33 Anesthesia and analgesia in pregnancy

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INTRODUCTION

The first public demonstration of the use of ether for anesthesia in 1846 was quickly followed by its application to obstetrics in January 1847 by James Young Simpson of Scotland. Almost immediately, controversy surrounded its use. In the United States, Charles D Meigs, Professor of Obstetrics at Jefferson Medical College, denounced attempts to ameliorate the pain of labor, claiming that it was inseparable from the effectiveness of uterine contractions. Simpson, on the other hand, claimed that the pain of labor was of no physiologic value (1). Eventually, then, as today, public demand for effective relief of labor pain settled the argument. By the latter half of the 20th century, there was nearly full agreement within the medical profession that relief of labor pain should not be withheld from a woman in active labor. This position was formally recognized in 1992 when the American College of Obstetricians and Gynecologists and the American Society of Anesthesiologists published a joint statement underscoring the importance of the availability of pain relief for the parturient:

“Labor results in severe pain for many women. There is no circumstance where it is considered acceptable for a person to experience untreated severe pain, amenable to safe intervention, while under a physician’s care. In the absence of a medical contraindication, maternal request is a sufficient medical indication for pain relief during labor. Pain management should be provided whenever medically indicated” (Joint ASA–ACOG Statement, American Society of Anesthesiologists, Park Ridge, IL: October 21, 1992; amended October 1997) (2). While many women may choose to labor without any pharmacologic intervention, the provision of pain relief during childbirth has become an integral part of obstetric practice.

NOCICEPTIVE PATHWAYS OF PARTURITION

During the first stage of labor, pain signals from nociceptors in the myometrium and cervix are transmitted via the paracervical and hypogastric plexi, and, traveling with sympathetic fibers of the lumbar sympathetic chain, enter the spinal cord at segments T10 to L1. These fibers synapse with secondary neurons in the Rexed laminae of the dorsal horns and are modulated by mu receptors in the substantia gelatinosa, also located in the dorsal horns of the spinal cord. The pain is perceived primarily as visceral pain. Pain signals in the second stage of labor are transmitted via the pudendal nerves, which enter the spinal cord via nerve roots S2–S4. From there, pain signals are transmitted via secondary neurons to the contralateral spinothalamic tract and on to the thalamus. Signals from the thalamus are then projected to cognitive cortical centers, where they are perceived primarily as somatic pain. Pain can be modulated or interrupted with blockade at several levels during its transmission. Paracervical block provides pain

relief during the first stage of labor as does epidural and/or spinal blockade with local anesthetics or with spinal opiates either alone or in combination with local anesthetics. Pain during the second stage of labor can be managed with pudendal block, spinal (saddle) blockade, or extension of epidural blockade. Since the pain of the second stage of labor is somatic, it is not as responsive to spinal opiates as is the pain of the first stage of labor.

NONPHARMACOLOGIC METHODS OF PAIN RELIEF

Psychoprophylaxis is probably the most common method of nonpharmacologic management of labor pain. Its premise is that knowledge, education, and preparation reduce the severity of the fear–tension–pain cycle. The process usually begins with childbirth education classes that inform the pregnant patient and her partner of the normal progress of pregnancy, labor, and delivery as well as the expectations. In addition, relaxation and distraction techniques are taught as an adjunct to the management of labor pain. These include breathing exercises, focal points, and massage. The patient’s partner plays an important role in the process. Emotional support decreases the level of isolation the patient may feel. Nonfamily individuals trained to provide support (doulas) have been shown to have a beneficial effect on the patient’s perception of pain and the progress of labor (3). Touch and massage are frequent components used to alleviate the pain of labor. These techniques may include effleurage, light touch, and/or counterpressure applied to the low back. The ultimate goals are for the parturient to take an active role in the management of her labor and labor pain. Indeed, studies have shown that patients who have successfully completed a program of childbirth education and utilized the above techniques have a lesser need for pharmacologic treatment as well as a lower incidence of obstetric interventions (4,5). Other non-pharmacologic techniques that have been used include transcutaneous electrical nerve stimulation (TENS), acupuncture, and hypnosis.

TENS has had no discernible adverse fetal effects. Its efficacy has been reported to be essentially of minimal benefit to possibly shorter labors (6–9). Acupuncture requires knowledgeable and skilled practitioners, which probably explains the varied results that have been reported (10–13). Because of the need for additional training as well as for cultural reasons, this technique is not likely to be widely practiced in the foreseeable future. Like acupuncture, hypnosis requires a trained practitioner. It is time consuming and at least partially depends on the susceptibility of the patient to this technique. Patients who are susceptible to hypnosis have been shown to require less systemic analgesia than patients in a control group as well as experience shorter labors. Patients who are not susceptible to hypnosis do not experience much benefit (14).

SYSTEMIC ANALGESIA

Systemic analgesics have been widely used throughout the latter half of the 20th century. The mainstay of this technique is the use of opioids, both naturally occurring and synthetic. Morphine is derived from opium and has a very long history of use. As with all opioids, it binds to mu receptors in the CNS and, in addition to providing analgesia, may also cause respiratory depression, nausea, vomiting, and sedation. Systemically administered morphine can induce histamine release and cause pruritus (15). An associated skin rash may also develop. When given intravenously (IV), its onset of action is within 3 to 5 minutes with peak effect in 20 minutes. The pharmacologic effect of morphine does not correlate well with plasma concentrations following intravenous administration. This is believed to be secondary to a delay in transfer across the blood-brain barrier since a large percentage of morphine is ionized at physiologic pH (16–18). An intramuscular (IM) injection will have an onset of 15 to 30 minutes with a peak effect of 45 to 90 minutes. Morphine undergoes hepatic metabolism. With the availability of more potent synthetic opioids such as fentanyl, remifentanyl, and the agonists/antagonists nalbuphine and butorphanol, morphine is more commonly used during prelabor or the very early stages of labor and less so during active labor.

Meperidine is a widely used opioid that has the benefit of low cost and a long history of successful administration. Usual doses are 25 to 50mg IV/IM. Like most opioids, it has the potential of causing respiratory depression in both the mother and the neonate. Onset is within 5 minutes of intravenous administration. The neonatal half-life of maternally administered meperidine is considerably longer than maternal half life, approximately 18 versus 3 hours (19,20). A limiting factor in the administration of meperidine is the accumulation of the metabolically active metabolite normeperidine, which can cause seizures when levels are sufficiently high (17). Normeperidine can remain in the neonate for as long as 60 hours (21). The pharmacokinetics of meperidine is such that the optimal time for delivery is either within 1 hour after maternal administration or more than 2 to 4 hours following administration, depending on the dose (22,23).

Fentanyl is a potent synthetic opioid. The potency relative to morphine is 100 to 1. It is most often administered IV and has a rapid onset of less than 1 minute. It has a relatively short duration of action and requires frequent dosing (18). Because of its short duration of action, it is titratable and hence it is attractive when administered as patient-controlled analgesia (PCA). Because its potency is much greater than morphine and meperidine, it has a greater potential for causing severe respiratory depression. Patients receiving fentanyl should be closely monitored. Nevertheless, studies have demonstrated a lesser degree of neonatal effects with the use of fentanyl than with the use of meperidine or morphine (24,25).

The agonists/antagonists nalbuphine and butorphanol have also been widely used in many institutions for labor analgesia. These drugs act primarily at the kappa receptor and more weakly at the mu receptor (18). Their advantage over pure opiates is a ceiling effect on respiratory depression. When compared with meperidine, nalbuphine causes less maternal nausea and vomiting, but lower neonatal

neurobehavioral scores at 2 to 4 hours of age (26). Butorphanol, when compared with meperidine, affords similar degrees of pain relief (27). Like nalbuphine, there is less maternal nausea and vomiting compared with meperidine. Fetal and neonatal effects are similar when comparing butorphanol and meperidine (28).

In the general patient population, PCA has been found to provide better pain relief than intermittent, nurse-administered analgesia (29). Nalbuphine has been shown to provide better labor analgesia when administered in a PCA mode, while PCA administration of meperidine does not demonstrate any significant improvement (30,31). Opioids that are shorter acting may lend themselves well to PCA administration. Fentanyl has been used in a PCA mode, but neonatal depression has been reported. In one retrospective study, the total dose of fentanyl received by mothers of infants who required naloxone was significantly higher than the group of mothers whose infants did not require naloxone (32). Remifentanyl is a synthetic opioid with a very short duration of action. It is rapidly metabolized by blood esterases with a half-life of 3.5 minutes. There are no active metabolites, no drug accumulation, and metabolism is not organ dependent (33). Remifentanyl has been administered in a PCA mode successfully for labor analgesia. Problems have been reported with respect to maternal respiratory depression and decreasing oxygen saturation, but adverse neonatal effects are few (34–38). Remifentanyl administered via PCA may be the best opioid analgesic alternative when epidural analgesia is contraindicated.

Ketorolac is a nonsteroidal anti-inflammatory agent that has good analgesic efficacy for various types of painful conditions. It is attractive in that it causes no sedation and no respiratory depression (39). There are concerns about its use in obstetrics in that it may decrease uterine contractions and/or close the fetal ductus arteriosus. In one study comparing the analgesic effect of ketorolac with meperidine, ketorolac was not found to be superior (40). Another study demonstrated potential adverse effects on neonatal platelet function (41). At present, there appears to be no benefit from the use of ketorolac for labor analgesia.

Placental Transfer

Virtually, all drugs administered maternally have the potential to transfer to the fetus. Several mechanisms are involved in the placental transfer of drugs from the maternal to fetal circulation, the more common of which being simple diffusion, facilitated diffusion, and active transport. Simple diffusion is governed by the Fick equation:

$$Q/T = [kA(C_m - C_f)]/D$$

Where Q/T is the rate of diffusion of a given drug and k is a diffusion constant determined by the lipid solubility, molecular configuration, and molecular weight. A is the area available for diffusion, C_m is the maternal blood concentration, and C_f is the fetal blood concentration. D is the thickness of the diffusion membrane. Thus the size and thickness of the placental membrane along with variations in the distribution of vascular flow determine the rate of placental drug transfer. Other determinants include drug ionization, protein binding, and maternal and

fetal metabolism. Protein binding can be an important factor in drug transfer. Differences in protein binding in the maternal and fetal circulations may either inhibit or facilitate the degree of transfer. Variations in maternal blood concentrations of protein as may occur in various disease states may also influence drug transfer. Substances of smaller molecular size (less than 500 daltons) are more likely to transfer than larger molecules. Large polar compounds such as muscle relaxants that are used in general anesthesia transfer only in small amounts.

The rate and degree of drug transfer are measured by comparing umbilical vein (UV) and maternal vein (MV) concentrations. UV drug concentration reflects the amount of drug transferred to the fetal circulation via the placenta. A UV/MV ratio close to 1 indicates a high degree of placental transfer. The degree of fetal drug distribution and metabolism is reflected by comparing the umbilical artery (UA) and UV concentrations of a drug. Thus a UA/UV ratio of 1 will indicate equilibrium between fetal drug delivery and fetal distribution. A UA/UV ratio of less than 1 will indicate continued fetal drug uptake and a UA/UV ratio greater than 1 will indicate fetal elimination of drug via distribution into the maternal circulation.

The placental transfer of morphine is rapid. UV to MV ratio is close to 1 at 5 minutes. Fetal heart rate (FHR) variability is often decreased following maternal administration of morphine; however, fetal metabolism of morphine is high. Studies of morphine metabolism in the fetal baboon show that it is limited primarily by hepatic blood flow (42–44). Because the fetal exposure to morphine is short, it may actually be more beneficial than meperidine when used for systemic labor analgesia.

Maternally administered intravenous meperidine appears in the fetal plasma within 2 minutes and reaches equilibrium in 6 minutes. The UV/MV ratio increases with greater time following IM administration (21,22,45,46). Like morphine and other opioids, a decrease in FHR variability can be expected (47). However, variability is not effected during fetal movements or uterine contractions (48).

Fentanyl rapidly crosses the placenta and is detectable in fetal blood within 1 minute (49). Depending on total dose, UV/MV ratios of 0.05 to 0.76 have been reported. A decrease in FHR variability has been noted with a duration of approximately 30 minutes (50).

The UV/MV ratio for nalbuphine is reported to be 0.61 to 0.74 (26,51,52). Fetal effects include decreases in frequency of accelerations, decreased FHR variability, and the appearance of sinusoidal patterns (53,54). In spite of these changes, the fetus will still respond to fetal acoustic stimulation (55).

Butorphanol rapidly crosses the placenta. In fetal sheep, butorphanol can be detected within 1 minute of maternal administration (56). The UV to MV concentration ratio is 0.84. When compared with meperidine, there were no differences in effect on FHR (27).

PARACERVICAL AND PUDENDAL BLOCKS

Up until the mid-1970s, paracervical and pudendal blocks were frequently used in many centers for analgesia for labor and vaginal delivery. Paracervical block interrupts nerve transmission at the paracervical plexus. It provides several

hours or more of pain relief during the first stage of labor, depending on the local anesthetic used. During long labors, it may need to be repeated. Paracervical block is useful only during the first stage of labor. It is of no value during the second stage of labor. In the 1970s, multiple reports of fetal bradycardia began to appear. The mechanism was believed to be a transfer of large amounts of local anesthetic to the fetal circulation via the uterine artery. Other mechanisms that have been proposed are uterine artery vasospasm, UA vasospasm, and uterine hypertonus (57–60). Currently, paracervical block for labor analgesia is rarely used because of the concerns regarding adverse fetal effects. It may have some utility in special circumstances such as in patients with intrauterine fetal death who, in addition, have contraindications to epidural analgesia.

Pudendal anesthesia is achieved by blocking the pudendal nerve as it exits the pelvis at the ischial spine. It provides anesthesia to the perineum and lower one-third of the vagina. It is useful for late second-stage labor and vaginal delivery. It is of no value during the first stage of labor or for intrauterine manipulation. Because of the flexibility and reliability of epidural analgesia for both the first and second stages of labor, the use of pudendal block has been declining. It is rarely used at the University of Missouri, and the Mayo Clinic recently reported declining usage as well (61). Nevertheless, it is a valuable option when neuraxial analgesia is contraindicated or unavailable.

NEURAXIAL ANALGESIA

Epidural analgesia has become a very successful and widely used technique for managing the pain of labor in the United States. In 1992, epidural analgesia was used in slightly greater than 50% of laboring women delivering in hospitals with greater than 1500 deliveries per year (62). Today, rates of 75% or greater are not uncommon. Continuous lumbar epidural analgesia provides pain relief that is superior to any other method of labor analgesia. Compared with parenteral opioids, epidural analgesia provides superior pain relief, greater maternal satisfaction, and less neonatal depression (63). Epidural analgesia has been shown to significantly decrease the stress response to labor. Stress indicators such as epinephrine, cortisol, and beta-endorphins decrease following epidural analgesia (64–68). This can be important when dealing with patients with cardiac disease (see below).

Epidural analgesia involves the placement of local anesthetics often combined with low-dose opioids in the epidural space via a small-gauge catheter. The posterior epidural space is bound by the ligamentum flavum posteriorly and the dura anteriorly. Typically, the patient is placed in a sitting or lateral decubitus position. The lumbar approach is commonly used, most often L2 to L5. Following an aseptic technique with local anesthetic injected at the chosen interspace, an epidural needle is inserted into the epidural space utilizing a “loss of resistance” technique with a syringe filled with saline or air. An epidural catheter is then threaded into the epidural space and the needle is removed. The catheter is then secured and local anesthetic infused until an appropriate level of analgesia is achieved. Since the epidural catheter can be placed intravascularly or in the subarachnoid space, a test dose is

performed to rule out placement at these sites. A small dose of local anesthetic with epinephrine is injected via the catheter following careful aspiration. Typical test doses include 45 mg of lidocaine and 15 mcg of epinephrine. If injected IV the small dose of epinephrine will cause a transient maternal tachycardia. If injected into the subarachnoid space, the parturient will develop a limited motor block. Neither of these responses will occur if the catheter is in the epidural space.

Utilizing an epinephrine containing test dose as a marker of intravascular catheter, placement is not always accurate, however. Colonna-Romano and colleagues showed that the epinephrine test dose has a 100% negative predictive value, but a 55% to 73% positive predictive value. They calculated that as many as 27% to 45% of epidural catheters with a positive epinephrine test dose would be unnecessarily removed (69). Other authors have questioned the value of an epinephrine containing test dose as a method of detecting an intravascularly placed epidural catheter (70,71). The catheter design may also affect the positive and negative predictive value of test doses. Closed-tip multiport catheters, which are popular among many anesthesiologists because of improved local anesthetic spread, may present problems with multi-compartment placement (72). Because of these limitations, anesthesiologists have taken the position that every dose of a local anesthetic administered via an epidural catheter should be considered a test dose. Local anesthetics are therefore administered in small aliquots and the patient is observed for signs of toxicity (intravascular placement) or unexpected levels of motor block (subarachnoid placement).

Once the epidural catheter is placed, secured, and tested, it is dosed with a low concentration of local anesthetic alone or in combination with an opioid to achieve a T10 level. This usually requires a bolus loading dose of volumes ranging from 8 to 16 mL given in 5-mL aliquots. While intermittent single "top up" doses were given in the past for maintenance, continuous infusions are now almost universal. Patient-controlled epidural analgesia (PCEA) has gained popularity in a number of centers. Usually a background infusion of dilute local anesthetic with or without opioid is maintained and the patient is allowed to self-administer a "top up" dose with a predetermined lockout and hourly maximum volume programmed into a pump device. PCEA has been shown to improve patient satisfaction and decrease the number of anesthetic interventions with lower total volumes of local anesthetic than conventional continuous infusion techniques (73–75). A number of regimens for both continuous and PCEA techniques have been proposed, each with varying results. At the University of Missouri, PCEA is used almost exclusively.

A modification of conventional epidural analgesia, the combined spinal-epidural (CSE) technique, has also been gaining usage at major centers over the past decade. Following placement of the epidural needle in the epidural space, a small-gauge pencil-point spinal needle is passed through the epidural needle and the dura is punctured. A small dose of preservative-free opioid or opioid local anesthetic combination is injected intrathecally. The epidural catheter is then passed through the epidural needle and tested. Analgesia is achieved rapidly and there is no need for a bolus loading dose of local anesthetic via the epidural catheter (76,77). Following placement and testing

of the epidural catheter, a maintenance infusion is begun. By the time the intrathecal dose has dissipated, the epidural infusion has reached a sufficient level to maintain satisfactory analgesia.

The CSE technique has several distinct advantages. If an opiate alone is administered intrathecally, then there is no motor block and the patient is able to ambulate for a period of time, usually 90 to 120 minutes (the so-called walking epidural). Some institutions will follow the intrathecal dose with an ultralow concentration of local anesthetic with opioid and epinephrine adjuvants to allow continued ambulation (78,79). The CSE technique allows confirmation of epidural placement of the epidural needle, which may decrease the need for replacement of failed epidural catheters (80,81). A recent retrospective study suggested that the quality of analgesia obtained with a CSE technique is better than that obtained with a traditional epidural technique (82). Because of the rapid onset of analgesia when the CSE technique is used, patients with advanced labor may still be able to benefit from neuraxial analgesia. At the University of Missouri, patients rarely fail to receive neuraxial labor analgesia because it is "too late." Comparisons of outcome of labor and complications between CSE and conventional epidural techniques have shown the two to be similar (83–85). A more recent study showed that when an epidural catheter is dosed for cesarean delivery, those catheters placed via a CSE technique are more likely to be successful than those placed via a traditional epidural technique (86). CSE is therefore used almost routinely at the University of Missouri.

While epidural and CSE analgesia for labor have distinct advantages over other methods of labor pain management, absolute and relative contraindications exist. Patient refusal, untreated sepsis, frank coagulopathy, uncorrected hypovolemia/hypotension, and infection at the injection site are the generally accepted absolute contraindications. Relative contraindications may include uncooperative patient, neurologic disease, severe obstructive cardiac lesions, thrombocytopenia, and prior spine surgery. Fortunately, absolute contraindications are rare and the greatest majority of parturients can benefit from neuraxial analgesia.

Complications of Neuraxial Analgesia and Anesthesia

Serious complications from epidural analgesia are rare, but include local anesthetic toxicity, high or total spinal anesthesia, epidural hematoma or abscess, and permanent neurologic injury. Less serious but more troublesome complications are hypotension and post-dural puncture headache.

Local Anesthetics and Local Anesthetic Toxicity

The local anesthetics most commonly used in obstetric anesthesia are bupivacaine, lidocaine, 2-chloroprocaine, ropivacaine, and levobupivacaine. Local anesthetics are composed of a lipophilic aromatic moiety and a hydrophilic amine moiety linked by either an amide or an ester intermediate chain. They are therefore classified as either amides or esters. Except for 2-chloroprocaine, all of the local anesthetics commonly used in obstetrics are in the class of amide local anesthetics. 2-Chloroprocaine is an ester local anesthetic. Of the above local anesthetics, bupivacaine is the most potent, most lipophilic, longest lasting and slowest in onset. Lidocaine

is intermediate in these characteristics and 2-chloroprocaine is the fastest in onset, least potent, least toxic, and shortest in duration. Bupivacaine has been popular as a local anesthetic for epidural labor analgesia because of its capacity to develop a "differential block," meaning that it can provide greater sensory block with less associated motor block at low doses. Bupivacaine, however, has greater cardiotoxic potential than does lidocaine and has been the limiting factor in its use. Generally, seizures will occur during a local anesthetic toxic reaction prior to the onset of cardiac arrhythmias or arrest. However, the cardiotoxic to central neurotoxic plasma ratio for bupivacaine is higher than that for lidocaine, and with a rapid intravascular injection of bupivacaine, cardiac toxicity may be the first event. In addition, bupivacaine has a very slow washout from cardiac tissue and makes resuscitation difficult (87). Indeed, cardio-pulmonary bypass may be needed as a last ditch heroic measure (88). More recently, lipid emulsions have been used successfully to treat toxicity from local anesthetics, specifically bupivacaine (89). Some anesthesia units are now keeping intralipid on their resuscitation carts. It has been thought that pregnancy confers a greater sensitivity to the cardiotoxic effects of bupivacaine (90). This, however, has not been borne out in more recent studies (91). Ropivacaine and levobupivacaine are newer local anesthetics that are related to bupivacaine. While potencies may vary from bupivacaine, they are less cardiotoxic (91). As a result, ropivacaine has become popular in obstetric anesthesia. Concentration of 0.1% or 0.2% ropivacaine with additional opiate is used almost exclusively for labor epidural analgesia at the University of Missouri.

In the event of a toxic reaction, seizures should be controlled with either propofol, midazolam, or thiopental; the airway should be controlled with endotracheal intubation; ventilation should be supported if necessary; and the parturient should be placed in left lateral uterine displacement position. Supplemental oxygen should be administered and fluids be begun. Blood pressure should be supported with additional fluids and vasopressors. Further therapy depends on the results of initial treatment. The administration of intralipid in the face of bupivacaine toxicity is worthy of serious consideration. Cardio-pulmonary resuscitation should be performed in the left lateral position to facilitate venous return and maintain uteroplacental blood flow.

Hypotension

Epidural analgesia has the potential of creating a sympathetic block and subsequent hypotension. This is primarily dependent on the level of block and the rate of administration. It is therefore common practice that patients are prehydrated with 500 to 1000 mL of crystalloid immediately prior to initiation of epidural analgesia. In some cases, a colloid such as hetastarch may be used. The need for routine prehydration with currently used epidural and CSE techniques, however, has been questioned (92). This may be important when caring for patients with conditions mandating limited fluid administration. Clinically significant hypotension that is otherwise asymptomatic to the mother may manifest itself as late decelerations of the FHR or fetal bradycardia. Treatment includes left uterine displacement to

increase venous return, cardiac output and uterine blood flow, intravenous fluids, and judicious administration of vasopressors and oxygen. Ephedrine is the vasopressor of choice. It is both an alpha and a beta receptor agonist and has the potential of causing maternal tachycardia. When maternal tachycardia preexists or is undesirable, then phenylephrine, a pure alpha agonist, can be used.

FHR Changes

Not long following the introduction of CSE analgesia for labor, reports of sudden fetal bradycardia appeared. This was believed secondary to the rapid onset of analgesia with a subsequent drop in circulating catecholamines, resulting in uterine disinhibition and markedly increased uterine activity (93). Subsequent studies comparing the fetal effect of CSE analgesia versus conventional epidural analgesia had varying results. A systematic review in 2002, however, demonstrated that there was indeed an increased risk of fetal bradycardia following CSE analgesia compared with conventional epidural analgesia. Surprisingly, there was no increased risk of cesarean section with CSE, nor was there an increased risk of cesarean delivery in yet another large study of the use of CSE (94,95). Another study in 2004, however, compared the incidence of fetal bradycardia among three groups of patients. Group 1 received a conventional epidural, group 2 received a CSE regimen consisting of low-dose intrathecal bupivacaine and low-dose opioid, and Group 3 received a CSE regimen of only high-dose intrathecal opioid. There was no difference in the incidence of fetal bradycardia between groups 1 and 2, but there was a higher incidence of fetal bradycardia in group 3. The authors recommended limiting the amount of opioid administered intrathecally (96). At the University of Missouri, we therefore use a combination of 3 mL of isobaric ropivacaine 0.1% and 6 µg of fentanyl intrathecally in our CSE regimen. When fetal bradycardia does occur following CSE secondary to uterine hyperactivity, we treat with either terbutaline or sublingual nitroglycerin, both of which have been reported to be effective (93,97,98).

Accidental Dural Puncture

Accidental dural puncture (ADP) is not an uncommon complication of epidural analgesia. The rate may vary from 0.6% to 4.2% in training institutions (83,99). ADP would not necessarily present a problem were it not for the 70% post-dural puncture headache rate associated with the use of 18-gauge epidural needles (100,101). Post-dural puncture headache (spinal headache) typically presents approximately 24 to 48 hours following dural puncture. It is rare for symptoms to appear before 24 hours. Patients typically present with a fronto-occipital headache that may be described as throbbing and severe with associated posterior cervical pain or stiffness. The headache will be totally or nearly totally gone with the supine position and reappear within minutes of obtaining an erect position. It cannot be overly stressed that the hallmark of a post-dural puncture headache is its positional nature. Almost universally, the relief of headache is very noticeable when taking the supine position. The headache is believed to be secondary to low cerebrospinal fluid (CSF) pressure when erect causing traction on meninges and/or reactive cerebral vasodilation (102,103).

Post-dural puncture headache can mimic other more serious conditions, which may include intracranial hemorrhagic disorders, mass lesions and cortical venous thrombosis (104–106). Not all postpartum headache is a post-dural puncture headache. Patients who do not present with classic features of a post-dural puncture headache should be evaluated with further studies such as MRI or CT scanning of the central nervous system.

Post-dural puncture headache can be very debilitating. While the nonpregnant patient recovering from surgery or illness may tolerate long periods of bed rest, the parturient must be able to care for an infant. Inability to maintain an erect posture may interfere with breast-feeding. Treatment of post-dural puncture headache in the obstetric patient population may therefore carry greater importance than that in the rest of the population.

Typical conservative measures of treatment include bed rest, hydration, caffeine, opioids, and nonsteroidal anti-inflammatory analgesics. Caffeine has vasoconstrictive properties that counteract the presumed vasodilation that occurs reactively to low CSF pressures. Sumatriptan, another medication with vasoconstrictor properties used to treat migraine headache, has been shown to be effective in one study but ineffective in another (107,108). Generally, it has not been used as a first-line drug for post-dural puncture headache in the obstetric population.

Epidural blood patch is considered the definitive treatment for post-dural puncture headache. The technique involves the injection of 10 to 20mL of autologous blood in the epidural space near the original epidural puncture site. Its effectiveness has been reported to be as high as 97% (109). A long-term follow-up study of nonobstetric patients, however, showed that only 61% of patients had a permanent resolution of headache despite an initial success rate of 88% to 96% (110). More recently, a study in an obstetric population showed that only 15% required a repeat blood patch (111). Epidural blood patch has a long history of effectiveness and safety. Nevertheless, if a patient should require more than two blood patches, a search for another cause of headache should be made.

Other Complications

High spinal anesthesia is a potentially lethal complication. Large volumes of local anesthetics are required to establish adequate labor analgesia for both the first and second stages of labor. An accidental intrathecal injection of a large volume of local anesthetic has the potential of causing respiratory arrest, hypotension, and even cardiac arrest. Treatment is supportive and requires respiratory assistance including tracheal intubation, fluids, and vasopressors until the block recedes. Careful use of an appropriate test dose prior to dosing the epidural catheter will markedly decrease the likelihood of this complication.

Epidural abscess and epidural hematoma are very rare complications that can be devastating if not diagnosed in a timely manner. Both present as mass spinal lesions with pain, sensory and/or motor loss, and, in the event of abscess, fever. Both almost always require surgical drainage. The risk of abscess can be decreased by paying close attention to sterile technique and by avoiding neuraxial analgesia/anesthesia in

the face of untreated bacteremia or septicemia. Epidural hematoma can be minimized by avoiding neuraxial regional analgesia/anesthesia in the patient at risk for coagulopathy.

Peripheral neuropathies are not rare in the obstetric patient population. When these problems occur in a patient who has had epidural analgesia, the anesthesiologist is often consulted. Lower extremity peripheral neuropraxia can result from stretch or compression lesions that occur during labor and delivery. Foot drop, quadriceps weakness, weak hip adduction, and meralgia paresthetica can result from lumbosacral trunk or peroneal nerve, femoral nerve, obturator nerve, and lateral femoral cutaneous nerve injury, respectively. Peroneal nerve injury can result from nerve compression at the knee due to positioning equipment. Femoral and lateral femoral nerve injury can result from prolonged hip flexion during the second stage of labor. If the patient has a dense epidural block at that time, she may not complain of pain or numbness with overzealous hip flexion. Detailed and conscientious evaluation will help differentiate peripheral obstetric neuropathies from direct nerve root or spinal cord injuries (112). Early neurology consultation and spine imaging may elucidate the etiology and direct appropriate treatment in a timely manner.

Epidural Analgesia and the Progress of Labor

The effect of epidural analgesia on the progress and outcome of labor has, in the past, been controversial. Retrospective studies have demonstrated an increased risk of cesarean delivery when epidural analgesia was utilized (113). Subsequent prospective randomized studies, however, did not show any significant difference in the cesarean delivery rate when patients were randomized to receive either epidural or parenteral analgesia (114,115). While prospective randomized studies provide good data, problems still exist. Patients do not always stay in their assigned group, leading to “intent to treat” analyses. Retrospective “sentinel” event studies overcome this confounding factor. These studies examine the cesarean delivery rate before and after the institution of an “on demand” epidural analgesia service (116). While retrospective in nature, there are no selection biases and no opportunity for patients to drop out of a study group. Results of these studies show that there is no increase in cesarean delivery rate when there is a sudden increase in the utilization of epidural analgesia. One study in particular did offer an interesting insight. While there was no change in cesarean delivery rate with a marked increase in epidural analgesia overall, it was noted that following the institution of epidural analgesia on demand, those women who went on to cesarean delivery for dystocia were approximately eight times more likely to have had an epidural. The authors concluded that dystocia is more painful and women who request epidural analgesia are already at risk for cesarean delivery for dystocia (117). This result may explain why retrospective studies that examined cesarean delivery rates in institutions where epidural analgesia services were well established showed higher rates of cesarean delivery in association with epidural analgesia. Patients who request epidural analgesia are different from those who do not. Epidural analgesia is therefore a risk marker, not a risk factor.

While epidural analgesia does not increase the risk of cesarean delivery for dystocia, it does slow labor. A meta-analysis of randomized trials published in 1998 concluded

that, overall, the first stage of labor increased by 42 minutes and the second stage of labor by 14 minutes (114,118). A more recent study concluded that while the first stage of labor is not prolonged, the second stage is (119). Not only does epidural analgesia not increase the incidence of cesarean delivery for dystocia but neither does the timing of epidural placement. A study published in 2005 examined the cesarean delivery rate of early (less than 4cm dilatation) versus late epidural placement and found no difference in the cesarean delivery rate for dystocia. Indeed, patients who had early CSE analgesia had shorter labors (120). At the University of Missouri, women are not required to reach a preset cervical dilatation before epidural analgesia is administered. This position is supported by the American College of Obstetricians and Gynecologists, which has recently stated:

... the decision of when to place epidural analgesia should be made individually with each patient, with other factors, such as parity, taken into consideration. Women in labor should not be required to reach 4–5cm of cervical dilatation before receiving epidural analgesia (121).

Epidural Analgesia and Maternal Fever

A rise in maternal temperature has been associated with the use of epidural analgesia (122). Studies that are retrospective and/or nonrandomized are likely to be biased because factors that lead to increased requests for epidural analgesia such as long labors complicated by dystocia are also likely to lead to maternal fever. Nevertheless, prospective randomized trials have shown that a rise in maternal temperature can occur in association with epidural use in the absence of infection (123). The reasons are unclear and have been attributed to alterations in vascular responsiveness and thermoregulatory control. Parturients who shiver immediately following induction of epidural analgesia are more likely to develop an earlier and greater rise in temperature than those who do not (124). While mild to modest increases in maternal temperature may not have significant physiologic significance, it has led to increases in neonatal sepsis evaluations (125). When criteria for neonatal sepsis evaluations are better refined, however, there are no increases in sepsis evaluations of neonates born to women with epidural-associated fevers (126). Currently, the wide use of epidural analgesia does not seem to be negatively effected by concerns regarding the association of epidural use and maternal fever (119).

ANESTHESIA FOR CESAREAN DELIVERY

The cesarean delivery rate in the United States has steadily increased during the past several decades. In high-risk tertiary care institutions, rates have climbed higher than 30% (127).

In 1981, general anesthesia was used more often than either epidural or spinal anesthesia in larger institutions (>1500 deliveries per year). By 2001, only 3% of elective cesarean deliveries were performed under general anesthesia, the remainder utilizing either spinal or epidural anesthesia (128). These data underscore the preference for regional anesthesia for cesarean deliveries. Significant advantages exist over general anesthesia: an awake mother with spontaneous respirations and ability to control the airway with a lower

risk of aspiration, contracted gut, more complete muscular relaxation, and an opportunity to provide excellent post-operative analgesia with the use of spinal opiates.

From 1979 to 1990, the maternal mortality rate from anesthesia-related causes for patients undergoing cesarean delivery in the United States steadily decreased for regional anesthesia but remained approximately the same for general anesthesia. By 1990, the relative risk of death from anesthesia-related causes in cesarean delivery patients was 16.7 for general versus regional anesthesia (129). By 1996, the relative risk decreased to 6.7 (130). The major risks from general anesthesia are primarily inability to intubate, inability to ventilate and aspiration. Pregnant patients at term and in labor are considered to be individuals with “full stomachs” due to increased gastric emptying time. In addition, pregnant patients at term are more likely to present with “difficult airways” that cannot be intubated by conventional means or ventilated (131). Because term pregnant patients are considered to have “full stomachs,” general anesthesia must be administered via a “rapid sequence” induction technique. With patients who are not at risk for aspiration, anesthesia is generally induced with an intravenous agent that usually renders the patient apneic. An attempt at mask ventilation is made and, if successful, a muscle relaxant is administered and mask ventilation is continued until the patient is ready for intubation. During this time, aspiration is possible since airway reflexes are obtunded and the airway is unprotected. This event is extraordinarily rare, however, in patients who have no risk factors for aspiration such as morbid obesity, full stomachs or trauma. In patients who are at risk of aspiration, such as pregnant women, an induction agent is administered and immediately followed with a rapidly acting muscle relaxant and intubation without first testing the airway with mask ventilation. Cricoid pressure is applied to reduce the chance of regurgitation. This technique, known as the rapid sequence induction, diminishes the time that the airway is unprotected and is therefore the standard technique used for patients who are at risk of aspiration. Patients who are unexpectedly found to have an airway that cannot be intubated or ventilated at this time, however, become susceptible to hypoxic injury or death. For this reason, all pregnant patients at risk for cesarean delivery should have their airways evaluated. At the University of Missouri, all patients admitted in labor are examined regardless of the anticipated need for analgesia/anesthesia. This allows the anesthesiologist to identify in advance patients who may have a “difficult airway.” Plans to avoid or limit the likelihood of general anesthesia for a “stat” cesarean delivery can then be made in advance for these at risk patients.

General Anesthesia

Despite the increased risks of general anesthesia over regional anesthesia, it still has indications and some advantages under specific circumstances. It can be administered quickly and reliably. Uterine relaxation responds to potent inhalation anesthetics (e.g., sevoflurane, isoflurane, and desflurane) in a dose-dependent manner. When marked uterine relaxation is required such as with in utero fetal surgery, intrauterine manipulations, and placental extractions, general anesthesia with potent inhalational anesthetics is reliable and effective. General anesthesia is most often chosen either because of

coexisting contraindications to regional anesthesia or because circumstances do not allow time to establish a sufficient level of regional anesthesia.

The usual technique for general anesthesia for cesarean delivery is to administer a non-particulate clear antacid shortly prior to induction. The patient is then placed in supine position with left uterine displacement, standard monitors are applied, and the patient is pre-oxygenated with four or five vital capacity breaths of 100% oxygen. Cricoid pressure is then applied just prior to induction with an intravenous agent such as propofol or thiopental and followed immediately with the administration of the rapid-onset, short-acting muscle relaxant succinylcholine. Following approximately 60 seconds, the trachea is orally intubated. Once intubation is confirmed via breath sounds and end-tidal CO₂, the cricoid pressure can be released and incision made. Potent inhalational agents are usually continued at low concentrations with or without the addition of nitrous oxide. Pregnancy confers a greater sensitivity to anesthetics, which is fortuitous because inhalational agents cause uterine relaxation in a dose-dependent manner. At low concentrations of inhalational agents, oxytocin can still be effective in providing uterine contractility and hemostasis. When necessary, the potent inhalational agent can be discontinued. Nitrous oxide does not cause uterine relaxation and can be initiated or continued with the addition of narcotics, benzodiazepines, and muscle relaxants. In order to decrease the risk of aspiration upon emergence, the patient should be extubated when sufficiently awake such that airway protective reflexes are intact and the risk of laryngospasm is low.

A misconception that many obstetricians have is that time is of the essence in performing a cesarean delivery under general anesthesia. Uterine incision to delivery time is more important in neonatal outcome than induction to delivery time. With regional anesthesia, neonates do not become acidotic until greater than 3 minutes have elapsed following uterine incision (132). Induction agents used for general anesthesia do not anesthetize the neonate when usual doses are given. The reasons for this are multifactorial and include dilution of the induction agent with blood from the fetal vena cava, first-pass fetal hepatic metabolism, and fetal shunting. Furthermore, in sheep models, a period of 15 to 20 minutes is required for isoflurane administered to the ewe to reach full anesthetizing levels in the fetal circulation (133). Even if a prolonged induction to delivery time is required, as long as maternal blood pressure and oxygenation are maintained, an anesthetized but not severely acidotic neonate is likely to be delivered as long as fetal distress was not present at the time of induction and uterine incision to delivery time was less than 3 minutes. It is probably better for the obstetrician to take sufficient time to perform a careful operation than risk maternal injury for fear of delivering an anesthetized infant.

Spinal Anesthesia

Spinal anesthesia is more correctly termed intrathecal or subarachnoid anesthesia as the local anesthetic drug is injected through the dura-arachnoid into the CSF below the terminal end of the spinal cord. The most common interspaces chosen are the L3–4 or L4–5 levels. Hyperbaric bupivacaine is most commonly used in the United States. A dosage of 12 mg

reliably offers a sufficient level of anesthesia to keep the patient comfortable, although some practitioners may use slightly more or less than 12 mg (134,135). This dosage may be less than what is commonly used in the nonobstetric patient population as pregnancy confers greater sensitivity to local anesthetics. In addition, engorged epidural vasculature may lead to lower spinal CSF volumes. While a lower abdominal incision is utilized in cesarean deliveries, a T4 anesthetic level is required for lower abdominal intraperitoneal operations. Pain from peritoneal traction may be referred to mid or upper thoracic levels. Testing the level of anesthesia at the lower abdomen prior to incision will therefore not guarantee a sufficient level of anesthesia once the peritoneal cavity is entered. A single injection spinal anesthetic utilizing 12 mg of hyperbaric bupivacaine will provide 90 to 120 minutes of anesthesia.

Hypotension is the most common side effect of spinal anesthesia and can be limited but not completely prevented by prehydration with 1000 to 1500 mL of crystalloid administered immediately prior to induction. The use of colloid may be more effective (136). When fluid administration is insufficient to prevent or treat hypotension, vasopressors are often required. In the past, ephedrine had been the drug of choice. Ephedrine has both alpha and beta agonist properties. Phenylephrine, however, is a pure alpha vasoconstrictor and was once considered to be potentially harmful as it was shown in sheep models that potent vasoconstrictors decrease uterine blood flow (137). More recently, it has been determined that, clinically, phenylephrine does not have deleterious fetal/neonatal effects when administered judiciously. Indeed, infants born to mothers receiving phenylephrine have higher umbilical cord arterial blood pH levels than those treated with ephedrine (138). Another troublesome side effect from spinal anesthesia is post-dural puncture headache. The use of small-gauge pencil-point needles, however, has reduced the incidence of post-dural puncture headache to an acceptable rate of 0.5% to 1% (139). In a 2001 survey, spinal anesthesia was the most commonly used anesthetic technique for elective cesarean delivery. Even for emergent cesarean deliveries, spinal anesthesia was used 45% to 59% of the time (128).

Epidural Anesthesia

Epidural anesthesia for cesarean deliveries is most often used for women who have been in labor with an active epidural analgesic already in place. The level of the block can be intensified and extended by dosing the catheter with 2% lidocaine with epinephrine, 3% 2-chloroprocaine, 0.5% bupivacaine, or 0.5% ropivacaine. Epidural anesthesia has the advantage of titration of the level of block, slower onset with greater ability to manage hypotension, and flexibility. The epidural catheter can be re-dosed as needed for procedures that end up being longer than anticipated. Lidocaine 2% with epinephrine 1:400,000 or 1:200,000 is probably the drug most often used. It is relatively rapid in onset and of intermediate duration lasting 90 to 120 minutes. 2-Chloroprocaine 3% has an onset time within 8 minutes or less in laboring patients with preexisting epidural catheters and can be used for urgent cesarean deliveries (140). It is rapidly metabolized in maternal serum with little transfer and accumulation in an acidotic fetus (141). 2-Chloroprocaine has a shorter duration of action,

however, lasting 40 to 50 minutes. When used, it must be followed up with additional local anesthetic, most often 2% lidocaine. 2-Chloroprocaine may interfere with the effectiveness of subsequently administered bupivacaine or epidurally administered opioids (142,143).

Epidural anesthesia for cesarean delivery may not be as reliable as spinal anesthesia. Incomplete or "patchy" block may limit its usefulness. This may require extra time to allow further distribution of the local anesthetic. The addition of epidural adjuvants such as fentanyl may be helpful. Intravenous additives such as opioid, small judicious doses of propofol, or ketamine may also be required. The anesthesiologist must be careful not to obtund the patient's airway reflexes. Ketamine in small doses is often useful under these circumstances as it provides profound amnesia and analgesia. It can cause dysphoria and therefore requires the addition of midazolam to limit this unpleasant side effect. When epidural anesthesia is ineffective, general anesthesia may be necessary. From the standpoint of airway protection, general endotracheal anesthesia is the most conservative approach to take. Ineffective or incomplete epidural anesthesia during cesarean delivery can be avoided if the effectiveness of the labor epidural is carefully evaluated prior to cesarean delivery. If there is any question, then proceeding to spinal anesthesia or repeat placement of the epidural catheter is in order (144).

If spinal anesthesia is chosen immediately following failed or unsuccessful epidural anesthesia, then caution must be taken to avoid a high spinal block, which may render the patient hypotensive and/or apneic. The reasons for this may be related to an already existing partial block or compression of the intrathecal sac from epidurally administered fluid. A downward adjustment of local anesthetic dose may therefore be necessary (145). If the anesthesiologist chooses to replace the epidural catheter, the potential for local anesthetic toxicity must be kept in mind as large doses of local anesthetic are typically used.

CSE Anesthesia

CSE anesthesia offers the advantages of both the techniques for cesarean delivery. Spinal anesthesia provides a more rapid onset and more reliable block than does epidural anesthesia (146). Because of its rapid onset, however, maternal hypotension may be problematic. In addition, spinal anesthesia provides a fixed time period of anesthesia. Should the operative time run beyond the length of the spinal anesthetic, then general anesthesia may be required for the remainder of the procedure. CSE anesthesia allows for the use of lower doses of spinal anesthetic, minimizing maternal hypotension, and has the flexibility to extend and prolong the duration of the block via epidural "top-ups" during the procedure (147,148). At the University of Missouri, we often use CSE anesthesia when a longer than usual procedure is anticipated such as multiple prior cesarean deliveries, morbid obesity, or anticipated cesarean hysterectomy. The more favorable hemodynamics and reliability of CSE anesthesia have allowed regional anesthesia to be utilized in patients with severe pre-eclampsia and obstructive cardiac lesions (149–151).

Post-cesarean Pain Management

The increasing use of regional anesthesia for cesarean delivery has been paralleled with an increasing use of spinal opioids for

the management of postoperative pain. Postoperative pain following cesarean delivery is unique in that the parturient must care for a newborn infant as well as for herself. Parenteral opioids have a long history of effectiveness, but can be associated with troublesome side effects, particularly somnolence. Spinal opioids administered epidurally or intrathecally can provide effective pain relief with a minimum degree of somnolence. Preservative free morphine is probably the most commonly used drug in the United States. It can be administered intrathecally at the time of spinal anesthesia or via the epidural catheter during or immediately following cesarean delivery. A single dose of morphine, 2 to 5mg, administered via an epidural catheter will provide pain relief for up to 24 hours (152). While a portion of the morphine administered into the epidural space will be absorbed into the vasculature and redistributed to the CNS, the remainder will transfer directly to the CSF and bind to mu receptors at the spinal cord level. Stimulation of mu receptors in turn blocks the transmission of nociceptive signals to higher levels (153). Administered intrathecally at the time of spinal anesthesia, small doses of morphine, ranging from 0.1 to 0.25mg, will provide analgesia for 18 to 24 hours (154,155). Unlike local anesthetics, spinal opiates do not cause motor block and allow for early ambulation.

Other opiates have been used in place of or in addition to morphine. Meperidine and hydromorphone have also been used successfully (156,157). Fentanyl is more lipid soluble than morphine. It quickly binds to mu receptors at the spinal cord level and is of much shorter duration lasting only a few hours. It is usually used as an adjunct to local anesthetics during cesarean delivery. If it is to be used at all for postoperative pain relief, it is usually added to a continuous epidural infusion of low-concentration local anesthetic.

While effective in providing pain relief, spinal opiates are not without troubling side effects. Nausea and vomiting, pruritus, and respiratory depression can complicate an otherwise excellent method of postoperative analgesia. These side effects are primarily mediated by mu receptors. Mu antagonists can therefore be used for treatment when side effects become particularly bothersome. It is important to note that pruritus from spinal opiates is not primarily histamine mediated. Antihistamines are therefore less likely to be effective in treating pruritus than mu antagonists. Low-dose naloxone either as a bolus or continuous intravenous infusion can effectively treat side effects without diminishing analgesia (158). Agonists–antagonists such as nalbuphine have also been used successfully (159).

Of the side effects that can occur with the use of spinal opiates, respiratory depression is the most concerning. Fortunately, most obstetric patients are young and healthy with a very low incidence of significant respiratory depression following the use of spinal opiates (152). Nevertheless, it is prudent to follow these patients closely with hourly nursing checks and/or continuous pulse oximetry. It is important to note that with spinal morphine, respiratory depression may be delayed by up to 12 hours following administration. Most anesthesiologists therefore wish to be consulted before any sedative drugs are administered to patients who have received spinal morphine during the first 24 postoperative hours. While side effects and the fear of respiratory depression may be

disconcerting, spinal opiates have become the mainstay of postoperative pain management following cesarean delivery in the United States.

ANESTHESIA FOR THE HIGH-RISK PATIENT

Of the myriad complications of pregnancy that have anesthetic implications, pre-eclampsia and deteriorating fetal status (fetal distress) are among the more common. In prior decades, patients with congenital heart disease did not often survive to reproductive age. Currently, however, more and more patients are living to childbearing age and it is becoming more common to encounter patients with corrected or partially corrected congenital heart lesions. With the obesity epidemic making its way into an ageing obstetric population, we can expect to see an increase in the frequency of cardiovascular diseases complicating pregnancy.

Pre-eclampsia/Eclampsia

Hypertensive disorders complicate 5% to 10% of pregnancies. While pre-eclampsia affects multiple systems, the cardio-pulmonary, hepatic, coagulation, and airway systems are of particular interest to the anesthesiologist. Patients with severe pre-eclampsia are intravascularly volume depleted even though there may be a positive water and sodium balance. Intravascular volume depletion may present a challenge to the anesthesiologist providing regional analgesia for labor or anesthesia for cesarean delivery. In addition, most patients with severe pre-eclampsia have some degree of increased systemic vascular resistance with varying degrees of cardiac function ranging from hyperdynamic to normal to impaired (160). In the past, epidural analgesia for labor was controversial in patients with severe pre-eclampsia because of the concern for marked reductions in blood pressure and utero-placental blood flow. Epidural analgesia, however, has been shown to provide superior pain relief, decrease blood pressure, decrease catecholamine levels, and improve utero-placental blood flow (161,162). Marked drops in blood pressure can be prevented with judicious use of crystalloids and or colloids for prehydration and treated with small doses of ephedrine. Indeed, in a 2001 study, the incidence of hypotension requiring treatment was only 11% (163). In patients whose severe pre-eclampsia is complicated by pulmonary edema and/or oliguria, further studies including invasive central monitoring and/or echocardiography may be indicated before initiating epidural analgesia.

General anesthesia for cesarean delivery in patients with severe pre-eclampsia can be particularly hazardous. An edematous airway can make intubation difficult or impossible, posing a serious threat to maternal safety. Tracheal intubation during general anesthesia is very stimulating and can be associated with dangerously high blood pressures placing the patient at risk for intracranial hemorrhage. For these reasons, regional anesthesia is the preferred method of anesthesia in patients with severe pre-eclampsia. When general anesthesia is necessary, blood pressure should be controlled with additional doses of antihypertensives. The response to intubation can be blunted with opioids and/or intravenous lidocaine just prior to induction. Awake intubation may be necessary to avoid the very dangerous cannot-intubate/cannot-ventilate scenario.

In the past, spinal anesthesia was not recommended in patients with severe pre-eclampsia undergoing a cesarean delivery. Many anesthesiologists believed that spinal anesthesia would lead to difficult-to-treat hypotension. More recent studies however have shown that the incidence or severity of hypotension is no greater in severe pre-eclamptic patients having spinal anesthesia than epidural anesthesia (164). It is interesting to note that a study as far back as 1950 demonstrated that severe pre-eclamptic patients were more resistant to hypotension following spinal anesthesia than were normal patients (165). At the University of Missouri, spinal anesthesia is frequently administered to patients with severe pre-eclampsia undergoing cesarean delivery.

The coagulopathy that may accompany severe pre-eclampsia is another major concern to the anesthesiologist. Uncorrected severe coagulopathy is an absolute contraindication to regional analgesia/anesthesia for fear of traumatizing the epidural vasculature, which in turn may lead to the formation of an epidural hematoma. Most anesthesiologists will place an epidural catheter or perform a spinal anesthetic with platelet counts above 100,000/mm³ in the absence of any clinical evidence of abnormal bleeding. There is no absolute cutoff for platelet counts below which regional anesthesia is contraindicated. Regional analgesia/anesthesia has been safely performed in parturients with platelet counts as low as 50,000/mm³ to 69,000/mm³ when other coagulation indices are normal and there is no clinical evidence of abnormal bleeding (166,167). The decision to perform regional analgesia/anesthesia in a patient with thrombocytopenia, however, must always be made on an individual basis keeping the risk/benefit ratio in mind. It is also worthwhile to keep in mind that epidural hematomas are very rare in the pregnant patient population. Difficult airways, unfortunately, are not.

Early anesthesia consultation is recommended when the obstetrics service admits a patient with severe pre-eclampsia. This is particularly true in patients who are at risk for an emerging coagulopathy. Many obstetric anesthesiologists are now advising early epidural placement when the patient is committed to delivery. As the disease progresses, regional anesthesia may not be possible further in labor if a coagulopathy is already well established. An epidural catheter placed early in labor can be continued even if the platelet count drops to very low levels. Not only would this allow the patient to receive the benefit of epidural analgesia for labor, but in the event of cesarean delivery, the epidural catheter can also be dosed to a surgical level of anesthesia and avoid the much greater hazards of general anesthesia.

Deteriorating Fetal Status

The term "fetal distress" is imprecise and nonspecific. Its use can often lead to unnecessary haste, placing both the mother and the fetus at risk for complications and medical errors. The American College of Obstetricians and Gynecologists has recommended that the term "fetal distress" be replaced with "non-reassuring fetal status" with further descriptors clarifying the abnormality or presumed etiology (168). Either regional anesthesia or general anesthesia can be used for cesarean deliveries performed for non-reassuring fetal status with comparable outcomes (169). In instances of non-reassuring fetal status, the degree of urgency and time limitations often

determine the choice of anesthesia. Some practitioners have the perception that general anesthesia can be administered more rapidly than regional anesthesia and have encouraged its use when “fetal distress” is diagnosed. It must be kept in mind, however, that the risk of maternal mortality from anesthetic causes is significantly greater for general anesthesia than regional anesthesia (130). Recognizing the increased maternal risks of general anesthesia versus regional anesthesia, the American College of Obstetricians and Gynecologists has recently stated:

The significant added morbidity of general anesthesia over regional anesthesia for cesarean delivery suggests that regional anesthesia is the preferred method of pain control and should be used unless a contraindication to regional anesthesia is present. Although general anesthesia may be indicated in some cases of fetal heart rate abnormality, the severity of the abnormality should be considered before incurring the excess risk of maternal mortality associated with general anesthesia (170).

Inability to intubate and aspiration of gastric contents present the greatest risk of general anesthesia to the parturient. The incidence of failed intubation has been estimated to be as high as 1 in 250 patients (171). When patients at risk for failed intubation are identified, close communication among obstetric and anesthesia team members is critical. These patients may benefit from early epidural catheter placement. When anesthesia team members are notified early in the process of initiating a “stat” cesarean delivery, dosing a well-established labor epidural catheter for cesarean delivery can be performed nearly as rapidly as general anesthesia (172). When an unexpected difficult airway is encountered, a decision must be made to proceed without the benefit of endotracheal intubation, incurring the risk of aspiration, or allowing the patient to awaken and proceeding with an awake intubation technique, which will usually require much more time to accomplish than the standard rapid sequence induction. Newer ventilation and intubation methods such as the laryngeal mask airway (LMA), intubating LMA, and Pro-Seal LMATM have been recognized as valuable techniques for managing these very stressful situations (173,174). If ventilation cannot be established, then either the patient must be awakened or a surgical airway be established (175).

The importance of close communication between obstetrician and anesthesiologist cannot be stressed more. The highest risk to the patient occurs when an anesthesiologist first encounters a patient already in the operating room prepped and draped for “stat” cesarean delivery. The anesthesiologist is given very little time to evaluate the patient and prepare for anticipated difficulties. Conversely, the obstetrician must be apprised as early as possible when the anesthesiologist anticipates difficulty. At the University of Missouri, when patients are brought to the operating room for “stat” cesarean delivery for rapidly deteriorating fetal status, FHR monitoring is continued. This allows the establishment of regional anesthesia to continue if the FHR returns to normal or to stable levels. If an internal electrode is in place, it is

not removed until just prior to incision or may be kept in place if general anesthesia is required. The real-time information gained with this approach may help guide the management of a failed intubation. In the event of a failed intubation, if fetal status has improved and remains stable, the patient can be awakened and a different course of action can be taken. If there is continued fetal deterioration, the anesthetic can then be continued by mask or LMA as noted above, with continuous cricoid pressure (176).

Cardiac Disease

The cardiac adaptations to pregnancy are well known. Blood volume and cardiac output increase significantly during gestation and are tolerated very well in healthy individuals. Women with cardiac disease who otherwise may be sufficiently compensated in the nonpregnant state, however, may deteriorate significantly when faced with the cardiac demands of pregnancy.

Congenital Heart Disease

In 2001, the majority of pregnant women presenting with cardiac disease were those with congenital heart disorders (177). This is not surprising since a greater number of women with congenital heart disease are living to childbearing age than that in earlier decades. Patients with fully corrected lesions with no residual dysfunction do well during pregnancy and do not require special attention other than prophylactic antibiotics. Those with partially corrected lesions or residual dysfunction, however, may require special considerations.

Individuals with shunts must maintain a balance between right- and left-sided pressures. Increasing left-sided pressures such as systemic hypertension may worsen preexisting left-to-right shunting. A right-to-left shunt will worsen if peripheral vascular resistance drops as it may with regional anesthesia. Patients with obstructive lesions who are preload dependent may decompensate if there is a significant drop in venous return. In the past, regional anesthesia was considered relatively contraindicated in these individuals. More recently, however, regional anesthesia has been shown to be of benefit in many patients and is recommended when it is advisable to avoid the high catecholamine levels of pain and stress, which may lead to maternal tachycardia, systemic hypertension and pulmonary hypertension (178). Patients with obstructive lesions and pulmonary hypertension who do not tolerate drops in venous return or systemic vascular resistance may still significantly benefit from epidural analgesia, provided that it is dosed slowly while maintaining preload and systemic vascular resistance. Patients with regurgitant lesions and left-to-right shunts may benefit from the decreased systemic vascular resistance that epidural analgesia provides as it promotes forward flow. The increased demands on cardiac output, workload, and oxygen consumption present during the second stage of labor can be ameliorated with a carefully managed epidural analgesic allowing for a passive second stage of labor. Patients with these lesions may require invasive monitoring as well as continuous oxygen saturation monitoring to optimize cardiac function and avoid the hemodynamic perturbations that regional anesthesia may cause.

Valvular Lesions

Patients with stenotic valvular lesions and dynamic obstructive cardiomyopathy do not tolerate tachycardia and decreased systemic vascular resistance well, nor do they tolerate the tachycardia and stress associated with the pain of labor. Epidural analgesia is beneficial in these individuals as long as preload and systemic vascular resistance are maintained. This is particularly true during the second stage of labor. When treating hypotension in these patients, beta agonists are to be avoided.

Epidural analgesia is the preferred pain management technique in patients with regurgitant valvular lesions. The decreased systemic vascular resistance that results from regional anesthesia decreases afterload, reduces the regurgitant fraction, and improves forward flow. In addition, it prevents the increase in systemic vascular resistance that results from the pain of labor.

Ischemic Cardiac Disease

Ischemic cardiac disease in pregnancy is rare. Nevertheless, as the pregnant patient population ages, particularly in association with assisted reproductive techniques used in an aging population, we can expect to see increasing numbers of patients with coronary artery disease. Epidural analgesia is well suited to this patient population. The sympathectomy associated with epidural analgesia decreases catecholamine levels and cardiac workload. A passive second-stage labor can be achieved, which will further decrease myocardial oxygen demand. Perfusion pressures must be maintained, however, but epinephrine-containing local anesthetic and beta agonists should be avoided as they may lead to troublesome tachycardia. Intensive cardiac monitoring may be necessary in patients who have significant myocardium at risk.

The successful management of the pregnant cardiac patient requires an interdisciplinary approach. Obstetrician, cardiologist, and anesthesiologist should be involved early in the patient's pregnancy. Clinical data, particularly results of echocardiograms and stress tests, should be shared among all involved prior to the patient's arrival on labor and delivery. It does not serve the patient well when the anesthesiologist is first consulted at the time that the patient is already in active labor or presents for cesarean delivery. Early consultation will provide for a coordinated team approach leading to the best results possible (178).

CONCLUSION

Obstetric anesthesia has made great strides over the past 50 years. Maternal mortality from anesthetic causes has declined dramatically, primarily due to increasing usage of regional anesthesia. Regional analgesia for labor is effective, safe, and has little effect on the course of labor or neonatal outcome. Newer techniques have led to the expansion of regional analgesia to allow for its application to a wide range of patients with pregnancy complications. In contemporary labor and delivery units, virtually all patients are able to enjoy the benefits of regional analgesia should they choose to do so.

Currently, a national effort is underway to improve patient safety. As part of this effort, anesthesiologists are becoming more and more proactive in perioperative and obstetric care. At the University of Missouri, strategies have been developed

and are continuing to be refined, to help reduce general anesthesia-related morbidity and mortality. An attempt is made for an anesthesiologist to evaluate all patients admitted to labor and delivery regardless of the anticipated need for anesthesia services. Patients who may present with potential anesthetic complications are referred for anesthesia consultation during gestation, prior to admission. This includes patients who are morbidly obese, have had prior anesthetic difficulties or a family history of anesthesia complications. This is also true for patients with heart disease, prior spine surgery, neurologic, hematologic, or significant pulmonary disorders. Patients with an anticipated or known difficult airway are encouraged to have an epidural catheter placed early in labor. This is also true for patients at risk of developing a coagulopathy, such as with severe pre-eclampsia or hemolysis, elevated liver enzymes, and low platelet count syndrome.

It cannot be overstressed that continuous close communication with all members of the obstetric team is vital to improving patient outcome.

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