

# Advances in Labor Analgesia

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## Abstract

Approximately two-thirds of all women in the United States receive analgesia for labor and delivery. The ideal labor analgesic technique would confer complete pain relief without side effects to either the mother or the neonate. The analgesic technique would not cause any lower extremity motor blockade nor interfere with the progress or course of labor and would be sufficiently flexible to produce anesthesia for forceps or cesarean deliveries. Modern obstetric analgesia techniques and medications come close to achieving these goals. The following article will review current labor analgesia techniques and medications used during labor and delivery.

**Key Words:** Advances, analgesia, epidural, combined spinal-epidural, local anesthetics.

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## Introduction

ANALGESIA FOR LABOR AND DELIVERY is now safer than ever. Anesthesia-related maternal mortality has decreased from 4.3 per million live births during 1979–1981 to 1.7 per million live births during 1988–1990. The increased use of regional anesthesia for the parturient is partially responsible for this decrease in mortality (1). The pain of labor is mediated by nerves that enter the neuraxis at the 10th, 11th, and 12th thoracic spinal segments and at the 1st lumbar spinal segment. These nerves can be blocked by administering medication into either the epidural or the subarachnoid space. Our goal is to provide labor analgesia, not anesthesia. Analgesia is the absence of sensation to pain whereas anesthesia is the absence of all sensation.

The epidural space is located between the ligamentum flavum and the dura mater and can be located by applying pressure to a fluid- or air-filled syringe connected to a needle as it is advanced through the back and ligamentum flavum. While the needle is in the ligamentum flavum, there is almost complete resistance to injection through the needle. As the needle tip passes into the epidural space, the resistance to injection disappears and the air or saline is easily injected. A catheter through which medica-

tion can be administered is threaded into the epidural space. The medication utilized is 10–15 mL of bupivacaine 0.125–0.25% with fentanyl 50–100 micrograms. The exact dose of medication is based on the severity of labor pain at the time of catheter placement. The subarachnoid space is found by advancing a needle through the dura mater and visualizing subarachnoid fluid in the hub of the needle. Fentanyl 25 micrograms with 1 mL of bupivacaine 0.25% is administered. The medication lasts only approximately 1.5–2 hours. A catheter is not threaded into the subarachnoid space. Subarachnoid analgesia is usually utilized in conjunction with epidural analgesia.

Safety is the first and foremost goal of obstetrical anesthesia. For labor analgesia, a secondary goal is to minimize or eliminate maternal lower extremity muscle weakness associated with epidural and subarachnoid local anesthetics. Patients with less motor block are more satisfied with their anesthetic experience (2). Also, decreasing motor blockade may improve obstetric outcome. Although controversial, motor blockade related to labor epidural analgesia has been implicated as a cause of forceps deliveries and cesarean delivery (3). Minimizing the motor blockade may attenuate or eliminate these effects (4) and may allow women to ambulate during labor. Single isomer local anesthetics such as levo-bupivacaine and ropivacaine have been developed that may be safer and produce less motor blockade than their stereoisomer counterparts. The purpose of this article is to review analgesic techniques and medications that are currently used to provide labor analgesia.

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Epidural analgesia has been the most popular technique for the relief of labor pain, because of its efficacy and safety. Women can obtain almost complete relief from the pain of labor. Because a catheter can be threaded into the epidural space, dilute solutions of local anesthetic can be injected during the earlier stages of labor to achieve analgesia. As labor progresses, a more concentrated solution of local anesthetic can be administered, or an adjunct, such as an opioid, can be added. Additionally, an epidural catheter can be utilized to maintain a low dermatomal level of analgesia for labor (T10–L1) and, if needed, the dermatomal level can be raised to T4 for cesarean delivery.

Local anesthetic are most commonly utilized for labor epidural analgesia. Opioids are often added to the local anesthetic to decrease the motor block, but they do not confer adequate analgesia for labor pain when used alone unless large doses are used (5). Continuous infusions of epidural local anesthetic combined with an opioid are frequently employed during labor. Continuous infusions provide a more stable level of analgesia than intermittent bolus techniques. This technique results in better analgesia for the mother and a decreased workload for the anesthesiologist (6). Without the frequent bolus injections, there may be less risk of maternal hypotension (7, 8). Interestingly, maternal satisfaction does not appear to be greater when continuous infusions are utilized compared with intermittent boluses (9). Most women who receive continuous infusions tend to receive greater doses of bupivacaine than those who received intermittent injections (8, 9). The continuous infusion solutions currently used usually contain 0.04–0.125% of a local anesthetic (bupivacaine or ropivacaine) plus an opioid (fentanyl or sufentanil) (10, 11).

Some anesthesiologists use patient-controlled epidural analgesia (PCEA). This technique allows the patient to self-medicate, thereby controlling her own analgesia. Because there are few well-controlled studies regarding PCEA, the optimal dosing regimens have not been determined. Compared with continuous infusion or intermittent bolus techniques, PCEA is associated with fewer anesthesiologist interventions and less motor block (7, 12). Less anesthesia also decreases the frequency of maternal hypotension (7). The total dose of local anesthetic used is less with PCEA (13, 14), and maternal satisfaction is greater than when standard epidural analgesia techniques are used

(15). Unfortunately, not all studies have documented all these advantages and therefore few hospitals offer this technique (16, 17). A commonly used PCEA regimen is bupivacaine 0.0625% with fentanyl 2 µg/mL with the following PCEA settings; basal rate of 10 mL/hr, bolus dose of 5 mL, 10 minute lockout, and a 30 mL/hr maximum limit. This author is not aware of any complications to the parturient with PCEA use. But theoretical risks include those that have been seen in the general surgical patient including high dermatomal level or overdose from excessive self-administration, from a helpful family member, or secondary to a catheter that has migrated into the subarachnoid space.

The safety of epidural opioids has been well documented. Despite decreased neonatal neurobehavioral scores shortly after delivery (18), epidural fentanyl has not been linked to any long-term (four years) developmental effects (19). The clinical relevance of lower neurobehavioral scores around the time of delivery is unknown, but some have suggested that epidural fentanyl may impact on the ability of the neonate to breast feed (20). This concern is not based on scientific evidence. Indeed, Halpern et al. (21) did not find any difference in breast feeding success among neonates whose mothers received epidural fentanyl versus those who did not (21). Respiratory depression in the neonate is also of little concern with epidural fentanyl. Respiratory parameters of neonates whose mothers received epidural fentanyl (up to 400 g) are similar to those whose mothers did not receive any fentanyl (22).

There are a number of problems with labor epidural analgesia that have prompted the use of alternative techniques. First, the time from epidural catheter placement until the patient is comfortable is variable, but depending on the local anesthetic used, can take up to 30 minutes. Other disadvantages of labor epidural analgesia include maternal hypotension, inadequate analgesia (15–20% of cases) (23) and motor block, even with the very dilute local anesthetic solutions (11).

Subarachnoid opioids offer rapid, intense analgesia with minimal changes in blood pressure (24) or motor function (25). The opioid is usually administered as part of a combined spinal epidural (CSE) technique. After locating the epidural space in the usual manner, a long small-gauge spinal needle with a pencil-point design is inserted through the epidural needle into the subarachnoid space. A subarachnoid

opioid, either alone or in combination with local anesthetic, is injected. The spinal needle is removed and an epidural catheter threaded for future use. Analgesia begins within 3–5 minutes and lasts 1–1.5 hours. When the analgesia wears off the epidural catheter is utilized for the remainder of labor. Or, a continuous epidural infusion of dilute local anesthetic/opioid solution is started immediately after securing the epidural catheter. Starting the epidural infusion immediately, versus waiting for pain to recur, prolongs the spinal medication by approximately 60 minutes with minimal side effects and is highly recommended (26). It would be tempting to thread a catheter into the subarachnoid space to enable administration of repeated doses of opioid into this space. Unfortunately, there may be a risk of cauda equina syndrome when placing subarachnoid catheters, especially microcatheters (27). A study is currently underway to evaluate the safety of subarachnoid microcatheters (28).

Subarachnoid administration of fentanyl 25 micrograms (0.5 mL) or sufentanil 5 micrograms (0.1 mL) are the opioids most commonly utilized with the CSE technique. Differences between the two drugs are subtle and choice of one over the other is based on personal preference. However, the cost of sufentanil is \$7.50 for a 2 mL ampule whereas a 2 mL ampule of fentanyl costs \$0.21. The balance of the opioid from the vial is generally saved for later use in the same patient or discarded if not used. Palmer et al. (29) found that the ED<sub>50</sub> of subarachnoid fentanyl is 14 µg and that the duration of action increased to 89 minutes as the dose increased to 25 µg. Above 25 µg the duration of action was not prolonged. Herman et al. (30) found that the ED<sub>50</sub> for subarachnoid sufentanil was 2.6 µg and the ED<sub>95</sub> was 8.9 µg. Adding 1 mL of bupivacaine 0.25% to either fentanyl or sufentanil does not hasten the onset of block, but prolongs the duration by about 20 min for fentanyl (31) and 30 minutes for sufentanil (32). Side effects of adding bupivacaine are minimal and may protect the patient from developing pruritus (33). Whether this added duration is worthwhile is based on personal preference. At Mount Sinai we commonly use fentanyl 25 µg with 1 mL of bupivacaine 0.25% for the subarachnoid dose.

The CSE technique has several advantages. The primary one is the rapid (3–5 min) onset of analgesia. Additionally, Collis et al. (2) found less motor block and greater patient satisfaction in parturients receiving the CSE technique ver-

sus the “standard” epidural technique of bupivacaine 0.25%. The greater satisfaction was related to the faster onset of action and less motor block.

There are some concerns about the CSE technique, most of which are only theoretical. There is no increased risk of subarachnoid catheter migration of the epidural catheter (34) and metallic particles are not produced as a result of passing one needle through another (35). Norris et al. (36) found that the incidence of postdural puncture headache is not increased with the CSE technique. An increase in end-tidal carbon dioxide has been reported in women who received subarachnoid sufentanil (37), but the risk of clinically significant respiratory depression is low (38). Also, the risk of hypotension with the CSE technique is not greater than with standard epidural regimens. Grant et al. (25) found minimal changes in maternal blood pressure in nonlaboring term parturients following 25 µg of subarachnoid fentanyl. This was true in women who received prehydration with 1,200 mL crystalloid solution and those who did not receive any prehydration. The most common side effect of subarachnoid opioids is pruritus, with a reported incidence as high as 95% (33, 39), which is easily treated with either an antihistamine or naloxone.

It is possible that the epidural catheter may not actually be in the epidural space after the CSE technique is performed, and this may not be detected until the analgesia from the subarachnoid opioid has dissipated (1–2 hours). If, during this time period, the woman requires an emergent cesarean delivery, the catheter may fail and the patient may require a general anesthetic. Norris et al. (40) found that the risk of failed epidural catheters was lower in women who received CSE analgesia than those who received epidural analgesia. However, it is prudent not to use the CSE technique in a woman who is a poor risk for general anesthesia, e.g., one with a bad airway or obesity, so that in these patients it is important to assure that an epidural catheter can and will function satisfactorily.

Clarke et al. (41), in 1994, reported fetal bradycardia associated with uterine hypertonus after subarachnoid opioid injection. One proposed theory for increased uterine tone is related to the rapid decrease in maternal catecholamines associated with the onset of pain relief. With the decrease in circulating beta adrenergic agonists, there is enhanced alpha activity that leads to uterine contractions (42). Three retrospective studies did not find any dif-

ference in the incidence of fetal heart rate abnormalities with CSE analgesia versus epidural analgesia (43–45). A large retrospective review found no difference in the incidence of emergency cesarean delivery in 1,217 women who received CSE analgesia versus 1,140 who did not receive neuraxial analgesia (46). If hypertonus occurs, treatment should include subcutaneous terbutaline or intravenous nitroglycerin (47).

There have been several recent prospective studies evaluating the effects of the CSE technique on the incidence of cesarean delivery. Nageotte et al. (48) randomized women to three groups: group 1 received CSE with sufentanil 10 µg, group 2 received the same technique and medication as those in group 1 but were encouraged to ambulate, and group 3 received epidural analgesia. They did not find any difference in the need for cesarean delivery between the three groups of patients. Gambling et al. (49) compared women who received CSE analgesia versus those who received intravenous meperidine during labor, and they too did not find any difference in the incidence of cesarean delivery between the 2 groups.

The term “walking epidural” has become popular especially in the lay community. It refers to any epidural or spinal technique that allows ambulation. Some studies have suggested that ambulating or being in the upright position is associated with a shorter first stage of labor, less pain in early labor, and decreased analgesia requirements (50, 51). These findings have not been confirmed in prospective, randomized studies. Indeed, two recent well-designed prospective and randomized studies have not been able to document any medical benefit of ambulating, either in terms of duration of labor or mode of delivery (48, 52).

In many centers, few patients want to ambulate. Most want to rest or sleep once they have pain relief. However, even if patients do not want to ambulate, using a technique that produces minimal motor blockade will improve patient satisfaction (2). Either epidural analgesia using dilute local anesthetic/opioid solutions or a CSE technique can be used to achieve this goal. Several precautions should be taken before allowing a parturient to walk during epidural or CSE analgesia. Maternal blood pressure and fetal heart rate should be monitored for 30–60 minutes after induction (49) and intermittently thereafter since small doses of subarachnoid and epidural local anesthetics can produce some motor deficits (2, 10). Motor

function should be assessed by having the parturient perform a modified deep knee bend or stepping up and down on a stool. The patient must have an escort at all times, and fetal heart rate and maternal blood pressure should be reassessed at least every 30 minutes.

### Local Anesthetics

Bupivacaine gained popularity for use in obstetrics because of its long duration of action and relative motor sparing as compared to other local anesthetics. It is also compatible with other medications commonly used during labor epidural analgesia, especially opioids. However, bupivacaine has a narrow margin of safety (dose that causes analgesia is close to the dose that causes cardiovascular symptoms). In 1979, Albright reported several cases of cardiovascular collapse, most of which were fatal, in the parturient who received inadvertent intravascular injections of bupivacaine (53). Because of these reports, the United States Food and Drug Administration (FDA) banned the use of epidural bupivacaine 0.75% in the parturient. This has led to the search for a safer local anesthetic for the parturient.

Local anesthetics produce their effects on nerve conduction by blocking the passage of sodium ions through the sodium channels in the plasma membrane. Amide local anesthetics exist as one of two enantiomers, levo or S(–) and dextro or R(+). In general, the levo form is more potent as an anesthetic, but is less cardiotoxic than the dextro form. The reduced cardiotoxicity is related to a lower affinity of the levo isomer for the sodium channels in the plasma membrane of cardiac cells (54). Bupivacaine is commercially produced as a racemic mixture of its two enantiomers, levo-bupivacaine and dextro-bupivacaine. The levo-isomer of ropivacaine, as well as levo-bupivacaine, are now available for use.

Initial studies suggested that ropivacaine may be less cardiotoxic and produce less motor block than bupivacaine, thus making it an ideal agent for labor analgesia. Feldman et al. (55) found, in the canine model, that the lethal dose of intravenous ropivacaine was greater than that of bupivacaine. Although there are no cardiotoxicity studies of ropivacaine in humans, Scott et al. (56) found, in human volunteers, that a larger intravenous dose of this drug was tolerated prior to the onset of neurologic symptoms than was the case for intravenous bupivacaine. In the surgical patient, Brockway et al.

(57) found that less motor block developed in the patients who received ropivacaine than in those who received bupivacaine. In the parturient, however, both McCrae et al. (58) and Stienstra et al. (59) were unable to detect less motor block when ropivacaine was utilized for labor analgesia as compared to bupivacaine. In these studies (55, 56, 58, 59), the same concentrations of ropivacaine and bupivacaine were utilized. Subsequently, two separate investigators (60, 61) demonstrated that epidural ropivacaine is significantly less potent than epidural bupivacaine by a factor of 0.57. The author is not aware of any study that has compared the potency of ropivacaine and levo-bupivacaine. Thus, the decrease in motor block or toxicity found in the previously studied ropivacaine groups may have been related to the lesser potency of ropivacaine.

Levo-bupivacaine is equipotent to racemic bupivacaine (62) and has been found to be less cardiotoxic than bupivacaine in human volunteers (63). Two studies have been completed in parturients comparing bupivacaine with levo-bupivacaine. Both studies found that the quality and onset of analgesia and lower extremity motor block were similar for the two drugs (64, 65).

The challenge facing obstetric anesthesiologists is to define the role of these new local anesthetics for the parturient. Although using a drug less toxic than bupivacaine is important, the risk of cardiac problems from modern day doses and concentrations of bupivacaine (0.625–1.25%) for labor is close to zero. Furthermore, even before the introduction of ropivacaine and levo-bupivacaine, modifications in clinical practice including the use and test-dosing of multi-orifice epidural catheters, the use of dilute concentrations of local anesthetic, and the fractionation of the total dose of local anesthetic has made epidural anesthesia very safe. Indeed, the estimated maternal mortality rate from regional anesthesia decreased from 8.6 per million regional anesthetics in 1979–1984 to 1.9 per million in 1985–1990 (1). Another important consideration is cost. At The Mount Sinai Hospital, a 30 mL vial of bupivacaine costs approximately \$1.00, whereas a similar volume and concentration of levo-bupivacaine and ropivacaine costs approximately \$6.00. Despite this cost differential, the author believes, in view of the information currently available, that these latter two drugs may be preferred for use in women with limited cardiac reserve, e.g., those with mitral stenosis, severe

preeclampsia, or pulmonary hypertension. The author also prefers using levo-bupivacaine or ropivacaine for women undergoing cesarean delivery where the otherwise larger amounts (both volumes and concentrations) of alternative local anesthetic agents may increase the likelihood of an adverse reaction.

In summary, techniques and drugs available to the obstetric anesthesiologist are vastly superior to what existed previously. The future of obstetric anesthesia lies in refining these techniques and drugs to make obstetric anesthesia even safer and more effective.

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