J Anesth (2003) 17:30–41

Journal of
Anesthesia

Review article

Recent advances in obstetric anesthesia

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Key words Combined spinal/epidural · Preeclampsia · Preloading · Conservation · Regional

Introduction

Obstetric anesthesia has developed over the last one and a half centuries, and has grown into a dominant specialty of its own. This parallels an important change in the philosophical thinking, and attitude, to the relief of pain in labor. The safety of obstetric anesthesia has increased, primarily due to the awareness of local anesthetic toxicity and the increased use of regional techniques. Maternal mortality, directly related to regional anesthesia, has dramatically decreased. This article will review the current opinion on the following areas of obstetric anesthesia: the combined spinal/epidural technique, the role of spinal anesthesia for cesarean section in severe preeclampsia, acute hydration prior to spinal anesthesia, and blood-conservation strategies in obstetrics.

1) Combined spinal/epidural analgesia

The combined spinal/epidural technique (CSE) has gained increasing popularity in recent years. In obstetric practice, it is employed for both labor analgesia and anesthesia for cesarean section. A recent survey in the United Kingdom indicates that 24% of obstetric anesthesia departments are now using the CSE technique [1]. The CSE technique is one wherein selected advantages of both spinal and epidural techniques are combined, without an increase in complications. It provides rapid onset of analgesia with minimal local anesthetic dosage and has the flexibility and unlimited duration of an epidural technique.

History

The earliest reference to CSE appeared in 1937. Soresi [2], a surgeon, described a technique whereby local anesthetic was injected, first into the epidural space, and then into the subarachnoid space, through the same spinal needle. In 1979, Curelaru, a Romanian anesthesiologist, utilized a two-segment technique. The spinal block was performed at one to two interspaces below the epidural catheter. Brownridge [3] described a similar technique for cesarean section in 1981. The epidural catheter was used to extend the surgical block, if necessary, and for postoperative analgesia. A single-space "needle-through-needle" technique was reported for orthopedic surgery in 1982, and for cesarean delivery, by Carrie and O'Sullivan [4], in 1984. In this technique, the epidural needle serves as an introducer for a long, fine spinal needle. In 1986, Rawal [5] described a two-stage, single-space technique, in which the epidural catheter was used to gradually raise the level of an intentionally low spinal block.

Technique

In the CSE technique, a long spinal needle (e.g., $4\frac{11}{16}$-inch 25-gauge Whitacre point) is placed through a properly sited epidural needle (typically $3\frac{1}{2}$ inches), cerebrospinal fluid (CSF) is obtained, medication is injected, and an epidural catheter is placed. This is the "needle-through-needle" technique [6]. Using this combination, 12 mm of spinal needle will protrude from the tip of the epidural needle. Administration of epidural

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Received: September 26, 2001 / Accepted: October 25, 2002

medications at this time is at the discretion of the anesthesiologist. If no medication is given initially, then an appropriate test dose should be used when the epidural catheter is subsequently used. The "needle-through-needle" is currently the most popular technique. There are also several commercially available combined-needle devices, which incorporate a specific channel for the spinal needle, distinct from the channel for the epidural catheter.

CSE for labor analgesia

The advantages of a CSE technique are that it provides a rapid onset of profound analgesia and includes the placement of an epidural catheter, for use if the extent or duration of the spinal analgesia is inadequate. Maternal satisfaction is high [7,8]. The adjuvant use of neuroaxial opioids allows for lower doses of local anesthetics to be used. This enhancement of analgesia comes without additive motor blockade or hypotension, with the exception of meperidine, which, because of its unique local anesthetic-like properties, may result in motor block, hypotension, or loss of proprioception [9]. Because CSE allows for ambulation of the parturient, it has been called the "walking epidural".

It has been observed that subsequent epidural analgesia can be achieved with lower doses of local anesthetic than if prior intrathecal opioid had not been used. The intrathecal route of opioid administration provides analgesia which is more profound and of more rapid onset than the epidural route [10]. Epidural opioids, alone, do not provide very effective labor analgesia. However, their combination with small amounts of local anesthetic dramatically enhances the efficacy of epidural opioids [11,12]. The presence of even a small-bore dural puncture has been shown to enhance the caudal spread of subsequently administered epidural medications, resulting in good sacral analgesia [13].

CSE for early labor generally involves a short-acting, lipid-soluble opioid such as fentanyl (10–25 μg) or sufentanil (5–15 μg), given intrathecally. Morphine (0.1–0.5 mg) can also be used, but it has a slower onset (30–60 min) and is associated with a higher incidence of severe pruritus and delayed respiratory depression. Because analgesic requirements are greater in advanced labor, the addition of a small dose of local anesthetic (2.5 mg bupivacaine) to the intrathecal opioid provides rapid onset of more prolonged effective analgesia (90–180 min), when compared with opioid alone. Undesired effects of local anesthetics, such as hypotension and motor blockade, are minimal with this combination [14,15]. With the employment of this opioid/local anesthetic combination, the patient may ambulate with assistance. A study by Stacey et al. [16], using 5 mg intrathecal bupivacaine, produced an unacceptably high incidence of motor blockade. The addition of epinephrine to the local anesthetic has been shown to significantly prolong the duration of effective analgesia [17].

When should the epidural infusion be started? Some practitioners wait for the spinal block to resolve, but it is our practice to give 1 ml (2.5 mg) of bupivacaine with 25 μg of fentanyl intrathecally, followed immediately by continuous epidural infusion of 0.125% bupivacaine with 2 μg/ml of fentanyl at 10 ml·h^{-1}. This allows for a smooth transition between the spinal and epidural portions of analgesia.

Intrathecal opioids are associated with dose-dependent side-effects, such as nausea, vomiting, sedation, pruritus, and respiratory depression. These side-effects may be increased if the patient has already received systemic opioids, and the incidence is higher with morphine than with fentanyl or sufentanil. The use of pulse oximetry is strongly recommended with intrathecal opioids.

CSE technique and the progress of labor

Several prospective, randomized clinical trials have examined the effect of CSE on the progress and outcome of labor. Nageotte et al. [18] compared CSE with standard epidural analgesia, and found no significant differences in the overall cesarean section rate, incidence of dystocia, or frequency of maternal or fetal complications between the two groups. Gambling et al. [19] confirmed that CSE does not increase the cesarean delivery rate for dystocia in parturients, regardless of parity, compared with intravenous meperidine. The effect on the outcome of labor is the same with CSE and standard epidural analgesia. CSE, however, may be associated with a more rapid progress of labor. A recent interesting study has demonstrated a more rapid cervical dilatation in nulliparous patients receiving CSE compared with conventional epidural analgesia [20]. In this study, the CSE technique was performed in early labor, at a cervical dilatation of less than 5 cm.

CSE for cesarean section

A CSE technique may also be adapted for cesarean delivery, to combine the rapidity and efficacy of spinal anesthesia with the unlimited duration and flexibility of an epidural catheter. This technique is useful in situations where the surgical procedure is anticipated to be of long duration, e.g., repeat cesarean section with multiple abdominal adhesions. CSE may be employed to provide spinal anesthesia for surgery and postoperative epidural analgesia. There is evidence that a "modified" CSE technique may reduce hemodynamic instability during cesarean section. Rawal et al. [21] used a "partial" spinal, with 7.5–10 mg of hyperbaric bupivacaine to achieve a T8-T10 sensory block. They waited 20 min to "fix" the spinal block, and then used the epidural catheter to extend the block to T4 with fractionated doses of 0.5% bupivacaine. The total local anesthetic dose used was lower, as was the incidence of maternal hypotension, in the CSE group. Although this technique obviates one of the prime advantages of spinal anesthesia, i.e., that of rapid onset, it deserves consideration.

Controversial aspects of CSE

Concerns regarding the CSE technique have focussed on the risk of postdural-puncture headache (PDPH), subarachnoid catheter migration, fetal bradycardia, metallic particle contamination, and potential problems posed by an untested catheter.

Postdural-puncture headache

The CSE technique inherently includes the risk of PDPH from both the intentional dural puncture and the possibility of unintended "wet tap" with the epidural needle. The latter is always a possibility, even with standard epidural anesthesia. The use of small-bore, pencil-tipped spinal needles reduces the additional risk of PDPH to 1% and the need for epidural blood patch even further. Several studies have demonstrated a lower incidence of "wet tap" with CSE than with routine epidural analgesia during labor. A retrospective review of the use of the CSE needle-through-needle technique, in more than 6000 patients, reported a PDPH incidence of 0.13% [22]. In these patients, a 27-gauge Whitacre spinal needle was passed no more than twice. It is postulated that, in cases of uncertain or inconclusive loss of resistance with the epidural needle, the spinal needle can be used as a guide to assess the proximity of the dura from the tip of the advancing epidural needle [23]. This will reduce the incidence of dural puncture by the epidural needle. In addition, the risk of CSF leakage through the intentional dural puncture made by the spinal needle is decreased. The increase in epidural pressure, resulting from the administration of epidural drugs, can be expected to splint the dura against the arachnoid membrane [16]. With a single-segment CSE technique, the spinal needle is deflected somewhat as it exits the epidural needle, and approaches the dura at an angle. The holes in the dura and subarachnoid are less likely to overlap, thereby reducing the risk of CSF leakage [16]. Finally, there are conflicting reports as to the prophylactic effect of epidural or spinal opioids against PDPH [24–26].

Subarachnoid catheter migration

Subarachnoid migration of the epidural catheter is a theoretical risk with the CSE technique. Failure to recognize an intrathecal catheter, and subsequent injection of an epidural dose of local anesthetic, could result in total spinal anesthesia. However, in practice, this does not seem to be a common occurrence. Holmstrom et al. [27] performed an epiduroscopic study, in a cadaveric model, during CSE administration, to assess this risk. They found that it was impossible to force an 18-gauge epidural catheter through the dural hole after a single dural puncture made by a 25-gauge spinal needle. After multiple punctures in the same area of the dura, the epidural catheter penetrated the perforated dura in 1 of 20 cases (5%). The epidural catheter penetrated the dural hole made by the Tuohy needle in 9 of 20 cases (45%). They concluded that the risk of epidural catheter migration through the dural hole during uncomplicated CSE block is very small. The possibility of subarachnoid or intravenous placement exists with any epidural catheter, and the danger of a massive intrathecal dose is not unique to the CSE technique. The real question is whether epidural catheter migration occurs with greater frequency during CSE than with routine epidural techniques [28]. Available evidence to date indicates that this is not the case. Catheter position should be confirmed by aspiration. The block should be frequently assessed, following injection of fractionated doses of local anesthetic, and every "top-up" should be considered a test dose.

Fetal/neonatal effects

Many studies have assessed the fetal and neonatal effects of CSE. No significant changes in neonatal Apgar scores or neurobehavioral examinations have been reported following clinically used doses of intrathecal or epidural opioids. Sufentanil is undetectable in the umbilical vessels after maternal administration of 10 μg epidurally during labor. Fentanyl is detectable in neonatal plasma following 25 μg intrathecal injection, but the levels are low, and no neonatal effects were noted.

In 1994, Clarke et al. [29] reported a case series of 30 mothers undergoing CSE for labor analgesia. Fetal bradycardia developed in 9 out of 30 cases, immediately after the intrathecal injection of fentanyl 50 μg. Uterine hypertonus was present in 5 out of the 9 bradycardia cases. Seven of these resolved spontaneously (or with terbutaline), but the remaining 2 had emergency cesarean deliveries. Neonatal and maternal outcome was excellent in all cases. Gambling et al. [19] compared the CSE technique with intravenous meperidine for labor analgesia. They found that 2% of the CSE patients (400 in total), had emergency cesarean deliveries for fetal bradycardia within 1 h of the intrathecal component of the CSE. No meperidine patients required emergency cesarean section.

There is an association with the CSE technique and fetal bradycardia, but is it causal? In three studies, with comparable patient groups, there was a significant incidence of fetal bradycardia (3%–20%) [30–32]. However, the incidence was similar whether the patient had a CSE or a standard epidural technique for labor analgesia. There was no cesarean delivery performed within 1 h of induction of analgesia. Likewise, Albright and Forster [33], in a series of 1240 CSEs, reported no emergency cesarean delivery within 90 min of induction of analgesia. The incidence of emergency cesarean delivery for fetal distress did not differ when using CSE or standard epidural analgesia. Comparisons between epidural with local anesthetics and intrathecal opioid-based CSE for labor analgesia (fentanyl 25 μg or sufentanil 10 μg) have shown similar incidences of significant fetal heart rate abnormalities.

This leads to the real question: why is there fetal bradycardia after the induction of labor analgesia? This may result from increased uterine tone due to abrupt decreases in maternal catecholamines, effects on uteroplacental blood flow, or rapid fetal descent. Satisfactory analgesia reduces the level of circulating catecholamines [34,35]. There is a relatively greater reduction in epinephrine than norepinephrine levels. Catecholamines exert a tocolytic effect on the gravid uterus. The abrupt reduction in circulating epinephrine may cause an increase in uterine tone, which, in turn, may decrease placental blood flow, with subsequent fetal bradycardia. The relative excess in norepinephine may cause uterine artery vasoconstriction and decreased placental perfusion, and may contribute to fetal bradycardia.

Should fetal bradycardia occur after performing a CSE, several measures may be employed for the in-utero resuscitation of the fetus. Uterine displacement is essential, and it should be remembered that right uterine displacement may be more successful in up to 15% of mothers. Any decrease in blood pressure must be corrected with fluids and/or ephedrine. Supplemental oxygen may increase the supply to the fetus. Oxytocin infusions should be terminated to permit uterine relaxation. Fetal scalp stimulation may be attempted by the obstetrician. Pharmacological measures to relax the uterus include nitroglycerine 200–400 μg intravenously, or terbutaline 25 mg administered subcutaneously.

Although significant changes in fetal heart rate (FHR) may occur occasionally with CSE, the incidence of emergency cesarean section due to fetal distress is no different from that in parturients having systemic opioid analgesia or epidural analgesia.

Metallic particle contamination

Concern has been raised that the needle-through-needle technique may cause metallic fragments to be deposited in the epidural or subarachnoid spaces [36]. Several investigators have studied this alleged problem, and found no evidence that such a phenomenon occurs [37].

Reliability of the epidural catheter

As the epidural component of a CSE is not utilized until after resolution of the initial spinal analgesia, the correct position of the catheter cannot be confirmed at the time of placement. In an emergency, this untested catheter may fail to provide adequate anesthesia. In situations where a well-functioning epidural catheter is of high priority (in patients at increased risk of cesarean delivery, or those with an anticipated difficult airway), the CSE technique may not be ideal. However, recent evidence suggests that epidural catheters placed as part of a combined technique are at least as successful, and possibly even more so, than catheters placed for standard epidural techniques [38,39]. Norris [39] compared the efficacy of catheters placed as part of an epidural or needle-through-needle CSE technique in laboring women. Of the 1495 catheters that were adequately tested, those inserted as part of a CSE technique were more likely to produce bilateral sensory change and adequate analgesia than were those inserted without prior spinal analgesia. It is estimated that when either epidural or spinal anesthesia is used alone for cesarean section, an alternative technique is required in approximately 4%. Lyons [40] has reported that the use of CSE reduced the need for rescue with general anesthesia to 1/900 cesarean deliveries.

2) The role of spinal anesthesia in severe preeclampsia

Epidural anesthesia is widely accepted as the method of choice for cesarean section in preeclamptic patients. The preeclamptic population has been recognized to be at increased risk for operative deliveries, general anesthetic-related complications, and bleeding disorders. Therefore, anesthesiologists have attempted to institute early epidural anesthesia in these patients, in order to reduce the stress of labor, and also to provide an anesthetic route for urgent cesarean delivery.

Is there a role for spinal anesthesia for cesarean section in this population? Selection of spinal anesthesia for severely preeclamptic patients requiring cesarean section has been controversial. These patients have a reduced plasma volume, which is thought to place them at an increased risk for hypotension in response to regional anesthesia-induced sympathetic blockade. Poor placental perfusion is seen in severe preeclampsia, and is reflected by high vascular resistance in the uterine arteries. Fetal wellbeing may be further jeopardized by reduced uteroplacental perfusion during maternal hypotension. Intravenous fluid administration, either prophylactically or as management of hypotension during regional anesthesia, is also thought to place the severely preeclamptic parturient at increased risk for iatrogenic pulmonary edema. This patient population is more sensitive to pressor agents, and it has been postulated that drugs such as ephedrine, which are commonly used to treat hypotension after induction of regional anesthesia, may be harmful in severely preeclamptic women. The epidural route has been considered safer for cesarean section because it allows for a more gradual onset of sympathectomy, thereby preventing potentially precipitous decreases in blood pressure.

The problem still remained that if epidural anesthesia was not feasible in the time required before emergency cesarean delivery, the only option remaining was general anesthesia. Reviews of maternal mortality have consistently shown preeclamptic patients to be at greater risk for airway difficulties [41]. The risks of general anesthesia in severe preeclampsia include hemodynamic instability at induction and intubation, and again at extubation. The pressor response to laryngoscopy may produce hypertension leading to raised intracranial pressure and pulmonary edema. Hodgkinson et al. [42], in a landmark study comparing general with epidural anesthesia for cesarean section in severe preeclampsia, demonstrated significant increases in systemic and pulmonary artery pressures during tracheal intubation and extubation. Furthermore, preeclampsia is associated with laryngeal edema, which may contribute to difficulties with tracheal intubation and postextubation obstruction of the upper airway. A study by Ahmed et al. [43] demonstrated a significantly higher incidence of complications following general anesthesia compared with spinal anesthesia for cesarean section in preeclamptic women.

Recent studies have questioned the avoidance of spinal anesthesia for preeclamptic patients, and whether the hemodynamic instability observed with spinal anesthesia in normal parturients can be extrapolated to the preeclamptic population. Most anesthesiologists would agree that spinal anesthesia may be administered safely in a woman with mild preeclampsia, but what about in severe preeclampsia? Hood and Boesse [44] reviewed the records of 48 patients with severe preeclampsia undergoing cesarean delivery with either epidural ($n = 34$) or spinal ($n = 14$) anesthesia. Blood pressure changes were identical in both groups.

There is only one randomized clinical trial which has evaluated the maternal and fetal effects of different anesthetic techniques. Wallace et al. [45] randomized 80 women with severe preeclampsia to receive general, epidural, or spinal anesthesia. Those assigned to the spinal group had a combined spinal/epidural (CSE) technique performed, with 1.5 ml, 0.75% hyperbaric bupivacaine given intrathecally, a dose that many anesthesiologists use for a “single-shot” technique. The mean preoperative blood pressure was 170/110 mmHg and all women had proteinuria. Noninvasive blood pressure monitoring was employed, and vasopressor support was only provided if the systolic blood pressure fell below 100 mgHg. Patients in the regional groups received acute hydration with 1000 ml of Ringer’s lactate solution on arrival in the operating room. Differences between the groups included longer induction-of-anesthesia to skin-incision time, greater crystalloid administration, and lower blood pressure, only at the time of incision, in the regional anesthesia groups compared with the general anesthesia group. Ephedrine use was greater for the spinal and epidural groups than for the general anesthetic group, but there was no statistically significant difference between the two regional techniques. Neonatal assessment (Apgar scores and cord arterial gases) was not different among groups, nor were outcomes related to maternal morbidity.

Karinen et al. [46] examined maternal and uteroplacental hemodynamics in 12 preeclamptic women during spinal anesthesia for elective cesarean section; 6 women had severe disease. These authors found that preloading with 1000 ml of Ringer’s lactate did hot prevent maternal hypotension, and that changes in uteroplacental blood flow, measured with a Doppler technique, were minor, when the systolic arterial pressure was 80% or more of baseline, during spinal anesthesia. The incidence of significant hypotension was 17%. The hypotensive episodes were easily corrected with further crystalloid infusion and small doses of intravenous ephedrine. These changes did not seem to have any effect on the clinical condition of the neonate, as assessed by Apgar scores and umbilical artery pH values.

Patel et al. [49] retrospectively examined epidural, spinal, and general anesthesia in patients with pregnancy-induced hypertension (PIH) and in normal gravida. PIH patients receiving spinal anesthesia for cesarean section did not become dramatically hypotensive, despite less use of ephedrine and fluids, when compared with non-PIH patients. Furthermore, as the severity of PIH increased, the incidence of hypotension, and fluid and pressor requirements, decreased.

Hood and Curry [47] retrospectively examined the medical records of all severely preeclamptic patients who received either spinal or epidural anesthesia for cesarean section over an 8-year period. Patients who had undergone labor were excluded. The lowest recorded blood pressures during the 20 min prior to induction of anesthesia, the period from induction to delivery, and the period from delivery to the end of surgery were compared. Changes in the lowest mean blood pressure were similar after epidural or spinal anesthesia. Intraoperative ephedrine use was similar for both groups. Intraoperative crystalloid administration was significantly greater for patients receiving spinal, compared with epidural anesthesia. Maternal and fetal outcomes (Apgar scores) were also similar. The presence or absence of antihypertensive therapy did not influence the subsequent decrease in blood pressure that followed induction of regional anesthesia.

In the studies by Wallace et al. [45] and Hood and Curry [47], severely preeclamptic women were studied, and the effects of spinal anesthesia were compared directly with the effects of epidural anesthesia. Both studies support the contention that the average reductions in mean arterial pressure are mild (15%–25%) for both spinal and epidural anesthesia.

A case report by Overdyk and Harvey [48] has described the first use of a continuous spinal anesthetic technique for cesarean delivery in a morbidly obese parturient with severe preeclampsia. They suggest that this is a viable alternative anesthetic method for operative delivery when epidural anesthesia cannot be established.

The Hood and Curry study, and others evaluating preeclamptic parturients (Hood and Boesse [44], Patel et al. [49]) are of an observational retrospective design. Therefore, all factors influencing outcome cannot be assured of being controlled. There is always the possibility of selection bias. This would affect the results if women with greater cardiovascular stability were more likely to receive spinal anesthesia than those receiving epidural anesthesia. The studies reporting the use of spinal anesthesia in women with PIH feel the hemodynamic instability is no greater than with general or epidural anesthesia, or when compared with women without PIH. Small numbers were examined in all studies (Hood and Boesse [44]; n = 80; Patel et al. [49]; n = 48, and Rout [63]; n = 118). Uncommon outcomes, such as unanticipated difficult intubation, pulmonary edema, maternal cerebrovascular events, or severe fetal asphyxia, were unlikely to have occurred, and estimation of the relative risk for the different anesthetic techniques could not be calculated.

Differences in design exist among the various studies published. Some studies included laboring patients, who, presumably, had pain and, as a result, had relatively elevated mean arterial pressures in the preanesthetic period. This increased blood pressure may produce an exaggerated decrease in blood pressure after the induction of spinal anesthesia. The choice of local anesthetic agent for epidural anesthesia may be an important factor for subsequent hypotension. The use of 3% epidural 2-chloroprocaine, exclusively, is associated with a greater incidence of hypotension in normal parturients undergoing elective cesarean section, compared with the use of epidural bupivacaine [50].

Over 50 years ago, Assali and Prystowski [51] reported a moderate decrease (approximately 20%) in blood pressure in severely preeclamptic patients receiving total spinal anesthesia. The reduction in blood pressure was less than that observed in normal gravida. They postulated that other humoral mechanisms tended to maintain blood pressure despite a total sympathectomy. The cause of this humoral pressor effect, which is independent of the sympathetic system, is not yet known. It is known that preeclampsia is associated with a relative excess of thromboxane, and that there are increased plasma levels of the potent vasoconstrictor endothelin-I.

The choice of regional anesthetic technique in severe preeclampsia should be made for clinical reasons, other than the anticipated decreases in blood pressure. At our institution, we consider spinal anesthesia to be a viable technique for severely preeclamptic women who do not have an epidural catheter in situ, and who need urgent cesarean delivery. In our experience, we have found it a safe anesthetic technique, and one which is preferable to the hazards of the emergency administration of general anesthesia.

3) Volume preloading and spinal anesthesia for cesarean section

Spinal anesthesia has become the anesthetic technique of choice for uncomplicated cesarean delivery. Among commonly performed regional techniques, spinal anesthesia is associated with the highest incidence of serious cardiovascular complications [52]. One complication that persists is arterial hypotension.

It is generally accepted that the hemodynamic consequences of spinal anesthesia are directly attributable to preganglionic sympathetic blockade. The most convincing evidence is the fact that spinal anesthesia administered to sympathectomized animals results in no change in mean arterial pressure. The precise mechanism by which sympathetic blockade leads to hypotension and bradycardia is less firmly established. The "classic model" emphasizes the dilatation of venous capacitance vessels, venous pooling, and diminished venous return to the heart as the predominant mechanism of hypotension during spinal anesthesia [53]. This occurrence has been well established in experimental studies. Arndt et al. [54] traced the redistribution of technetium-labeled red blood cells to the lower extremities, at the expense of venous return to the heart following a sympathetic block. Arterial dilatation, and the potentially negative inotropic/chronotropic effects of blockade of cardiac sympathetic fibers, is thought to play only a minor role in the setting of significant hypotension. Therefore, prevention or treatment of significant hypotension should focus on efforts to enhance venous return. Clinically, it is observed that spinal hypotension is accentuated by hypovolemia, reverse Trendelenburg's position, and mechanical obstruction to venous return (gravid uterus), and that it is relieved by fluids, vasopressors, and Trendelenburg's position.

The level and extent of the sympathetic block, relative to the sensory block height, appears to be complex. It is classically taught that sympathetic blockade occurs approximately two dermatomes higher than the pinprick level. Greene [55] demonstrated that perception of a cold ether-soaked sponge was blocked up to two dermatomes above the sensory level. More recent attempts to map the extent of the sympathetic blockade by measuring changes in skin temperature [56], skin conductance [57], and skin blood flow, by Doppler flowmetry [56,58], found that sympathetic responses could be elicited six to ten dermatomes below the sensory level, as determined by pin-prick. In contrast, Chamberlain, and Chamberlain [59], using a sensitive thermographic imaging technique, determined that at least partial sympathetic blockade extends six or more spinal segments above the level of sensory blockade.

Pregnant women comprise a unique patient population, due to the extensive physiological changes that occur during pregnancy. We will briefly review the hemodynamic alterations and changes in the nervous system. At term, there is a 50% increase in cardiac output, due to increases in heart rate and stroke volume. Central venous and pulmonary arterial and wedge pressures are within the normal range for nonpregnant individuals. The degree of compression of the aorta and the inferior vena cava by the term gravid uterus depends on the position of the pregnant woman, and is most evident in the supine position. Blood volume may be increased by 50%, with a relatively greater increase in plasma volume than red cell volume. Maternal colloid osmotic pressure decreases by approximately 5 mmHg during pregnancy.

Maintenance of hemodynamic stability is progressively dependent on the sympathetic nervous system throughout pregnancy. The effect is primarily on the venous capacitance vessels of the lower limbs, which counteracts the adverse effects of uterine compression of the inferior vena cava on venous return. Assali and Prystowski [51] produced a complete sympathectomy, without a fluid preload, in pregnant and nonpregnant women. Pregnant women exhibited a 50% fall in blood pressure. Nonpregnant women exhibited only a 10% fall. In addition, animal studies have demonstrated diminished arterial, but increased venous sensitivity to pressor agents during pregnancy. Enhanced venous sensitivity is consistent with the increased dependence of maternal venous return on sympathetic nervous system activity.

Uterine blood flow is not autoregulated, and is dependent on perfusion pressure. Spinal-associated hypotension may result in reduced uterine blood flow, with a potential compromise in fetal oxygenation. Maternal nausea and vomiting may occur. Various interventions have been applied to decrease the significance of the sympathectomy induced by spinal anesthesia. Avoidance of aortocaval compression, by employing left uterine displacement, is essential when positioning the gravid patient after induction of sympathetic blockade.

Prevention of hypotension using crystalloid preload

Methods developed for the prevention of hypotension associated with spinal anesthesia are pelvic tilt and prehydration, a concept that was introduced into clinical practice by Gertie Marx (Wollman and Marx [60]; Marx et al. [61]). Marx et al. [61] demonstrated a 0% incidence of hypotension when patients received 1 l of Ringer's lactate with 5% dextrose within 30 min before the administration of spinal anesthesia. Although this observation has not been replicated, fluid loading with crystalloid prior to spinal anesthesia has been common practice for years. Recently, the role of preload in the prevention of hypotension has been questioned. Two studies, by Jackson et al. [62] and Rout et al. [63], have found little value in crystalloid preloads. Neither study showed a clinical difference between groups receiving and not receiving a fluid bolus, in terms of hypotension, severity of hypotension, Apgar scores, or cord gases. Another study by Rout et al. [64] showed that the rapid administration of crystalloid had no influence on the incidence of hypotension. In this study, patients received 20 $ml \cdot kg^{-1}$ crystalloid over 10 min. Park et al. [65] compared small and large volumes of fluid preload (10 ml, 20 ml, or 30 $ml \cdot kg^{-1}$), and found no advantage to the larger preloads. They also reported a significant decrease in colloid osmotic pressure with large crystalloid preloads.

Prophylactic fluid administration may not prevent hypotension, but it does restore blood pressure in hypovolemic patients. It has been suggested that, in normovolemic patients, infusion of fluids stimulates the release of atrial natriuretic peptide (ANP), a potent endogenous vasodilator and diuretic. ANP may be responsible for the apparent failure of prehydration to prevent spinal-anesthesia-related hypotension. Pouta et al. [66] demonstrated increased ANP levels after the infusion of either crystalloid or colloid solutions. They concluded that a significant increase in the release of ANP, in response to volume loading, may decrease vascular tone and initiate diuresis, thereby attenuating the effect of volume loading on blood pressure during elective cesarean delivery. Park et al. [65] have shown that, with volume loading of 10 or 2 $ml \cdot kg^{-1}$ of crystalloid, systemic vascular resistance, measured by electrical bioimpedance, decreases. This supports the theory that ANP causes vasodilation. More recently, Frolich [67] measured atrial natriuretic factor (ANF) levels before and 10 min after subarachnoid block in patients undergoing scheduled cesarean section. One group received 15 $ml \cdot kg^{-1}$ crystalloid immediately before spinal anesthesia. Another group received the same volume, but starting at the time of subarachnoid injection. Frolich included a third, control group, who received no prehydration. ANF levels increased significantly in prehydrated patients, but not in the control group. However, the incidence of hypotension was not significantly different among the groups. This study questions the role of ANF in short-term cardiovascular hemostasis after spinal anesthesia and also demonstrates a failure of crystalloid prehydration in preventing hypotension.

Prevention of hypotension using colloid preload

Colloid solutions remain in the intravascular compartment for a longer period of time than crystalloid solutions. Ueyama et al. [68] used a dye dilution technique to measure the change in blood volume and cardiac output, before and after volume loading with either 1.5 l Ringer's lactate (RL), or 0.5 l or 1.0 l hydroxyethylstarch (HES) solution. After volume preload, the blood volume significantly increased in all three groups. The volume of HES solution infused correlated closely with the increase in blood volume. The crystalloid solution was not as effective. The incidence of hypotension was 75% for the RL group, 58% for the 0.5 l HES group, and 17% for the 1.0-l HES group. A significant correlation between the percentage increase in blood volume, achieved by volume preloading, and the increase in cardiac output was observed. The authors demonstrated that greater volume expansion resulted in less hypotension. They concluded that the augmentation in blood volume with preloading, regardless of the fluid used, must be large enough to result in a significant increase in cardiac output for effective prevention of hypotension.

There is little doubt that a colloid bolus decreases the incidence of hypotension, when given prior to spinal anesthesia for cesarean delivery [69–72]. Mathru et al. [69] also found a significant improvement in Apgar scores in the colloid group. Riley et al. [70] demonstrated lower ephedrine requirements in the colloid group, and showed that when hypotension occurred, it was later and not as severe as in the crystalloid group. In addition, the use of colloid solutions does not decrease colloid oncotic pressure (COP). Maintenance of a higher COP should result in less tissue edema, provided that capillary permeability remains normal. The disadvantages of colloid solutions include expense and a small risk of allergic reaction.

No intervention completely eliminates the hypotension associated with spinal anesthesia. Certain interventions may decrease its incidence and severity. Uterine displacement is a standard intervention for all patients undergoing cesarean section. If hypotension occurs, the tilt may be increased to relieve any residual aortocaval compression. Morgan et al. [73] conducted a meta-analysis of 23 randomized trials, including a total of 1504 patients, to examine the effects of an increase in central blood volume before spinal anesthesia for cesarean delivery. Some of the studies are limited, in that a wide variation in preload volume (750–1800 ml) was employed and criteria for vasopressor administration were not always standardized. The authors found that crystalloid preload was inconsistent in preventing hypotension, whereas colloid appeared to be effective in all but one study. Leg-wrapping and thromboembolic stockings decreased the incidence of hypotension compared with leg elevation or control. Few differences in fetal outcomes or maternal nausea and vomiting were reported. They concluded that increasing blood volume by using colloid and leg-wrapping decreases, but does not abolish, the incidence of hypotension with spinal anesthesia for cesarean section.

4) Blood-conservation strategies in obstetrics

Obstetric hemorrhage is a leading cause of maternal mortality. In the *Report on Confidential Enquiries into Maternal Deaths in the United Kingdom* for the triennium 1994–1996, hemorrhage was the third leading cause of maternal mortality, with a death rate of 5.5 per million maternities [74]. There were 12 deaths during this triennium—4 due to placental abruption, 3 to placenta previa, and 5 to postpartum hemorrhage. Hemorrhage remains the leading cause of maternal mortality in developing countries. Because of the unexpected onset of massive obstetric hemorrhage, treatment often necessitates the transfusion of multiple units of allogeneic blood products. Transfusion is required in 1%–3% of vaginal deliveries and 3%–5% of cesarean deliveries [75]. With the advent of the human immunodeficiency virus (HIV) and the recognition of hepatitis C, the use of blood transfusion has come under increasing scrutiny, both by the medical profession and by the public at large.

We will review the roles of the following blood-conservation strategies in obstetric practice: autologous transfusion, antepartum donation, acute normovolemic hemodilution, intraoperative blood salvage, and erythropoietin.

Autologous transfusion

The main advantage of autologous blood transfusion lies in the avoidance of the complications that are associated with homologous transfusion, i.e., transmission of infection, incompatibility, and immune reactions. The primary disadvantage is that these techniques require advance preparation and planning, and, as such, are not suitable in emergency settings.

Antepartum blood donation

Preoperative blood donation, before elective surgery, is a well-established blood-conservation strategy. The safety of this technique in obstetric patients has been documented in several reports [76–78]. Droste et al. [76], measured cardiac output, total peripheral vascular resistance, and fetal umbilical artery systolic/diastolic ratios, before and after donation of 450 ml of blood. They reported no significant maternal or fetal effects. Women with a stable placenta previa, not requiring urgent delivery, and those with rare blood types, may be suitable candidates for antepartum blood donation.

A hemoglobin level of $11\,g{\cdot}dl^{-1}$, or hematocrit (Hct) of 33%, is required by the American Association of Blood Banks prior to autologous predonation of blood. This would exclude some pregnant patients with physiological or iron-deficient anemia. Many practitioners consider a predonation hemoglobin level of $10\,g{\cdot}dl^{-1}$ acceptable; however, most studies in the literature have required higher levels (Hct, 34%). Another disadvantage of autologous blood donation is that most parturients do not require blood transfusion. Andres et al. [79] have suggested that the commonly accepted risk factors for postpartum hemorrhage and transfusion (repeat cesarean section, placenta previa, multiple gestation) do not accurately identify those patients who will require blood transfusion. Many patients who donate blood may not require a transfusion. In their retrospective study of 251 patients with traditionally accepted risk factors for hemorrhage, Andres et al. [79] found that only 1.6% required blood transfusion. Furthermore, 92% of those patients requiring transfusion were given more than one unit of blood; as such, it is likely that additional, homologous, blood would be needed. Camann and Datta [80] reviewed the blood transfusion practice over a 4-year period during which 9596 cesarean sections were performed. The overall incidence of transfusion declined from 6.2% to 3.2% during the study period. Most patients (68.4%) received two units of blood. The cost efficiency of antepartum blood donation has also been examined. Combs et al. [81] suggested that a hypothetical antepartum blood-donation program would cost \$32 800 to \$130 700 to prevent one case of transfusion-related hepatitis and \$26 000 000 to \$78 000 000 to prevent one case of HIV infection. Of 14 267 term deliveries (without placenta previa) studied, only 1.1% of the patients required transfusion. They concluded that the need for peripartum blood transfusion cannot be predicted with sufficient accuracy to justify the costs of antepartum autologous blood donation.

The lack of cost-efficiency, the limited collection volume (generally only one to two units retrieved), and the unpredictable timing of delivery have limited the widespread application of autologous predonation. In addition, autologous blood is still susceptible to bacterial contamination and clerical errors, and is not devoid of risks. However, antepartum blood donation may become beneficial if there is better identification of parturients at very high risk for significant hemorrhage.

Acute normovolemic hemodilution

The potential advantages of this technique include reduction of the red blood cell mass lost for a given volume during surgery; the fact that collected blood is reinfused, not wasted, and the fact that reinfused blood is fresh, with active clotting factors and platelets; and there is limited risk of storage or clerical errors.

However, there is limited experience with this technique in obstetric practice. Grange et al. [82] employed acute normovolemic hemodilution for cesarean section in 38 healthy parturients at high risk for hemorrhage (placenta previa, placenta accreta). The prehemodilution hemoglobin level was $10.9\,g{\cdot}dl^{-1}$; 750 ml to 1000 ml of blood was collected and replaced by an equal volume of 10% pentastarch, and the hemoglobin level decreased to $8.3\,g{\cdot}dl^{-1}$ (range, 6.7–9.5 g·dl). All collected blood was reinfused. There were no adverse maternal or fetal effects in terms of fetal heart rate monitoring, Apgar scores, or umbilical venous blood gases. This is still a very new technique in the obstetric setting and warrants further evaluation.

Intraoperative blood salvage

This technique is capable of providing large quantities of autologous blood rapidly, and is widely employed in general and vascular surgery. The major concern with intra-operative blood salvage during cesarean section is the potential to transfuse blood that may be contaminated with fetal or amniotic substances, causing amniotic fluid embolism or disseminated intravascular coagulation. Recently, several investigators have challenged this fear, and used salvaged blood from cesarean deliveries for reinfusion, without apparent adverse sequelae. Bernstein et al. [83] have reported the in-vitro removal of functionally active tissue factor, to non-detectable levels, from salvaged blood contaminated with amniotic fluid, by processing in a cell saver. Jackson and Lonser [84] have also reported the successful use of intraoperative blood salvage at cesarean section. Over an 11-year period, 64 women received a total of 136 salvaged units of blood. There were no cases of clinical amniotic fluid embolism or other adverse effects. Catlin et al. [85] demonstrated that the cell saver effectively removed all α-fetoprotein (AFP), if the initial gush of amniotic fluid was removed by separate suction. Cell-saver processing and leucocyte depletion filtration also completely removed trophoblastic tissue and white cells. Rainaldi et al. [86], in a randomized study, observed fewer homologous blood transfusions, and a shorter hospital stay, in patients who had intraoperative blood salvage during cesarean delivery, than in the control group.

The results of these studies are reassuring, and intraoperative blood salvage is a promising blood-conservation strategy in obstetrics. However, when assessing the safety of this technique, one must bear in mind that the incidence of amniotic fluid embolus is extremely low (1:80000 births), and that the published studies have relatively small numbers of subjects. Nevertheless, this technique may provide a feasible alternative to transfusion, in cases of unanticipated, massive hemorrhage. It may also be acceptable to some Jehovah's witnesses.

Erythropoietin

Although clinical experience with the use of erythropoietin during pregnancy is still very limited, we have included its use for completion. The permeability of erythropoietin across the placenta is very low [87], and it has been used during pregnancy without significant maternal or fetal effects. It may be given as indicated in general medical practice, or to maintain hemoglobin levels during autologous blood donation.

Summary

The low-dose technique of combined spinal/epidural analgesia is to be welcomed in obstetrics. Its merits include rapid onset of analgesia, with the flexibility of an epidural technique, and high maternal satisfaction. It is a safe and effective technique. Pulse oximetry should be employed when using intrathecal opioids. Commercially available combined-needle devices may make this technique more attractive to users. The role of spinal anesthesia for emergency cesarean section in severe preeclampsia has been reevaluated recently. We consider it a feasible option for those severely preeclamptic women requiring urgent cesarean section who do not have an epidural catheter in place. The choice of anesthetic technique for this patient population should be made on clinical judgment and not on anticipated hemodynamic changes. Spinal anaesthesia for cesarean section is associated with hypotension; however, certain interventions may reduce the incidence and severity of the hypotension. An increase in cardiac output appears to be key in attenuating the hypotensive response to spinal anesthesia. Colloids have exhibited most success in this regard. At our institution, we do not delay spinal anesthesia for urgent cesarean section in order to administer a predetermined volume of fluid; in such cases, we simultaneously administer a fluid preload and spinal anesthesia. Recent studies regarding the use of cell savers for blood conservation in obstetrics are based on small numbers of patients. These studies show great promise, particularly with the modern emphasis on avoiding blood transfusion, which can be massive in this usually young patient population.

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