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Does Early Administration of Epidural Analgesia Affect Obstetric Outcome in Nulliparous Women Who Are in Spontaneous Labor?

David H. Chestnut, M.D., Joan M. McGrath, M.D.,† Robert D. Vincent, Jr., M.D.,‡ Donald H. Penning, M.D.,‡ Won W. Choi, M.D.,§ James N. Bates, M.D., Ph.D.,# Claude McFarlane, M.D.†*

Background: **Some studies suggest that epidural analgesia prolongs labor and increases the incidence of cesarean section, especially if it is administered before 5 cm cervical dilation. The purpose of the current study was to determine whether early administration of epidural analgesia affects obstetric outcome in nulliparous women who are in spontaneous labor.**

Methods: **Informed consent was obtained from 344 healthy nulliparous women with a singleton fetus in a vertex presentation, who requested epidural analgesia during spontaneous labor at at least 36 weeks' gestation. Each patient was randomized to receive either early or late epidural analgesia. Randomization occurred only after the following conditions were met: (1) the patient requested pain relief at that moment, (2) a lumbar epidural catheter had been placed, and (3) the cervix was at least 3 cm but less than 5 cm dilated. Patients in the early group immediately received epidural bupivacaine analgesia. Patients in the late group received 10 mg nalbuphine intravenously. Late-group patients did not receive epidural analgesia until they achieved a cervical dilation of at least 5 cm or until at least 1 h had elapsed after a second dose of nalbuphine. Ten of the 344 patients were excluded because of a protocol violation or voluntary withdrawal from the study.**

Results: **Early administration of epidural analgesia did not increase the incidence of oxytocin augmentation, prolong the interval between randomization and the diagnosis of complete cervical dilation, or increase the incidence of malposition of the vertex at delivery. Also, early administration of epidural analgesia did not result in an increased incidence of cesarean section or instrumental vaginal delivery. Seventeen (10%) of 172 women in the early group and 13 (8%) of 162 women in the late group underwent cesarean section (relative risk for the early group 1.22; 95% confidence interval 0.62–2.40). Patients in the early group had lower pain scores between 30 and 150 min after randomization. Infants in the late group had lower umbilical arterial and venous blood *p*H and higher umbilical venous blood carbon dioxide tension measurements at delivery.**

Conclusions: **Early administration of epidural analgesia did not prolong labor, increase the incidence of oxytocin augmentation, or increase the incidence of operative delivery, when compared with intravenous nalbuphine followed by late administration of epidural analgesia, in nulliparous women who were in spontaneous labor at term. (Key words: Anesthetic techniques: epidural. Anesthetics, local: bupivacaine. Opioids: nalbuphine. Pregnancy.)**

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* Professor of Anesthesia and Obstetrics and Gynecology.

† Associate in Anesthesia.

‡ Assistant Professor of Anesthesia.

§ Professor of Anesthesia.

Associate Professor of Anesthesia.

Received from the Department of Anesthesia and the Department of Obstetrics and Gynecology, University of Iowa College of Medicine, Iowa City, Iowa. Accepted for publication March 14, 1994.

Reprints will not be available. Address correspondence to Dr. Chestnut: Department of Anesthesiology, University of Alabama at Birmingham, 619 South 19th Street, Birmingham, Alabama 35233.

EPIDURAL analgesia during labor is associated with an increased risk of prolonged labor and operative delivery (*i.e.*, cesarean section or instrumental vaginal delivery). It is unclear whether there is a cause-and-effect relationship between the use of epidural analgesia and prolonged labor or operative delivery. Some physicians contend that epidural analgesia prolongs the first stage of labor and increases the likelihood that the patient will require oxytocin augmentation, especially if it is administered during the latent phase.[1–3] Two studies suggested that administration of epidural analgesia before 5 cm cervical dilation increases the risk of cesarean section in nulliparous women.[4,5] In a previous study, we observed that early administration of epidural analgesia did not prolong labor or increase the incidence of operative delivery, when compared with intravenous nalbuphine followed by late administration of epidural analgesia, in nulliparous women who were receiving intravenous oxytocin for induction or augmentation of labor.[6] The purpose of the current study was to determine whether early administration of epidural analgesia

affects obstetric outcome in nulliparous women who are in spontaneous labor.

Materials and Methods

The protocol was approved by the University of Iowa institutional review board for research involving human subjects. Informed consent was obtained from healthy, nulliparous women with a singleton fetus in a vertex presentation, who requested epidural analgesia during spontaneous labor at no sooner than 36 weeks' gestation, between January 1, 1990, and December 31, 1993. Exclusion criteria included (1) preeclampsia, (2) insulin-dependent diabetes mellitus, (3) estimated fetal weight 4,500 g or more, (4) prior or planned administration of oxytocin, and (5) a cervical dilation of 5 cm or more.

A patient was randomized to one of two groups by opening a sealed, opaque envelope that contained the identity of the group assignment. The envelopes were numbered, and the group assignments were made according to a computer-generated table of random numbers.

Each patient was randomized to receive either early or late epidural analgesia. A patient was randomized only after the following conditions were met: (1) the patient requested pain relief at that moment; (2) a 20-G epidural catheter had been placed *via* the L3–L4 interspace; and (3) the cervix was at least 3 cm but less than 5 cm dilated, according to a vaginal examination performed during the 30 min before opening the randomization envelope. Time 0 was the time that the randomization envelope was opened.

At time 0, patients in the early group received a 500-ml bolus of lactated Ringer's solution intravenously. Five minutes after time 0, patients in the early group received 3 ml 1.5% lidocaine with epinephrine *via* the epidural catheter. At 10 min, patients in the early group received 5 ml 0.25% bupivacaine *via* the epidural catheter. Subsequently, these patients received additional boluses of 0.25% bupivacaine as needed to maintain analgesia and to maintain a sensory level of at least T10. When the cervix was at least 5 cm dilated, each patient received a continuous epidural infusion of 0.125% bupivacaine at an initial rate of 12 ml/h. The cephalad dermatomal level of anesthesia was determined by pinprick at 30-min intervals. The anesthesiologist adjusted the epidural infusion rate to maintain satisfactory analgesia while minimizing motor block and optimizing expulsive efforts during the second stage of labor.

Five minutes after time 0, patients in the late group received 10 mg nalbuphine intravenously. Late-group patients could receive a second dose of nalbuphine, on request, at least 1 h after the first dose. Late-group patients did not receive epidural analgesia until they achieved a cervical dilation of at least 5 cm or until at least 1 h had elapsed after the second dose of nalbuphine. (The latter criterion was included as a rescue alternative.) At that time, late-group patients received a 500-ml bolus of lactated Ringer's solution intravenously. Subsequently, epidural analgesia was achieved and maintained using a protocol identical to that used for the early-group patients.

Vaginal examinations were performed for obstetric indications and/or at any time that a patient requested analgesia. The cervical dilation was assessed using 0.5-cm increments (*e.g.*, a cervical dilation of 3–4 cm was considered 3.5 cm). The fetal heart rate was monitored continuously before, during, and after administration of nalbuphine and/or epidural analgesia in every patient. Adequate left uterine displacement was maintained at all times. An automated blood pressure monitor was used to determine maternal blood pressure every 2 min for the first 20 min after a bolus injection of local anesthetic. Subsequently, maternal blood pressure was measured every 15 min. Maternal hypotension was defined as a systolic blood pressure lower than 100 mmHg or a 20% or greater decrease in the systolic blood pressure. Hypotension was treated by intravenous administration of 5 or 10 mg ephedrine followed by administration of a bolus of lactated Ringer's solution.

The anesthesiologist asked each patient to indicate her pain score on an unmarked 100-mm visual analog pain scale (0 = no pain, 100 = worst possible pain) at time 0 and at 30-min intervals during the first stage of labor. Also, each patient was asked two additional questions at 60, 120, and 180 min after randomization. The first question was as follows: "How would you rate the quality of analgesia during the last hour—excellent, good, fair, or poor?" The second question was as follows: "How satisfied are you with your analgesia during the last hour—very satisfied, satisfied, unsatisfied, or very unsatisfied?"

Statistical analysis was by chi-square, Fisher's exact test, Student's *t* test, and Mann-Whitney U test as indicated. The Bonferroni correction was used to correct for multiple comparisons of pain scores. $P < 0.05$ was

considered significant, except for the analysis of pain scores, where $P < 0.005$ was required for significance.

Results

Three hundred forty-four patients were randomized to receive either early or late epidural analgesia. Two patients in the early group were excluded because of a protocol violation: one for a breech presentation and the second for an antepartum diagnosis of fetal macrocephaly. Both of these patients underwent cesarean section. Five patients in the late group were excluded because of a protocol violation. In each case, the anesthesiologist mistakenly administered early epidural analgesia rather than nalbuphine. One of those five patients underwent cesarean section for dystocia. An additional three patients in the late group were excluded because of voluntary withdrawal from the study. All three of those patients received early epidural analgesia, and all three delivered vaginally. Among the remaining 334 patients, the two groups were similar with regard to maternal characteristics, except that the early group included a slightly higher percentage of white patients than the late group (table 1).

Table 2 summarizes data for the progress of labor. Early administration of epidural analgesia did not increase the incidence of oxytocin augmentation, and it did not prolong the interval between randomization and the diagnosis of complete cervical dilation. Also, early administration of epidural analgesia did not increase the incidence of malposition of the vertex at delivery.

Early administration of epidural analgesia did not result in an increased incidence of instrumental vaginal delivery or cesarean section (table 3). Seventeen (10%) of 172 women in the early group and 13 (8%) of 162 women in the late group underwent cesarean section (relative risk for the early group 1.22; 95% confidence interval 0.62–2.40). Likewise, early administration of epidural analgesia did not increase the incidence of a prolonged second stage of labor (*i.e.*, ≥3 h).

Patients in the early group received a greater total dose of bupivacaine, as expected from the study design (table 4). Patients in the early group had lower pain scores 30–150 min after randomization (fig. 1). Likewise, patients in the early group had analgesia of better quality and were more satisfied with their analgesia at 60, 120, and 180 min after randomization (fig. 2). Among those patients who delivered vaginally, 72 (46%) of 155 women in the early group and 71 (48%) of 149 women in the late group had satisfactory anesthesia immediately before delivery and did not require a supplemental injection of local anesthetic.

Table 1. Maternal Characteristics

	Early (n = 172)	Late (n = 162)	*P*
Age (yr)*	23 ± 5	23 ± 5	NS
Race			
White	153 (89%)	130 (80%)	<0.05
Other†	19 (11%)	32 (20%)	
Socioeconomic status			
Private	80 (47%)	76 (47%)	NS
Indigent	92 (53%)	86 (53%)	
Attended prepared childbirth class			
Lamaze	43 (25%)	45 (28%)	NS
Other	31 (18%)	39 (24%)	
None	98 (57%)	78 (48%)	
Gestational age (weeks)*	39.9 ± 1.5	39.9 ± 1.3	NS
Weight (kg)*	78 ± 16	77 ± 13	NS
Height (cm)*	165 ± 7	166 ± 7	NS
Membranes ruptured before randomization	144 (84%)	124 (77%)	NS

* Mean ± SD.
† Black, Hispanic, Asian, Indian, Native American.

Forty-nine (28%) of 172 women in the early group and 49 (30%) of 162 women in the late group had hypotension during the 1st hour after administration of epidural analgesia (P = NS). Likewise, there was no significant difference between groups in the incidence of nausea, emesis, or urinary retention (data not shown).

There was no significant difference between groups in the incidence of meconium-stained amniotic fluid, infant weight, or 1- or 5-min Apgar scores (table 5). Also, there was no significant difference between groups in the incidence of fetal scalp blood *p*H determination after randomization. No infant in the early group and five (3%) infants in the late group received naloxone after delivery ($P < 0.05$). Infants in the late group had lower umbilical arterial and venous blood *p*H and higher umbilical venous blood P_{CO_2} measurements at delivery. There was no significant difference between groups in umbilical arterial or venous blood P_{O_2} or base deficit.

Discussion

Some physicians contend that epidural analgesia prolongs the first stage of labor and increases the incidence

Table 2. Progress of Labor

	Early (n = 172)	Late (n = 162)	*P*
Cervical dilation at randomization (cm)*	4 (0.5)	4 (0.5)	NS
Cervical dilation at time of epidural test dose (cm)*†	4 (0.5)	5 (0.25)	<0.0001
Interval between randomization and epidural test dose (min)‡	5 ± 2	134 ± 101	<0.0001
Required oxytocin after randomization	53 (31%)	62 (38%)	NS
Interval between randomization and complete cervical dilation (min)‡§	329 ± 197	359 ± 214	NS
Second stage of labor (min)*	85 ± 65	88 ± 62	NS
Position of vertex at delivery			
Occiput anterior	149 (87%)	142 (88%)	NS
Occiput posterior or transverse	23 (13%)	20 (12%)	
	(n = 155)	(n = 149)	
Position of vertex at vaginal delivery			
Occiput anterior	142 (92%)	135 (91%)	NS
Occiput posterior or transverse	13 (8%)	14 (9%)	

* Median (quartile deviation). Eighty-two (48%) of 172 women in the early group and 77 (48%) of 162 women in the late group had a cervical dilation <4 cm at the time of randomization.

† Twenty-four women in the late group received epidural analgesia ≥1 h after their second postrandomization dose of nalbuphine, before they achieved a cervical dilation of 5 cm.

‡ Mean ± SD.

§ Excludes 12 patients in the early group and 11 patients in the late group who underwent cesarean section before complete cervical dilation.

of cesarean section, primarily if it is administered during the latent phase. Friedman and Sachtleben[1] retrospectively evaluated the progress of labor in 330 women who received "early" caudal anesthesia (*i.e.*, before 7 cm cervical dilation) at their hospital between January 1955 and December 1957. The authors observed no difference in the duration of either the first or the second stage of labor between two groups of women who received early caudal epidural anesthesia and two control groups. The authors concluded that "caudal anesthesia does not necessarily affect the course of labor. . . ." Nonetheless, they stated that "proper administration entails withholding it until the

Table 3. Method of Delivery

	Early (n = 172)	Late (n = 162)	*P*
Spontaneous vaginal	92 (53%)	80 (49%)	NS
Instrumental vaginal	63 (37%)	69 (43%)	
Cesarean section	17 (10%)	13 (8%)	
Indication for instrumental vaginal delivery			
Elective	27 (16%)	21 (13%)	NS
Nonreassuring FHR tracing	22 (13%)	35 (22%)	
Prolonged second stage (≥3 h)	14 (8%)	13 (8%)	
Indication for cesarean section			
Dystocia	14 (8%)	8 (5%)	NS
Nonreassuring FHR tracing	3 (2%)	5 (3%)	

FHR = fetal heart rate.

Table 4. Management of Analgesia

	Early (n = 172)	Late (n = 162)	*P*
Doses of nalbuphine before randomization*			
None	112 (65%)	125 (77%)	<0.05
One	49 (28%)	28 (17%)	
Two	11 (6%)	9 (6%)	
Doses of nalbuphine after randomization			
None	172 (100%)	0 (0%)	<0.0001
One	0 (0%)	96 (59%)	
Two	0 (0%)	66 (41%)	
Total dose of bupivacaine (mg)†	128 ± 106	102 ± 65	<0.01

* If a patient received one or more doses of nalbuphine before randomization, those doses did not count toward the two-dose limit after randomization. Each of the eight patients in the late group who were excluded had received at least one dose of nalbuphine before randomization. If those eight patients had remained in the study, there would have been no significant difference between groups in the number of patients who received nalbuphine before randomization.

† Mean ± SD.

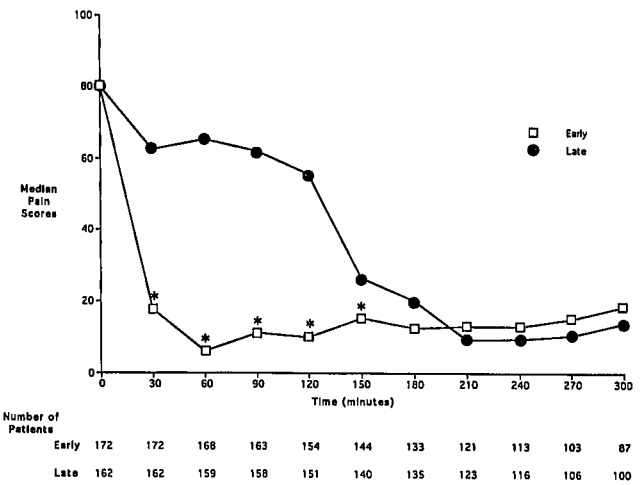

Fig. 1. Median pain scores over time. Patients in the early group had significantly lower pain scores at 30, 60, 90, 120, and 150 min after randomization ($P < 0.005$). Pain score assessments were discontinued when a patient achieved complete cervical dilation. Thus, the x-axis lists the number of patients who had not achieved complete cervical dilation at each period of assessment.

active phase of labor is entered. . . ." Read *et al.*[3] concluded, "There can be no reasonable doubt that epidural analgesia delays the progress of labour, particularly if it is given early, in the latent phase."

At the University of Iowa, longstanding policy has dictated that nulliparous women not receive epidural analgesia until they achieve a cervical dilation of 5 cm. However, a substantial number of nulliparous women experience severe pain during early labor. The current study represents the second of two studies designed to determine whether early administration of epidural analgesia affects obstetric outcome in nulliparous women. The previous study was limited to women who were receiving intravenous oxytocin for induction or augmentation of labor at the time of randomization.[6] The current study was limited to women who were in spontaneous labor at the time of randomization. In the previous study, 27 (18%) of the 149 patients in the two groups underwent cesarean section.[6] In contrast, in the current study, only 30 (9%) of the 334 patients in the two groups underwent cesarean section ($P < 0.01$). This difference underscores the fact that patients who require intravenous oxytocin for induction or augmentation of early labor are at increased risk for cesarean section, when compared with similar patients who labor spontaneously. For this reason, studies that assess the effect of epidural analgesia on obstetric outcome should be limited to a homogeneous group of patients (*i.e.*, either patients who are in spontaneous labor or patients who are receiving intravenous oxytocin for induction or augmentation of labor at the time of administration of epidural analgesia).

Because all patients were in spontaneous labor at the time of randomization, the current study includes an outcome measure not included in our previous study. Specifically, in the current study, early administration of epidural analgesia did not increase the incidence of oxytocin augmentation of labor. The current study does not confirm that early epidural analgesia does not affect the progress of labor in patients who are in spontaneous labor. Rather, it suggests that the effect, if any, of early epidural analgesia does not differ from that of intravenous nalbuphine. Some studies have suggested that opioids may decrease uterine activity and prolong the first stage of labor.[7-12]

Thorp *et al.*[5] performed a prospective study in which healthy nulliparous women were randomized to receive either epidural bupivacaine or intravenous meperidine analgesia. The authors used an epidural analgesia regimen similar to that used in the current study; namely, women in the epidural group received an initial bolus of 0.25% bupivacaine, followed by a continuous infusion of 0.125% bupivacaine. All subjects had a spontaneous onset of labor, but 9 of 48 women in the epidural group and 3 of 45 women in the meperidine group were receiving intravenous oxytocin at the time of the first dose of an analgesic drug. Twelve (25%) of 48 women in the epidural group, *versus* 1 (2%) of 45 women in the meperidine group, underwent cesarean section. Eleven of the 12 cesarean sections in the epidural group were performed in women who received epidural analgesia before 5 cm cervical dilation.

In the previous study, early administration of epidural analgesia did not significantly increase the incidence of cesarean section.[6] The current study does not exclude the potential for early administration of epidural analgesia to result in an increased incidence of cesarean section. However, under the conditions of the current study, it appears that such an effect—if it exists at all—is small. Results of the current study differ from the 12-fold increase in the cesarean section rate in the epidural group in the study by Thorp *et al.*[5] Reasons for this discrepancy are unclear. In the current study, all patients ultimately received epidural analgesia, whereas, in the study by Thorp *et al.*,[5] only 1 of the 45 women in the meperidine group ultimately received epidural analgesia. In the study by Thorp *et al.*,[5] the

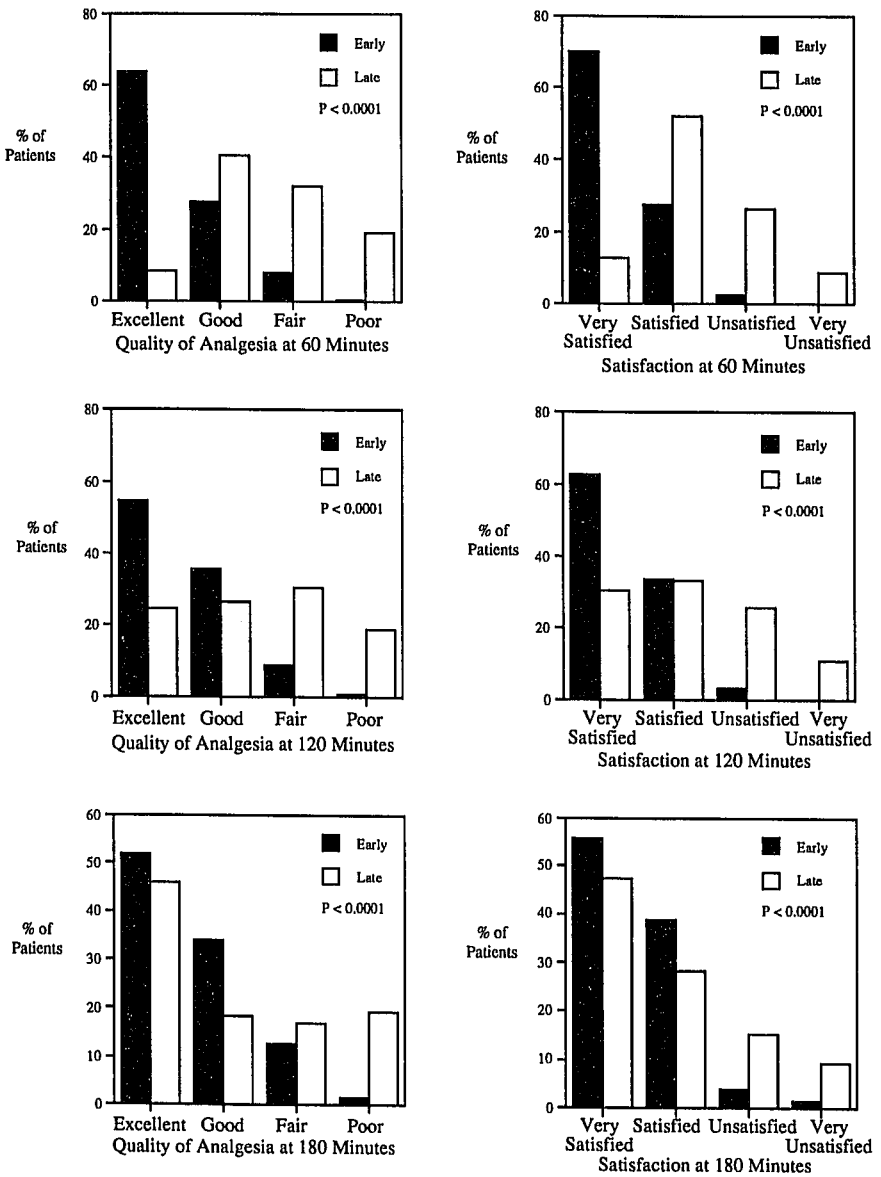

Fig. 2. Assessment of analgesia quality and patient satisfaction at 60, 120, and 180 min after randomization. Patients in the early group had analgesia of better quality than did patients in the late group at 60, 120, and 180 min after randomization ($P < 0.0001$). Similarly, patients in the early group were more satisfied with their analgesia than were patients in the late group at 60, 120, and 180 min after randomization ($P < 0.0001$).

authors also assumed responsibility for decisions regarding the method of delivery.[13] The study by Thorp *et al.*[5] was limited to a population of indigent women,** whereas the current study included a population that was almost evenly divided between private and indigent patients. Finally, unstated differences in obstetric and/or anesthetic management may be partly responsible for the different results.

In our previous study, there was an increased incidence of transient hypotension after induction of epidural analgesia in the early group.[6] The reason for this difference was unclear, and we did not speculate as to the reason for that difference. In the current study, there was no difference between groups in the incidence of hypotension after induction of epidural analgesia. In both studies, infants in the late group had lower umbilical arterial and venous blood *p*H and higher umbilical venous blood P_{CO_2} measurements at delivery. These differences likely reflected higher maternal blood

** McNitt J: Personal communication. 1993.

Table 5. Neonatal Condition

	Early (n = 172)	Late (n = 162)	*P*
Meconium-stained amniotic fluid			
Yes, noted before randomization	15 (9%)	11 (7%)	NS
Yes, noted after randomization	25 (15%)	19 (12%)	
No	132 (77%)	132 (81%)	
Scalp *p*H determined after randomization	7 (4%)	14 (9%)	NS
Infant weight (g)*	3,368 ± 459	3,408 ± 467	NS
1-min Apgar score ≥7	130 (76%)	125 (77%)	NS
5-min Apgar score ≥7	168 (98%)	158 (98%)	NS
Naloxone administered to infant	0 (0%)	5 (3%)	<0.05
Umbilical arterial blood			
*p*H*	7.25 ± 0.07	7.23 ± 0.07	<0.05
P_{CO_2} (mmHg)*	46 ± 9	48 ± 9	NS
P_{O_2} (mmHg)*	20 ± 6	20 ± 6	NS
Base deficit (mEq/L)*	6.4 ± 2.9	6.8 ± 2.9	NS
Umbilical venous blood			
*p*H*	7.33 ± 0.06	7.31 ± 0.07	<0.01
P_{CO_2} (mmHg)*	37 ± 6	39 ± 8	<0.05
P_{O_2} (mmHg)*	29 ± 6	28 ± 6	NS
Base deficit (mEq/L)*	5.3 ± 2.3	5.8 ± 2.7	NS

* Mean ± SD.

P_{CO_2} in the late groups. Mild maternal hypercarbia may have resulted from the administration of nalbuphine, followed by the administration of epidural analgesia. In the current study, no infant in the early group and five infants in the late group received naloxone after delivery. Otherwise, there was no evidence that late-group infants were at increased risk for hypoxemia or metabolic acidosis at delivery.

Unfortunately, labor represents one of the few circumstances when the provision of effective analgesia is alleged to interfere with the parturient's and obstetrician's goal (*i.e.*, spontaneous vaginal delivery). Anesthesiologists should participate in ongoing assessments of obstetric outcome to identify those techniques that provide the most effective analgesia without adverse effect on the progress of labor and method of delivery. However, anesthesiologists, obstetricians, and third-party payers should remember that pain relief is itself a worthy goal. As noted by the American Society of Anesthesiologists and the American College of Obstetricians and Gynecologists, "There is no other circumstance where it is considered acceptable for a person to experience severe pain, amenable to safe intervention, while under a physician's care." ††

We conclude that early administration of epidural analgesia did not prolong labor, increase the incidence of oxytocin augmentation, or increase the incidence of operative delivery, when compared with intravenous nalbuphine followed by late administration of epidural analgesia, in nulliparous women who were in spontaneous labor at term. Early administration of epidural bupivacaine provided analgesia that was clearly superior to that provided by intravenous nalbuphine. Infants in the late group had slightly lower umbilical cord blood *p*H measurements at delivery. It is unnecessary to await an arbitrary cervical dilation of 5 cm before administration of epidural analgesia in nulliparous women who are in spontaneous labor at term.

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