Hypertension and Pregnancy: Mechanisms and Management

1Mie Saiki, 2Vesna D Garovic

ABSTRACT

Hypertensive pregnancy disorders encompass a spectrum of conditions, including preeclampsia, a multisystem hypertensive disease that is unique to pregnancy, eclampsia, and gestational and chronic hypertension. Severe forms of preeclampsia, including its convulsive form – eclampsia – represent obstetrical emergencies, the therapy of which is immediate delivery. The goal of antihypertensive therapy in these patients is to prevent maternal cardiac, cerebrovascular, and renal complications. Central to the medical management of hypertension in pregnancy is the careful balance between maternal benefits from improved blood pressure control and fetal risks from intrauterine drug exposure and changes in uteroplacental perfusion. Women with chronic hypertension and hypertension onset before pregnancy should undergo prepregnancy counseling regarding medication safety during pregnancy and evaluation for end-organ damage, which will help define their blood pressure goals during pregnancy. Women with gestational hypertension (hypertension onset in the second half of pregnancy) require close monitoring for signs of progression to preeclampsia. Adequate care of these patients relies on regular follow-ups, judicious use of antihypertensive medications, and close monitoring for early signs of preeclampsia. While these patients are typically cared for by high-risk obstetricians, input from internists and related subspecialties increasingly is being recognized as important for optimization of patient blood pressure treatment and overall pregnancy outcomes.

Keywords: Blood pressure management, Hypertensive pregnancy disorders, Preeclampsia.

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HYPERTENSIVE DISORDERS OF PREGNANCY: CLASSIFICATION, PRESENTATION, AND MECHANISMS

Hypertensive pregnancy disorders affect 10% of pregnancies and include preeclampsia, eclampsia, and chronic and gestational hypertension (Table 1). In 2000, the Working Group of the National High Blood Pressure Education Program (NHBPEP) defined hypertension in pregnancy as a blood pressure ≥140 mm Hg systolic and/or ≥90 mm Hg diastolic on two occasions, at least 6 hours apart.1 For the diagnosis of preeclampsia, both hypertension and proteinuria (300 mg or greater in a 24-hour urine specimen, or 1+ dipstick) were required. The American College of Obstetricians and Gynecologists (the College) assembled a task force of specialists in the management of hypertension in pregnancy in 2013 to issue evidence-based recommendations for clinical practice.2 With respect to the diagnostic criteria for preeclampsia, the most notable changes made by the College related to the importance of proteinuria, which now is neither mandatory for the diagnosis of preeclampsia, nor is it considered a marker of preeclampsia severity. Based on these recommendations, the diagnosis of preeclampsia can be entertained in the absence of proteinuria on the basis of clinical and laboratory abnormalities in women

<table>
<thead>
<tr>
<th>Table 1: Hypertension in pregnancy: Classification and definitions</th>
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<tbody>
<tr>
<td><strong>Preeclampsia</strong></td>
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<tr>
<td><strong>Gestational hypertension</strong></td>
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<tr>
<td><strong>Chronic hypertension</strong></td>
</tr>
<tr>
<td><strong>Preeclampsia superimposed on chronic hypertension</strong></td>
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</tbody>
</table>

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with new-onset hypertension (Table 1). Common labora-
tory tests for the diagnosis of and differential diagnosis
among the hypertensive pregnancy disorders include
urinalysis, hemoglobin, hematocrit, platelet count, serum
uric acid, albumin, and kidney and liver function tests.

Preeclampsia, unlike the other hypertensive disorders
of pregnancy, is a systemic disease, commonly associated
with proteinuria. It occurs after 20 weeks of gestation and
affects approximately 5% of all pregnancies. Together with
its related conditions, namely eclampsia, its convulsive form,
and HELLP syndrome (an acronym for Hemolysis, Elevated
Liver enzymes, and Low Platelet count), preeclampsia
remains one of the leading causes of fetal and maternal mor-
bidity and mortality. Preeclampsia traditionally has been
considered a disease of first pregnancy. However, women
with a history of preeclampsia are at increased risk during
their subsequent pregnancies. Several other risk factors
are well recognized, which may aid in the early recogni-
tion of patients at risk (Table 2). Preeclampsia may develop
denovo in previously healthy pregnant women or occur in
women with preexisting conditions, such as renal disease
or chronic hypertension, i.e., superimposed preeclampsia.
Maternal complications occur as a consequence of hyper-
tensive end-organ damage of the central nervous system
(stroke), kidneys (acute renal failure), and heart (acute
cardiac decompensation). In a recent study examining all
maternal deaths after the 20th week of pregnancy, pre-
eclampsia and eclampsia were responsible for 790 of 4,024
deaths between 1979 and 1992. The overall preeclamp-
sia–eclampsia case-fatality rate was 6.4 cases per 10,000
cases at delivery. The burden is even higher in developing
countries. The etiology of this condition remains elusive;
thus, specific screening, preventive, and treatment strate-
gies are not available.

Pathophysiology of Preeclampsia

The role of maternal vascular adaptation and placental
angiogenesis in normal pregnancy has been well recog-
nized and studied. The fact that hypertension rapidly
resolves upon the removal of the products of conception
has led to several theories implicating structural and/
or functional changes in the developing placenta as
factors contributing to preeclampsia. The failure of the
placental spiral arteries to lose their musculoelastic layers,
ultimately leading to decreased placental perfusion, was
considered to be the central pathophysiological event in
preeclampsia for decades. Placental hypoxia ensues
following the decrease in placental perfusion, resulting
in placental production of vasoactive soluble factors,
which, when released into the maternal circulation, result
in endothelial dysfunction and clinical features of pre-
eclampsia. Over the last decade, preeclampsia has been
associated with elevated levels of the soluble receptor for
vascular endothelial growth factor (VEGF) of placental
origin. This soluble receptor, commonly referred to as
soluble fms-like tyrosine kinase receptor-1, may bind and
neutralize VEGF and limit the availability of free VEGF
for placental angiogenesis, thus representing the
missing link between placental ischemia and maternal
endothelial dysfunction. However, this mechanism may
not necessarily account to a similar extent for all cases of
preeclampsia, as many pathophysiological processes
that ultimately result in endothelial dysfunction may
contribute to its pathophysiology. Notably, an imbal-
ance between vasodilatory and vasoconstricting pros-
taglandins, favoring the latter, may be a contributing
factor, as well as the presence of agonistic antibodies
to angiotensin II, reduced heme oxygenase-1 levels, nitric
oxide dysfunction, and upregulation of several
vasoactive mediators, including cellular fibronectin, von
Willebrand factor, cell adhesion molecules, and
cytokines.

Preeclampsia is a Heterogeneous Disease

It has been increasingly recognized that preeclampsia is
a heterogeneous disease, with the different clinical sub-
types possibly reflecting distinct underlying pathological
mechanisms. It is common in clinical practice, e.g., to
subcategorize preeclampsia as early versus late onset
(before and after 34 weeks of gestation respectively),
with early preeclampsia commonly presenting with
severe features, including thrombocytopenia, impaired
liver function tests, the new development of renal insuf-
siciency, pulmonary edema, or new-onset cerebral or
visual disturbances.

Recent evidence suggests that women with early,
severe preeclampsia may have a more pronounced anti-
angiogenic imbalance and less favorable outcome than
those with late preeclampsia. Early preeclampsia can
also further be viewed as placental preeclampsia, as
it is commonly associated with poor placentation,
the pathological substrate for fetal growth restriction.
In contrast, late preeclampsia is not associated with

Table 2: Risk factors for preeclampsia

<table>
<thead>
<tr>
<th>Risk Factor</th>
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<tbody>
<tr>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Renal disease</td>
</tr>
<tr>
<td>History of preeclampsia with previous pregnancies</td>
</tr>
<tr>
<td>Extremes of maternal age</td>
</tr>
<tr>
<td>Nulliparity</td>
</tr>
<tr>
<td>Multiple gestations</td>
</tr>
<tr>
<td>Family history of preeclampsia</td>
</tr>
<tr>
<td>Chronic hypertension (either essential or secondary)</td>
</tr>
<tr>
<td>Thrombophilias</td>
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<tr>
<td>Trophoblastic disease (i.e., hydatidiform mole)</td>
</tr>
<tr>
<td>Autoimmune and connective tissue diseases</td>
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</tbody>
</table>
abnormal placentation and the associated decreased perfusion. This late form occurs in women with vascular dysfunction that is present prior to pregnancy (commonly due to hypertension, diabetes, or obesity), in whom pregnancy acts as a physiological stress that exacerbates preexisting vascular inflammation and endothelial dysfunction (i.e., maternal preeclampsia).

The dichotomous view of preeclampsia (e.g., early, severe, placental versus late, mild, maternal) is likely overly simplistic, and it is more likely that there is an overlap between maternal preexisting systemic inflammation (such as that which is present in obesity) and impaired angiogenesis. Further understanding of the relative contributions of inflammation, antiangiogenesis, or other mechanisms to the different subtypes of preeclampsia may be the first step toward developing targeted therapies. Of note, several therapeutic/preventive strategies have been studied in preeclampsia. None has been applicable to all patients, likely due to the failure to identify the preeclampsia subtype and to provide targeted treatments.23,25

Over the last five decades, much progress has been made in improving blood pressure control in preeclampsia and in the prevention of eclamptic seizures (see Management). Delivery, however, remains the mainstay of therapy for severe forms and anticipated life-threatening complications. As the severe forms of preeclampsia tend to develop early in pregnancy, labor induction, commonly for maternal indications, usually results in a preterm delivery, with low birth weight and related neonatal complications.

Chronic hypertension in pregnant women is diagnosed based on the presence of hypertension before the 20th week of gestation.1 The diagnosis may be difficult in young women with little or no medical history. Physiologic changes during pregnancy lead to a fall in blood pressure during the first and second trimesters. In a woman with undiagnosed hypertension prior to pregnancy, this may lead to normal readings early in pregnancy. During the third trimester, the return to prepregnancy hypertensive values may lead to the false diagnosis of new-onset hypertension.

The epidemiology of chronic hypertension in pregnancy has changed significantly over the last couple of decades. This is predominantly due to a trend toward advanced age at first pregnancy, further confounded by the sophisticated techniques of assisted reproduction, such as in vitro fertilization (IVF), that have made pregnancy possible for women with infertility conditions that are associated with cardiovascular disease (CVD) risk factors (such as polycystic ovary syndrome). The care of these patients imposes two major challenges. First, the classical approach that suggests that pregnant women with chronic hypertension are at low risk for cardiovascular complications within the short duration of pregnancy and, therefore, do not require blood pressure treatment may be suboptimal for this particular group. These women, furthermore, may be at even a greater risk for superimposed preeclampsia, due to preexisting comorbidities (such as diabetes, renal disease, and hypertension). In addition, several studies have reported an increased risk of preeclampsia in pregnancies conceived by IVF.26

Up to 30% of pregnancies in women with chronic hypertension may be affected. In women with chronic hypertension, but no proteinuria at baseline, preeclampsia is heralded by the development of proteinuria after 20 weeks of gestation. Some women may have proteinuria at baseline, and this can significantly complicate the diagnosis. In general, the development of severe hypertension (≥160 mm Hg systolic and/or ≥110 mm Hg diastolic) or any of the signs or symptoms of severe preeclampsia (Table 3) signify the development of superimposed preeclampsia; these women are at a particularly high risk for cerebral hemorrhage and placental abruption.

Gestational hypertension is characterized by new-onset hypertension after the 20th week of gestation, in the absence of proteinuria.1 Women who develop gestational hypertension after 30 weeks gestation have a 10% risk of progressing to preeclampsia; this risk increases to 30% in women who present before 30 weeks gestation. Women who do not develop proteinuria are diagnosed with either transient hypertension (normalization of blood pressure by 12 weeks postpartum) or chronic hypertension (elevated blood pressure and need for blood pressure treatments that persist after pregnancy and delivery).

During the first five postpartum days, blood pressure in normotensive women tends to be higher compared with

### Table 3: Diagnostic criteria for severe preeclampsia

<table>
<thead>
<tr>
<th>Any of these findings:</th>
<th></th>
</tr>
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<tbody>
<tr>
<td>Severe hypertension</td>
<td>Blood pressure ≥160 systolic or ≥110 diastolic on two occasions, 4 hours apart</td>
</tr>
<tr>
<td>Renal impairment</td>
<td>Serum creatinine &gt;1.1 mg/dL or its doubling in the absence of other renal disease</td>
</tr>
<tr>
<td>Hepatic involvement*</td>
<td>Elevated liver function tests (twice upper limit of normal)</td>
</tr>
<tr>
<td></td>
<td>Right upper quadrant pain (unresponsive to medications, or not related to other causes, or both)</td>
</tr>
<tr>
<td>Thrombocytopenia*</td>
<td>Platelet count &lt;100 × 10⁹/L</td>
</tr>
<tr>
<td>Neurological signs and symptoms**</td>
<td>New onset of cerebral or visual disturbances</td>
</tr>
<tr>
<td>Cardiovascular compromise</td>
<td>Pulmonary edema</td>
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</tbody>
</table>

*Presence of these findings should prompt consideration of HELLP syndrome

**May represent impending eclampsia
their pregnancy values, likely due to fluid shifts from the interstitial space and the resultant transient rise in the intravascular volume. While hypertension in most of these women resolves by 2 to 4 weeks postpartum, some of these women may remain hypertensive and require antihypertensive treatment. A subset of these patients may progress to pre eclampsia/eclampsia that, due to the onset of hypertension after delivery (i.e., postpartum pre eclampsia), may represent a diagnostic challenge leading to delayed treatment. An increasing awareness of this clinical entity led to a new set of recommendations by the College advising close blood pressure monitoring in the hospital and outpatient surveillance up to 10 days postpartum of women with gestational hypertension. In addition, all women should receive discharge instructions regarding signs and symptoms of preeclampsia and the need to see their health care providers immediately should signs/symptoms develop. Treatment of postpartum preeclampsia relies on blood pressure control and magnesium sulfate administration for prevention of seizures.

At the mechanistic level, postpartum preeclampsia is particularly interesting as it occurs in the absence of the placenta, thus challenging one of the widely accepted concepts in the pathogenesis of preeclampsia: The role of the placenta as the major culprit. Postpartum preeclampsia likely represents a clinical subtype with a distinct underlying mechanism; its clinical presentation further supports the evolving concept of preeclampsia being a heterogeneous disease rather than a single clinical entity.

The HELLP syndrome is believed to be a deceptive form of preeclampsia, which presents with the distinctive and ominous triad of microangiopathic hemolytic anemia, hepatocellular injury, and consumption of platelets. Right upper quadrant and epigastric pain may occur as a consequence of a hepatic hematoma and resultant stretching of Glisson's capsule. It may herald hepatic rupture, which is associated with high maternal and fetal mortality rates. Urgent delivery remains the mainstay of treatment for patients with HELLP syndrome. Retrospective analyses of HELLP syndrome patients, in whom urgent delivery was not undertaken, have documented an extremely high perinatal infant mortality of 70%. In an extremely high perinatal infant mortality of 70%.

Eclampsia refers to the development of seizures in a woman with preeclampsia or gestational hypertension. While the classic presentation is the development of seizures in a woman with severe preeclampsia, up to 20% of cases occur in women with no evidence of proteinuria, and many cases occur in patients with mild hypertension. The mainstay of treatment is intravenous magnesium sulfate, which has been shown to be more effective than either phenytoin or diazepam for seizure prophylaxis in women with severe preeclampsia and for prevention of recurrent seizures in those with eclampsia.

**MANAGEMENT OF HYPERTENSIVE PREGNANCY DISORDERS**

The goal for the treatment of hypertensive pregnancy disorders is to prevent maternal complications without compromising fetal well-being and safety. The factors that affect management decisions are maternal, including the duration and severity of hypertension and the presence of end-organ damage, as well as fetal, such as safety of blood pressure medications and the potential for uteroplacental and fetal circulation compromise due to overzealous blood pressure control. The following discussion will address preventive strategies, preconception counseling, blood pressure treatment goals and options, and timing of delivery.

**Preeclampsia Prevention**

Several different strategies have been evaluated for the prevention of preeclampsia, including a low-salt diet, diuretics, low-dose aspirin, antioxidants, and calcium and magnesium supplements. With the exception of calcium supplementation for calcium-deficient women, and low-dose aspirin for women at high risk (i.e., those with a history of chronic hypertension and preeclampsia in a previous pregnancy), these approaches have failed to provide reproducible benefits.

**Preconception Counseling**

Women with a history of hypertension should be evaluated before pregnancy for target organ damage, such as left ventricular hypertrophy, hypertensive nephropathy, and retinopathy, which will help establish blood pressure treatment goals. Patients with clinical clues suggestive of secondary hypertension (e.g., hard-to-control hypertension requiring more than three antihypertensive agents and/or indicative laboratory and clinical findings) should undergo a workup for secondary hypertension (primary hyperaldosteronism, pheochromocytoma, and renal artery stenosis). Therefore, preconception counseling of women with chronic hypertension may require expertise outside the realm of obstetrics. Some forms of secondary hypertension, particularly pheochromocytoma and renovascular hypertension, may further increase the risk for adverse pregnancy outcomes beyond that of essential hypertension; thus, surgery (for pheochromocytoma) or revascularization (for renal artery stenosis) should be considered before pregnancy. In this population of young women of childbearing age, these interventions may result in cure of hypertension. The preconception evaluation should also address changes in medications to those that have acceptable safety profiles in pregnancy and include counseling related to pregnancy risks. It is estimated that as many as 25% of women with chronic
hypertension may develop superimposed preeclampsia. These women are at a particularly high risk for cerebral hemorrhage and placental abruption. It remains unclear whether early treatment of chronic hypertension in pregnancy prevents preeclampsia. In the absence of randomized prospective trials adequately powered to address this important clinical question, practicing physicians should treat chronically hypertensive women according to currently accepted national guidelines, which are presented and discussed below.

**Blood Pressure Treatment Goals and Options**

It is useful to divide hypertensive pregnancy disorders into two general categories for purposes of optimizing hypertension evaluation and treatment. The first includes the acute hypertensive syndromes of preeclampsia/eclampsia/HELLP syndrome, which carry a high-risk for maternal and fetal morbidity and mortality. The most important reason for the initiation of antihypertensive treatment in these patients is to prevent maternal cerebrovascular and cardiac complications. While hypertension in these settings can be treated medically, the definitive treatment remains delivery. The second general category is chronic hypertension. Ideally, these women should be evaluated before pregnancy, which will help establish blood pressure treatment goals (see Preconception Counseling). The treatment of gestational hypertension depends upon whether proteinuria subsequently develops. In the absence of proteinuria, blood pressure either returns to normal by 12 weeks postpartum (transient hypertension) or fails to normalize, leading to the diagnosis of chronic hypertension. Women with gestational hypertension who subsequently develop proteinuria are then considered to have developed preeclampsia and are treated accordingly.

**Hypertension in Preeclamptic Patients**

The most important reason to initiate antihypertensive treatment in these patients is to prevent maternal cerebrovascular and cardiac complications. While hypertension in these settings can be treated medically, the definitive treatment remains delivery.

The most recent College guidelines suggest medical therapy for severe hypertension (sustained systolic blood pressures of at least 160 mm Hg and/or sustained diastolic blood pressures of at least 110 mm Hg) in order to decrease the incidence of maternal cardiac and cerebral events. The medications most commonly used for urgent control of hypertension include intravenous hydralazine and labetalol. Medications that may be used, along with their safety profiles and dosing schedules, are summarized in Tables 4 and 5, respectively. Control of blood pressure does not cure preeclampsia or prevent its progression: Eclamptic seizures can occur when the blood pressure is only mildly elevated. Therefore, in addition to antihypertensive therapy, preeclamptic patients should receive seizure prophylaxis with intravenous magnesium sulfate, which should be continued during labor and delivery, and for at least 24 hours after delivery. As magnesium is renally excreted, the rate of continuous

<table>
<thead>
<tr>
<th>Table 4: Classes and specific medications useful for hypertension in pregnancy</th>
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<tr>
<td><strong>Benefits</strong></td>
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<tr>
<td><strong>Central agents</strong></td>
</tr>
<tr>
<td><strong>Alternative</strong> Clonidine Efficacy similar to methyldopa Unproven safety</td>
</tr>
<tr>
<td><strong>Beta blockers</strong></td>
</tr>
<tr>
<td><strong>Contraindicated</strong> Atenolol None compared with labetalol Intrauterine growth restriction</td>
</tr>
<tr>
<td><strong>Calcium channel blockers</strong></td>
</tr>
<tr>
<td><strong>Alternative</strong> Verapamil Similar efficacy to other oral agents Untested safety profile, risk of interaction with magnesium</td>
</tr>
<tr>
<td><strong>Direct vasodilators</strong></td>
</tr>
<tr>
<td><strong>Alternative</strong> Nitroprusside Effective in severe hypertension Cyanide and thiocyanate toxicity</td>
</tr>
<tr>
<td><strong>Diuretics</strong></td>
</tr>
<tr>
<td><strong>Contraindicated</strong> Spironolactone None Possible fetal antiandrogen effects</td>
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</table>

HTN: Hypertension; HF: Heart failure

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infusion, but not the loading dose, should be adjusted, i.e., decreased in women with renal failure. Serum magnesium levels should also be checked more frequently (every 1–2 hours) in these women, compared with women with normal renal function (every 4–6 hours). For women with severe preeclampsia at ≤34 gestational weeks, corticosteroids should be administered to accelerate fetal lung development. Delivery can be deferred for 48 hours for stable patients and in the absence of fetal compromise.

**Chronic Hypertension in Pregnancy**

Medications prescribed before pregnancy in women with chronic hypertension can be continued during pregnancy (Tables 4 and 5), except angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, renin inhibitors, atenolol, and spironolactone. According to the College recommendations, for pregnant patients with chronic hypertension, antihypertensive therapy is recommended for a systolic pressure ≥160 mm Hg and/or diastolic blood pressure ≥105 mm Hg. It is suggested that blood pressure levels be maintained between 120/80 and 160/105 mm Hg.

Thresholds for blood pressure treatment are higher for pregnant than for nonpregnant patients due to a lack of studies to support the benefit of treatment for mild diastolic hypertension (90–99 mm Hg) and concerns for fetal safety, as treatment-induced blood pressure drops were shown to be associated with impaired fetal growth in a meta-analysis of published studies. It is important to notice that the threshold which was set for the initiation of antihypertensive therapy does not reflect common clinical practice, as antihypertensive therapy is usually instituted for a systolic pressure ≥150 mm Hg and/or diastolic blood pressure ≥100 mm Hg. Another exception is made in women with evidence of end-organ damage: In the presence of renal disease, proteinuria, left ventricular hypertrophy, and retinopathy, antihypertensive therapy is commonly initiated for a diastolic blood pressure ≥90 mm Hg. Recent evidence argues that this approach may be beneficial for the mother without having detrimental fetal effects. A study that compared less tight control of hypertension (target diastolic blood pressure of 100 mm Hg) vs tight control (85 mm Hg), among pregnant women with either gestational or chronic hypertension, showed that tight control of hypertension in pregnancy conferred no apparent benefit to the fetus, but also did not pose a risk to the fetus or newborn. Tight control showed moderate benefit in preventing progression to severe hypertension in the mother. This finding is supported further by a meta-analysis that included 49 trials (with 4,723 patients), which showed that antihypertensive therapy for mild-to-moderate hypertension in pregnancy reduced the risk (by half) of developing severe hypertension.

**Timing of Delivery**

Hypertensive pregnant patients are typically cared for by high-risk obstetricians, and the decision to proceed with delivery is made only after a careful assessment of risks to the fetus and mother. Input provided by internists and related subspecialties increasingly is being recognized as important for the optimization of patient blood pressure treatment and pregnancy outcomes.

Consideration commonly is given to postponing delivery in pregnancies affected by preeclampsia before 34 weeks of gestation, as the fetus is still immature and may suffer profound consequences due to incomplete respiratory development. This approach is only reasonable in cases in which the maternal risk is relatively low. Induction of labor should be entertained in circumstances of adequate fetal development or progression to severe forms of hypertensive disease, irrespective of fetal maturity. The indications for urgent delivery include uncontrollable severe hypertension, eclampsia, pulmonary edema, placental abruption, and fetal distress.

**HYPERTENSIVE PREGNANCY DISORDERS AND FUTURE CARDIOVASCULAR HEALTH**

The cardiovascular complications of hypertensive pregnancy disorders traditionally were believed to be confined to pregnancy. In recent years, however, epidemiological studies consistently have demonstrated an association between an increased risk for CVD in adulthood and low birth weight, which, in children born to preeclamptic mothers, may occur as a consequence of either prematurity or intrauterine growth restriction.

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<table>
<thead>
<tr>
<th>Indication</th>
<th>Specific drug</th>
<th>Dose</th>
</tr>
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<tbody>
<tr>
<td>Urgent blood pressure control</td>
<td>Labetalol</td>
<td>20 to 80 mg IV every 10 min, maximum of 220 mg</td>
</tr>
<tr>
<td></td>
<td>Hydralazine</td>
<td>5 to 10 mg IV or IM every 20 min, no success by 30 mg total, consider alternatives</td>
</tr>
<tr>
<td>Chronic blood pressure control</td>
<td>Methyldopa</td>
<td>Initial 250 mg oral TID, max 3,000 mg daily</td>
</tr>
<tr>
<td></td>
<td>Labetalol</td>
<td>100 mg oral BID, titrate to 600 mg BID</td>
</tr>
<tr>
<td></td>
<td>Hydralazine</td>
<td>Initiate 10 mg QID, titrate to 50 mg QID, maximum of 300 mg</td>
</tr>
<tr>
<td></td>
<td>Hydrochlorothiazide</td>
<td>12.5 to 25 mg orally daily</td>
</tr>
<tr>
<td></td>
<td>Nifedipine ER</td>
<td>Initial 30 to 60 mg oral daily, max 120 mg daily</td>
</tr>
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IV: Intravenous; IM: Intramuscular; TID: Thrice a day; BID: Twice a day; QID: Four Times a day
In addition, women with a history of hypertensive compared with normotensive pregnancies are at increased risk for the development of hypertension, ischemic heart disease, or stroke later in life. The highest risk was reported for women with severe forms of preeclampsia who delivered prematurely. The likely mechanism for this association is that these two conditions share several common risk factors, such as renal disease and diabetes mellitus, which may lead to hypertensive pregnancy disorders and CVD at different times in a woman’s life. Thus, a history of hypertensive pregnancy disorders may aid in identifying women at risk for future CVD. Primary prevention in these women should focus on lifestyle modifications (exercise, weight loss, and smoking cessation), early detection of CVD risk factors, and treatment according to evidence-based national guidelines.

CONCLUSION

Hypertensive pregnancy disorders remain a major therapeutic challenge. Their etiologies and underlying pathophysiologies remain poorly understood, thus not allowing for targeted therapeutic approaches. Emerging evidence argues against several postulates that are commonly used to justify different approaches to treatment of hypertension in pregnancy compared with hypertension in the general population. First, the prevailing view that hypertensive pregnant women are at low risk for cardiovascular complications within the short duration of pregnancy may not apply to women with advanced age at first pregnancy (a trend increasingly described in many countries) and/or those who underwent fertility treatments for the conditions that are associated with increased CVD risks. Second, despite the lack of studies to indicate that treatment for mild hypertension is beneficial for the fetus, recent data suggest that it prevents progression to severe hypertension in the mother, without posing a risk to the newborn. This recent evidence sets the stage for future studies that should be powered adequately to explore the effects of tight blood pressure control in subgroups of women with preexisting CVD risks, including those with advanced age at pregnancy. In addition, as hypertensive pregnancy disorders have been associated with future CVD, it is plausible that better blood pressure control during pregnancy may improve future cardiovascular outcomes. Additional studies in this developing field are needed that may lead to improvements in both pregnancy and long-term outcomes.

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