We have invited select authorities to present background information on challenging clinical problems and practical information on diagnosis and treatment for use by practitioners.

Diagnosis and Management of Gestational Hypertension and Preeclampsia

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Gestational hypertension and preeclampsia are common disorders during pregnancy, with the majority of cases developing at or near term. The development of mild hypertension or preeclampsia at or near term is associated with minimal maternal and neonatal morbidities. In contrast, the onset of severe gestational hypertension and/or severe preeclampsia before 35 weeks' gestation is associated with significant maternal and perinatal complications. Women with diagnosed gestational hypertension–preeclampsia require close evaluation of maternal and fetal conditions for the duration of pregnancy, and those with severe disease should be managed in-hospital. The decision between delivery and expectant management depends on fetal gestational age, fetal status, and severity of maternal condition at time of evaluation. Expectant management is possible in a select group of women with severe preeclampsia before 32 weeks' gestation. Steroids are effective in reducing neonatal mortality and morbidity when administered to those with severe disease between 24 and 34 weeks' gestation. Magnesium sulfate should be used during labor and for at least 24 hours postpartum to prevent seizures in all women with severe disease. There is an urgent need to conduct randomized trials to determine the efficacy and safety of antihypertensive drugs in women with mild hypertension–preeclampsia. There is also a need to conduct a randomized trial to determine the benefits and risks of magnesium sulfate during labor and postpartum in women with mild preeclampsia. (Obstet Gynecol 2003;102:181–92. © 2003 by The American College of Obstetricians and Gynecologists.)

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Hypertension is the most common medical disorder during pregnancy.[1] Approximately 70% of women diagnosed with hypertension during pregnancy will have gestational hypertension–preeclampsia. The term "gestational hypertension–preeclampsia" is used to describe a wide spectrum of patients who may have only mild elevation in blood pressure (BP) or severe hypertension with various organ dysfunctions including acute gestational hypertension; preeclampsia; eclampsia; and hemolysis, elevated liver enzymes, low platelets (HELLP) syndrome. The exact incidence of gestational hypertension–preeclampsia in the United States is unknown. Estimates range from 6% to 8% of all pregnancies.[1] Here I will focus the discussion on gestational hypertension and preeclampsia. The subjects of eclampsia and HELLP syndrome will be covered in a subsequent review.

DEFINITION AND CLASSIFICATION

Gestational Hypertension

Defined as a systolic BP of at least 140 mm Hg and/or a diastolic BP of at least 90 mm Hg on at least two occasions at least 6 hours apart after the 20th week of gestation in women known to be normotensive before pregnancy and before 20 weeks' gestation. The BP recordings used to establish the diagnosis should be no more than 7 days apart.[1] Gestational hypertension is considered severe if there is sustained elevations in systolic BP to at least 160 mm Hg and/or in diastolic BP to at least 110 mm Hg for at least 6 hours.[2]

Gestational hypertension is the most frequent cause of hypertension during pregnancy. The rate ranges between 6% and 17% in healthy nulliparous women and between 2% and 4% in multiparous women.[3–6] The rate is further increased in women with previous preeclampsia and in women with multifetal gestation. Some women

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with gestational hypertension will subsequently progress to preeclampsia. The rate of progression depends on gestational age at time of diagnosis; the rate reaches 50% when gestational hypertension develops before 30 weeks' gestation.[7] In addition, some of these women may have undiagnosed chronic hypertension.

Preeclampsia

Preeclampsia is primarily defined as gestational hypertension plus proteinuria (300 mg or more per 24-hour period). If 24-hour urine collection is not available, then proteinuria is defined as a concentration of at least 30 mg/dL (at least 1+ on dipstick) in at least two random urine samples collected at least 6 hours apart.[1] The urine dipstick measurements used to establish proteinuria should be no more than 7 days apart.[1] The concentration of urinary protein in random urine samples is highly variable. Recent studies have found that urinary dipstick determinations correlate poorly with the amount of proteinuria found in 24-hour urine determinations in women with gestational hypertension.[8] Therefore, the definitive test to diagnose proteinuria should be quantitative protein excretion in a 24-hour period. Severe proteinuria is defined as protein excretion of at least 5 g per 24-hour period. Urine dipstick values should not be used to diagnose severe proteinuria.[8]

In the absence of proteinuria, preeclampsia should be considered when gestational hypertension is associated with persistent cerebral symptoms, epigastric or right upper quadrant pain with nausea or vomiting, or thrombocytopenia and abnormal liver enzymes.

Preeclampsia is considered severe if there is severe gestational hypertension in association with abnormal proteinuria or if there is hypertension in association with severe proteinuria (at least 5 g per 24-hour period). In addition, preeclampsia is considered severe in the presence of multiorgan involvement such as pulmonary edema, seizures, oliguria (less than 500 mL per 24-hour period), thrombocytopenia (platelet count less than 100,000/mm^3), abnormal liver enzymes in association with persistent epigastric or right upper quadrant pain, or persistent severe central nervous system symptoms (altered mental status, headaches, blurred vision or blindness).

The rate of preeclampsia ranges between 2% and 7% in healthy nulliparous women.[3,4] The rate is substantially higher in women with twin gestation (14%)[9] and those with previous preeclampsia (18%).[6]

ETIOLOGY AND PATHOPHYSIOLOGY

The etiology of preeclampsia is unknown. During the past centuries several etiologies have been suggested, but most of them have not withstood the test of time. Some of the remaining potential etiologies include abnormal trophoblast invasion of uterine blood vessels, immunological intolerance between fetoplacental and maternal tissues, maladaptation to the cardiovascular changes or inflammatory changes of pregnancy, dietary deficiencies, and genetic abnormalities.

The pathophysiologic abnormalities of preeclampsia are numerous. Some of the reported abnormalities include placental ischemia, generalized vasospasm, abnormal hemostasis with activation of the coagulation system, vascular endothelial dysfunction, abnormal nitric oxide and lipid metabolism, leukocyte activation, and changes in various cytokines as well as in insulin resistance. These abnormalities have been the subject of a recent review[10] and will not be discussed here.

Table 1. Risk Factors for Preeclampsia

Nulliparity
Multifetal gestation
Obesity
Family history of preeclampsia–eclampsia
Preeclampsia in a previous pregnancy
Abnormal uterine Doppler studies at 18 and 24 wk
Pregestational diabetes mellitus
Presence of thrombophilias
Hypertension or renal disease

PREDICTION AND PREVENTION

Prevention of any disease process requires knowledge of its etiology and pathogenesis, as well as the availability of methods to predict or identify those at high risk for this disorder. Numerous clinical, biophysical, and biochemical tests have been proposed for the prediction or early detection of preeclampsia. Unfortunately, most of these tests suffer from poor sensitivity and poor positive predictive values, and the majority of them are not suitable for routine use in clinical practice.[11]

At present, there is no single screening test that is considered reliable and cost-effective for predicting preeclampsia.[11] As a result, all studies on prevention have included women with various risk factors for preeclampsia[12] (Table 1).

During the past 2 decades, numerous clinical reports and randomized trials described the use of various methods to reduce the rate and/or the severity of preeclampsia. The results of these studies were the subject of a recent review.[12] There are few randomized trials evaluating magnesium, zinc, or fish oil supplementation to prevent preeclampsia. These trials had limited sample size; however, results reveal minimal to no benefit. There are at least nine placebo-controlled trials evaluat-

Table 2. Pregnancy Outcome in Women With Mild Gestational Hypertension

	Knuist et al[4] (n = 396)	Hauth et al[3] (n = 715)	Barton et al[7] (n = 405)	Sibai et al[9] (n = 186)
Gestation at delivery (wk)*	NR	39.7	37.4†	39.1
<37 (%)	5.3	7.0	17.3	5.9
<34 (%)	1.3	1.0	4.9	1.6
Birth weight (g)*	NR	3303	3038	3217
SGA (%)	1.5‡	6.9	13.8	7.0
<2500 g (%)	7.1	7.7	23.5	NR
Abruptio placentae (%)	0.5	0.3	0.5	0.5
Perinatal deaths (%)	0.8	0.5	0	0

NR = not reported; SGA = small for gestational age.
* Mean values.
† Women who developed hypertension at 24–35 weeks.
‡ Less than the third percentile.

ing calcium supplementation during pregnancy. Results of these trials conflict.[12] Of note is the trial sponsored by the National Institute of Child Health and Human Development that included 4589 healthy nulliparous women and revealed no reduction in the rate of preeclampsia.[13] On the other hand, trials conducted in women considered at very high risk demonstrated significant reductions in the rate of preeclampsia. The majority of randomized trials for the prevention of preeclampsia have used low-dose aspirin.[12] Results of early single-center trials demonstrated an average reduction of 70% with low-dose aspirin. However, results of eight recent large trials that included over 30,000 women demonstrated minimal to no benefit.[12–14] A recent large multicenter National Institute of Child Health and Human Development–sponsored study that included 2539 women with pregestational insulin-treated diabetes mellitus, chronic hypertension, multifetal gestation, or preeclampsia in a previous pregnancy showed no beneficial effects from low-dose aspirin in such high-risk women.[15] Moreover, there was a recent trial that demonstrated reduced rates of preeclampsia with vitamins C and E in women identified to be at risk by means of abnormal uterine Doppler studies[16] (elevated resistance index and presence of notch). However, there was no improvement in perinatal outcome in the vitamin supplement group.

Based on the available data, neither calcium supplementation nor low-dose aspirin should be routinely prescribed for preeclampsia prevention in nulliparous women. In addition, zinc, magnesium, fish oil, and vitamins C and E should not be routinely used for this purpose. Even in studies revealing beneficial effects, the results reveal reductions in a "definition of preeclampsia" without concomitant improvement in perinatal outcome. There is a suggestion that low-dose aspirin improves pregnancy outcome in women with persistent elevations in the uterine Doppler resistance index at both 18 and 24 weeks' gestation.[17]

MATERNAL AND PERINATAL OUTCOME

Gestational Hypertension

In general, the majority of cases of mild gestational hypertension develop at or beyond 37 weeks' gestation, and thus pregnancy outcome is similar or superior to that seen in women with normotensive pregnancies (Table 2). Both gestational age at delivery and birth weight in these pregnancies are higher than those in normotensive pregnancies.[3,4,8,9] However, women with gestational hypertension are more likely to have higher rates of induction of labor for maternal reasons and higher rates of cesarean delivery than women with normotensive gestation.[3–5] The increased rate of cesarean delivery in such women is mainly related to failed medical induction or dystocia.[3–5]

On the other hand, maternal and perinatal morbidities are substantially increased in women with severe gestational hypertension.[3–5] Indeed, these women have higher morbidities than women with mild preeclampsia.[3–5] In addition, the rates of abruptio placentae, preterm delivery (at less than 37 and 35 weeks), and small for gestational age (SGA) infants in these women are similar to those seen in women with severe preeclampsia. However, whether this increase in rates of preterm delivery is secondary to an increase in early delivery by the physician or because of the disease process itself remains unknown. Therefore, these women should be managed as if they had severe preeclampsia.[5]

Preeclampsia

Maternal and perinatal outcomes in preeclampsia are usually dependent on one or more of the following: gestational age at onset of preeclampsia as well as at time of delivery, the severity of the disease process, the presence of multifetal gestation, and the presence of preexisting medical conditions such as pregestational diabetes, renal disease, or thrombophilias. In women with mild

Table 3. Pregnancy Outcome in Women With Mild and Severe Preeclampsia

	Hauth et al[3]		Buchbinder et al[5]		Hnat et al[6]	
	Mild (n = 217)	Severe (n = 109)	Mild* (n = 62)	Severe* (n = 45)	Mild (n = 86)	Severe (n = 70)
Delivery (wk)						
<37 (%)	NR	NR	25.8	66.7	14.0	33.0
<35 (%)	1.9†	18.5†	9.7	35.6	2.3	18.6
SGA infant (%)	10.2	18.5	4.8	11.4	NR	NR
Abruptio placentae (%)	0.5	3.7	3.2	6.7	0	1.4
Perinatal death (%)	1.0	1.8	0	8.9	0	1.4

Abbreviations as in Table 2.

* This study included women with previous preeclampsia. The other studies included only nulliparous women.

† These rates are for delivery at less than 34 weeks.

preeclampsia, the perinatal death rate and rates of preterm delivery, SGA infants, and abruptio placentae are similar to those of normotensive pregnancies[3,5,6] (Table 3). The rate of eclampsia is less than 1%, but the rate of cesarean delivery is increased because of increased rates of induction of labor.[3,5,6]

In contrast, perinatal mortality and morbidities as well as the rates of abruptio placentae are substantially increased in women with severe preeclampsia (Table 3). The rate of neonatal complications is markedly increased in those who develop severe preeclampsia in the second trimester, whereas it is minimal in those with severe preeclampsia beyond 35 weeks' gestation.

Severe preeclampsia is also associated with increased risk of maternal mortality (0.2%) and increased rates of maternal morbidities (5%) such as convulsions, pulmonary edema, acute renal or liver failure, liver hemorrhage, disseminated intravascular coagulopathy, and stroke. These complications are usually seen in women who develop preeclampsia before 32 weeks' gestation and in those with preexisting medical conditions.[18]

ANTEPARTUM MANAGEMENT OF MILD HYPERTENSION–PREECLAMPSIA

The optimal treatment of women with mild gestational hypertension or preeclampsia before 37 weeks' gestation is controversial. There is disagreement regarding the benefits of hospitalization, complete bed rest, and use of antihypertensive medications.

Hospitalization

In the past, treatment of these women has involved bed rest in the hospital for the duration of pregnancy with the belief that such treatment diminishes the frequency of progression to severe disease and allows rapid intervention in case of abrupt progression to abruptio placentae, eclampsia, or hypertensive crisis.[1] However, these complications are extremely rare among compliant women with mild hypertension or mild preeclampsia and absent symptoms. In addition, the results of two randomized trials in women with gestational hypertension and several observational studies in women with mild hypertension and mild preeclampsia suggest that most of these women can be safely treated at home or in a daycare facility provided they undergo frequent maternal and fetal evaluation. It must be emphasized that most of the patients included in these studies had mild hypertension only.[19] Therefore, there is a definite need for randomized trials in women with mild preeclampsia.

Bed Rest

Complete or partial bed rest for the duration of pregnancy is often recommended for women with mild hypertension–preeclampsia. There is no evidence to date suggesting that such recommendation improves pregnancy outcome. In addition, there are no published randomized trials comparing complete bed rest and restricted activity in the treatment of women with mild preeclampsia. On the other hand, prolonged bed rest for the duration of pregnancy increases the risk of thromboembolism.

Blood Pressure Medications

There are several randomized trials describing the use of antihypertensive drugs versus no treatment or a placebo in the treatment of women with mild hypertension or preeclampsia remote from term. Overall, these trials revealed lower rates of progression to severe disease, with no improvement in perinatal outcome.[20] Of note, the sample size of these trials was inadequate to evaluate differences in fetal growth restriction, abruptio placentae, perinatal death, or maternal outcome.[20]

Fetal and Maternal Surveillance

There is universal agreement that fetal testing is indicated during expectant treatment of women with gestational hypertension or preeclampsia.[1,2] However, there

is disagreement regarding the test to be used as well as the frequency of testing. Most authorities in the United States recommend daily fetal movement counts in association with either a nonstress test (NST) or a biophysical profile (BPP) to be performed at time of diagnosis and serially thereafter until delivery (one to two times a week.).[1,2] Because uteroplacental blood flow may be reduced in some of these women, ultrasound estimation of fetal weight as well as amniotic fluid status is also recommended at time of diagnosis and serially thereafter every 3 to 4 weeks. Doppler flow velocimetry is usually recommended by authorities outside the United States, particularly in the presence of suspected fetal growth restriction. The frequency of these tests usually depends on the severity of hypertension or preeclampsia, gestational age at time of diagnosis, and fetal growth findings. Most clinical series suggest testing once weekly in women with mild gestational hypertension or preeclampsia, twice weekly if there is suspected fetal growth restriction, and daily during expectant treatment of women with severe preeclampsia at less than 32 weeks' gestation.[1] However, there are no large prospective studies assessing the benefits or harms of these monitoring techniques in women with gestational hypertension or preeclampsia.

Maternal surveillance is indicated in all women with gestational hypertension and preeclampsia. The goal of monitoring in women with mild gestational hypertension is to observe progression of the condition to severe hypertension or to preeclampsia.[1,2] In women with mild preeclampsia, the goal is early detection of severe preeclampsia. In those with severe preeclampsia, the goal is to observe for the development of organ dysfunction. Therefore, all such women should be evaluated for symptoms of organ dysfunction such as severe headaches, visual changes, altered mentation, right upper quadrant or epigastric pain, nausea or vomiting, shortness of breath, and decreased urine output.[1] In addition, they should undergo laboratory testing for 24-hour urine protein, serum creatinine, platelet count, and liver enzymes. Coagulation function tests are not needed in the presence of a normal platelet count and liver enzymes.[21] The frequency of subsequent testing will depend on the initial findings, severity of the maternal condition, and the ensuing clinical progression. Most authorities recommend evaluation and testing of platelet count, liver enzymes, and serum creatinine once weekly for women with mild gestational hypertension or mild preeclampsia, and performing these tests daily during expectant treatment of women with severe preeclampsia remote from term.[1,2]

EXPECTANT MANAGEMENT OF SEVERE PREECLAMPSIA?

The clinical course of severe preeclampsia may be characterized by progressive deterioration in both maternal and fetal conditions. Because these pregnancies have been associated with increased rates of maternal morbidity and mortality and with significant risks for the fetus (growth restriction, hypoxemia, and death), there is universal agreement that all such patients should deliver if the disease develops after 34 weeks' gestation. Prompt delivery is also clearly indicated when there is imminent eclampsia (persistent severe symptoms), multiorgan dysfunction, severe fetal growth restriction (fifth percentile), suspected abruptio placentae, or nonreassuring fetal testing before 34 weeks' gestation.[22]

There is disagreement about treatment of patients with severe preeclampsia before 34 weeks' gestation where maternal condition is stable and fetal condition is reassuring. In such patients, some authors consider delivery as the definitive treatment regardless of gestational age, whereas others recommend prolonging pregnancy until development of maternal or fetal indications for delivery or until achievement of fetal lung maturity or 34 weeks' gestation.[22]

Although delivery is always appropriate for the mother, it may not be optimal for the fetus that is extremely premature. In the past, it was believed that infants born prematurely to severely preeclamptic women had lower rates of neonatal mortality and morbidity than infants of similar gestational age born to nonpreeclamptic women. This belief was based on the clinical impression that fetuses of preeclamptic women have accelerated lung and neurologic maturation as a result of stress in utero. This phenomenon, however, has never been documented in case–control studies.[22] In contrast, several recent case–control studies have demonstrated that premature infants born after severe preeclampsia have neonatal complications and mortality similar to those of other premature infants of similar gestational age and have higher rates of admission to neonatal intensive care units.[22] In addition, case–control studies have revealed that fetuses of preeclamptic women do not exhibit accelerated lung or neurological maturation.[22]

In the past, there was uncertainty regarding the efficacy and safety of corticosteroids in women with severe preeclampsia before 34 weeks' gestation. A prospective, double blind, randomized trial of 218 women with severe preeclampsia and gestational age between 26 and 34 weeks receiving either betamethasone ($n = 110$) or a placebo ($n = 108$) reported a significant reduction in the rate of respiratory distress syndrome (relative risk [RR]

0.53; 95% confidence interval [CI] 0.35, 0.82) in the steroids group.[23] Corticosteroid use also was associated with a reduction in the risks of neonatal intraventricular hemorrhage (RR 0.35; 95% CI 0.15, 0.86), neonatal infection (RR 0.39; 95% CI 0.39, 0.97), and neonatal death (RR 0.5; 95% CI 0.28, 0.89). However, there were no differences in maternal complications between the two groups. Thus, the data support the use of steroids to reduce neonatal complications in women with severe preeclampsia at 34 weeks' gestation or less.

RECOMMENDED MANAGEMENT

The primary objective of management in women with gestational hypertension–preeclampsia must always be safety of the mother and then delivery of a mature newborn who will not require intensive and prolonged neonatal care. This objective can be achieved by formulating a management plan that takes into consideration one or more of the following: the severity of the disease process, fetal gestational age, maternal and fetal status at time of initial evaluation, presence of labor, cervical Bishop score, and the wishes of the mother.

Mild Hypertension or Preeclampsia

Once the diagnosis of mild gestational hypertension or mild preeclampsia is made, subsequent therapy will depend on the results of maternal and fetal evaluation (Figure 1). In general, women with mild disease developing at 37 weeks' gestation or longer have a pregnancy outcome similar to that found in normotensive pregnancy. Thus, those who have a favorable cervix at or near term and patients who are considered noncompliant should undergo induction of labor for delivery. In addition, cervical ripening with prostaglandins and induction of labor can be used in women with mild preeclampsia and an unfavorable cervix at 37 weeks or more because the mother is at slightly increased risk for development of abruptio placentae and progression to severe disease. I also recommend delivery in those with a gestational age of 34 weeks or more in the presence of progressive labor or rupture of membranes, abnormal fetal testing, or fetal growth restriction.

In women who remain undelivered, close maternal and fetal evaluation is essential. These women are instructed to eat a regular diet with no salt restriction, and they are instructed to restrict their activity but not to complete bed rest. I do not use diuretics or antihypertensive medication because of the potential to mask the diagnosis of severe disease. In addition, the current data suggest that antihypertensive therapy in women with mild gestational hypertension or preeclampsia does not improve perinatal outcome. Only women considered to have severe disease should be started on antihypertensive medications, and they require in-hospital management. At the time of initial and subsequent visits, the women are educated and instructed about reporting symptoms of severe preeclampsia. They are also advised to immediately come to the hospital or office if they develop abdominal pain, uterine contractions, vaginal spotting, or decreased fetal movement.

In women with mild gestational hypertension, fetal evaluation should include an NST and an ultrasound examination of estimated fetal weight and amniotic fluid index. If the results are normal, then there is no need for repeat testing unless there is a change in maternal condition (progression to preeclampsia or severe hypertension) or there is decreased fetal movement or abnormal fundal height growth.[1] The development of any of these

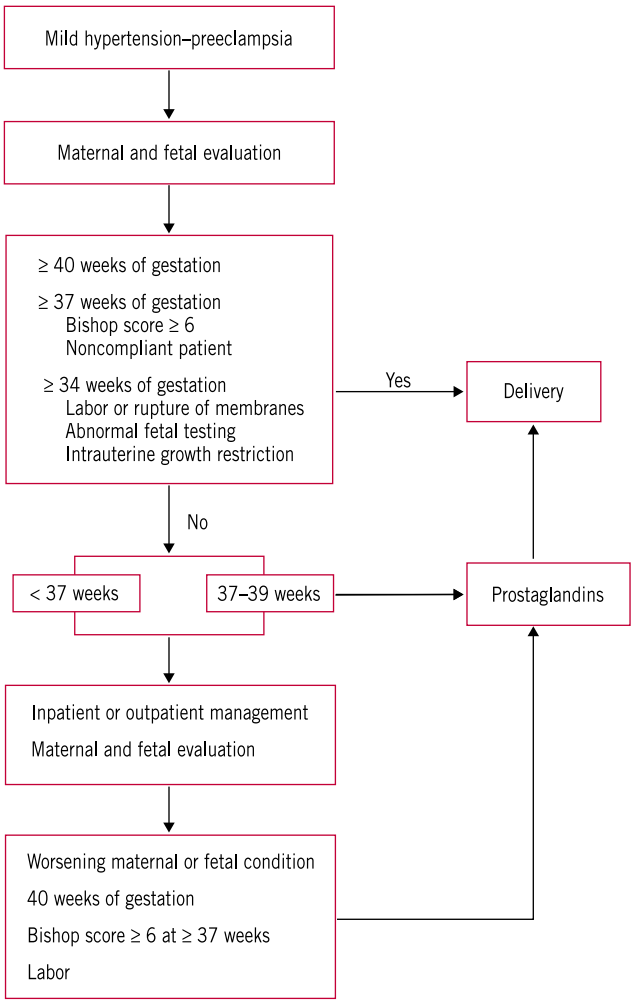

Figure 1. Recommended management of mild gestational hypertension or preeclampsia.
Sibai. Gestational Hypertension–Preeclampsia. Obstet Gynecol 2003.

findings requires prompt fetal testing with a nonstress test or biophysical profile.

Maternal evaluation includes measurements of hematocrit, platelet count, liver function tests, and 24-hour urine protein testing once weekly. The women are usually seen twice a week for evaluation of maternal BP, urine protein by dipstick, and symptoms of impending eclampsia. This evaluation is extremely important for early detection of progression to preeclampsia or severe hypertension. The onset of maternal symptoms, a sudden increase in BP to severe values, or development of proteinuria (2+ or more on dipstick) requires prompt hospitalization for close evaluation.

In women with mild preeclampsia at less than 37 weeks' gestation, my policy is to use outpatient management in those with a systolic BP of 150 mm Hg or less and/or a diastolic BP of 100 mm Hg or less and a urine protein count of 1000 mg or less per 24 hours if they have no symptoms and have normal liver enzymes and a normal platelet count (more than 100,000/mm^3). Women who do not satisfy these criteria are managed in-hospital. During ambulatory management, the women are instructed to have relative rest at home, to have BP and urine (dipstick) checked daily, and to promptly report symptoms of severe disease. These women are then seen twice weekly, during which time they have a laboratory evaluation of platelet count and liver enzymes. Fetal evaluation includes daily fetal movement count, NST twice weekly, and ultrasound evaluation of fetal growth and fluid every 3 weeks. If there is evidence of disease progression (significant increase in BP or proteinuria to levels above the threshold mentioned previously), if they have a new onset of symptoms, or if there is evidence of abnormal blood tests or abnormal fetal growth, these women are then hospitalized for the duration of pregnancy. Women managed in-hospital receive similar maternal and fetal evaluations. All women then deliver according to the plan described in Figure 1.

Severe Preeclampsia

The presence of severe disease mandates immediate hospitalization in labor and delivery. My policy is to start intravenous (IV) magnesium sulfate to prevent convulsions and antihypertensive medications to lower severe levels of hypertension (systolic pressure greater than 160 mm Hg and/or diastolic pressure of at least 110 mm Hg). The aim of antihypertensive therapy is to keep systolic BP between 140 and 155 mm Hg and diastolic BP between 90 and 105 mm Hg. During the observation period maternal and fetal conditions are assessed and a decision is made regarding the need for delivery (Figure 2). Those with gestational ages of 24–34 weeks are given corticosteroids to accelerate fetal lung maturity. Maternal evaluation includes monitoring of BP, urine output, cerebral status, and the presence of epigastric pain, tenderness, labor, or vaginal bleeding. Laboratory evaluation includes a platelet count and liver enzyme and serum creatinine testing. Fetal evaluation includes continuous fetal heart monitoring, a BPP, and ultrasonographic assessment of fetal growth and amniotic fluid. Patients with resistant severe hypertension despite maximum doses of IV labetalol (220 mg) plus oral nifedipine (50 mg) or persistent cerebral symptoms while on magnesium sulfate deliver within 24–48 hours irrespective of fetal gestational age. In addition, patients with either thrombocytopenia (platelet count less than 100,000) or elevated liver enzymes with epigastric pain and tenderness or with serum creatinine of 2.0 mg/dL or more also deliver within 48 hours.[24]

Patients with gestational ages of 33 to 34 weeks are given corticosteroids and then deliver after 48 hours. Patients with gestational age below 23 weeks are offered termination of pregnancy. Patients at 23–32 weeks' gestation receive individualized treatment based on their clinical response during the 24-hour observation period. If BP is adequately controlled and fetal tests are reassuring, magnesium sulfate is discontinued and the patients are then observed closely on the antepartum high-risk ward until 34 weeks' gestation or development of a maternal or fetal indication for delivery. During hospitalization, they receive antihypertensive drugs if needed, usually oral nifedipine (40–120 mg per day) plus labetalol (600–2400 mg per day), to keep systolic BP between 140 and 155 mm Hg and diastolic pressure between 90 and 105 mm Hg. The patients also receive daily assessment of maternal and fetal well-being.[24] In general, most patients will require delivery within 2 weeks, but some patients may continue their pregnancies for several weeks. It is important to emphasize that this therapy is appropriate only in a select group of patients and should be practiced only in a tertiary-care center with adequate maternal and neonatal intensive care facilities. In addition, once the decision is made for delivery, the patients should receive magnesium sulfate in labor and for at least 24 hours postpartum.

Intrapartum Management

The goals of treatment of women with gestational hypertension–preeclampsia are early detection of fetal heart rate abnormalities, early detection of progression from mild to severe disease, and prevention of maternal complications. Pregnancies complicated by preeclampsia, particularly those with severe disease and/or fetal growth restriction, are at risk for reduced fetal reserve and abruptio placentae. Therefore, all women with pre-

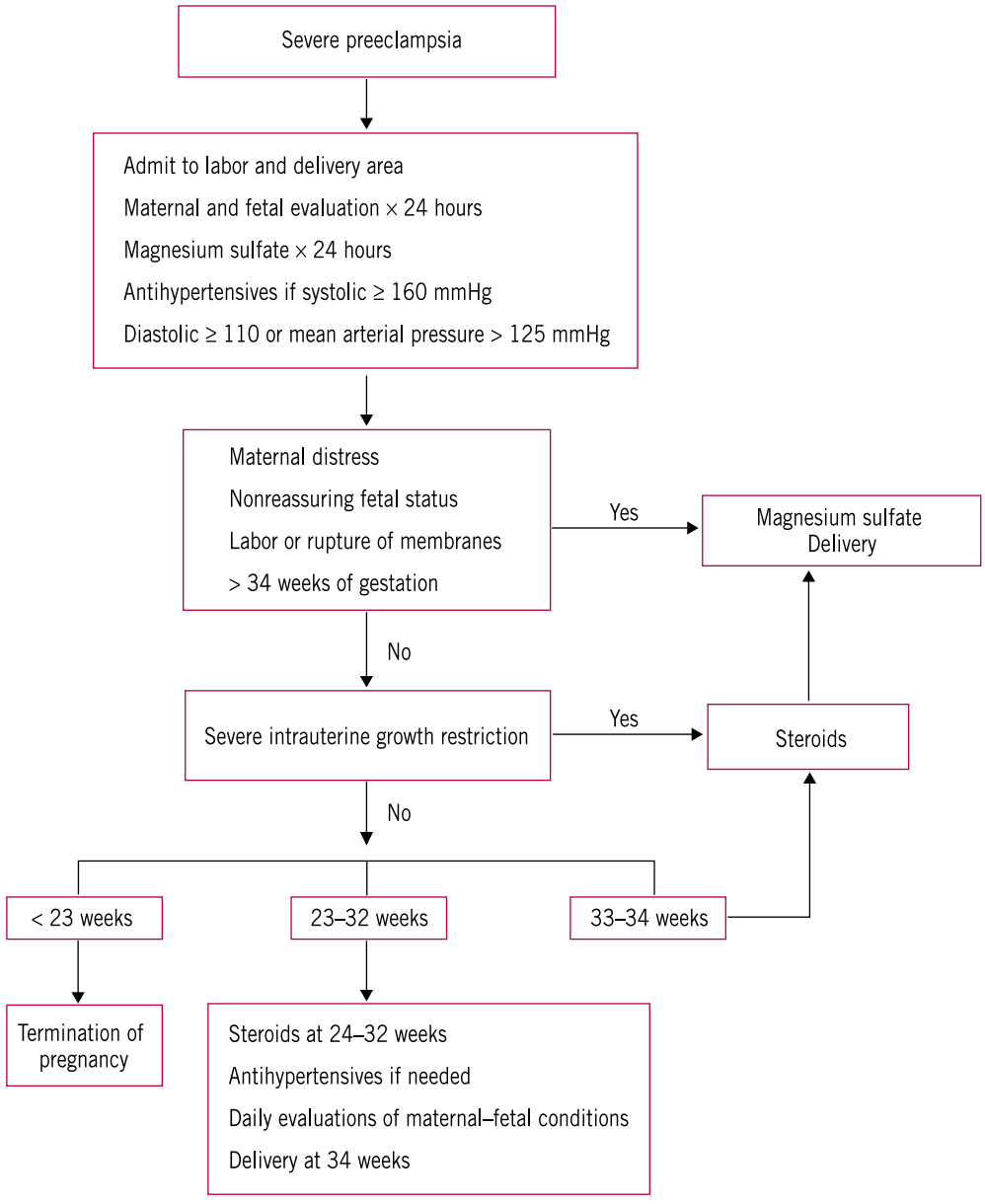

Figure 2. Recommended management of severe preeclampsia. Maternal distress: thrombocytopenia, imminent eclampsia, pulmonary edema, and hemolysis plus elevated liver enzyme levels.
Sibai. Gestational Hypertension-Preeclampsia. Obstet Gynecol 2003.

eclampsia should receive continuous monitoring of fetal heart rate and uterine activity, with special attention to hyperstimulation and development of vaginal bleeding during labor. The presence of uterine irritability and/or recurrent variable or late decelerations may be the first sign of abruptio placentae in these women.

Some women with mild hypertension–preeclampsia will progress to severe disease as a result of changes in cardiac output and stress hormones during labor. Therefore, all women with gestational hypertension–preeclampsia should have BP recordings every hour and need to be questioned about the new onset of symptoms suggesting severe disease. Those who develop severe hypertension and/or symptoms should be treated as having severe preeclampsia.

Maternal pain relief during labor and delivery can be provided by either systemic opioids or segmental epidural anesthesia. Epidural analgesia is considered the preferred method of pain relief in women with mild gestational hypertension and mild preeclampsia. Al-

though there is no unanimity of opinion regarding the use of epidural anesthesia in women with severe preeclampsia, a significant body of evidence indicates that epidural anesthesia is safe in these women.[1,25] A randomized trial of 116 women with severe preeclampsia receiving either epidural analgesia or patient-controlled analgesia reported no differences in cesarean delivery rates, and the group receiving epidural analgesia had significantly better pain relief during labor.[26]

Either epidural, spinal, or combined techniques or regional anesthesia are considered by most obstetric anesthesiologists to be the method of choice during cesarean delivery. In women with severe preeclampsia, general anesthesia increases the risk of aspiration and failed intubation due to airway edema and is associated with marked increases in systemic and cerebral pressures during intubation and extubation.[1] Women with airway or laryngeal edema may require awake intubation under fiber optic observation with the availability of immediate tracheostomy. Changes in systemic and cerebral pressures may be attenuated by pretreatment with labetalol or nitroglycerine injections. It is important to emphasize that regional anesthesia is contraindicated in the presence of coagulopathy or severe thrombocytopenia (platelet count less than 50,000/mm^3).

Prevention of Convulsions

Magnesium sulfate is the drug of choice to prevent convulsions in women with preeclampsia. Two recent randomized trials showed that magnesium sulfate is superior to a placebo for prevention of convulsions in women with severe preeclampsia.[27,28] One of the largest randomized trials to date enrolled 10,141 women with preeclampsia in 33 nations (largely in the Third World).[28] Almost all of the enrolled patients had severe disease by US standards: 50% received antihypertensives before randomization, 75% received antihypertensives after randomization, and the remainder had severe preeclampsia or imminent eclampsia. Among all enrolled women, the rate of eclampsia was significantly lower in those assigned to magnesium sulfate (0.8% versus 1.9%; RR 0.42; 95% CI 0.29, 0.60). However, among the 1560 women enrolled in the Western world, the rates of eclampsia were 0.5% in the magnesium group and 0.8% in the placebo, a difference that was not significant (RR 0.67; 95% CI 1.19, 2.37).[28]

There are two randomized placebo-controlled trials evaluating the efficacy and safety of magnesium sulfate in women with mild preeclampsia.[29,30] One of these trials included 135 women[29] and the other included only 222.[30] There were no instances of eclampsia in either group in both of these trials. In addition, the findings of both studies revealed that magnesium sulfate does not affect the duration of labor or the rate of cesarean delivery. However, neither of these studies had an adequate sample size to determine the efficacy of magnesium sulfate in preventing convulsions.[29,30] Therefore, the benefit of magnesium sulfate in women with mild preeclampsia remains unclear. A randomized trial to answer this question is urgently needed. My policy is to give IV magnesium sulfate during labor and postpartum for all women with diagnosed severe preeclampsia. I do not use this therapy in women with mild gestational hypertension or preeclampsia in the absence of symptoms. In women having elective cesarean delivery, magnesium sulfate is given at least 2 hours before the procedure and continued during surgery and for at least 12 hours postpartum.

Control of Severe Hypertension

The objective of treating acute severe hypertension is to prevent potential cerebrovascular and cardiovascular complications such as encephalopathy, hemorrhage, and congestive heart failure.[1] For ethical reasons, there are no randomized trials to determine the level of hypertension to treat to prevent these complications. Antihypertensive therapy is recommended by some for sustained systolic BP values of at least 180 mm Hg and for sustained diastolic values of at least 110 mm Hg. Some experts recommend treating systolic levels of 160 mm Hg or greater, others recommend treating diastolic levels of 105 mm Hg or greater, whereas others use a mean arterial BP of 130 mm Hg or greater.[1,2] The definition of sustained hypertension is not clear, ranging from 30 minutes to 2 hours.

The most commonly used and advocated agent for the treatment of severe hypertension in pregnancy is IV hydralazine given as bolus injections of 5–10 mg every 15–20 minutes for a maximum dose of 30 mg. Recently, several drugs were compared with hydralazine in small, randomized trials. The results of these trials were the subject of a recent systemic review that suggested that IV labetalol or oral nifedipine is as effective as and has fewer side effects than IV hydralazine.[31] The recommended dose of labetalol is 20–40 mg IV every 10–15 minutes for a maximum of 220 mg, and the dose of nifedipine is 10–20 mg orally every 30 minutes for a maximum dose of 50 mg.[1] I generally use sustained BP values of at least 170 mm Hg (systolic) or at least 110 mm Hg (diastolic) to initiate therapy intrapartum. For women with thrombocytopenia and those in the postpartum period I use systolic values of at least 160 mm Hg or diastolic values of at least 105 mm Hg. My first-line agent is IV labetalol, and if maximum doses are ineffective, I add oral nifedipine.

Mode of Delivery

There are no randomized trials comparing optimal methods of delivery in women with gestational hypertension–preeclampsia. A plan for vaginal delivery should be attempted for all women with mild disease and for the majority of women with severe disease, particularly those beyond 30 weeks' gestation.[1] The decision to perform cesarean delivery should be based on fetal gestational age, fetal condition, presence of labor, and cervical Bishop score. In general, the presence of severe preeclampsia is not an indication for cesarean delivery. My policy is to recommend elective cesarean delivery for all women with severe preeclampsia below 30 weeks' gestation who are not in labor and whose Bishop score is below five. In addition, I recommend elective cesarean delivery to those with severe preeclampsia plus fetal growth restriction if the gestational age is below 32 weeks in the presence of an unfavorable cervical Bishop score.

Postpartum Management

During the immediate postpartum period, women with preeclampsia should receive close monitoring of BP and symptoms consistent with severe disease and accurate measurements of fluid intake and urinary output.

These women usually receive large amounts of IV fluids during labor, as a result of prehydration before the administration of epidural analgesia, and IV fluids given during the administration of oxytocin and magnesium sulfate in labor and postpartum. In addition, during the postpartum period there is mobilization of extracellular fluid leading to increased intravascular volume. As a result, women with severe preeclampsia–particularly those with abnormal renal function, those with capillary leaks, and those with early onset–are at increased risk for pulmonary edema and exacerbation of severe hypertension postpartum. These women should receive frequent evaluation of the amount of IV fluids, oral intake, blood products, and urine output as well as monitoring by pulse oximetry and pulmonary auscultation.

In general, in most women with gestational hypertension the BP becomes normotensive during the first week postpartum.[32] In contrast, in women with preeclampsia the hypertension takes a longer time to resolve.[32] In addition, in some women with preeclampsia there is an initial decrease in BP immediately postpartum, followed by development of hypertension again between days 3 and 6.[33] My policy is to use antihypertensive drugs if the systolic BP is at least 155 mm Hg and/or if the diastolic BP is at least 105 mm Hg. My drug of choice is oral nifedipine (10 mg every 6 hours) or long-acting nifedipine (10 mg twice daily) to keep BP below that level.[34] If BP is well controlled and there are no maternal symptoms, the woman is then discharged home with instructions for daily BP measurements by a home visiting nurse for the first week postpartum or longer as necessary. Antihypertensive medications are discontinued if the pressure remains below the hypertensive levels for at least 48 hours.

Severe hypertension or severe preeclampsia may develop for the first time in the postpartum period. Hence, all postpartum women should be educated about the signs and symptoms of severe hypertension or preeclampsia. These women are at increased risk for eclampsia, pulmonary edema, stroke, and thromboembolism. Therefore, medical providers as well as personnel who answer patient's phone calls should be educated and instructed about the important information to report to physicians.[35] In addition, women who have persistent severe headaches, visual changes, epigastric pain with nausea or vomiting, and severe hypertension require immediate evaluation and potential hospitalization. My policy is to give these women magnesium sulfate for at least 24 hours and to give antihypertensive drugs to keep the BP below the severe range. If the patient does not respond to such therapy, then I perform brain imaging to rule out the presence of other cerebral pathology.[35,36]

SUMMARY

The etiology and pathogenesis of gestational hypertension and preeclampsia remain unknown. Despite all the recent research efforts, there are no reliable tests to predict the development of preeclampsia and there are no effective therapeutic methods to prevent preeclampsia. As a result, gestational hypertension and preeclampsia remain a major obstetric problem, accounting for a large percentage of maternal and perinatal morbidities. At present, there are few, if any, multicenter randomized studies available to evaluate the safety and efficacy of the various fetal evaluation techniques or of the various antihypertensive drugs recommended during the management of gestational hypertension and preeclampsia. There is solid evidence to treat severe hypertension and to use magnesium sulfate as a prophylaxis against convulsions in women with severe disease. However, there are inadequate data to support the use of magnesium sulfate in women with mild gestational hypertension or mild preeclampsia. Therefore, until multicenter trials are performed in this area, management of women with preeclampsia will continue to be based on consensus and expert opinion.

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