Hypertensive disorders in pregnancy

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Hypertensive disorders of pregnancy occur in approximately 10% of pregnant women and preeclampsia in approximately 3% of pregnancies in the United States (1). The American College of Obstetricians and Gynecologists Task Force on Hypertension in Pregnancy defined chronic hypertension as a systolic blood pressure of 140 mmHg or more or a diastolic blood pressure of 90 mmHg or more on two separate occasions at least 2 h apart occurring before pregnancy or developing less than 20 weeks during pregnancy (2). Mild hypertension is a systolic blood pressure of 140–149 mmHg or a diastolic blood pressure of 90–99 mmHg (3). Moderate hypertension during pregnancy is a systolic blood pressure of 150–159 mmHg or a diastolic blood pressure of 100–109 mmHg (3). Severe hypertension during pregnancy is a systolic blood pressure of 160 mmHg or higher or a diastolic blood pressure of 110 mmHg or higher (3). Gestational hypertension occurs after 20 weeks during pregnancy (2). Preeclampsia is diagnosed if the woman has hypertension after 20 weeks of pregnancy with proteinuria greater than 300 mg in a 24-hour urine collection or a urinary protein/creatinine ratio ≥0.3 (2). Severe features of preeclampsia include thrombocytopenia, renal insufficiency, impaired liver function, pulmonary edema, and cerebral or visual symptoms (2). Modifiable risk factors for hypertensive disorders in pregnancy include increased body mass index, anemia, increased dietary sodium, and decreased dietary potassium intake (4,5).

A study of 12,055 Finnish women demonstrated that gestational hypertension was associated at a mean follow-up of 39.4 years with a 44% increase in ischemic heart disease, a 75% increase in myocardial infarction, a 3 times increase in death from myocardial infarction, a 78% increase in heart failure, a 59% increase in ischemic stroke, and a 91% increase in kidney disease (6). A study of Danish women showed that the risk of subsequent hypertension was increased 5.31 times after gestational hypertension, 3.61 times after mild preeclampsia, and 6.07 times after severe preeclampsia (7). This study showed that the risk of subsequent type 2 diabetes mellitus was increased 3.12 times after gestational hypertension and 3.68 times after severe preeclampsia. The risk of ischemic heart disease was increased 1.48 times after gestational hypertension, 1.57 times after mild preeclampsia, and 1.61 times after severe preeclampsia (7). The risk of stroke was also increased 1.51 times after gestational hypertension, 1.43 times after mild preeclampsia, and 1.58 times after severe preeclampsia (7).

A meta-analysis of 3,488,160 women included 198,252 women with preeclampsia (8). Women with preeclampsia had a 3.70 times increased risk of hypertension after 14.1 years, a 2.16 times increased risk of ischemic heart disease after 11.7 years, and a 1.81 times increased risk of stroke after 10.4 years (8). A Scottish cohort study showed that the risk of stroke was increased 2.42 times by gestational hypertension and 3.39 times by preeclampsia/eclampsia (9).

A Danish study showed that the risk of subsequent cardiomyopathy was increased 2.06 times by gestational hypertension, 1.89 times by moderate preeclampsia, and 2.20 times by severe preeclampsia (10). A Canadian study showed that the risk of subsequent heart failure or atrial or ventricular arrhythmias at a mean duration of 7.8 years was increased 2 times by a hypertensive disorder of pregnancy (11). Preeclampsia also increased the risk of stage B heart failure 4.3 times (12).

A meta-analysis of seven studies showed at 7.1 years postpartum that women with preeclampsia had a 4.31 times

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increased risk of microalbuminuria (13). A Taiwanese study showed that women with hypertensive disorders during pregnancy had a 9.38 times increased risk of chronic kidney disease and a 12.4 times increased risk of end-stage renal disease (14). A Scottish record linkage study showed that the subsequent risk of chronic kidney disease was increased 1.36 times by gestational hypertension and 1.93 times by preeclampsia (15).

There are three Cochrane database reviews of treatment of mild to moderate hypertension during pregnancy (16-18). One study showed that oral beta blockers reduced the risk of severe hypertension by 63% and the need for additional antihypertensive drugs by 56% (16). There were insufficient data to show the effect of beta blockers on perinatal mortality or preterm birth (16). Another study of two small trials showed insufficient evidence to determine whether reduction of the blood pressure to less than 130/80 mmHg was better than reduction of the blood pressure to less than 140/90 mmHg to improve maternal and fetal-neonatal outcomes (17). A third study showed that antihypertensive drug treatment reduced the risk of severe hypertension by 51% (18). Compared with methyldopa, beta blockers and calcium channel blockers reduced the risk of developing proteinuria/preeclampsia by 27% (18).

A randomized study of 987 women with non-proteinuric preexisting or gestational hypertension randomized to a diastolic blood pressure below 85 mmHg or to less than 100 mmHg showed that severe hypertension developed in 40.6% of women with less tight control versus 27.5% of women with tighter control (19). A prospective observational study of 222 women with mild to moderate hypertension demonstrated that cessation of antihypertensive drug therapy increased maternal and fetal morbidity (20). Forty-six studies showed that mild chronic hypertension during pregnancy increased the risk for perinatal mortality 3.4 times and increased the risk for placental abruption 2.1 times (21). This review emphasized that use of angiotensin-converting enzyme (ACE) inhibitors during the second or third trimester increases renal failure and use of atenolol early in pregnancy restricts fetal growth (21). In addition to use of ACE inhibitors or angiotensin receptor blockers (ARBs) causing fetal renal damage in pregnancy, these drugs cause lower birth weight and gestational age and increase the risk for miscarriage (22). ARBs also cause a high prevalence rate of oligohydramnios (23). Direct renin inhibitors should also not be administered (2).

The European Society of Cardiology (ESC) guidelines recommend treating mild to moderate hypertension with antihypertensive drug therapy to a level below 140/90 mmHg in pregnant women with gestational hypertension, pre-existing hypertension with the superimposition of gestational hypertension, and hypertension with subclinical organ damage or symptoms at any time during pregnancy (24). Nifedipine and labetalol are considered first-line drugs for treatment of hypertensive disorders in pregnancy (1). Methyldopa may also be used (1). Hypertensive emergencies should be treated with intravenous labetalol, oral nifedipine, or intravenous hydralazine (1,25) or with intravenous sodium nitroprusside (24). Sodium nitroprusside should be used only in extreme emergencies and used for the shortest amount of time possible because of cyanide and thiocyanate toxicity in the mother and fetus or newborn and increased intracranial pressure in the mother (26). The antihypertensive drugs labetalol, nifedipine, methyldopa, and hydralazine are considered safer in breastfeeding (1).

The ESC guidelines recommend induction of delivery in patients with gestational hypertension with proteinuria with adverse conditions such as fetal distress, visual disturbances, or coagulation abnormalities (24). A Cochran database review published in 2017 included five studies with 1,819 women with hypertensive disorders randomized to planned early delivery by induction of labor or by caesarean section compared with expectant management from 34 weeks gestation (27). Women randomized to receive planned early delivery had a 31% reduction in maternal mortality and severe morbidity, a 60% lower risk of the HELLP syndrome, and a 64% reduction in severe renal impairment (27). There were insufficient data to draw any conclusions about the effect of planned early delivery on infant mortality and severe morbidity.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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