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Pre-eclampsia: fluids, drugs, and anesthetic management

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Hypertensive disorders are the most common complications of pregnancy. They occur in 6% to 8% of pregnancies and account for approximately 15% of maternal deaths in the United States [1]. These disorders also contribute significantly to stillbirths, neonatal morbidity, and mortality. The National Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy recently reported on and defined hypertensive disorders in pregnancy [2]. They accepted a classification that included the four forms of hypertension in pregnancy, namely, gestational hypertension, chronic hypertension, chronic hypertension with superimposed pre-eclampsia, and pre-eclampsia–eclampsia with or without HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome.

Pre-eclampsia is a pregnancy-specific syndrome of unknown etiology that always occurs after 20 weeks of gestation in a previously normotensive woman. It is characterized by hypertension and proteinuria. The incidence varies depending on the population studied and is reported to be 3% to 7% in primiparas and 1% to 5% in multiparas [1]. Pre-eclampsia can be mild or severe. Mild pre-eclampsia is characterized by a sustained systolic blood pressure equal to or greater than 140 mm Hg, a diastolic blood pressure equal to or greater than 90 mm Hg, and proteinuria of 300 mg in a 24-hour urine collection. Pre-eclampsia is considered severe when systolic pressure is 160 mm Hg or higher, diastolic pressure is 110 mm Hg or higher, and there is proteinuria of at least 5 g in 24-hour urine collection. Other manifestations of severe pre-eclampsia are oliguria (<400 mL in 24 hours), cerebral and visual disturbances,

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pulmonary edema, thrombocytopenia, and impaired liver function. Eclampsia is defined as the occurrence of a seizure in a woman with pre-eclampsia that cannot be attributed to other causes.

A detailed discussion of the etiology and pathogenesis of pre-eclampsia and eclampsia is beyond the scope of this review. Briefly, abnormal trophoblast invasion at the time of placentation has been implicated as one of the factors in the development of pre-eclampsia [3]. During normal pregnancy, the migratory action of interstitial and endovascular trophoblasts into the walls of spiral arteries transforms the uteroplacental bed into a ''low resistance, low pressure, high flow system.'' The trophoblast-induced changes extend all the way from the intervillous space (first wave of migration into the decidual segments) to the origin of the spiral arteries in the inner third of the myometrium (second wave of migration into the myometrial segments). In pre-eclampsia, this second wave of migration fails to occur, which leaves the musculo-elastic portions of arteries intact. Therefore, these arteries respond readily to vasomotor stimuli causing vasoconstriction. In addition, widespread vascular endothelial dysfunction occurs. Damaged vascular endothelium not only promotes coagulation but also exhibits increased sensitivity to all vasopressor agents [4]. Another pathognomonic feature is a reversal of the ratio of prostacyclin and thromboxane levels, which leads to increased vasospasm, endothelial injury, and platelet activation and consumption [5].

Pathophysiology

Hemodynamic profile

Women with pre-eclampsia present with a wide spectrum of cardiovascular changes. There is a wealth of information on the hemodynamic changes in severe pre-eclampsia [6–17]. Many of these are observational studies using pulmonary artery (PA) catheters. In normal term pregnancy, heart rate (HR) and stroke volume (SV), and therefore, cardiac output (CO) increase, whereas systemic (SVR) and pulmonary (PVR) vascular resistances decrease [8]. Pulmonary artery

Table 1
Hemodynamic changes in nonpregnant and healthy term pregnant women

	Nonpregnant (n = 10)	Healthy pregnant (n = 10)
MAP (mm Hg)	86 ± 7.5	90 ± 5.8
Heart rate (beats/min.)	71 ± 10	83 ± 10
Cardiac ouput (L/min)	4.3 ± 0.9	6.2 ± 1.0
SVR (Dynes sec cm^{-5})	1530 ± 520	1210 ± 265
PCWP (mm Hg)	6.3 ± 2.1	7.5 ± 1.8
CVP (mm Hg)	3.7 ± 2.6	3.6 ± 2.5
LVSWI (g mm^2)	41 ± 8	48 ± 6
COP (mm Hg)	21 ± 1	18 ± 1.5

Data from Clark S, Cotton DB, Lee W. Central hemodynamic assessment of normal term pregnancy. Am J Obstet Gynecol 1989;161:1439–42.

wedge pressure (PCWP), central venous pressure (CVP), and left ventricular stroke work index (LVSWI) remain unchanged (Table 1).

In women with severe pre-eclampsia, hemodynamic changes are variable and are based on factors such as the duration and severity of pre-eclampsia, previous administration of IV fluids or antihypertensive drugs, and concurrent medical problems such as chronic hypertension and peripartum cardiomyopathy. Other factors including labor and the mode of delivery may also influence these findings. In untreated patients with severe pre-eclampsia, the hemodynamic findings are characterized by high SVR, low left and right ventricular filling pressures, low to normal cardiac index (CI), and hyperdynamic left ventricular function (Table 2). In those treated with IV fluids and/or antihypertensives, the findings are quite different [10,15]. In general, most patients have normal to high SVR, elevated CI, and a normal to high PCWP (Table 2). The left ventricular function is hyperdynamic in the majority of patients (Fig. 1). Often, CVP and PCWP do not correlate.

Bolte and colleagues recently published PA catheter data collected from 30 severe preeclamptic patients [6]. The data were collected prospectively before and after initiation of therapy with fluids and vasodilators. They found that before treatment with fluids and vasodilators, there was a modest correlation between CVP and PCWP with $r = 0.64$, $P < 0.0002$. After volume expansion, the correlation was poor with $r = -0.039$, probably due to a time lag in the development of changes between the left and right sides. They concluded that reliance on CVP alone for making therapeutic decisions regarding fluid loading and drug administration was unacceptable. Others believe that the lack of

Table 2
Hemodynamic changes in severe pre-eclampsia

Hemodynamic variables	Untreated patients[a] ($n = 87$)	Treated patients[b] ($n = 45$)	Treated patients[c] ($n = 41$)	Pulmonary edema[c] ($n = 8$)
MAP (mm Hg)	—	138 ± 3	130 ± 2	136 ± 3
CVP (mm Hg)	2	4 ± 1	4.8 ± 0.4	11 ± 1
PCWP (mm Hg)	7	10 ± 1	8.3 ± 0.3	18 ± 1
Cardiac index (l min^{-1} m^{-2})	3.3	—	—	—
Cardiac output (L/min)		7.5 ± 0.2	8.4 ± 0.2	10.5 ± 0.6
SVR (dynes s cm^{-5})	3003	1496 ± 64	1226 ± 37	964 ± 50
PVR (dynes s cm^{-5})	131	70 ± 5	65 ± 3	71 ± 9
LVSWI (g mm^2)	—	81 ± 2	84 ± 4	87 ± 10

[a] *Data from* Wallenburg HCS. Hemodynamics in hypertensive pregnancy. In: Rubin PC, editor. Handbook of Hypertension. The Netherlands: Elsevier; 1988. p. 66–101.

[b] *Data from* Cotton DB, et al. Hemodynamic profile of severe pregnancy-induced hypertension. Am J Obstet Gynecol 1988;158:523–9.

[c] *Data from* Mabie WC, et al. The central hemodynamics of severe pre-eclampsia. Am J Obstet Gynecol 1989;161:1443–8.

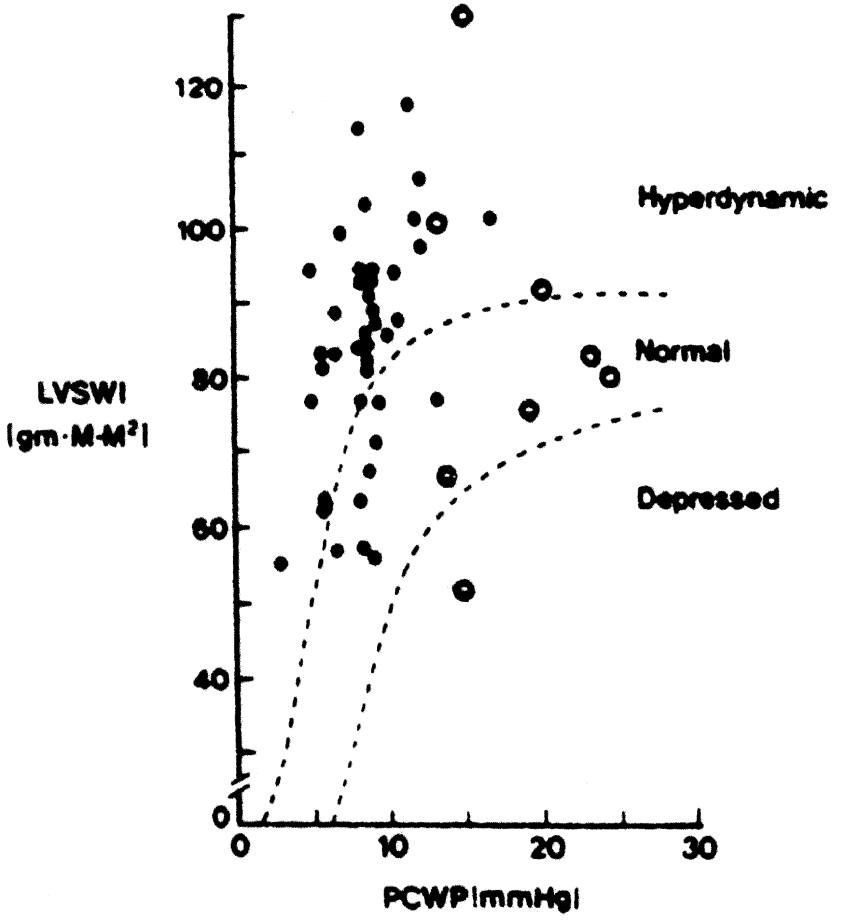

Fig. 1. Left ventricular function curve in patients with severe pre-eclampsia: 41 patients with no pulmonary edema (*solid circles*) and 8 patients with pulmonary edema (*open circles*). (*From* Mabie WC, Ratts T, Sibai B. The central hemodynamics of preeclampsia. Am J Obstet Gynecol 1989;161:1443–8; with permission.)

correlation between right- and left-sided filling pressures may be due to high SVR and a high CO leading to high left ventricular pressure [10]. The right-sided pressure remains normal or low [10].

Pulmonary edema is a serious complication of severe pre-eclampsia with an incidence of approximately 3% [16]. Pulmonary edema in pre-eclampsia may be either cardiogenic or noncardiogenic [16]. Cardiogenic pulmonary edema is due to either impaired left ventricular systolic or diastolic function. The presence of low CO, high PCWP, high CVP, and high SVR characterizes systolic dysfunction, whereas diastolic dysfunction is associated with normal or high CO, high PCWP, and a normal SVR. Diastolic dysfunction is due to a combination of

impaired ventricular relaxation and volume overload resulting in high filling pressures and pulmonary edema [16,18]. Cardiogenic pulmonary edema may also develop in those with other concurrent conditions such as chronic hypertension and peripartum cardiomyopathy.

Noncardiogenic pulmonary edema results from such factors as increased capillary permeability, iatrogenic fluid overload, an imbalance between colloid osmotic pressure (COP) and hydrostatic pressure, or a combination of these. In normal term pregnancy, the COP values vary from 18 to 21 mm Hg. In patients with pre-eclampsia, the baseline COP values are significantly lower at approximately 17 mm Hg [19]. This is due to albuminuria and decreased hepatic synthesis of albumin. Further reduction of values as low as 13 mm Hg occurs after delivery, which narrows COP–PCWP differences even more. The hemodynamic data from patients with pulmonary edema show a right shift of the data points (Fig. 2). Thus, the hemodynamic changes associated with pulmonary edema in severe pre-eclampsia are complex, and invasive monitoring with a PA catheter is recommended.

In severe pre-eclampsia, expansion of blood volume fails to occur. This causes decreased intravascular volume, generalized vasoconstriction, and hemoconcentration [20]. In mild pre-eclamptics, plasma volume is 9% lower than normotensives, and in severe pre-eclampsia is further reduced by 30% to 40%. Hematocrit and hemoglobin values are therefore elevated.

Renal dysfunction and oliguria

Renal plasma flow and glomerular filtration rate (GFR) increase during normal pregnancy with a fall in serum creatinine, urea, and uric acid concentrations. In pre-eclampsia, vasospasm and capillary endothelial swelling lead to a reduction in GFR. Serum creatinine and uric acid are elevated. Rising serum creatinine and oliguria signal rapid deterioration of renal function. Clark et al described three distinct types of hemodynamic findings with oliguria [9]. In their first group, they found classic signs of hypovolemia as evidenced by low filling pressures, elevated SVR, and hyperdynamic cardiac function. The patients in this group responded well to IV fluids. Their second group of oliguric patients had normal or elevated filling pressures, elevated CO, and a high SVR. These patients were treated with vasodilators and fluid restriction. One patient had elevated SVR and PCWP, and depressed cardiac function. She responded well to after-load reduction.

Hepatic dysfunction

The extent of hepatic involvement is evident from hypoalbuminemia and rising levels of serum transaminase and lactic dehydrogenase. Although cholinesterase levels decrease [21], the duration of action of succinylcholine and ester local anesthetics is seldom affected.

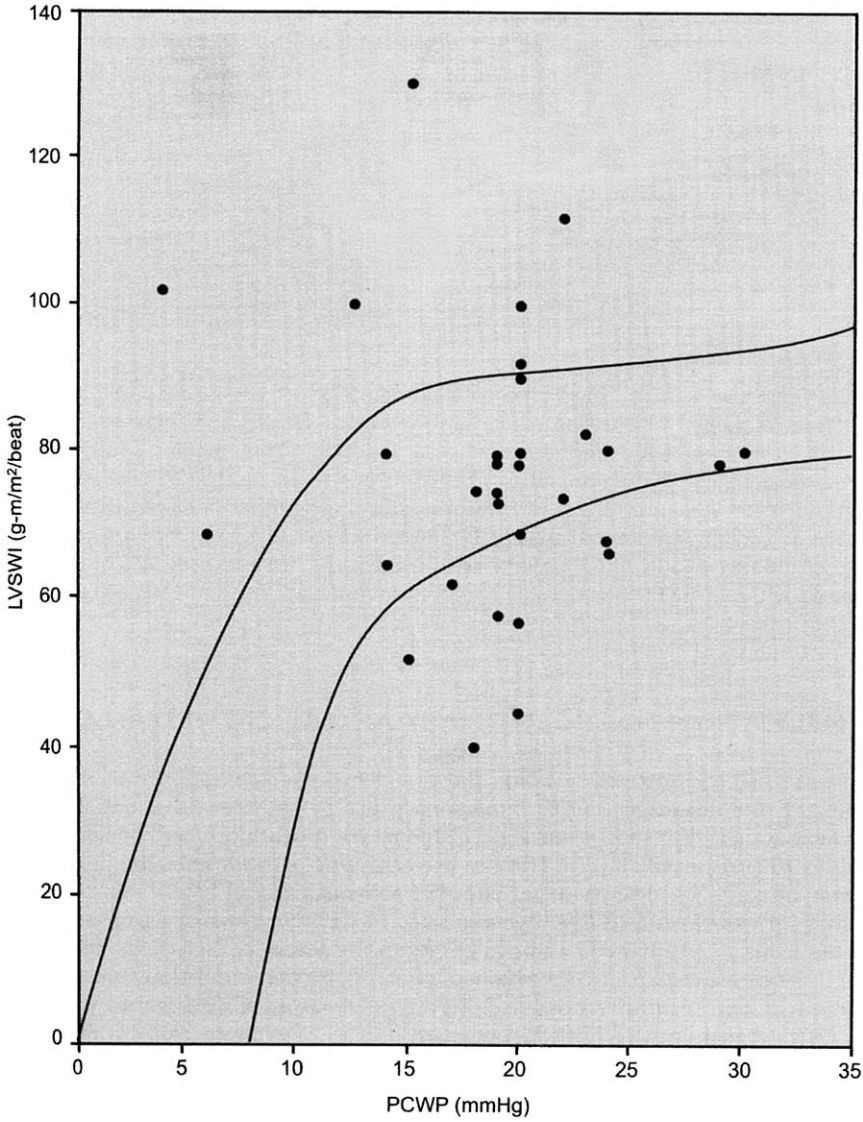

Fig. 2. Left ventricular function curve in 32 patients with pulmonary edema. (*From* Young P, Johanson R. Haemodynamic, invasive and echocardiographic monitoring in the hypertensive parturient. Best Practice & Research Clinical Obstetric and Gynecology 2001;15:605–22; with permission.)

Coagulation abnormalities

Endothelial injury in the microvasculature results in increased platelet activation, consumption, and thrombocytopenia. The incidence of thrombocytopenia ranges from 15% to 20% and may be as high as 50% in severe preeclampsia [22–24]. Platelet destruction may also be due to an autoimmune

mechanism as indicated by elevated levels of platelet-specific immunoglobin [22]. In addition to thrombocytopenia, platelet function is also adversely affected, and the severity of platelet dysfunction is directly related to the severity of the disease [22,25].

There is a general consensus that a platelet count of 100,000/mm^3 is adequate for the administration of neuraxial blocks. Controversy only arises when the platelet count is less than 100,000/mm^3. There are reports of apparent safety of epidural anesthesia in healthy women with very low platelet counts [26]. In some pre-eclamptic women, the template bleeding time is prolonged even in those with adequate platelet counts [25,27].

Recently, a few investigators have used the Thromboelastograph (TEG) to examine platelet function in women with pre-eclampsia and low platelet counts. In one study, Wong et al found that an abnormal maximum amplitude TEG value always correlated with a prolonged bleeding time [28]. They concluded that TEG is useful in the presence of thrombocytopenia for the assessment of platelet function. In another study, Sharma et al evaluated coagulation changes using TEG and platelet counts in 52 healthy parturients, 140 mild pre-eclamptics, and 114 patients with severe pre-eclampsia [29]. They found that TEG was useful tool for assessment of platelet function. The conclusion of this study was that "severe pre-eclamptic women with a platelet count less than 100,000/mm^3 are hypocoagulable when compared to healthy pregnant women and other pre-eclamptic women" [29]. Recently, in a retrospective study, McDonagh and colleagues calculated the correlation between the platelet count and bleeding time in 87 pre-eclamptic women [30]. They found that a platelet count below 75,000/mm^3 appeared to be moderately insensitive but quite specific for identifying those with a prolonged bleeding time. The authors acknowledged the potential for bias in retrospective studies and discussed the need for a large prospective study to identify the hematological markers that might predict epidural bleeding. Other coagulation tests such as prothrombin time, partial thromboplastin time, and fibrinogen levels deteriorate with the onset of disseminated intravascular coagulation (DIC).

Respiratory system changes

Marked upper airway edema, swelling of the tongue and soft tissues can cause difficulties with tracheal intubation, which can be severe enough to cause total upper airway obstruction. Maternal carboxyhemoglobin level increases and 2,3-diphosphoglycerate decreases causing a leftward shift of the oxyhemoglobin dissociation curve [31].

Changes in the central nervous system

Diffuse vasospasm of cerebral vessels leads to focal areas of cerebral ischemia, which is considered a pathognomonic feature leading to seizures and eclampsia [20,32]. Eclampsia is a serious condition and is associated with high

maternal and fetal morbidity and mortality [32,33]. Both computerized tomographic and magnetic resonance imaging studies reveal widespread ischemic lesions involving occipital and parietal lobes [32,33]. Severe hypertension can cause an increase in cerebral blood flow (CBF) velocity. A positive correlation exists between CBF velocity and systemic blood pressure. Persistent hypertension can cause overdistension of cerebral vessels, forced vasodilatation, loss of cerebral autoregulation, and vasogenic cerebral edema. Maternal middle cerebral

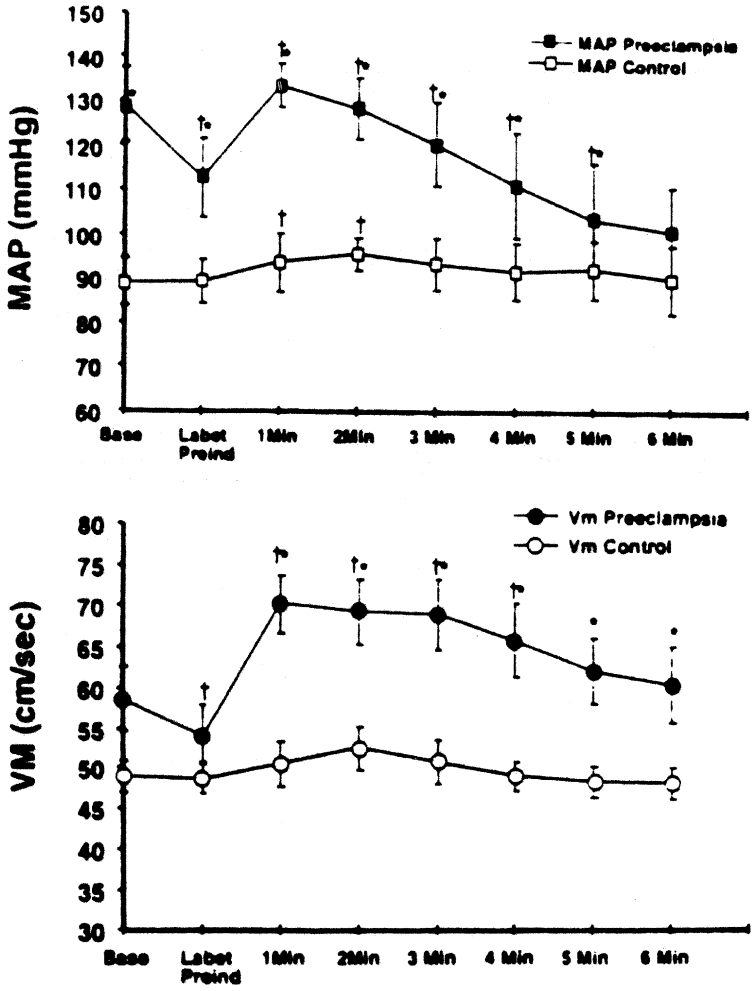

Fig. 3. Changes in mean arterial pressure (MAP) and mean middle cerebral artery flow velocity (VM) before and after induction of general anesthesia and tracheal intubation in pre-eclampsia and control groups.

artery blood flow velocity increases dramatically during rapid sequence induction of general anesthesia and tracheal intubation in patients with pre-eclampsia (Fig. 3) [34]. In this study, the increase in flow velocity showed a direct correlation with the rise in MAP with intubation. Prophylactic administration of antihypertensives or a β-adrenergic blocking agent is essential before induction of general anesthesia.

Treatment

The goals of treatment are threefold: prevention of convulsions, control of hypertension, and optimization of intravascular volume status.

Prevention of convulsions

Magnesium sulfate

In the United States, magnesium sulfate (Mg^{++}) is considered the drug of choice for prevention of convulsions [35]. The mechanism of action of Mg^{++} involves generalized CNS depression as well as cerebral arterial dilatation relieving cerebral ischemia. Other beneficial effects include a mild antihypertensive effect, tocolytic activity, and lowering of plasma endothelin-1 levels. Magnesium impairs peripheral neuromuscular transmission and the intensity of neuromuscular block correlates with elevated serum Mg^{++} and decreased serum calcium levels [36]. Magnesium prolongs the actions of all muscle relaxants. A recent TEG study indicated that Mg^{++} does not affect overall coagulation [37].

Magnesium is usually administered IV, 4 to 6 g as a bolus over 20 minutes followed by a 2 to 3 g/h infusion. The therapeutic range is 5.0–7.0 mg/dL. Even within this therapeutic range, pulmonary function may be transiently affected [38]. Toxic reactions (Table 3) are rare but can occur with overdose or decreased renal elimination. The treatment is administration of calcium chloride to reverse effects of Mg^{++} and cardio-respiratory support. Fetal Mg increases steadily, and prolonged maternal administration results in neonatal respiratory depression and hypotonia. Magnesium is also used for the treatment of eclampsia in bolus doses of 4 g IV.

Table 3
Plasma magnesium levels and clinical effects

Plasma magnesium (mEq/L)	Clinical effects
1.5–2.0	Normal level
4.0–4.8	Therapeutic range
5.0–10.0	Prolonged P–Q interval Wide QRS
>10.0	Respiratory depression/arrest
25.0	Cardiovascular collapse

Control of hypertension

Antihypertensive agents

Direct acting vasodilators

Hydralazine. Hydralazine is preferred by most obstetricians as the first-line of treatment for control of hypertension. Hydralazine is given IV in doses of 5 to10 mg to lower the diastolic pressure to less than 110 mm Hg. The onset of action is approximately 20 minutes. Hydralazine is a direct vasodilator that lowers MAP and SVR, increases CO and HR without affecting PCWP [11]. The slow onset, delayed peak effect, and compensatory tachycardia make hydralazine a less than an ideal agent to prevent the hypertensive response during intubation.

Sodium nitroprusside (SNP). The use of SNP is limited to situations such as acute hypertensive crisis, severe intractable hypertension, and occasionally blunting of hypertensive response to tracheal intubation. It is a potent arteriolar dilator [39]. The recommended dose is 0.5 to5μg/kg/min. Sodium nitroprusside is also a cerebral vasodilator and may increase intracranial pressure. The major concern is the potential for fetal cyanide toxicity [40]. However, SNP has been safely used for the treatment of hypertension, pulmonary congestion, and heart failure without any adverse fetal effects [41]. Administration of low doses of SNP for a short duration is deemed safe.

Nitroglycerin (NTG). Nitroglycerin is a venodilator and the indications for its use are similar to those for SNP. In patients with severe pre-eclampsia, NTG lowers MAP, PCWP, and CI, but has no effect on CVP, SV, and HR [12]. Nitroglycerin can be given prophylactically to blunt the hypertensive response to tracheal intubation [14].

Ganglion blocking agents

Trimethaphan. Trimethaphan is a drug with a large molecular weight and therefore has limited placental transfer. It is given as an infusion or bolus doses. Unfortunately, this drug inhibits plasma pseudocholinesterase and prolongs the action of succinylcholine [42]. Other side effects, such as histamine release and tachyphylaxis, limit the usefulness of this drug.

β-Adrenergic blocking agents

Labetalol. Labetalol is a combined β- and α-adrenergic blocking agent. When given IV, the β to α blocking ratio is 7:1. When compared to hydralazine, labetalol is found to be as effective, if not more effective, than hydralazine [43]. Furthermore, compared with hydralazine, labetalol has a faster onset, causes a smooth fall in blood pressure, and reduces maternal heart rate. Labetalol crosses

the placental barrier and the fetal:maternal ratio is 1:1. Despite the high drug levels in the fetus, labetalol does not cause β blockade and therefore, neonatal hypoglycemia and hypotension are rarely present. Labetalol has no adverse effects on uteroplacental and fetal blood flow. In doses of 1 mg/kg, labetalol can be used for blunting the hypertensive response to tracheal intubation [44].

Esmolol. Esmolol is a pure β-receptor antagonist which selectively blocks the β-1 receptors of the heart. It has a rapid onset and offset of action with a half-life of 9 minutes in the mother. Esmolol is a popular agent for preventing or blunting the hypertensive response to tracheal intubation in nonpregnant patients. It has not gained popularity in obstetrics because of its adverse effects in the fetus. Esmolol crosses the placenta and causes persistent β blockade in the fetus [45]. Animal studies showed decreased fetal oxygenation, fetal β blockade, and reduced fetal tolerance to asphyxia [45]. In humans, severe fetal bradycardia can occur after maternal administration [46]. There are no prospective studies on esmolol attesting to its safety and efficacy in obstetric population; therefore, it is not recommended for use in this setting.

Calcium-channel blocking agents

Nifedipine and nicardipine. Nifedipine has been used for treatment of hypertension in pregnancy for several years. Nifedipine, given orally or sublingually, lowers MAP reliably and safely within 10 to 30 minutes. Although nifedipine crosses the placental barrier, it does not have any appreciable effects on fetal hemodynamics [47,48]. Nicardipine has less negative ionotropic effects than nifedipine and has more selective action on peripheral vasculature. Intravenous nicardipine can be used for control of blood pressure during a hypertensive crisis in severe pre-eclampsia [47]. Both nifedipine and nicardipine enhance the cardiotoxic effects of magnesium. Administration of magnesium and a calcium-channel blocking agent can cause severe hypotension and myocardial depression [48]. Furthermore, nifedipine potentiates and prolongs the neuromuscular blocking effects of magnesium [49].

Fluid management

Intravenous hydration before regional anesthesia is a routine practice to minimize hypotension resulting from sympathetic blockade. Recent evidence suggests that prior hydration fails to prevent a decrease in MAP in healthy pregnant women, and many investigators question the need for prophylactic fluid administration [50]. Because patients with severe pre-eclampsia may have significant intravascular volume deficit and reduced uteroplacental perfusion, it is prudent to administer fluids before any anesthetic interventions.

There is a paucity of data regarding the ideal volume and the type of IV fluid for patients with pre-eclampsia [51]. As discussed earlier, pre-eclampsia is

associated with a complex set of hemodynamic changes. Not uncommonly, the CVP may be low, whereas the left-sided filling pressures (PCWP) may be quite high. In addition, with fluid infusion, PCWP may increase earlier than CVP and may be disproportionately high [6,7]. It is often difficult to predict how patients will respond to fluid loading. Furthermore, the correlation between CVP and PCWP is poor. Nevertheless, the consensus is that invasive hemodynamic monitoring is not essential for safe fluid management of all cases of severe pre-eclampsia.

Patients with mild pre-eclampsia do not need any special monitoring and will tolerate prophylactic hydration. In most instances, patients with severe pre-eclampsia can be similarly managed, especially if the urine output is adequate. If the urine output is inadequate, a fluid challenge is done with 250 to 500 mL of crystalloid infused over 20 minutes. If the patient responds with an increase in urine output, additional fluid boluses may be given cautiously before the regional block. If there is no response to the initial fluid bolus, CVP or PCWP monitoring becomes necessary. If CVP monitoring alone is contemplated, the following facts should be considered [18]. Currently a volume expansion to CVP of at least 6 to 8 mm Hg is considered to be safe and effective. However, the CVP–PCWP gradients in severe pre-eclampsia may be as high as 8 to10 mm Hg [18]. Therefore, a CVP of 8 mm Hg might correspond to a PCWP as high as 18 mm Hg. This results in volume overload and possibly pulmonary edema. In a study of 50 patients with pre-eclampsia, Wallenburg et al showed that none of the patients with a CVP of 4 mm Hg or less had PCWP values exceeding 12 mm Hg [52]. Therefore, if CVP alone is being monitored for fluid management, volume expansion to achieve a CVP of 4 mm Hg or less is sufficient [18]. Monitoring with a PA catheter is indicated in patients with pulmonary edema or oliguria unresponsive to fluid therapy or intractable hypertension.

As a routine, crystalloid is used for hydration before regional anesthesia. In these patients volume expansion may further reduce the COP and therefore, in theory, it would be advantageous to use colloid for volume expansion. A review of recent studies compared outcome in nonpregnant patients receiving albumin for plasma volume expansion versus no albumin and concluded that albumin increased the risk of death [53]. Similarly, increased mortality was associated with the use of colloid for resuscitation when compared with crystalloid [54]. At this time, there is insufficient evidence to choose colloid over crystalloid in patients with pre-eclampsia [7]. If large volumes of colloid are chosen for hydration, invasive monitoring of filling pressures is recommended.

Anesthetic management

Preanesthetic evaluation and patient preparation

For patients with severe pre-eclampsia, it is important to have a flexible anesthetic plan, preferably with more than one option as the situation may change

suddenly without prior warning. Before any anesthetic intervention, it is important to ensure that hypertension is well controlled, and concurrent problems, such as eclampsia and pulmonary edema, treated. Physical examination should include evaluation of the upper airway to document airway classification. Laboratory investigations include complete blood count, coagulation panel, liver function tests, and urine analysis. Blood and blood products should be ordered as necessary. As discussed earlier, patients with platelet counts of 100,000/mm^3 and above may receive regional anesthesia safely. For those with platelet counts less than 100,000/mm^3, the decision to administer regional anesthesia is based primarily on the clinical situation. The incidence of difficult airway problems in obstetric patients is approximately 1:300 [55]. Whereas the exact incidence of epidural hematoma is unknown, and quite rare. A regional anesthetic may be a safer option in this very difficult situation.

Monitoring

For patients with mild pre-eclampsia, routine monitoring with EKG and automatic blood pressure cuff is often sufficient. For those with severe pre-eclampsia, a radial arterial line is recommended for accurate monitoring of arterial pressures and for sampling of blood for arterial blood gases, coagulation panel, liver function tests, and serum Mg^{++} levels. As discussed earlier, hemodynamic monitoring should be initiated as needed.

Analgesia for labor and vaginal delivery

Epidural analgesia

Epidural analgesia is suitable for providing pain relief for labor and delivery. There are numerous benefits from an epidural block. With pain relief, the serum concentration of catecholamines decreases resulting in an increase in uteroplacental and intervillous blood flow [56]. This is highly beneficial in pre-eclamptic patients who already have vasospasm of placental circulation. Should the need arise for rapid delivery of the fetus via cesarean section, epidural block can be extended to provide adequate anesthesia. With judicious hydration and slow induction of block, hypotension can be minimized with little change in CVP, CI, and PCWP [17].

Technique

Hydration with 500 to 1000 mL of crystalloid is necessary. Maternal EKG, BP, as well as FHR should be monitored continuously. Administration of oxygen with a facemask or nasal cannulae is beneficial. Among the local anesthetics, a low concentration of bupivacaine, 0.125%, with 2 μg/mL of fentanyl as an initial bolus provides excellent analgesia with minimal motor block. This mixture is given by epidural infusion at a rate of 10 to 12 mL/hour. Other local anesthetics, such as ropivacaine and levobupivacaine, may be used but the superiority of these agents compared to bupivacaine is not established.

Epinephrine-containing local anesthetics should be avoided, although not all agree. Hypotension is treated with IV ephedrine 5 to 10 mg, left uterine displacement, and additional fluids.

Combined spinal–epidural anesthesia (CSE)

This elegant technique can be used safely to provide analgesia for labor and delivery in patients with pre-eclampsia [57]. For the intrathecal dose, an opioid alone such as fentanyl or sufentanil may be used or a combination of bupivacaine 1.25 to 2.5 mg with fentanyl 25 μg or sufentanil 10 μg. Epidural infusion of the same local anesthetic combination as described previously is used to maintain analgesia until delivery.

Anesthesia for cesarean section

Regional anesthesia

Regional anesthesia is the method of choice for cesarean deliveries due to its proven record of maternal and fetal safety [55]. The maternal mortality rate directly related to anesthesia is approximately 16 times greater in those receiving general anesthesia compared to those receiving regional anesthesia [55]. The mother remains conscious and is able to interact with her infant. There are no significant changes in PCWP, CVP, and CI from baseline during epidural anesthesia for cesarean section [13]. The serum levels of stress-related hormones such as catecholamines, β endorphins, ACTH, and cortisol remain unchanged [58].

The use of single-shot spinal anesthesia is somewhat controversial. Pre-eclamptic women have a depleted intravascular volume and decreased uteroplacental perfusion. With spinal anesthesia, the onset of sympathetic blockade can be quite rapid and profound hypotension can occur. Prophylactic hydration does not reliably prevent hypotension even in healthy parturients. The vasodilatory actions of magnesium and the use of antihypertensive medications such as labetalol and hydralazine may exaggerate hypotension. Despite these concerns, recent evidence indicates that spinal anesthesia may be safely used with no adverse maternal or fetal sequalae [59]. In this study, the authors compared the maternal and neonatal outcomes in severely preeclamptic patients who either received epidural (n = 35) or spinal (n = 103) anesthesia for cesarean section. They found similar BP declines, lowest BP, intraoperative ephedrine use, and neonatal Apgar scores [59].

An alternative plan is to use the CSE technique. Recent evidence indicates that hyperbaric bupivacaine in doses as low as 7.5 mg with 25 μg fentanyl provides adequate anesthesia for cesarean section [57]. The presence of the epidural catheter provides the flexibility to extend the level and the duration of block [57]. The suggested technique of epidural anesthesia for cesarean delivery is given in Box 1. Transfusion of blood and blood products may become necessary in cases of placental abruption and atony of uterus from prior administration of tocolytic agents, including magnesium.

Box 1. Suggested technique for regional anesthesia for cesarean section

- Give aspiration prophylaxis.
- Make sure that blood and blood products are available as needed.
- Start a second peripheral intravenous line.
- Start CVP or PCWP monitoring as indicated.
- Hydrate with 1000 mL of crystalloid or infuse enough fluids to increase CVP to no more than 4 mm Hg or a PCWP of 5–8 mm Hg.
- Monitor the fetal heart rate until the beginning of surgery.
- Insert epidural catheter and start administering either 2% lidocaine or 0.5% bupivacaine with 100 μg of fentanyl in incremental doses to extend the sensory level of block to T4.
- Maintain left uterine displacement.
- Treat hypotension with ephedrine, volume, or both.
- At the end of surgery, start epidural fentanyl infusion or give a dose of preservative free epidural morphine 4 mg for post-operative pain relief.

For CSE: Administer 7.5 mg of hyperbaric bupivacaine with 25μg of fentanyl intrathecally. The level of sensory block can be extended/ maintained with 2% lidocaine or 0.5% bupivacaine epidurally as needed

General anesthesia

General anesthesia is indicated in cases of coagulopathy, fetal distress requiring emergency cesarean section (no pre-existing epidural catheter), and patient refusal of regional anesthesia.

The three most important considerations are airway edema and the possibility of difficult airway management, exaggerated hypertensive responses to endotracheal intubation, and drug interaction between magnesium and muscle relaxants. Different sizes of endotracheal tubes, oral or nasal airways, and laryngeal mask airways and a flexible fiberoptic bronchoscope should be available in the operating room. Magnesium prolongs the action of muscle relaxants and therefore, neuromuscular block should be monitored with a nerve stimulator. To blunt the hypertensive response to tracheal intubation, labetalol is effective. The use of NTG or SNP should be guided by invasive hemodynamic monitoring. The recommended technique for general anesthesia is given in Box 2.

Box 2. Recommended technique for general anesthesia

- Administer aspiration prophylaxis.
- Start additional intravenous lines.
- Place an arterial line. Start invasive hemodynamic monitoring with CVP or PCWP if required
- Keep smaller endotracheal tubes and different sizes and types of laryngoscope blades in the operating room. Make sure all the necessary equipment for the management of a difficult airway is readily available.
- Begin preoxygenation. Apply all the routine monitors such as EKG, pulse oximeter, endtidal CO_2 monitor and temperature probe.
- Monitor fetal heart rate. Gradually lower MAP as tolerated by the fetus, with labetalol 1.0 mg/kg, or use vasodilators guided by CVP/PCWP.
- Induce anesthesia with thiopental 4 mg/kg and succinylcholine 1 mg/kg. Maintain anesthesia with 50% nitrous oxide and isoflurane 0.5% until delivery. Use vecuronium or atracurium for muscle relaxation in reduced doses.
- At the end of surgery, reverse neuromuscular block. Give labetalol 5–10 mg IV before extubation to prevent emergence hypertension.

Postoperative care

The patient is monitored in the recovery room or the obstetric intensive care unit for the next 12 to 24 hours. Magnesium infusion is continued to prevent eclampsia. As discussed earlier, the risk of pulmonary edema is high and careful monitoring for evidence of pulmonary congestion is required so that treatment can be initiated, as needed.

Summary

Severe pre-eclampsia is a complex disease, which taxes the expertise of even the most experienced obstetric anesthesiologist. The treatment should focus on stabilization of blood pressure, optimization of fluid status, and prevention of convulsions. Neuraxial blocks for labor and delivery offer many benefits to the mother and her infant. For cesarean section, there is unequivocal evidence of superiority of neuraxial anesthesia over general anesthesia. If general anesthesia is needed, careful preanesthetic preparation and meticulous airway management is essential. The successful and safe peripartum management of the pre-eclamptic patient and her infant is a team effort among the anesthesiologist, obstetrician, and neonatologist.

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