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

Chronic Hypertension in Pregnancy

Baha M. Sibai, MD

Chronic hypertension in pregnancy is associated with increased rates of adverse maternal and fetal outcomes both acute and long term. These adverse outcomes are particularly seen in women with uncontrolled severe hypertension, in those with target organ damage, and in those who are noncompliant with prenatal visits. In addition, adverse outcomes are substantially increased in women who develop superimposed preeclampsia or abruptio placentae. Women with chronic hypertension should be evaluated either before conception or at time of first prenatal visit. Depending on this evaluation, they can be divided into categories of either "high risk" or "low risk" chronic hypertension. High-risk women should receive aggressive antihypertensive therapy and frequent evaluations of maternal and fetal well-being, and doctors should recommend lifestyle changes. In addition, these women are at increased risk for postpartum complications such as pulmonary edema, renal failure, and hypertensive encephalopathy for which they should receive aggressive control of blood pressure as well as close monitoring. In women with low-risk (essential uncomplicated) chronic hypertension, there is uncertainty regarding the benefits or risks of antihypertensive therapy. In my experience, the majority of these women will have good pregnancy outcomes without the use of antihypertensive medications. Antihypertensive agents are recommended and are widely used in these women despite absent evidence of either benefits or harm from this therapy. These recommendations are based on dogma and consensus rather than on scientific evidence. There is an urgent need to conduct randomized trials in women with mild chronic hypertension in pregnancy. (Obstet Gynecol 2002;100:369–77. © 2002 by The American College of Obstetricians and Gynecologists.)

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According to data derived from the National Health and Nutrition Examination Survey, 1988–1991, the prevalence of chronic hypertension among women of childbearing age increases from 0.6–2.0% for women 18–29 years old to 4.6–22.3% for women 30–39 years old. The lower prevalences are for whites, and higher rates are for blacks.[1] Because of the current trend of childbearing at an older age, it is expected that the incidence of chronic hypertension in pregnancy will continue to rise. During the new millennium, and estimating a prevalence of chronic hypertension during pregnancy of 3%, at least 120,000 pregnant women (3% of 4 million pregnancies) with chronic hypertension per year will be seen in the United States.

DEFINITION AND DIAGNOSIS

In pregnant women chronic hypertension is defined as elevated blood pressure that is present and documented before pregnancy. In women whose prepregnancy blood pressure is unknown, the diagnosis is based on the presence of sustained hypertension before 20 weeks of gestation, defined as either systolic blood pressure of at least 140 mm Hg or diastolic blood pressure of at least 90 mm Hg on at least two occasions measured at least 4 hours apart. The diagnosis may be difficult in women with previously undiagnosed chronic hypertension who begin prenatal care after 16 weeks' gestation because a physiologic decrease in blood pressure usually begins at that time. This decrease may result in normal blood pressure findings at that time, which will eventually increase again during the third trimester. These women are more likely to be erroneously diagnosed as having gestational hypertension.[2]

Women with chronic hypertension are at increased risk of superimposed preeclampsia. The development of superimposed preeclampsia is associated with high rates of adverse maternal and perinatal outcomes.[3] The diag-

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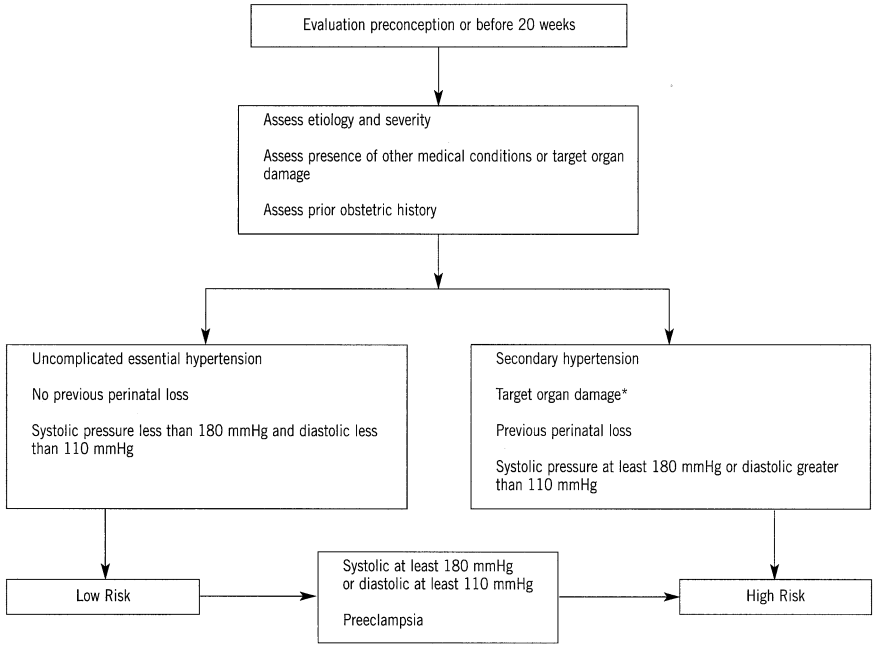

Figure 1. Initial evaluation of women with chronic hypertension. *Left ventricular dysfunction, retinopathy, dyslipidemia, maternal age above 40 y, microvascular disease, stroke.

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nosis of superimposed preeclampsia should be made in the presence of any of the following findings:

1. In women with chronic hypertension and without proteinuria early in pregnancy (less than 20 weeks' gestation), preeclampsia is diagnosed if there is new-onset proteinuria (0.3 g of protein or more in a 24-hour specimen).
2. In women with chronic hypertension and pre-existing proteinuria before 20 weeks' gestation, the diagnosis is confirmed if there is an exacerbated increase in blood pressure to the severe range (systolic pressure of 180 mm Hg or more or diastolic pressure of 110 mm Hg or more) in a woman whose hypertension has previously been well controlled with antihypertensive drugs, particularly if associated with headaches, blurred vision, or epigastric pain, or if there is significant increase in liver enzymes (unrelated to methyldopa), or if the platelet count is less than 100,000/mm.[4]

ETIOLOGY AND CLASSIFICATION

The etiology and severity of chronic hypertension are important considerations in the management of pregnancy. Chronic hypertension is subdivided into primary (essential) and secondary. Primary hypertension is by far the most common cause of chronic hypertension seen during pregnancy (90%). In 10% of the cases, chronic hypertension is secondary to one or more underlying disorders such as renal disease (glomerulonephritis, interstitial nephritis, polycystic kidneys, renal artery stenosis), collagen vascular disease (lupus, scleroderma), endocrine disorders (diabetes mellitus with vascular involvement, pheochromocytoma, thyrotoxicosis, Cushing disease, hyperaldosteronism), or coarctation of the aorta.[4,5]

Chronic hypertension during pregnancy can be subclassified as either mild or severe, depending on the systolic and diastolic blood pressure readings. Systolic and diastolic (Korotkoff phase V) blood pressures of at

Table 1. Rates of Adverse Pregnancy Outcome in Observational Studies Describing Mild Chronic Hypertension in Pregnancy

	Preeclampsia (%)	Abruptio placentae (%)	Delivery at <37 wk (%)	SGA (%)
Sibai et al[2] ($n = 211$)	10	1.4	12.0	8.0
Rey and Couturier[6] ($n = 337$)	21	0.7	34.4	15.5
McCowan et al[7] ($n = 142$)	14	NR	16.0	11.0
Sibai et al[3] ($n = 763$)	25	1.5	33.3	11.1

NR = not reported; SGA = small for gestational age.

least 180 mm Hg and 110 mm Hg, respectively, constitute severe hypertension.[4,5]

For management and counseling purposes, chronic hypertension in pregnancy is also categorized as either low risk or high risk, as described in Figure 1. The patient is considered to be at low risk when she has mild essential hypertension without any organ involvement. Blood pressure criteria are based on blood pressure measurements at initial visit irrespective of whether patients are on antihypertensive medications. For example, if the patient has a blood pressure of 140/80 mm Hg on antihypertensive drugs, she is still classified as low risk. The medications will be discontinued and blood pressure monitored very closely. If it reaches severe levels, she would then be classified as high risk, and managed as such. A patient initially classified as low risk early in pregnancy may become high risk if she later develops severe hypertension or if she develops preeclampsia.

MATERNAL-PERINATAL RISKS

Pregnancies complicated by chronic hypertension are at increased risk for the development of superimposed preeclampsia and abruptio placentae. The reported rates of preeclampsia in the literature in mild hypertension range from 10% to 25% (Table 1).[2,3,6,7] The rate of preeclampsia in women with severe chronic hypertension approaches 50%.[7,8] Sibai et al[3] studied the rate of superimposed preeclampsia among 763 women with chronic hypertension observed prospectively at several medical centers in the United States. The overall rate of superimposed preeclampsia was 25%. The rate was not affected by maternal age, race, or presence of proteinuria early in pregnancy. However, the rate was significantly greater in women who had hypertension for at least 4 years (31% versus 22%), in those who had had preeclampsia during a previous pregnancy (32% versus 23%), and in those whose diastolic blood pressure was 100–110 mm Hg when compared with those whose diastolic blood pressure was below 100 mm Hg at baseline (42% versus 24%).[3]

The reported rate of abruptio placentae in women with mild chronic hypertension has ranged from 0.7% to 1.5% (Table 1). The rate in those with severe or high risk hypertension may be 5–10%.[8] In a recent multicenter study that included 763 women with chronic hypertension, the overall rate of abruptio placentae was reported at 1.5%, and the rate was significantly higher in those who developed superimposed preeclampsia than in those without this complication (3% versus 1%, $P = .04$).[3] However, the rate was not influenced by either maternal age, race, or duration of hypertension.[4] In addition, the results of a systematic review of nine observational studies revealed that the rate of abruptio placentae is doubled (odds ratio [OR] 2.1; 95% confidence interval [CI] 1.1, 3.9) in women with chronic hypertension compared with either the normotensive or the general obstetric population.[9]

In addition to preeclampsia and abruptio placentae, women with high-risk chronic hypertension are at increased risks for life-threatening maternal complications such as pulmonary edema, hypertensive encephalopathy, retinopathy, cerebral hemorrhage, and acute renal failure.[4] These risks are particularly increased in women with uncontrolled severe hypertension, in those with significant renal dysfunction early in pregnancy, and in those with left ventricular dysfunction before conception.[10,11]

Fetal and neonatal complications are also increased in women with chronic hypertension. The risk of perinatal mortality is increased three to four times compared with the general obstetric population (OR 3.4; 95% CI 3.0, 3.7).[9] The rates of premature deliveries and small for gestational age (SGA) infants are also increased in women with chronic hypertension (Table 1). In women with severe chronic hypertension in the first trimester, the reported rates of preterm deliveries were 62–70% and the rates of SGA infants were 31–40%.[7,8] Recently, Sibai et al[3] reported risk factors for adverse perinatal outcome among 763 women with mild chronic hypertension who were enrolled in a multicenter trial comparing low-dose aspirin to a placebo. They found that the development of superimposed preeclampsia was associated with higher rates of preterm delivery (OR 3.9; 95% CI 2.7, 5.4), higher rates of neonatal intraventricular hemorrhage (OR 4.5; 95% CI 1.5, 14.2), and higher rates of perinatal death (OR 2.3; 95% CI 1.4, 4.8). In addition, the presence of proteinuria early in pregnancy was also an independent risk factor associated with higher rates of preterm delivery (OR 3.1; 95% CI 1.8, 5.3), higher rates of SGA infants (OR 2.8; 95% CI 1.6, 5.0), and higher rates of neonatal intraventricular hemorrhage (OR 3.9; 95% CI 1.3, 11.6).[3]

GOALS OF ANTIHYPERTENSIVE THERAPY IN PREGNANCY

In nonpregnant individuals, long-term blood pressure control can lead to significant reductions in the rates of stroke and cardiovascular morbidity and mortality.[12] In those with mild to moderate hypertension, the benefit is achieved after at least 5 years of treatment.[12] The side effects of therapy are restricted to the treated individual. Hypertension in pregnancy is different because the duration of therapy is shorter, the benefits to the mother may not be obvious during the short time of treatment,

and the exposure to drugs will include both mother and fetus. In this respect, one must balance the potential short-term maternal benefits against possible short- and long-term benefits and risks to the fetus and infant.[9,13]

Most women with chronic hypertension during pregnancy have mild essential uncomplicated hypertension and are at minimal risk for cardiovascular complications within the short time frame of pregnancy.[9,13] Several retrospective[2,3,6,7] and prospective[14–17] studies have been conducted to determine whether antihypertensive therapy in these women would improve pregnancy outcome. An overall summary of these studies revealed that, regardless of the antihypertensive therapy used, maternal cardiovascular and renal complications were minimal or absent.[9,13] Based on the available data, there is no compelling evidence that short-term antihypertensive therapy is beneficial for the mother in women with low-risk hypertension, except for a reduction in the rate of exacerbation of hypertension.[18,19]

There are no placebo-controlled trials examining the benefits of antihypertensive therapy in women with severe hypertension in pregnancy, and none are likely to be performed because of the potential risks of untreated severe hypertension.[8] Antihypertensive therapy is necessary in these women to reduce the acute risk of stroke, congestive heart failure, or renal failure. In addition, control of severe hypertension may also permit pregnancy prolongation and thereby improve perinatal outcome. However, there is no evidence that control of severe hypertension reduces the rates of either superimposed preeclampsia or abruptio placentae.[7,8]

There are no trials examining the treatment of women with chronic hypertension and other risk factors, such as pre-existing renal disease, diabetes mellitus, or cardiac disease.[9] On the other hand, there is evidence from retrospective and observational studies that uncontrolled mild to moderate hypertension may exacerbate target organ damage during pregnancy in women with renal disease, in those with diabetes mellitus with vascular disease, and in those with left ventricular dysfunction.[20,21] Therefore, some authors recommend aggressive treatment of mild hypertension in these women because of the belief that such management may reduce both short- and long-term cardiovascular complications.[20,21]

There are many retrospective and prospective studies examining the potential fetal-neonatal benefits of pharmacologic therapy in women with mild essential uncomplicated hypertension (low risk).[9,19] Some compared treatment with no treatment or with a placebo, others compared two different antihypertensive drugs, and others used a combination of drugs. In addition, the gestational age at time of treatment, the level of blood pressure achieved during treatment, and the duration of therapy were highly variable. Only four of these studies were randomized trials that included women enrolled prior to 20 weeks' gestation.[14–17] Only two of the trials had a moderate sample size to evaluate the risks of superimposed preeclampsia and abruptio placentae.[16,17] The findings of these two trials revealed contradictory results regarding the effects of antihypertensive therapy on the rates of superimposed preeclampsia (a significant reduction in the study by Steyn and Odendaal[17]) and abruptio placentae (a moderate but not significant reduction in the study by Steyn and Odendaal). Antihypertensive therapy did not affect gestational age at time of delivery in any of the four trials; only the small trial by Butters et al[15] demonstrated a significantly lower average birth weight and significantly higher rate of SGA infants in the atenolol-treated group. The total number of women enrolled in these trials was only 450, and the largest trial included 263 women.[16] In addition, there was imbalance in the number of women with risk factors for preeclampsia and abruptio placentae between the study groups in the trial by Steyn and Odendaal.[17] This imbalance favored the treated arm of the study. Therefore, none of these trials had a sample size with adequate power to detect moderate (20–30%) reductions or increase in rates of preeclampsia, SGA infants, or abruptio placentae.[9]

THE SAFETY OF ANTIHYPERTENSIVE DRUGS IN PREGNANCY

The potential adverse effects for most commonly prescribed antihypertensive agents are either poorly established or unclearly quantified.[9] Most of the evidence on harm associated with antihypertensives in pregnancy is limited to case reports. The interpretation of these reports is difficult because it is impossible to ascertain the exact number of women exposed to antihypertensive drugs during pregnancy.[9] Also, it is likely that the number of published case reports is an underestimate of the actual number of women experiencing the reported adverse reaction. This limitation is amplified by the fact that rechallenge and information related to previous exposure during pregnancy are nonexistent. Furthermore, the condition for which pregnant women are treated with antihypertensive drugs can be partially responsible for the adverse fetal and neonatal outcomes.

In general, available information about teratogenecity, except in laboratory animals, is limited and selective. All available data have been obtained from registries such as state medical registry data.[22] Because of absent multicenter randomized trials in women with chronic hypertension, there are no placebo-controlled evaluations regarding the safety of these drugs when used at the time of

conception and throughout pregnancy. At the present time, there are few data to help the clinician evaluate the benefits or risks of most antihypertensive drugs when used in pregnancy. Nevertheless, the limited data in the literature suggest that there are potential adverse fetal effects such as oligohydramnios and fetal-neonatal renal failure when angiotensin-converting enzyme inhibitors are used in the second or third trimester.[9,22] Similar effects are to be expected with the use of angiotensin II receptor blockers. Therefore, these agents should be avoided if possible in the second and third trimesters.[13,22]

The use of atenolol during the first and second trimesters is associated with significantly reduced fetal growth along with decreased placental growth and weight.[15,23] On the other hand, no such effects on fetal or placental growth were reported with other β-blockers, such as metoprolol, pindolol, and oxprenolol, but data on the use of these agents in early pregnancy are very scarce.[9]

Prospective trials that studied the effect of either methyldopa or labetalol in women with mild chronic hypertension revealed no adverse maternal or fetal outcome with the use of these medications.[9,13] In a large and unique trial in which methyldopa or labetalol was started between 6 and 13 weeks' gestation in patients with chronic hypertension, none of the exposed newborns had major congenital anomalies.[16]

There is a large clinical experience with the use of thiazide diuretics during pregnancy. The available data suggest that the use of diuretics in the first trimester and throughout gestation is not associated with increased risk of major fetal anomalies or adverse fetal-neonatal events.[9,13] However, their use was associated with reduced plasma volume expansion. There is little information regarding the use of calcium channel blockers in women with mild chronic hypertension. The available evidence suggests that the use of calcium channel blockers, particularly nifedipine in the first trimester, was not associated with increased rates of major birth defects.[22,24] The effects of nifedipine on fetal-neonatal outcome were evaluated in a prospective randomized trial of 283 women with mild to moderate hypertension in pregnancy in which 47% of the participants had chronic hypertension.[25] Sixty-six of these women were enrolled between 12 and 20 weeks' gestation. In this study, the use of slow-release nifedipine was not associated with adverse fetal-neonatal outcomes.[25]

The long-term effects on children of mothers exposed to antihypertensive drugs during pregnancy are lacking, except for limited information concerning the use of methyldopa and nifedipine.[26,27] A follow-up study of infants after 7.5 years showed no long-term adverse effects on development among those exposed to methyldopa in utero, as compared with infants not exposed to such treatment.[26] A similar study examining the effects of slow-release nifedipine after 1.5 years of follow-up demonstrated no adverse effects on development.[27]

SUMMARY

Many important clinical issues faced by clinicians who care for pregnant women with pre-existing chronic hypertension remain unresolved. There is lack of agreement regarding the blood pressure levels at which to initiate antihypertensive therapy, and there is lack of information regarding the optimal blood pressure to be achieved during antihypertensive therapy. The evidence to date regarding benefits and risks of antihypertensive drugs remains scant and provides little direction to clinicians. There are no studies assessing the costs, benefits, or risks of various fetal evaluation techniques (ultrasound examinations, serial nonstress testing, or biophysical profile testing) in women with chronic hypertension. Various international and national societies recommend different guidelines and different antihypertensive agents as the management of choice.[4,5,28,29] These recommendations are based on consensus rather than on solid scientific evidence. Therefore, until multicenter trials are performed in this area, management of women with chronic hypertension in pregnancy will continue to be based on expert opinion.

MANAGEMENT

The primary objective in the management of pregnancies complicated by chronic hypertension is to reduce maternal risks and achieve optimal perinatal survival. This objective can be achieved by formulating a rational approach that includes preconceptual evaluation and counseling, early antenatal care, frequent antepartum visits to monitor both maternal and fetal well-being, timely delivery with intensive intrapartum monitoring, and proper postpartum management.

Evaluation and Classification

Management of patients with chronic hypertension should ideally begin before pregnancy, whereby extensive evaluation and a complete workup are undertaken to assess the etiology, severity, and presence of other medical illnesses, and to rule out the presence of target organ damage of long-standing hypertension. An in-depth history should delineate in particular the duration of hypertension, the use of antihypertensive medications, their type, and the response to these medications. Also, attention should be given to the presence of cardiac or renal disease, diabetes, thyroid disease, and a history

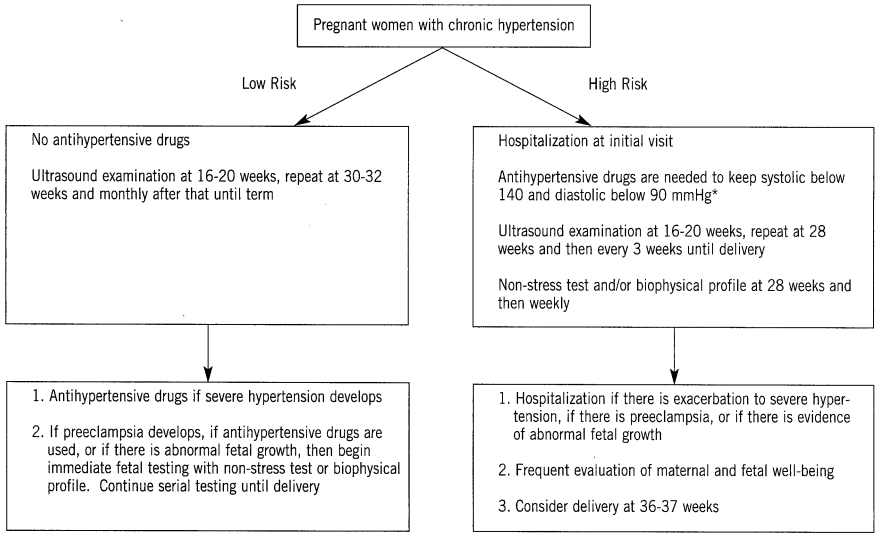

Figure 2. Antepartum management of chronic hypertension. *For women with target organ damage.

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of cerebrovascular accident, or congestive heart failure. A detailed obstetric history should include maternal as well as neonatal outcome of previous pregnancies, with stresses on history of development of abruptio placentae, superimposed preeclampsia, preterm delivery, small for gestation infants, intrauterine fetal death, and neonatal morbidity and mortality.

Laboratory evaluation is obtained to assess the function of different organ systems that are likely to be affected by chronic hypertension, and as a baseline for future assessments. These should include the following for all patients: urine analysis, urine culture and sensitivity, 24-hour urine evaluations for protein, electrolytes, complete blood count, and glucose tolerance test.

Women with long-standing hypertension for several years, particularly those with histories of poor compliance or poor blood pressure control, should be evaluated for target organ damage, including left ventricular hypertrophy, retinopathy, and renal injury. These women should receive an electrocardiogram (ECG) examination and echocardiography if the ECG is abnormal, ophthalmologic evaluation, and creatinine clearance.

Certain tests should be done selectively to identify secondary causes of hypertension such as pheochromocytoma, primary hyperaldosteronism, or renal artery stenosis. These conditions require selective biochemical testing and are amenable to diagnosis with either computed tomograpy or magnetic resonance imaging.[4,5] Pheochromocytoma should be suspected in women with paroxysmal severe hypertension, hyperglycemia, and sweating. Primary aldosteronism is extremely rare in pregnancy and should be considered in women with severe hypertension and marked hypokalemia. Based on this evaluation, the patient is then classified as having low- or high-risk chronic hypertension and managed accordingly (Figure 2).

Low-Risk Hypertension

Women with low-risk chronic hypertension without superimposed preeclampsia usually have a pregnancy outcome similar to that in the general obstetric population.[2,6,16] In addition, discontinuation of antihypertensive therapy early in pregnancy does not affect the rates of preeclampsia, abruptio placentae, or preterm delivery in these women.[2,16] My policy is to discontinue antihypertensive treatment at the first prenatal visit because the majority of these women will have good pregnancy outcome without such therapy.[2] Although these women do not require pharmacologic therapy, a careful management is still essential (Figure 2). At the time of initial and subsequent visits, the patient is educated about nutritional requirements, weight gain, and sodium intake (maximum of 2.4 g of sodium per day). She is also counseled that consumption of alcohol and smoking during pregnancy can aggravate maternal hypertension and are associated with adverse effects on the fetus such as fetal growth restriction and abruptio placentae. During each subsequent visit patients are observed very closely for early signs of preeclampsia and fetal growth restriction.

Fetal evaluation should include an ultrasound examination at 16–20 weeks' gestation, to be repeated at 30–32 weeks' gestation, and monthly thereafter until term. Antihypertensive medications with either nifedipine or labetalol are initiated if the patient develops severe hypertension before term. The development of severe hypertension, preeclampsia, or abnormal fetal growth requires immediate fetal testing with a nonstress

Table 2. Drugs Used to Treat Hypertension in Pregnancy

Drug	Starting dose	Maximum dose
Acute treatment of severe hypertension		
Hydralazine	5–10 mg IV every 20 min	30 mg*
Labetalol†	20–40 mg IV every 10–15 min	220 mg*
Nifedipine	10–20 mg orally every 30 min	50 mg*
Long-term treatment of hypertension		
Methyldopa	250 mg BID	4 g/d
Labetalol	100 mg BID	2400 mg/d
Nifedipine	10 mg BID	120 mg/d
Thiazide diuretic	12.5 mg BID	50 mg/d

IV = intravenous; BID = twice daily.

* If desired blood pressure levels are not achieved, switch to another drug.

† Avoid in women with asthma or congestive heart failure.

test or biophysical profile. Women who develop severe hypertension, those with documented fetal growth restriction by ultrasound examination, and those with superimposed preeclampsia at or beyond 37 weeks require hospitalization and delivery. In the absence of these complications, the pregnancy may be continued until 40 weeks' gestation.

High-Risk Hypertension

Women with high-risk chronic hypertension are at increased risk for adverse maternal and perinatal complications. The frequency and the maternal-fetal effects of these complications will depend on the etiology of the hypertension as well as the degree of target organ damage. Women with significant renal insufficiency (serum creatinine greater than 1.4 mg/dL), diabetes mellitus with vascular involvement (class R/F), severe collagen vascular disease, cardiomyopathy, or coarctation of the aorta should receive thorough counseling regarding the adverse effects of pregnancy before conception. These women should be advised that pregnancy may exacerbate their condition with the potential for congestive heart failure, acute renal failure requiring dialysis, and even death. In addition, perinatal loss and neonatal complications are markedly increased in these women. All such women should be managed by or in consultation with a subspecialist in maternal-fetal medicine, as well as in association with other medical specialists as needed. In addition, these women must be observed and have their deliveries at a tertiary care center with adequate maternal-neonatal care facilities.

My policy is to hospitalize women with high-risk hypertension at the time of the first prenatal visit for evaluation of cardiovascular and renal status and for regulation of antihypertensive medications, as well as other prescribed medications (insulin, cardiac drugs, thyroid drugs, etc) if needed. Women receiving atenolol, angiotensin-converting enzyme inhibitors, or angiotensin II receptor antagonists should have these medications discontinued under close observation. Antihypertensive therapy with one or more of the drugs listed in Table 2 is subsequently used in all women with systolic blood pressure of 180 mm Hg or more or diastolic blood pressure of 110 mm Hg or more. In women without target organ damage, the aim of antihypertensive therapy is to keep systolic blood pressure between 140 and 150 mm Hg and diastolic blood pressure between 90 and 100 mm Hg. In addition, antihypertensive therapy is indicated in women with mild hypertension plus target organ damage because there are short-term maternal benefits from lowering blood pressure in such women. In these women, I recommend keeping systolic blood pressure below 140 mm Hg and diastolic blood pressure below 90 mm Hg. In some women, blood pressure may be difficult to control initially, demanding the use of intravenous therapy with hydralazine or labetalol or oral short-acting nifedipine with doses as described in Table 2. For maintenance therapy, one may choose either oral methyldopa, labetalol, slow-release nifedipine, or a diuretic. Methyldopa is the drug most commonly recommended to treat hypertension during pregnancy.[4,5] However, it is rarely used in nonpregnant hypertensive women. Therefore, it is not practical to switch maternal medications to methyldopa because of their pregnancy. In addition, methyldopa is associated with dry mouth and drowsiness in many pregnant women. Other side effects include liver function abnormalities. My first drug of choice for control of hypertension in pregnancy is labetalol, starting at 100 mg twice daily and increasing to a maximum of 2400 mg per day. If maternal blood pressure is not controlled with maximum doses of labetalol, a second drug such as a thiazide diuretic or nifedipine may be added. For women with diabetes mellitus and vascular disease, my preference is oral nifedipine. Oral nifedipine or a thiazide diuretic is the drug of choice

for young black women with hypertension because these women often manifest a low-renin type or salt-sensitive hypertension.[13] If maternal blood pressure is adequately controlled with these medications, the patient can continue with the same drug after delivery.

Diuretics are commonly prescribed in women with essential hypertension before conception.[12,13] The use of diuretics throughout pregnancy is controversial. The primary concern relates to the fact that women who use diuretics from early in pregnancy do not have an increase in plasma volume to the degree usual in normal pregnancy.[14] However, this reduction in plasma volume was not shown to be associated with an adverse effect on fetal outcome.[14,30] Therefore, it is appropriate to start diuretics as a single agent during pregnancy or to use them in combination with other agents, particularly in women with excessive salt retention.[4] However, diuretics should be discontinued immediately if superimposed preeclampsia develops or if there is evidence of suspected fetal growth restriction because of the potential of reduced uteroplacental blood flow secondary to reduced plasma volume in women with such complications.[14]

Early and frequent prenatal visits are the key for successful pregnancy outcome in women with high-risk chronic hypertension. These women need close observation throughout pregnancy and may require serial evaluation of 24-hour urine protein excretion and a complete blood count with metabolic profile at least once every trimester. Further laboratory testing can be performed, depending on the clinical progress of the pregnancy. During each visit, the woman should be advised about the adverse effects of smoking and alcohol abuse, and should receive nutritional advice regarding diet and salt intake.

Fetal evaluation should include an ultrasound examination at 16–20 weeks' gestation, to be repeated at 28 weeks and subsequently every 3 weeks until delivery. A nonstress test or biophysical profile testing is usually started at 28 weeks and then repeated weekly. The development of uncontrolled severe hypertension, preeclampsia, or evidence of fetal growth restriction requires maternal hospitalization for more frequent evaluation of maternal and fetal well-being. The development of any of these complications at or beyond 34 weeks' gestation should be considered an indication for delivery. In all other women, consider delivery at 36 to 37 weeks' gestation after documenting fetal lung maturity.

Postpartum Management

Women with high-risk chronic hypertension are at risk for postpartum complications such as pulmonary edema, hypertensive encephalopathy, and renal failure.[10,11] These risks are particularly increased in women with a target organ involvement, superimposed preeclampsia, or abruptio placentae.[11] In these patients, blood pressure must be closely controlled for at least 48 hours after delivery. Intravenous labetalol or hydralazine can be used as needed, and diuretics may be appropriate in women with circulatory congestion and pulmonary edema.[10] This therapy is usually needed in those who develop exaggerated and sustained severe hypertension in the first week postpartum.

Oral therapy may be needed to control blood pressure after delivery. In some women, it is often necessary to switch to a new agent such as an angiotensin-converting enzyme inhibitor, particularly in those with pregestational diabetes mellitus and those with cardiomyopathy. Some patients may wish to breast-feed their infants. All antihypertensive drugs are found in the breast milk, although differences are found in the milk-plasma ratio of these drugs.[22] Additionally, the long-term effect of maternal antihypertensive drugs on breast-feeding infants has not been specifically studied. Milk concentrations of methyldopa appear to be low and are considered to be safe. The β-blocking agents (atenolol and metoprolol) are concentrated in breast milk, whereas labetalol or propanolol has a low concentration.[22,31] Concentrations of diuretic agents in breast milk are low; however, they may induce a decrease in milk production.[22]

There is little information about the transfer of calcium channel blockers to breast milk, but there are no apparent side effects. Angiotensin-converting enzyme inhibitors and angiotensin II receptor antagonists should be avoided because of their effects on neonatal renal function, even though their concentrations appear to be low in breast milk.

Finally, in breast-feeding women, the use of methyldopa as a first-line oral therapy is a reasonable choice. If methyldopa is contraindicated, labetalol may be used.

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