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Epidural Anesthesia for Cesarean Section:

A Comparison of Bupivacaine, Chloroprocaine, and Etidocaine

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The authors studied three groups of patients undergoing elective cesarean section during lumbar epidural anesthesia with bupivacaine, 0.75 per cent (15 patients), chloroprocaine, 3 per cent (15 patients) or etidocaine, 1 per cent (ten patients). Excellent sensory and motor block were obtained with chloroprocaine and bupivacaine; sensory anesthesia was inadequate with etidocaine in most patients. Onset of anesthesia, induction–delivery interval, and stay in the recovery room were all longer with bupivacaine when compared with chloroprocaine. Fetal outcomes, as determined by Apgar scores, acid–base status and neurobehavioral testing, were equally good in all groups. At delivery, fetal/maternal concentration ratio of bupivacaine was 0.31 and that of etidocaine, 0.25. The umbilical artery–umbilical vein blood concentration difference for etidocaine was significantly higher than that for bupivacaine. Excellent clinical results were obtained using either bupivacaine, 0.75 per cent, alone, or chloroprocaine, 3 per cent, for induction and maintenance of anesthesia, supplemented with bupivacaine, 0.25 per cent, before removal of the catheter. (Key words: Anesthesia, obstetric. Anesthetics, local: bupivacaine; chloroprocaine; etidocaine. Anesthetic techniques: epidural; peridural. Fetus: Apgar score: neurobehavioral score.)

ALTHOUGH THE USE of epidural anesthesia for delivery by cesarean section is increasing, the issue of the choice of appropriate local anesthetic agent remains unsettled. Bupivacaine,[1–4] etidocaine,[5,6] and chloroprocaine[7] have all been advocated, but no detailed comparative study by one group has been reported. Our aim was to compare bupivacaine, 0.75 per cent, chloroprocaine, 3 per cent, and etidocaine, 1 per cent, in epidural anesthesia for elective cesarean section. We evaluated the onset and quality of the block in the mother and effects in the newborn.

Methods

Forty healthy parturients, without maternal or fetal complications, undergoing elective primary or repeat cesarean section at term, were selected at random, and informed consent was obtained. Fifteen patients were each given bupivacaine or chloroprocaine and ten received etidocaine. The same technique of epidural anesthesia was used in every case. With an intravenous infusion of dextrose, 5 per cent, in lactated Ringer's solution, established, each patient was placed in the left lateral decubitus position. An epidural catheter was inserted at the L2–3 interspace and directed caudad 1 to 2 cm. A test dose of 2 ml of local anesthetic was injected. The patient was then placed in the supine semi-sitting position, with the head up at a 35–40-degree angle. After 3–5 min had elapsed without evidence of subarachnoid or intravascular injection, the remainder of the local anesthetic agent was administered. The dose was chosen to provide analgesia to a level of T4–6, taking into consideration the height of the patient. Epinephrine-containing solutions were not used.

In accordance with our previously described protocol,[4] during the first 10 min, all patients were kept supine and semi-sitting with the uterus manually displaced to the left. Thereafter, during the development of full surgical anesthesia, the patients were kept in the left lateral decubitus position with the head up at the same angle. The interval between the injection of the final dose and the spread of sensory anesthesia to T6 was recorded as the time to onset of surgical anesthesia.

In every patient, 1 liter of intravenous fluid was infused before induction and a second liter of fluid infused slowly thereafter. Maternal blood pressure was measured every minute for the first 15 min and every 3 min thereafter. Fetal heart rate was monitored by auscultation at 5-min intervals. Maternal hypotension was considered to be present whenever systolic blood pressure decreased more than 30 torr, or to less than 100 torr. Hypotension was corrected by increasing the rate of intravenous fluid infusion.

With the onset of surgical anesthesia, the patient was taken to the operating room. All parturients were tilted to the left with a blanket roll under the right hip and torso until the delivery of the baby. In the operating room, all mothers received oxygen through a plastic face mask at a flow rate of 6 l/min. The time from injection of the final dose of local anesthetic to delivery of the infant was recorded as the induction–

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delivery (I-D) interval. At delivery, samples of blood from a maternal radial artery, an antecubital vein and the umbilical artery and vein from a doubly-clamped segment of umbilical cord were collected. Blood-gas and *p*H values of all samples were immediately determined in duplicate with a Radiometer® microelectrode system. Base deficit was calculated using the Siggaard-Andersen nomogram.[8] In ten of the parturients who received bupivacaine and five who received etidocaine, the concentrations of local anesthetic in maternal blood and fetal blood were determined by a previously described gas chromatographic technique sensitive to concentrations of local anesthetics as low as 0.02 μg/ml ± 10 per cent.[9] Apgar scores at 1 and 5 min were assigned by a pediatrician. Neurobehavioral testing, according to a previously described protocol,[10] was performed on all infants between 2 and 4 hours of age by the same person, who was not involved in the anesthetic management of the patients.

All patients were observed for at least an hour in the recovery room. Thereafter, the patients were discharged as soon as they were able to flex their knees and lift their hips, unless there was a surgical complication necessitating continued observation in the recovery room. Time of stay in the recovery room was recorded from the time the patient arrived in the recovery room until she was discharged.

The overall quality of the block was determined by assignment of a score by the anesthesiologist, based upon observation and questioning of the patient. A score of 3, or excellent, was given when the parturient needed no supplemental drug; 2, or satisfactory, when an analgesic or sedative was needed; 1, or unsatisfactory, when discomfort following delivery was so intense that general anesthesia was necessary. Intravenous medication was offered to every patient who complained of discomfort. The surgeon scored the adequacy of abdominal muscle relaxation on a three-point scale: 3, excellent; 2, satisfactory; 1, unsatisfactory.

In the case of chloroprocaine, the block was reinforced routinely at 40-min intervals, based on our clinical experience. In the first four patients, we were struck by the very abrupt nature with which chloroprocaine anesthesia terminated, unlike anesthesia with either bupivacaine or etidocaine, resulting in severe discomfort for the patients in the recovery room. Therefore, we altered our protocol so that the remaining 11 of 15 patients, all of whom had had one reinjection of chloroprocaine during the operative procedure, received bupivacaine, 0.25 per cent, 8–10 ml, prior to removal of the catheter in the operating room. Reinforcement was not necessary in the bupivacaine- and etidocaine-treated groups.

TABLE 1. Clinical Results (Mean ± SE)

	Bupivacaine (n = 15)	Chloroprocaine (n = 15)	Etidocaine (n = 10)
Total initial dose			
mg	128 ± 8	480 ± 20	220 ± 10
ml	17 ± 1	16 ± 1	22 ± 1
Onset of anesthesia (min)	35 ± 1	15 ± 1*	15 ± 1*
Induction–delivery interval (min)	53 ± 3	36 ± 2*	38 ± 2*
Sensory anesthesia score of 3 (number of patients)	15	14	3*
Muscle relaxation score of 3 (number of patients)	15	15	10
Hypotension (number of patients)	1	3	1

* $P < 0.001$.

All data were analyzed for statistical significance by computation of multiple correlation coefficients, t tests, or chi-square method where appropriate.

Results

There was no significant difference among the three groups with respect to maternal age (mean = 29 years), height (64 inches), or weight (159 pounds), or infant gestational age (40 weeks) or weight (3,400 g). Onset of surgical anesthesia was significantly slower, and hence the induction–delivery interval was longer, in the bupivacaine-treated group (table 1). Excellent anesthesia was achieved in all patients receiving bupivacaine and in 14 of 15 given chloroprocaine. In all ten patients who received etidocaine, anesthesia was adequate to permit delivery of the infant. Following delivery, because of increasing discomfort, two patients needed supplementation with intravenously administered narcotics and diazepam; five patients needed general anesthesia. Excellent muscle relaxation was reported for all patients in the three groups.

Hypotension was an infrequent event. In no case did it last longer than 2 min, nor was any vasopressor drug needed. Since acid–base data for those patients who had had episodes of hypotension did not differ from the remainder, the data were combined (table 2). There was no significant difference among the three groups at delivery.

There was a higher concentration difference for local anesthetic between umbilical-vein blood and umbilical-artery blood for etidocaine as compared with bupivacaine (table 3). All infants had Apgar scores of 7 or higher at both 1 and 5 min of age, had uncomplicated hospital stays, and were discharged with their mothers. Neurobehavioral tests of the neo-

TABLE 2. Maternal and Neonatal Acid–Base Data (Mean ± SE)

	Bupivacaine (n = 15)	Chloroprocaine (n = 15)	Etidocaine (n = 10)
Maternal arterial (MA) blood			
*p*H	7.42 ± 0.01	7.43 ± 0.01	7.43 ± 0.01
P_{O_2} (torr)	196 ± 6	180 ± 5	184 ± 8
P_{CO_2} (torr)	31 ± 1	30 ± 1	33 ± 1
Base deficit (mEq/l)	2.0 ± 0.5	1.8 ± 0.4	0.9 ± 0.8
Umbilical-vein (UV) blood			
*p*H	7.35 ± 0.01	7.35 ± 0.01	7.35 ± 0.01
P_{O_2} (torr)	34 ± 2	32 ± 1	36 ± 2
P_{CO_2} (torr)	40 ± 1	41 ± 1	43 ± 2
Umbilical-artery (UA) blood			
*p*H	7.31 ± 0.01	7.29 ± 0.01	7.30 ± 0.01
P_{O_2} (torr)	18 ± 1	17 ± 1	22 ± 2
P_{CO_2} (torr)	51 ± 2	52 ± 1	53 ± 3
Base deficit (mEq/l)	3.0 ± 0.6	3.5 ± 0.5	3.1 ± 0.8
Δ Base deficit: UA base deficit − MA base deficit (mEq/l)	1.0 ± 0.5	1.7 ± 0.4	2.2 ± 0.8

nates showed no significant difference in performances among the three groups. Eighty to 90 per cent of the neonates in each group had high scores in all the test variables; none was markedly depressed. There was no significant difference among the groups.

No patient in any of the groups needed reinforcement of the block before delivery of the infant. Hence, all of the acid–base data, blood levels of the local anesthetics, and infant scores reflect exposure to a single maternal induction dose of local anesthetic.

The late injection of bupivacaine, 0.25 per cent, did not alter the recovery room stay, since it provided continuation of sensory anesthesia without motor involvement. Despite the addition of bupivacaine, time of stay in the recovery room was shortest in the chloroprocaine-treated group, with all patients discharged within 60 min of admission. By contrast, patients who had received only bupivacaine remained in the recovery room for two to three hours.

Discussion

There appear to be distinct advantages to the use of bupivacaine, chloroprocaine, or etidocaine for epidural anesthesia in the obstetric patient, when compared with lidocaine or mepivacaine. A detailed review of this subject has recently been presented by Ralston and Shnider.[11] One factor is the association between the use of lidocaine or mepivacaine and modification of neurobehavioral performance in the newborn[10,12]; such effects have not been found with bupivacaine[3,13,14] or chloroprocaine.[15] Another is the relatively low blood levels of bupivacaine or etidocaine in the fetus as a result of the high degree of binding of these agents to maternal plasma proteins. Finally, one would expect minimal transfer from mother to fetus of chloroprocaine, owing to its rapid hydrolysis in maternal blood.

TABLE 3. Local Anesthetic Concentrations (Mean ± SE)

	Bupivacaine (0.75 Per Cent) (n = 10)	Etidocaine (1 Per Cent) (n = 5)
Maternal-vein (MV) blood (μg/ml)	0.41 ± 0.05	0.60 ± 0.03
Umbilical-vein (UV) blood (μg/ml)	0.12 ± 0.01	0.15 ± 0.01
Umbilical-artery (UA) blood (μg/ml)	0.10 ± 0.02	0.07 ± 0.01
UV/MV concentration ratio	0.29 ± 0.06	0.25 ± 0.01
UV-UA concentration difference (μg)	0.02 ± 0.01	0.08 ± 0.01*

* $P < 0.005$.

The present study compares results and effects of bupivacaine, chloroprocaine, and etidocaine in patients undergoing elective repeat cesarean deliveries with lumbar epidural anesthesia. The most striking finding was the inadequate sensory block provided by etidocaine, 1 per cent, despite the use of a relatively high dose. Lund *et al.*[5] reported adequate sensory anesthesia in 78 of 81 patients who were given etidocaine, 1 per cent, 250 mg, with or without epinephrine, 1:200,000, despite the fact that an unspecified number of their patients needed supplementation with thiamylal, 100–200 mg. Bromage *et al.*,[6] who used etidocaine, 1 per cent, with epinephrine, 1:200,000, in doses ranging from 140 to 225 mg, reported the need for supplemental analgesia in 12 of their 15 patients. The data strongly suggest that etidocaine is not a reliable anesthetic for use in epidural block for cesarean delivery.

By contrast, we[4] and others[1–3] have reported excellent results with bupivacaine, confirmed by the data in the present study. In addition, we have found that similar results can also be obtained with chloroprocaine, as previously reported.[7] Our comparison of bupivacaine with chloroprocaine revealed no difference in Apgar scores, acid–base data, or neuro-

behavioral performances in the newborn, all within normal expected limits for both drugs.

Our results clearly differ from those recently reported by Wright and his associates,§ who found significantly more maternal hypotension and fetal acidosis with chloroprocaine, compared with bupivacaine. No explanation for these differences is readily apparent. Chloroprocaine has the advantage of a quicker onset of action and hence a shorter induction–delivery interval than bupivacaine. The average induction–delivery interval with bupivacaine, 0.75 per cent, in the present series (53 min) is not greatly different from those reported by others (42 min,[3] 50 min,[1] 55 min§). However, disadvantages of chloroprocaine are the abrupt termination and short duration of its action, which, in our experience, necessitated reinforcement every 40 min. The injection of a small amount of bupivacaine, 0.25 per cent (8–10 ml), into the epidural space just before removal of the catheter resulted in good postoperative pain relief in the recovery room without prolonged patient stay, a drawback with the use of bupivacaine alone.

Our study also confirms those of others[1,3,5,6] in finding relatively low fetal/maternal concentration ratios for both bupivacaine and etidocaine. Indeed, our values of 0.29 and 0.25, respectively, are even lower than those reported by Magno *et al.* (0.41 for bupivacaine),[1] Lund *et al.* (0.38 for etidocaine without epinephrine),[5] and Bromage *et al.* (0.35 for etidocaine with epinephrine).[6] These relatively low concentrations in fetal blood are probably the result of the high degree of binding of these two drugs to maternal plasma proteins. In addition, the uptake of these two highly lipid-soluble local anesthetics into fetal tissues may keep the blood levels low.[11]

Our finding of a significantly higher umbilical vein–umbilical artery concentration difference with etidocaine (0.08 μg) as compared with bupivacaine (0.02 μg) may have been the result of the shorter induction–delivery interval in the case of etidocaine, with less time for equilibration between mother and fetus as well as within the fetus. It may also reflect the higher lipid solubility of etidocaine, which may result in greater uptake by the fetal tissues and lower levels in umbilical-artery blood. Both of these factors should, at least theoretically, contribute to the observed difference.

Our data suggest that excellent results with epidural anesthesia for cesarean section can be obtained through the use of either chloroprocaine or bupivacaine. With bupivacaine, 0.75 per cent, alone, onset of anesthesia is slower, induction–delivery interval longer, and stay in the recovery room longer. By contrast, the use of chloroprocaine, 3 per cent, for induction and maintenance of anesthesia, with the addition of a small dose of bupivacaine, 0.25 per cent, at the end of the surgical procedure, provides quicker onset of block, shorter induction–delivery interval, and shorter recovery room stay. Both techniques yield excellent anesthesia and infant outcomes.

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