Hypertensive Disorders of Pregnancy

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Hypertension is the most common medical problem encountered during pregnancy, complicating 2-3% of pregnancies. Hypertensive disorders during pregnancy are classified into 4 categories, as recommended by the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy: 1) chronic hypertension, 2) preeclampsia-eclampsia, 3) preeclampsia superimposed on chronic hypertension, and 4) gestational hypertension (transient hypertension of pregnancy or chronic hypertension identified in the latter half of pregnancy) (1). This terminology is preferred over the older but widely used term pregnancy-induced hypertension (PIH) because it is more precise.

Chronic Hypertension in pregnancy

Chronic hypertension is high blood pressure that either precedes pregnancy, is diagnosed within the first 20 weeks of pregnancy, or does not resolve by the 12-week postpartum checkup. Two categories of severity are recognized: mild (up to 179 mm Hg systolic and 109 mm Hg) and severe (≥ 180 systolic or 110 diastolic). Chronic hypertension complicates about 5% of all pregnancies, and prevalence rates are increasing due to delayed childbearing. Medications should be reviewed when pregnancy is first diagnosed. We cannot recommend with certainty to either stop, start, or continue antihypertensive medications: evidence is mixed whether such actions improve outcome. Methyldopa is the most studied of all antihypertensive medications and is generally the first choice in pregnancy because it has a limited effect on uteroplacental blood flow. Sometimes an alternative must be found because of elevated liver enzymes or complaints of headache. Labetalol, a combined alpha-blocker and beta-blocker, is the first alternative to methyldopa and is becoming a first-line choice as experience with the drug during pregnancy increases. It is generally well tolerated and has an easier (twice-a-day) dosing schedule than methyldopa. Calcium channel blockers, particularly nifedipine, are being used more frequently, probably because doctors have become familiar with their use to stop premature labor. They seem to be safe and effective, but evidence is sparse. Diuretics have been used in pregnancy despite the theoretical risk of preventing normal blood volume expansion. Most studies have not found adverse pregnancy outcomes. Nonetheless, caution should be used in cases of impaired uteroplacental perfusion, such as preeclampsia or intrauterine growth restriction. Atenolol and other pure beta-blockers should be avoided: they have been associated with babies born small for their gestational age. Angiotensin-converting enzyme (ACE) inhibitors are contraindicated in the second and third trimester because they are associated with a myriad of congenital anomalies, including renal failure, oligohydramnios, renal dysgenesis, reduced ossification, pulmonary hypoplasia, and fetal and neonatal death. Patients presenting in the first trimester on an ACE inhibitor should either be taken off antihypertensive medications or switched to another agent. Exposure during this time is not an indication for pregnancy termination, however. Angiotensin II receptor antagonists are considered guilty by association because of their similarity to ACE inhibitors, but there are no data to confirm this. Chronic hypertension accounts for a disproportionate amount of maternal and perinatal morbidity and mortality, mostly because of an increased risk of superimposed preeclampsia. There is an increased risk of prematurity, birth of infants who are small for their gestational age, intrauterine death, placental abruption, and cesarean delivery.
Complication rates are directly related to the severity and duration of elevated blood pressures. For instance, patients with severe hypertension in the first trimester

have a greater than 50% risk of developing superimposed preeclampsia. All hypertensive patients should undergo increased surveillance, serial laboratory tests throughout pregnancy, serial ultrasound scans to follow growth, and antenatal testing. The baby should be delivered vaginally if possible.

Gestational Hypertension

Gestational hypertension, formerly known as pregnancy-induced hypertension or PIH, is the new onset of hypertension after 20 weeks of gestation. The diagnosis requires that the patient have:

- Elevated blood pressure (systolic ≥ 140 or diastolic ≥ 90 mm Hg, the latter measured using the fifth Korotkoff sound)
- Previously normal blood pressures
- No protein in the urine
- No manifestations of preeclampsiaeclampsia.

Also known as transient hypertension, gestational hypertension is actually diagnosed retrospectively when the patient does not develop preeclampsia and if blood pressure returns to normal by the 12-week postpartum visit. Fifty percent of women diagnosed with gestational hypertension between 24 and 35 weeks develop preeclampsia (2). The diagnosis of gestational hypertension mandates increased surveillance. Women who progress to severe gestational hypertension based on the degree of blood pressure elevation have worse perinatal outcomes than do women with mild preeclampsia, and require management similar to those with severe preeclampsia (3).

Preeclampsia

Preeclampsia is a multiorgan disease process of unknown etiology (11) characterized by the development of hypertension and proteinuria after 20 weeks of gestation.

There are various theories of pathogenesis of preeclampsia. The most popular theory is immunologic.

During a normal pregnancy, fetal syncytial trophoblasts penetrate and remodel maternal spiral arteries, causing them to dilate into large, flaccid vessels. This remodeling accommodates the vast, increased maternal circulation needed for adequate placental perfusion. This remodeling is somehow prevented in preeclamptic pregnancies: the placenta is unable to properly burrow into the maternal blood vessels, leading to intrauterine growth restriction and other fetal manifestations of the disorder. Investigators speculate that this incomplete placentation is due to maternal immunologic intolerance of foreign fetal genes. Evidence in support of this theory is that the risk of preeclampsia is highest in a first pregnancy and decreases with the length of time a woman has lived with the father before becoming pregnant. Furthermore, risk is also increased in multiparous women who are pregnant by a new partner. Others theories of pathogenesis of preeclampsia are angiogenic factors (increased sFlt-1, decreased placental growth factor levels) (4, 5) cardiovascular maladaptation and vasoconstriction, genetic predisposition (maternal, paternal, thrombophilias) (6, 7) immunologic intolerance between fetoplacental and maternal tissue (8), platelet activation, vascular endothelial damage or dysfunction (8). Several factors are associated with preeclampsia and they are antiphospholipid antibody syndrome, chronic hypertension, chronic renal disease, elevated body mass index, maternal age older than 40 years, multiple gestation, nulliparity, preeclampsia in a previous pregnancy (particularly if severe or before 32 weeks of gestation), pregestational diabetes mellitus. Prevention through routine supplementation with calcium, magnesium, omega-3 fatty acids, or antioxidant vitamins is ineffective (9-12) calcium supplementation reduces the risk of developing preeclampsia in high-risk women and those with low dietary calcium intakes (13).

Diagnosis

Preeclampsia is defined as elevated blood pressure after 20 weeks of gestation (≥ 140 mm Hg systolic or ≥ 90 mm Hg diastolic) plus proteinuria (> 0.3 g/24 hours). In clinical practice, we usually use the criteria of two elevated bloodpressure measurements 6 hours apart and a proteinuria of 300 mg in a 24-hour urine specimen. A 24-hour determination is most accurate because urine dipsticks can be affected by variable excretion, maternal dehydration, and bacteriuria (8). A random urine protein/creatinine ratio of less than 0.21 indicates that significant proteinuria is unlikely with a negative predictive value of 83 percent; however, confirmatory 24-hour urine protein determination is recommended (14). Preeclampsia used to be diagnosed by the “30-15” rule: systolic pressure more than 30 mm Hg above baseline and diastolic pressure more than 15 mm Hg above baseline. That rule, however, is now discredited because it is too nonspecific. Similarly, generalized edema (affecting the face and hands) may be impressive and was once considered a diagnostic criterion, but it is no longer regarded as one because it is too variable. Preeclampsia can range from mild to severe. Severe preeclampsia is defined as any of the following:

- Markedly elevated blood pressure measurements (systolic ≥ 160 mm Hg or diastolic ≥ 110 mm Hg) taken at least 6 hours apart with the patient on bed rest
- Proteinuria (≥ 5 g/24 hours or ≥ 3+ on two random samples 4 hours apart)
- Manifestations of end-organ disease: oliguria (< 500 mL in 24 hours), cerebral or visual disturbances, pulmonary edema, cyanosis, epigastric or right-upper-quadrant pain, impaired liver function, thrombocytopenia, or fetal growth restriction.

Hematologic changes include:

- Thrombocytopenia—platelets are dramatically reduced, probably consumed by endothelial injury. Counts can be as low as 20 to 50 x 10^9/L.
- Hemoconcentration—doctors used to follow preeclampsia with serial hematocrits.
- Microangiopathic hemolysis—eventually, red cells are sheared through the microcirculation.

Hepatic changes are usually limited to hepatocellular necrosis, demonstrated by elevated alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels.

Occasionally there is subcapsular hemorrhage and even hepatic rupture, which has a 60% maternal mortality rate.

Neurologic changes are common and include headache, blurred vision, scotoma (seeing spots or "snow"), hyperreflexia, and rarely, cortical blindness, and the generalized seizures of eclampsia.

Renal changes. Glomerular endotheliosis is the pathognomonic lesion of preeclampsia: the glomeruli are enlarged, distorted, and filled with occlusions, with hypertrophy of the intracapillary cells. Laboratory testing shows a decreased glomerular filtration rate, decreased renal blood flow (the former more than the latter), and nonselective proteinuria (ie, all proteins including albumin; what a urine dip stick detects).

Fetal changes. Intrauterine growth restriction is very common. Oligohydramnios also occurs, because the amniotic fluid is essentially fetal urine; with poor perfusion through the placenta, the fetus has diminished urine output. Intrauterine demise and placental abruption are not uncommon. Doppler waveforms are typically abnormal, and antenatal testing suggests that the fetus is in jeopardy. We use the ratio of forward flow of blood in the umbilical artery during systole to that during diastole (the "umbilical artery S:D ratio") to assess the degree of resistance to flow in the placenta. The higher the ratio, the less diastolic flow. The greater the resistance to flow, the greater the peril to the fetus.

HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets) used to be classified as a separate syndrome, but current thinking categorizes it as a manifestation of preeclampsia, occurring in about 20% of severe cases. It is associated with significant maternal and perinatal morbidity. A decreasing platelet count and an increasing l-lactate dehydrogenase level (indicative of both hemolysis and liver dysfunction) reflect disease severity (15, 16).

Management of preeclampsia

Preeclampsia places both mother and fetus at risk. It is, however, a maternal disorder. The mainstay of treatment is early detection and managed delivery to minimize both maternal and fetal risks. If the pregnancy is at term, the decision is easy: the baby should be delivered. The decision to deliver involves balancing the risks of worsening preeclampsia against those of prematurity. Delivery is generally not indicated for women with mild preeclampsia until 37 to 38 weeks of gestation and should occur by 40 weeks (1, 7). If remote from term, the mother should be admitted for evaluation. She will need:

- Baseline and serial laboratory tests (complete blood cell count, BUN, creatinine, uric acid, ALT, AST).
- Ultrasonography to measure fetal growth and amniotic fluid volume and Doppler ultrasonography.Umbilical artery systolic/diastolic ratios measured by Doppler ultrasonography may detect early uteroplacental insufficiency (17, 18).
- Antenatal testing (nonstress test or biophysical profile). The biophysical profile is an assessment of fetal well-being. Fetuses that are well oxygenated behave normally by twisting, squirming, flexing and extending extremities, and breathing. Fetuses that are hypoxic lie still, trying to conserve oxygen.
- A 24-hour urine collection for protein.

The goals of treatment are to prevent seizures, lower blood pressure to avoid maternal end-organ damage, and expedite delivery.

Magnesium sulfate is still the drug of choice for preventing and arresting eclamptic seizures. It has the additional benefit of reducing the incidence of placental abruption (19). Serum magnesium levels should be monitored in women with elevated serum creatinine levels, decreased urine output, or absent deep tendon reflexes (20). Magnesium toxicity can lead to respiratory paralysis, central nervous system depression, and cardiac arrest. The antidote is calcium gluconate, 1 g infused intravenously over two minutes (21).

Antihypertensive medications are used solely to prevent maternal morbidity and have no effect on disease progression or preventing eclampsia. Medications must be given with caution: if blood pressure is lowered too fast, it can have a dramatic effect on uteroplacental perfusion and can cause an already compromised fetus to rapidly decompensate and become bradycardic. Preferred medications are hydralazine (5-10 mg intravenous bolus every 10-15 minutes), labetalol, nicardipine, and sodium nitroprusside. Intravenous labetalol and hydralazine are commonly used for the acute management of preeclampsia (22, 23).

Diuretics are usually contraindicated because of the already collapsed intravascular volume. However, if the pulmonary capillary wedge pressure is high, diuretics are necessary.

Intravenous hydration for oliguria must be given cautiously to avoid pulmonary edema, ascites and cardiopulmonary overload. If there is no evidence of pulmonary edema, a trial of fluid resuscitation (500 mL over an hour) should be given.

Delivery Decisions in Severe Preeclampsia

Delivery is the only cure for preeclampsia. Corticosteroids are administered to accelerate fetal lung maturity (8). Interventionist management advocates induction or cesarean delivery 12 to 24 hours after corticosteroid administration (24). Contraindications to expectant management include persistent severe symptoms, multiorgan dysfunction, severe IUGR (i.e., estimated fetal weight below the 5th percentile), suspected placental abruption, or nonreassuring fetal testing (24).

Method of delivery can be vaginal delivery or caesarean section. Vaginal delivery may be commenced in vertex presentation by: amniotomy + oxytocin if the cervix is favourable or prostaglandin vaginal tablet (PGE2) if the cervix is not favourable. Caesarean section is indicated in foetal distress, late deceleration occurs with oxytocin challenge test, failure of induction of labour and other indications as contracted pelvis and malpresentations. Some experts recommend cesarean delivery for fetuses younger than 30 weeks when the cervix is not ripe, but a trial of induction may be considered (8, 22). In patients with HeLLP syndrome, cesarean delivery carries special risks, such as bleeding from thrombocytopenia and difficulty controlling blood pressure because of depleted intravascular volume (15, 25).

Postpartum Management

Eclampsia may occur postpartum; the greatest risk of postpartum eclampsia is within the first 48 hours (20). Magnesium sulfate is continued for 12 to 24 hours, or occasionally longer if the clinical situation warrants. Generally, once the placenta is delivered, the disease rapidly improves. Large fluid shifts should occur immediately postpartum, and diuresis indicates that the syndrome is resolving. However, women with severe and early onset of disease may worsen before getting better. The physiologic changes of preeclampsia are completely reversible after delivery. However, maternal morbidity caused by severe hypertension, hemorrhage, or anesthetic complications may be permanent.

Eclampsia

Eclampsia is the development of convulsions in a pre-existing pre-eclampsia or it may appear unexpectedly in a patient with minimally elevated blood pressure and no proteinuria. The exact cause is unknown but cerebral ischaemia and oedema were suggested. The timing of an eclamptic seizure can be antepartum (53 percent), intrapartum (19 percent), or postpartum (28 percent) (26).

Management of eclampsia

General measures include:
- Care for respiratory system by:
  - head-down tilt to help drainage of bronchial secretion,
  - frequent change of patient position,
  - keep upper respiratory tract clear by aspiration of mucous through a plastic airway,
  - prophylactic antibiotic and
  - oxygen is administered during and after fits.
  - a medical professional skilled in performing intubations should be immediately available (27).
- The tongue is protected from biting by a plastic mouth gauge.
- After sedation, a self-retained Foley's catheter is applied. The hourly output of urine is charted. Proteinuria, haematuria and specific gravity are noticed.
- Efficient nursing in a single quiet semi-dark room to prevent any auditory or visual stimuli.
- Observation for maternal
  - pulse
  - temperature
  - blood pressure
  - respiratory rate
  - tendon reflexes
  - urine (see before)
  - number of fits and duration of coma
  - uterine contraction
- Observation for foetal:
  - FHS.

Magnesium sulfate is the drug of choice because it is more effective in preventing recurrent seizures than phenytoin (Dilantin) or diazepam (Valium) (28, 29-31). If a patient has already received a prophylactic loading dose of magnesium sulfate and is receiving a continuous infusion, an additional 2 g should be given intravenously. otherwise, a 6-g loading dose is given intravenously over 15 to 20 minutes, followed by maintenance infusion of 2 g per hour. A total of 8 g of magnesium sulfate should not be exceeded over a short period of time (20, 27).

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