any clinical response to the bupivacaine that would indicate that the catheter was in the intrathecal space. Therefore, the investigators believe that the catheter became dislodged from the intrathecal space in these 23 patients.

In the epidural group, 3 patients (3%) experienced inadvertent dural puncture during catheter placement. Two had their epidural replaced, and 1 was managed with the epidural catheter placed intrathecally. During the initial epidural bolus, 7 patients (7%) encountered difficulty. Three intravenous catheters were diagnosed. An additional 3 patients had no or an inadequate level. One catheter could not be injected and was removed. This catheter was found kinked under the skin upon removal. Ninety-three epidural patients (93%) were comfortable after the initial bolus. One catheter disconnected during labor, and the patient was discontinued from the study at that point.

Maternal Neurologic and Other Safety Outcomes

The primary hypothesis of this study was that there would be no difference in the incidence of neurologic complications presenting during the postpartum period in women who received continuous intrathecal analgesia compared with those who received continuous epidural analgesia. No patient developed cauda equina syndrome. There was no difference in the incidence of back pain between the two groups, with 4.6% and 3.0% (difference, 1.6%; 95% CI, −2.88% to 6.19%; $P = 0.486$) of the CIT and CEPI patients, respectively, reporting postpartum back pain. Eighteen patients (n = 17 CIT, n = 1 CEPI) had minor or transient postpartum change from baseline in their neurologic examination. The clinical course of these 18 patients is described as follows. Ten, all in the CIT group, had slightly depressed, slightly increased, or asymmetrical deep tendon reflexes at baseline, which were assessed as normal after delivery. There were no other neurologic findings in these 10 patients. Two patients, 1 in the CIT group and 1 in the CEPI group, had an abnormal gait after cesarean delivery. Both of these gait changes were assessed as related to pain from the surgery. One, in the CIT group, had a bilateral increase in her deep tendon reflexes assessed by the site investigator to be caused by severe preeclampsia. Another CIT patient had significant changes, including a decrease in the right patellar deep tendon reflex and right-sided muscle weakness. Neurologic consultation concluded that these changes were consistent with nerve compression by the fetal head during delivery. Four CIT patients, one of whom delivered by cesarean section, had minor transient changes including depression of a deep tendon reflex or a change in symmetry between the right and left side that were not believed to be significant by the site investigators and did not require neurologic consultation. Reports of postpartum weakness or loss of sensation occurred equivalently, with 4.0% and 6.0% (difference, 2.0%; 95% CI, −6.62% to 2.69%; $P = 0.395$) of the patients in the CIT and CEPI groups, respectively, having a symptom of this type during the study period. All of these reported changes were transient, and none required specific treatment. Only 1 study participant, noted above, underwent neurologic consultation for any postpartum neurologic finding. There were no permanent neurologic changes associated with either catheter used in this study.

Catheter Removal and Breakage. The intrathecal catheter was significantly more difficult to remove than the epidural catheter. Twenty-six (8.1%) and 22 (7%) intrathecal catheters were rated difficult or moderately

Table 3. Postpartum Headache

	n	Any Headache	PDPH	Nonpositional Headache	Epidural Blood Patch
CIT	322	39 (12%)	29 (9%)	10 (3%)	17 (5.3%)
CEPI	100	4 (4%)	4 (4%)	0	2 (2%)
P value		0.019	0.103	0.159	0.269

CEPI = continuous epidural group; CIT = continuous intrathecal group; PDPH = post–dural puncture headache.

Table 4. Obstetric Outcome

	n	SVD	IVD	C/D	GA
CIT	322	253 (78.6%)	24 (7.4%)	43 (13.3%)	2 (0.6%)
CEPI	100	79 (79%)	7 (7%)	14 (14%)	0

$P > 0.05$ between the two groups for each category.

C/D = cesarean delivery; CEPI = continuous epidural group; CIT = continuous intrathecal group; GA = general anesthesia; IVD = instrumented vaginal delivery; SVD = spontaneous vaginal delivery.

difficult to remove, respectively. In the CEPI group, no catheters were rated difficult to remove, and 2 (2%) were rated moderately difficult to remove (difference, 13%; 95% CI, −5.66% to 20.16%; $P < 0.001$). One intrathecal catheter was broken, inside of the patient's body, during removal. The individual who removed this catheter was not a member of the study team, had no training in the proper removal of the catheter, and had no authorization to remove the catheter. An estimated 4 cm of catheter was left in the patient's back. The patient was followed up with weekly phone calls for 1 month and then monthly phone calls for 6 months. This patient developed no symptoms or complaints from this incident.

Post–Dural Puncture Headache. There was no statistical difference in the incidence of PDPH between the two groups (table 3). Twenty-nine patients (9%) in the CIT group had signs and symptoms consistent with PDPH, compared with 4 (4.0%) in the epidural group (difference, 5%; 95% CI, −1% to 11%; $P = 0.103$). When the incidence of both positional and nonpositional headaches was compared, headache of any type occurred more frequently in the CIT group (table 3). Of the 4 epidural patients with signs and symptoms consistent with PDPH, 2 had recognized dural puncture during catheter placement. One of these 2 patients had the epidural catheter inserted intrathecally to provide labor analgesia and subsequently underwent an epidural blood patch postpartum. The other patient with an obvious dural puncture and symptoms of PDPH did not require epidural blood patch. The remaining 2 epidural patients with signs and symptoms consistent with a PDPH had no identified cause for headache. One of these patients received an epidural blood patch postpartum with complete resolution of her symptoms. The other recovered with conservative measures. One CEPI group patient who experienced a dural puncture had no postpartum headache. Seventeen (5.3%) of the CIT patients underwent epidural blood patch, compared with 2 (2%) of the epidural patients (difference, 3.3%; 95% CI, −1% to 8%; $P = 0.269$).

Respiratory Depression. Respiratory depression, defined as a respiratory rate of less than or equal to 10 breaths/min, was observed in two CIT patients. One patient had a 10-min interval of 10 breaths per minute that resolved without treatment. The second patient was undergoing cesarean delivery at 862 min from baseline. She had received a total of 68.6 μg intrathecal sufentanil at a rate of 5 μg/h during labor with a total of 7.5 mg bupivacaine, 0.25%, in three doses, for breakthrough pain. In addition, she had received 10 mg bupivacaine, 0.5%, for cesarean delivery anesthesia. Two minutes before the delivery of the baby, and in conjunction with the application of fundal pressure, her respiratory rate was observed to be 1–2 breaths/min. She received 400 μg intravenous naloxone, with prompt return of normal respirations.

Maternal Blood Pressure and Ephedrine Use. Maternal hypotension occurred infrequently. A total of 22 CIT patients (6.8%) and 8 CEPI patients (8.0%) received ephedrine during the study period (difference, 1.2%; 95% CI, −6.93% to 4.60%; $P = 0.674$).

Obstetric and Neonatal Outcomes

Obstetric. Obstetric outcomes were comparable between the two groups (table 4). Indications for cesarean delivery were comparable between the two groups, with 56% and 64% of the CIT and CEPI group cesarean delivery patients, respectively, diagnosed as "failure to progress." In the CIT group, 25.6% of the cesarean deliveries were for fetal indications and 18.6% were for maternal indications. In the CEPI group, 36% of the cesarean deliveries were for fetal indications. No patients in the CEPI group underwent cesarean delivery for a maternal indication. Four women, three of whom were in the CIT group, gave birth to twins. Two patients in the CIT group received general anesthesia for their cesarean delivery. One patient received general anesthesia due to a complete placental abruption with significant hemorrhage. The intrathecal catheter of the second patient became dislodged during transport to the operating room. This was recognized as the patient was being moved to the operating room table. No patient in the epidural group received general anesthesia.

Neonatal. Neonatal outcomes were comparable between the two groups (table 5). One neonate in the CIT group was born with Apgar scores of 0 at 1, 5, and 10 min. In this case, the mother was obese, with poor prenatal care. Delivery was complicated by severe shoulder dystocia. After 15 min of resuscitation, the neonate had an Apgar score of 3 and was transported to the neonatal intensive care unit. A second neonate in the CIT group was born with Apgar scores of 2 at 1 and 5

Table 5. Neonatal Outcome

	CIT*	CEPI†
n	325	101
Fetal bradycardia	15 (4.6%)	2 (2%)
95% CI	−1.74% to 7.01%	
Apgar score 1 min, median (range)	8 (0–10)	8 (3–9)
Apgar score 5 min, median (range)	9 (0–10)	9 (6–10)
Neonatal weight, mean (SD), g	3,499 (499)	3,390 (497)
Admission to normal newborn nursery	300 (92.3%)	92 (91%)

$P > 0.05$ between the two groups for each category.

* Includes three sets of twins. † Includes one set of twins.

CEPI = continuous epidural group; CI = confidence interval; CIT = continuous intrathecal group.

min. The mother had received 59 μg intrathecal sufentanil and 5 mg bupivacaine over approximately 8½ h and underwent spontaneous vaginal delivery. Resuscitation included a brief period of chest compressions. The baby was not intubated and did not receive naloxone. Venous umbilical cord blood values were as follows: pH, 7.29; carbon dioxide, 40.2 mmHg. Arterial umbilical cord values were as follows: pH, 7.21; carbon dioxide, 59.8 mmHg; base excess, 12.6. There was no obvious cause for the severe depression at birth. This neonate recovered fully and was discharged home with his mother 48 h later. When any neonate was admitted to a transitional or intensive care nursery, investigators were required to ask the neonatal team whether there were any indications that the maternal analgesia or anesthesia had any impact on the neonate. All investigators reported "no effect" in response to this query.

Maternal Efficacy Assessments

Two hundred seventy-four of 310 (88.4%) CIT patients who received the initial bolus of medication had adequate analgesia or anesthesia through delivery, compared with 92 of 100 CEPI patients (92%) (difference, 3.6%; 95% CI, −10.59% to 3.36%; $P = 0.31$). Pain scores were significantly lower in the CIT group for 60 min after initial drug injection (fig. 4). Using a Kaplan-Meier plot, figure 5 illustrates the percentage of women who dropped to a visual analog pain score of less than or equal to 1 cm at least once by each time point ($P < 0.001$ by log-rank test). The CIT group reported significantly higher pruritus scores for 180 min after initial drug injection (fig. 6). There were no differences in nausea scores between the two groups at any time point. Bromage motor blockade scores were higher (less blockade) in the CIT group, with 15 (4.9%) *versus* 13 (13%) of the CIT and CEPI group patients, respectively, having a Bromage score less than 4 at any point (difference, 8.1%; 95% CI, −15.00% to −3.12%; $P = 0.006$). Women in the CIT group were more satisfied with their pain relief at 24 h (table 6). There was no difference between the groups in the percentage of women who would choose the same analgesic technique for a future labor (table 6).

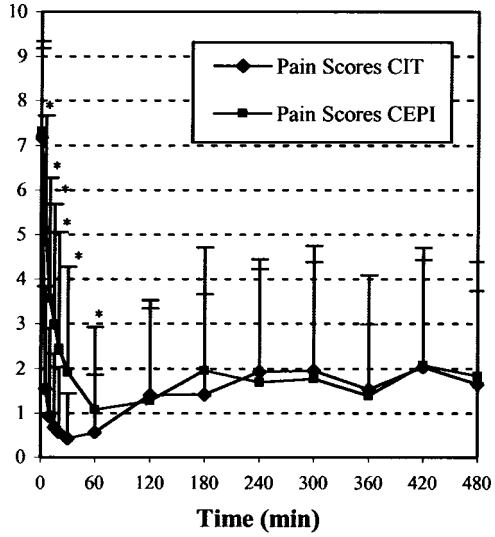

Fig. 4. Visual analog pain scores (mean ± SD). Pain scores were significantly lower in the continuous intrathecal group (CIT) *versus* the continuous epidural group (CEPI) for the first 60 min. * $P < 0.05$ between groups.

In comparing the overall efficacy of the two catheters between all women who were enrolled in this trial, fewer women in the CIT group, 274 of 329 (83%), *versus* the CEPI group, 92 of 100 (92%), delivered successfully with the assigned catheter (difference, 9%; 95% CI, −16.64% to −0.80%; $P = 0.031$). This comparison, based on intent-to-treat analysis, includes 7 women, assigned to the CIT group, who did not participate in the study (fig. 3).

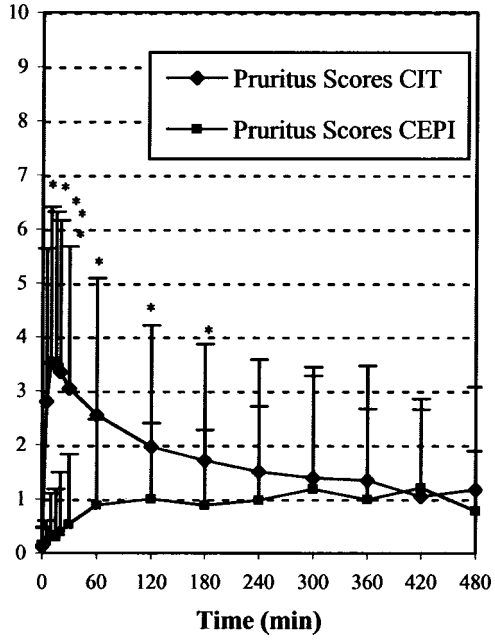

Fig. 5. Visual analog pruritus scores (mean ± SD). Pruritus scores were significantly higher in the continuous intrathecal group (CIT) *versus* the continuous epidural group (CEPI) for the first 180 min. * $P < 0.05$ between groups.

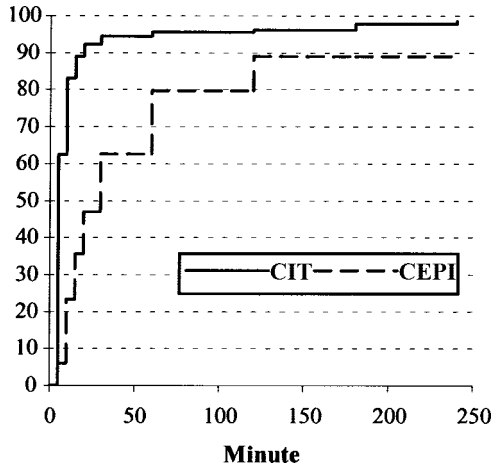

Fig. 6. Kaplan-Meier plot of the percentage of women in the continuous intrathecal group (CIT) *versus* the continuous epidural group (CEPI) who recorded a visual analog pain score less than or equal to 1 at least once by each time point. $P < 0.001$ by log-rank test.

Medication Use and Pharmacokinetic Results

Patients in the CIT received significantly less bupivacaine than the CEPI group patients ($P < 0.000$; table 7). The two groups received a comparable amount of sufentanil. A total of 16 CIT patients participated in the sufentanil pharmacokinetic substudy. No sufentanil was detected in maternal serum or cord blood serum (table 8). Limits of detection ranged from 0.05 to 0.5 ng/ml, depending on the serum sample size (table 8).

Discussion

This study found no occurrence of permanent neurologic deficit associated with the use of either catheter. Therefore, given the sample size of the CIT group, the likelihood of a permanent neurologic deficit occurring with the 28-gauge intrathecal catheter coupled with the medication regimens used in this study is less than 1%. If we assume that permanent neurologic deficits occur with the intrathecal catheter in the same rate as an epidural catheter, approximately 0.02%,[18] to detect one case of CES with an 80% power of detection using a two-tailed test would require approximately 8,000 observations of CIT labor analgesia.

Although there was no statistical difference in the incidence of PDPH, the CIT group patients showed a trend toward more PDPH. The upper limit of the 95% CI of the difference in PDPH rates suggests that we can rule out an absolute difference of 11% or more in PDPH between the two groups. Of relevance to comparing the difference in PDPH between the two groups is the 4% (4 of 100) rate of PDPH in the CEPI group. Only 2 of these 4 patients experienced recognized dural punctures. The epidural trays used for this study were new to all of the investigators and this may have contributed to this relatively high epidural PDPH rate.

Recent reports of very small groups of patients receiving intrathecal catheters have documented headache rates ranging from 0 to 78%.[25–27] In the study reporting a 78% rate of PDPH, subjects aged 18–30 yr underwent dural puncture with either a 23-gauge Crawford cutting spinal needle (catheter-through-the-needle technique) or a 27-gauge Quincke cutting spinal needle (catheter-over-the-needle technique). In the current study, a less traumatic pencil-point needle was used. In addition, intrathecal catheters remained in place for several hours in many patients. There is recent retrospective evidence that leaving an intrathecal catheter in place for 24 h after dural puncture with an 18-gauge Tuohy needle may reduce the subsequent incidence of PDPH.[15] Elucidation of the expected PDPH rate using a pencil-point needle with a 28-gauge catheter in obstetric patients, as well as approaches that may reduce that rate, will require further prospective, randomized study.

One patient during this trial required naloxone for the treatment of respiratory depression. Interestingly, this coincided with the application of fundal pressure during cesarean delivery after 14 h of labor. Although this particular patient did not participate in the sufentanil phar-

Table 6. Maternal Satisfaction with Pain Relief

	CIT	CEPI	*P* Value
24-Hour satisfaction*	n = 311	n = 98	
Median (range)	5 (1–5)	4 (1–5)	0.004
Have again? % yes			
7 days	n = 287	n = 87	
	88.9%	93.1%	0.159
30 days	n = 269	n = 84	
	90.3	95.2%	0.250

* Patients rated satisfaction as poor (1), fair (2), good (3), very good (4), or excellent (5).

CEPI = continuous epidural group; CIT = continuous intrathecal group.

Table 7. Total Medication Used during Labor by Catheter and Type of Delivery

	CIT	CEPI	*P* Value
Sufentanil, μg	n = 310	n = 100	0.183†
SVD	29.09 (19.36)	29.48 (16.25)	
IVD	33.64 (20.53)	42.16 (21.24)	
C/D	46.24 (28.24)	38.25 (21.43)	
Bupivacaine, mg	n = 284*	n = 100	<0.000†
SVD	4.39 (3.87)	53.45 (30.39)	
IVD	7.95 (4.81)	72.52 (41.6)	
C/D	9.07 (9.85)	65.89 (48.79)	

Results are mean (SD). Medication used for cesarean delivery anesthesia is *not* included in these results.

* Not all CIT group patients received bupivacaine. † *P* value for overall comparison of CIT and CEPI groups.

C/D = cesarean delivery; CEPI = continuous epidural group; CIT = continuous intrathecal group; IVD = instrumented vaginal delivery; SVD = spontaneous vaginal delivery.

Table 8. Plasma Sufentanil Levels (ng/ml)/Limit of Detection (ng/ml)

Patient No.	Time 0	5 min	30 min	45 min	60 min	90 min	3 h	5 h	8 h	12 h	Maternal Serum at Delivery	Umbilical Cord Blood	Sufentanil Infusion Rate during First 4 h, μg/h
78	0/0.05	0/0.05	0/0.1	0/0.05	0/0.1							0/0.1	5
90	0/0.05	0/0.05	0/0.05	0/0.05	0/0.05	0/0.2					0/0.05	0/0.1	5
91	0/0.05	0/0.05	0/0.05	0/0.05	0/0.1	0/0.05	0/0.05	0/0.05			0/0.1	0/0.5	5
81	0/0.2	0/0.2	0/0.2	0/0.2	0/0.2	0/0.2	0/0.2	0/0.2	0/0.2	0/0.20	0/0.2	0/0.2	7
104	0/0.1	0/0.1	0/0.1	0/0.1	0/0.1	0/0.1	0/0.1	0/0.1			0/0.1	0/0.1	7
106	0/0.1	0/0.1	0/0.1	0/0.1	0/0.1	0/0.1	0/0.1	0/0.1			0/0.1	0/0.1	7
107	0/0.1	0/0.1	0/0.1	0/0.1	0/0.1	0/0.1	0/0.1				0/0.1	0/0.1	7
108	0/0.1	0/0.1	0/0.1	0/0.1	0/0.1	0/0.1					0/0.1	0/0.1	7
109	0/0.1	0/0.1	0/0.1	0/0.1	0/0.1	0/0.1	0/0.1	0/0.1	0/0.1		0/0.1	0/0.1	7
110	0/0.05	0/0.05	0/0.05	0/0.05	0/0.05	0/0.05					0/0.05	0/0.05	7
3047	0/0.05	0/0.05	0/0.05	0/0.05	0/0.05	0/0.05	0/0.05	0/0.05	0/0.05		0/0.05	0/0.05	7
3048	0/0.05	0/0.05	0/0.05	0/0.05	0/0.05	0/0.05	0/0.05				0/0.05	0/0.05	7
3049	0/0.05	0/0.05	0/0.05	0/0.05	0/0.05	0/0.05	0/0.05	0/0.05			0/0.05	0/0.05	7
3050	0/0.05	0/0.05	0/0.05	0/0.05	0/0.05	0/0.05	0/0.05	0/0.05			0/0.05	0/0.05	7
3052	0/0.05	0/0.05	0/0.05	0/0.05	0/0.05	0/0.05	0/0.05	0/0.05	0/0.05		0/0.05	0/0.05	7
3062	0/0.2	0/0.2	0/0.2	0/0.2	0/0.2	0/0.2					0/0.2	0/0.2	7

macokinetic substudy, another patient had no detectable systemic sufentanil levels after 12 h of sufentanil infusion. This suggests that the respiratory depression was caused by intrathecal, rather than systemic, sufentanil. In ewes, intrathecal sufentanil is capable of migrating spontaneously from the lower lumbar space to the brainstem.[28] This raises the question of whether the application of fundal pressure can raise spinal fluid pressure sufficiently that a depot of medication in the spinal space could undergo enhanced cephalad spread. The incidence of respiratory depression after intrathecal sufentanil has been estimated at approximately 1 in 5,000.[29] In our case, the respiratory depression responded immediately to a single dose of intravenous 400 μg naloxone.

Technical difficulties such as locating the proper space, insertion, drug injection, and removal affected the use of both catheters. Although all principal investigators had used the 28-gauge catheter before its removal from the market in 1992, at the time this trial began enrolling patients, approximately 5 yr had passed since any investigator had placed a catheter in a patient. This may have contributed to early difficulties with catheter insertion, use of the connector, and breakage outside of the body. The incidence of insertion difficulties was not different between the catheters; however, intrathecal catheters were significantly more difficult to remove. One intrathecal catheter broke inside the body during removal. This catheter was removed by an individual who was neither authorized to remove the catheter nor trained in the proper removal technique. This event underscores both the importance of proper training in the use of any new device and the fact that the tensile strength of any catheter decreases with size. By example, the maximal tensile strength of a 22-gauge polyamide catheter is 29.56 ± 1.56 N, compared with 5.07 ± 0.59 N for a 28-gauge nylon catheter, at room temperature.[30]

Women in the CIT group experienced better pain control for the first hour; however, pain scores in both groups were low. Efficacy measures were secondary outcomes in this trial meaning that the randomization was not stratified for variables that might impact maternal comfort after the initiation of neuraxial labor analgesia, such as parity, cervical dilation, and oxytocin use. Because there were no differences in these variables between the two groups, the CIT group patients may have experienced better analgesia than the CEPI group during the first hour. It seems unlikely that the CEPI group patients had inadequate analgesia because they were able to receive 0.25% bupivacaine 15 min after the initial bolus dose.

There was no statistical difference between the two groups in the number of patients who received the initial bolus of medication and whose catheter functioned adequately for the entire labor and delivery. However, in the CIT group, there were 23 patients who remained uncomfortable after receiving the hourly maximum dose of sufentanil and bupivacaine and had to be dropped from the study at that point. The investigators believe that either the intrathecal catheter became dislodged in these patients or their medication requirements exceeded the allowed maximum doses. In the 23 patients who received the maximum dose of 7.5 mg bupivacaine, there was little or no evidence of intrathecal drug injection, such as maternal motor blockade. Therefore, the most likely explanation is that the catheters in these patients became dislodged. Further supporting this hypothesis, the average total bupivacaine dose for women undergoing spontaneous vaginal delivery was 4.39 mg. Therefore, if the entire supplemental bupivacaine dose of 7.5 mg was delivered to the intrathecal space, it is likely that most women would be comfortable. Because

the primary purpose of this study was to assess safety, the dosing regimens were strictly prescribed. For example, only sufentanil was infused continuously in the CIT group with bupivacaine bolus doses administered as needed. Some patients may have benefited from an infusion consisting of both bupivacaine and sufentanil. Elucidating optimal methods for securing a 28-gauge catheter as well as the most advantageous analgesic regimens await future studies.

When comparing the overall analgesic effectiveness of the two catheters between all women enrolled in the trial, the intrathecal catheter was less effective. This comparison includes seven women who were assigned to the CIT group but ultimately did not participate in the trial. We cannot exclude the possibility that, had this group of women received the catheter, they would not have been problematic in some way associated with catheter failure.

Increased pruritus in the CIT group was consistent with this known and well-documented side effect of intrathecal opioids. The occurrence of less motor blockade in the CIT group, despite bolus doses of bupivacaine in the majority of patients, was a reassuring finding. Future studies can consider whether this may impact obstetric outcome. Maternal satisfaction at 24 h was higher in the CIT group; however, similar numbers of women would choose the same technique again for a future labor.

This study has determined that providing intrathecal labor analgesia with sufentanil and bupivacaine *via* a 28-gauge catheter has an incidence of neurologic complication that is less than 1% and produces better initial pain relief and higher maternal satisfaction compared with epidural analgesia. Intrathecal catheters are associated with a trend toward more PDPH and are more difficult to remove. Additional, substantially larger studies are needed to better define the expected rate of permanent neurologic complications and assess how this compares with the 0.02% rate associated with the continuous epidural technique. Larger studies would also improve our understanding of the expected rate of PDPH, optimal analgesic regimens, and patient populations who can benefit the most from this technique. However, future access to this catheter is unclear. At the time of this writing, the study sponsor has no plans to complete the FDA submission process that would enable this catheter to be marketed in the United States. Therefore, if this challenge cannot be overcome, investigative work will need to continue outside of the United States in countries where small-gauge intrathecal catheters continue to be available.

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References

1. Carpenter SL, Ceravolo AJ, Foldes FF: Continuous-drop subarachnoidal block with dilute procaine solution for labor and delivery. Am J Obstet Gynecol 1951; 61:1277–84
2. Benedetti C, Tiengo M: Continuous subarachnoid analgesia in labour. Lancet 1990; 335:225
3. Johnson MD, Hurley RJ, Gilbertson LI, Datta S: Continuous microcatheter spinal anesthesia with subarachnoid meperidine for labor and delivery. Anesth Analg 1990; 70:658–61
4. Huckaby T, Skerman JH, Hurley RJ, Lambert DH: Sensory analgesia for vaginal deliveries: A preliminary report of continuous spinal anesthesia with a 32-gauge catheter. Reg Anesth 1991; 16:150–3
5. Honet JE, Arkoosh VA, Norris MC, Huffnagle HJ, Silverman NS, Leighton BL: Comparison among intrathecal fentanyl, meperidine, and sufentanil for labor analgesia. Anesth Analg 1992; 75:734–9
6. Arkoosh VA: Continuous spinal analgesia and anesthesia in obstetrics. Reg Anesth 1993; 18:402–5
7. Rigler ML, Drasner K, Krejcie TC, Yelich SJ, Scholnick FT, DeFontes J, Bohner D: Cauda equina syndrome after continuous spinal anesthesia. Anesth Analg 1991; 72:275–81
8. US Food and Drug Administration: FDA Safety Alert: Cauda Equina Syndrome Associated with the Use of Small-bore Catheters in Continuous Spinal Anesthesia. May 29, 1992
9. Lambert LA, Lambert DH, Strichartz GR: Irreversible conduction block in isolated nerve by high concentrations of local anesthetics. ANESTHESIOLOGY 1994; 80:1082–93
10. Drasner K, Sakura S, Chan VWS, Bollen AW, Ciriales R: Persistent sacral sensory deficit induced by intrathecal local anesthetic infusion in the rat. ANESTHESIOLOGY 1994; 80:847–52
11. Sakura S, Chan VWS, Ciriales R, Drasner K: The addition of 7.5-percent glucose does not alter the neurotoxicity of 5-percent lidocaine administered intrathecally in the rat. ANESTHESIOLOGY 1995; 82:236–40
12. Lambert DH, Hurley RJ: Cauda equina syndrome and continuous spinal anesthesia. Anesth Analg 1991; 72:817–19
13. Rigler ML, Drasner K: Distribution of catheter-injected local anesthetic in a model of the subarachnoid space. ANESTHESIOLOGY 1991; 75:684–92
14. Robinson RA, Stewart SFC, Myers MR, Lien LF, Rinaldi JR, Swisher JL, Drasner K: *In vitro* modeling of spinal anesthesia. ANESTHESIOLOGY 1994; 81: 1053–60
15. Ayad S, Demian Y, Narouze SN, Tetzlaff JE: Subarachnoid catheter placement after wet tap for analgesia in labor: Influence on the risk of headache in obstetric patients. Reg Anesth Pain Med 2003; 28:512–5
16. Gravenstein N, Blackshear RH, Wissler R: An approach to spinal or epidural catheters that are difficult to remove (letter). ANESTHESIOLOGY 1991; 75:544
17. Boey SK, Carrie LES: Withdrawal forces during removal of lumbar epidural catheters. Br J Anaesth 1994; 73:833–5
18. Dawkins CJM: An analysis of the complications of extradural and caudal block. Anaesthesia 1969; 24:554–63
19. Altman DG: Practical Statistics for Medical Research. London, Chapman & Hall, 1999, pp 66–71
20. Hanley JA, Lippman-Hand A: If nothing goes wrong, is everything all right? JAMA 1983; 249:1743–5
21. Rumke CL: Implications of the statement: No side effects were observed. N Engl J Med 1975; 292:372–3
22. Hollmen A, Jouppila R, Pihlajaniemi R, Karvonen P, Sjostedt E: Selective lumbar epidural block in labour: A clinical analysis. Acta Anaesth Scand 1977; 21:174–81
23. Crawford JS: The second thousand epidural blocks in an obstetric hospital practice. Br J Anaesth 1972; 44:1277–87
24. Sutter PA, Gamulin Z, Forster A: Comparison of continuous spinal and continuous epidural anaesthesia for lower limb surgery in elderly patients: A retrospective study. Anaesthesia 1989; 44:47–50
25. Whittaker S: Continuous spinal analgesia/anaesthesia in obstetrics. Int J Obstet Anes 2007; 16:183
26. Imbelloni LE, Gouveia MA: Continuous spinal anesthesia with Spinocath® for obstetric analgesia (letter). Int J Obstet Anesth 2006; 15:171–2
27. Gosch UW, Hueppe M, Hallschmid M, Born J, Schmucker P, Meier T: Post-dural puncture headache in young adults: Comparison of two small-gauge spinal catheters with different needle design. Br J Anaesth 2005; 94:657–61
28. Swenson JD, Owen J, Lamoreaux W, Viscomi C, McJames S, Cluff M: The effect of distance from injection site to the brainstem using spinal sufentanil. Reg Anesth Pain Med 2001; 26:306–9
29. Ferouz F, Norris MC, Leighton BL: Risk of respiratory arrest after intrathecal sufentanil. Anesth Analg 1997; 85:1088–90
30. Deusch E, Benrath J, Weigl L, Neumann K, Kozek-Langenecker SA: The mechanical properties of continuous spinal small-bore catheters. Anesth Analg 2004; 99:1844–7

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