DECISIONS

Hypertension in a woman planning pregnancy

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A 30-year-old woman who has never been pregnant and has chronic hypertension presents for preconception counselling. She received her diagnosis of hypertension at 25 years of age, and an evaluation at that time failed to show an underlying cause. The patient is otherwise healthy. Her blood pressure has been well controlled with lisinopril (40 mg/d) and hydrochlorothiazide (25 mg/d), and there is no evidence of target-organ damage. The patient does not smoke, consume alcohol or use illicit drugs.

Is this patient at increased risk of complications during pregnancy?

Chronic hypertension during pregnancy has been associated with a number of adverse pregnancy outcomes, including premature delivery, fetal growth restriction, fetal death, placental abruption and cesarean delivery.[1] The incidence of these complications appears to be related to the duration and severity of the hypertension and the presence of superimposed preeclampsia.[1]

The consensus definition of chronic hypertension during pregnancy is use of antihypertensive medications before pregnancy, onset of hypertension before the 20th week of pregnancy or hypertension that persists for more than 12 weeks after delivery.[1]

Women with mild hypertension (systolic pressure 140–159 mm Hg or diastolic pressure 90–109 mm Hg) should be counselled that their risk of preeclampsia is about 20%; the risk for women with severe hypertension (systolic pressure > 160 or diastolic pressure > 110 mm Hg) is about 50%, and the risk for women with target-organ damage or secondary hypertension is as high as 75%.[2,3]

What investigations should be done?

As a baseline, women with hypertension considering pregnancy should undergo laboratory investigations including a complete blood count, serum creatinine level and hepatic transaminase levels, as well as 24-hour urine collection to test protein and creatinine clearance.[1] In pregnant women, spot urine protein–creatinine ratio has a sensitivity of 82% to detect protein levels higher than 300 mg over 24 hours, and a sensitivity of 89% for levels higher than 2000 mg over 24 h; this lack of sensitivity could lead to an inappropriate and avoidable delay in diagnosis.[4] Normal protein excretion during pregnancy is less than 300 mg over 24 hours.[4]

Additional testing might include an electrocardiogram to detect left ventricular hypertrophy. If hypertrophy is detected, obtaining an echocardiogram should be considered. In patients with poorly controlled disease or known heart or kidney disease, other evaluations for target-organ damage, such as hypertensive retinopathy, could be considered before conception.[1]

What are the goals of treatment for this patient?

Because there is no evidence that maternal blood pressure control can decrease the risk of preeclampsia, the purpose of treatment is to decrease the short-term risks of severely elevated blood pressure, especially in cases of superimposed preeclampsia. Consensus guidelines suggest maintaining systolic pressure under 150 mm Hg and diastolic pressure under 100 mm Hg, regardless of the presence of target-organ damage.[1]

Will this patient require medication throughout her pregnancy?

Although blood volume increases during the first 2 trimesters of pregnancy, the corresponding decrease in systemic vascular resistance leads to a 10–20 mm Hg reduction in blood pressure. Blood pressure reaches a nadir at 18–20 weeks of gestation and returns to prepregnancy levels by the third trimester.[1] Thus, antihypertensive medication dosages can be reduced or stopped altogether during the first and second trimesters, but dosages may need to increase or be resumed during the third trimester.

The need for medications is variable and will be determined by the patient's baseline blood pressure and the size of the reduction in pressure.

What medications should be prescribed?

Based on retrospective data, tolerability and data regarding in utero exposure, labetalol (combined

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α- and β-adrenergic blocking agents) and methyldopa (an α-adrenergic agonist) are first-line medications.[1] Labetalol is preferred because it is less likely than methyldopa to cause fatigue, and because methyldopa can cause drug-induced lupus erythematosus.[1] Long-acting formulations of nifedipine (a calcium channel blocker) can be used as an additional second-line agent if blood pressure is not adequately controlled by labetalol or methyldopa. Propanolol has been associated with premature labour, and atenolol has been associated with intrauterine growth restriction; thus, these drugs are best avoided. Thiazide diuretic agents can be continued as long as volume depletion is avoided.[1] Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers should not be used during pregnancy, because they are associated with serious fetal anomalies such as renal dysgenesis and malformations of the cardiovascular and central nervous systems.[1,5]

Randomized controlled trials examining the benefit of low-dose acetylsalicylic acid (ASA, 81 mg/d) to prevent preeclampsia have shown conflicting results: one study found no benefit, whereas another found a benefit that was accompanied by an increased risk of placental abruption.[6,7] A meta-analysis concluded that starting ASA therapy before 16 weeks' gestation, but not after, may offer a benefit, but the number needed to treat is large.[8] Consensus statement recommendations to offer ASA therapy to some women before 16 weeks' gestation are driven by the results of this meta-analysis.[9]

What follow-up should be arranged?

Once the patient conceives, blood pressure should be assessed about every 4 weeks, because adjustments to the medication dose may be needed. Laboratory investigations and 24-hour urine collection should be repeated during the pregnancy if the patient shows symptoms or signs of preeclampsia, if fetal growth restriction is seen on ultrasonography or to help differentiate a physiologic increase in blood pressure from superimposed preeclampsia.[1] The patient should be counselled to seek care urgently if she has any symptoms of preeclampsia: new and persistent changes in vision, headaches, swelling of the face or hands, upper abdominal pain or hyperreflexia (as evidenced by the presence of clonus).

There is currently no consensus regarding a defined protocol for fetal monitoring. However, consensus guidelines and reviews of the topic recommend obtaining baseline ultrasonography early in the first trimester to confirm gestational age, and again at 18–20 weeks for an anatomic survey with Doppler evaluation of uterine arteries if there is a high potential for superimposed preeclampsia or intrauterine growth restriction.[1,10,11] If growth restriction is suggested or present, the physician might consider serial sonographic assessments in addition to twice-weekly nonstress testing or biophysical profile.[1,10,11]

The case revisited

At the initial consultation, the patient's medication was switched to labetalol (200 mg, twice daily), which she tolerated well. The patient conceived about 1 month later, and her dose of labetalol was lowered to 100 mg twice daily shortly thereafter. The dose was increased to 200 mg twice daily early in the third trimester because her blood pressure had started to increase. The patient received regular fetal monitoring and proceeded to have an uneventful pregnancy. She delivered a healthy infant vaginally at term. Her blood pressure remained stable during the postpartum period, and she returned to her prepregnancy antihypertensive regimen within a week of her discharge from hospital.

References

1. American College of Obstetricians & Gynecologists. ACOG practice bulletin no. 125: chronic hypertension in pregnancy. *Obstet Gynecol* 2012;119:396-407.
2. Chappell LC, Enye S, Seed P, et al. Adverse perinatal outcomes and risk factors for preeclampsia in women with chronic hypertension: a prospective study. *Hypertension* 2008;51:1002-9.
3. Vigil-De Gracia P, Lasso M, Montufar-Rueda C. Perinatal outcome in women with severe chronic hypertension during the second half of pregnancy. *Int J Gynaecol Obstet* 2004;85:139-44.
4. Gao YF, Huang QT, Zhong M, et al. Diagnostic value of random spot albuminuria to creatinine ratio in women with preeclampsia. [article in Chinese]. *Zhonghua Fu Chan Ke Za Zhi* 2012;47:166-70.
5. Cooper WO, Hernandez-Diaz S, Arbogast PG, et al. Major congenital malformations after first-trimester exposure to ACE inhibitors. *N Engl J Med* 2006;354:2443-51.
6. Sibai BM, Caritis SN, Thom E, et al. Prevention of preeclampsia with low-dose aspirin in healthy, nulliparous pregnant women. The National Institute of Child Health and Human Development Network of Maternal–Fetal Medicine Units. *N Engl J Med* 1993; 329:1213-8.
7. Caritis S, Sibai B, Hauth J, et al. Low-dose aspirin to prevent preeclampsia in women at high risk. National Institute of Child Health and Human Development Network of Maternal–Fetal Medicine Units. *N Engl J Med* 1998;338:701-5.
8. Bujold E, Roberge S, Lacasse Y, et al. Prevention of preeclampsia and intrauterine growth restriction with aspirin started in early pregnancy: a meta-analysis. *Obstet Gynecol* 2010;116:402-14.
9. Lindheimer MD, Taler SJ, Cunningham FG, et al.; American Society of Hypertension. ASH position paper: hypertension in pregnancy. *J Clin Hypertens* 2009;11:214-25.
10. Freeman RK. Antepartum testing in patients with hypertensive disorders in pregnancy. *Semin Perinatol* 2008;32:271-3.
11. Sibai BM. Chronic hypertension in pregnancy. *Obstet Gynecol* 2002;100:369-77.

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