

USE OF ANTIHYPERTENSIVE DRUGS DURING PREGNANCY

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<https://doi.org/10.5281/zenodo.11394011>

Abstract. Guidelines for the classification, diagnosis, and treatment of hypertensive disorders (including preeclampsia) are available from the American College of Obstetricians and Gynecologists (ACOG [1]).

In 2017, the American College of Cardiology (ACC) and the American Heart Association (AHA) published new guidelines for evaluating high blood pressure (BP). When determining hypertension, they lowered the blood pressure limits as follows:

Normal < 120/80 mm Hg. Art.

Elevated: 120-129/< 80 mm Hg. Art.

Stage 1 hypertension: 130-139 / 80-89 mm Hg. Art.

Stage 2 hypertension: \geq 140/90 mmHg. Art.

Keywords: hypertensive encephalopathy, Stroke, Kidney failure, Left ventricular failure.

The American College of Obstetricians and Gynecologists (ACOG) defines chronic hypertension as systolic blood pressure \geq 140 mm Hg before 20 weeks of gestation. Art. or diastolic blood pressure \geq 90 mm Hg. Art. in two dimensions. ACC/AHA data on this issue is limited. Thus, pregnancy management may change.

Hypertension during pregnancy can be classified as one of the following:

Chronic: high blood pressure before pregnancy or before 20 weeks of pregnancy. Chronic hypertension complicates 1-5% of all pregnancies.

Pregnancy: hypertension develops after 20 weeks of pregnancy (usually after 37 weeks) and disappears up to 6 weeks after delivery; It occurs in 5-10 percent of pregnancies, often in multiple pregnancies.

Both types of hypertension increase the risk of preeclampsia and eclampsia, as well as other causes of maternal morbidity and mortality, including

HELLP syndrome (hemolysis, increased liver enzymes and low platelet count)

The risk of fetal death or morbidity is increased by decreased uteroplacental blood flow, which can lead to vasospasm, growth restriction, hypoxia, and premature placental abruption. If hypertension is severe (systolic blood pressure \geq 160, diastolic blood pressure \geq 110 mmHg, or both) or renal insufficiency (eg, creatinine clearance < 60 mL/min, serum creatinine > 2 mg/min), results worsen [> 180 m mol/l]).

CLINICAL CALCULATOR

Creatinine clearance (measured)

CLINICAL CALCULATOR

Determination of glomerular filtration rate using MDRD formula

Diagnosis of hypertension during pregnancy

Investigations to rule out other causes of hypertension

A pregnant woman's blood pressure is measured at each prenatal visit. If severe hypertension occurs for the first time in pregnant women without multiple pregnancies or gestational trophoblastic disease, conducting tests to exclude other causes of hypertension (for

example, renal artery stenosis, coarctation of the aorta, Cushing's syndrome, systemic lupus erythematosus) need, pheochromocytoma).

Treatment of hypertension during pregnancy

Conventional therapy is used for mild hypertension, and then antihypertensive drugs should be prescribed if necessary.

Therapy begins with methyldopa, beta blockers, or calcium channel blockers.

Angiotensin converting enzyme inhibitors (ACE inhibitors), angiotensin II receptor blockers (ARBs) and aldosterone antagonists should be avoided.

Treatment for moderate or severe hypertension includes antihypertensive therapy, close monitoring, and if the condition worsens, termination of pregnancy or labor depending on gestational age.

Treatment recommendations for pregnant women with chronic and gestational hypertension are the same and depend on severity. However, chronic hypertension can be more severe. High blood pressure with gestational hypertension often occurs late in pregnancy and does not require treatment.

Treatment of mild to moderate hypertension without renal failure during pregnancy is controversial; Challenging questions are whether treatment improves pregnancy outcomes and to what extent the risks of drug therapy outweigh the risks of untreated disease. Since the uteroplacental blood flow is not self-regulating, lowering the mother's blood pressure can reduce it dramatically. Diuretics reduce the effective circulating blood volume of the mother; Consistent and persistent contractions increase the risk of fetal growth restriction. However, hypertension, even mild or moderate, can be treated together with kidney failure.

Physical activity restriction for mild to moderate hypertension (systolic blood pressure 140-159 mmHg or diastolic blood pressure 90-109 mmHg) or labile blood pressure can lower blood pressure and improve fetal well-being, thereby reducing perinatal risks in women without hypertension. reduces However, if this conservative measure does not reduce blood pressure, many experts recommend drug therapy. Strategies to reduce blood pressure < 140/90 mmHg in pregnant women with moderate chronic arterial hypertension. Art. associated with a reduction in preeclampsia and preterm birth, without increasing the risk of small-for-gestational-age infants (1). Women who received methyldopa, beta blockers, calcium channel blockers, or a combination of these before pregnancy may continue to take these medications. In contrast, ACE inhibitors and ARBs should be discontinued immediately after pregnancy is confirmed.

For severe hypertension (systolic blood pressure ≥ 160 mm Hg or diastolic blood pressure ≥ 110 mm Hg), drug therapy is indicated. The risk of maternal (development of organ dysfunction, preeclampsia) and fetal (premature birth, growth retardation, preeclampsia) complications increases significantly. You may need to take several antihypertensive medications.

With systolic blood pressure > 180 mm Hg. Art. or diastolic blood pressure > 110 mm Hg. Art. immediate evaluation is required. It is often necessary to take a large dose of medicine. Hospitalization may also be required for most of the second half of pregnancy. If the woman's condition worsens, sometimes it is recommended to terminate the pregnancy.

All women with chronic hypertension during pregnancy should be taught self-monitoring of blood pressure; they should also be evaluated for target organ damage. Assessments at the start of the study and periodically thereafter include:

Serum creatinine, electrolytes, uric acid concentration

Liver function tests

Platelet count

Determination of protein concentration in urine

A funduscopy is usually performed

If women have hypertension for more than 4 years, maternal echocardiography should be considered. After an initial ultrasound to assess fetal anatomy, monthly ultrasounds are performed beginning at approximately 28 weeks to monitor fetal growth; Antenatal diagnosis often begins at 32 weeks. If women develop additional complications (eg, kidney abnormalities) or fetal complications (eg, growth restriction), ultrasound can be started early to monitor fetal growth and antenatal diagnosis. Delivery should be from 37 to 39 weeks, but early delivery is possible if gestosis or intrauterine growth retardation is detected, as well as unsatisfactory test results.

Pharmacological treatment

First-line drugs for hypertension during pregnancy

Methyldopa

Beta blockers

Calcium channel blockers

The initial dose of methyldopa is 250 mg orally 2 times a day; in case of excessive drowsiness, depression or symptomatic orthostatic hypotension, it can be increased to a total of 2 g per day.

The most commonly used beta-blocker is labetalol (a beta-blocker with some properties of an alpha-1-blocker), which can be used alone or in combination with methyldopa once the maximum dose of methyldopa has been reached. The standard dose of labetalol is 100 mg 2-3 times a day, if necessary, it can be increased to a maximum of 2400 mg a day. Side effects of beta-blockers include increased risk of fetal growth restriction, fatigue, and maternal depression.

Long-acting nifedipine, a calcium channel blocker, may be preferable because it is taken once daily (starting dose 30 mg; maximum daily dose 120 mg); side effects include headache and swelling of the ankles. Thiazide diuretics are only used to treat chronic hypertension during pregnancy if the potential benefit outweighs the potential risk to the fetus. Dosage may be adjusted to reduce side effects such as hypokalemia.

Some classes of antihypertensive drugs that should be avoided during pregnancy include:

The use of ARBs is contraindicated because they increase the risk of fetal renal dysfunction, pulmonary hypoplasia, skeletal malformations, and death.

Aldosterone antagonists (spironolactone and eplerenone) should be excluded, as they may cause feminization of the male fetus.

Many maternal infections (such as UTIs, skin and respiratory diseases) do not usually complicate pregnancy, although some genital infections (bacterial vaginosis and genital herpes) affect the choice of delivery method. Thus, the main concern is the use and safety of antibacterial drugs.

However, some maternal infections can harm the fetus, which can occur in the following cases:

Congenital cytomegalovirus infection

Neonatal herpes simplex virus infection

Congenital rubella

Congenital toxoplasmosis

Hepatitis B in newborns

Congenital syphilis

HIV infection can be transmitted from mother to child transplacentally or perinatally. If left untreated by the mother, the risk of transmission at birth is about 25-35%.

Listeriosis often occurs during pregnancy. Increases the risk of listeriosis

Spontaneous abortion

Early birth

Stillbirth

Listeriosis can be transmitted from mother to child transplacentally or perinatally.

Bacterial vaginosis and possibly genital chlamydia are prone

Premature rupture of the membrane

Early birth

Tests for these infections are done during routine prenatal testing or when symptoms appear.

During childbirth, genital herpes can be transmitted to the newborn. The risk is high enough to justify a cesarean in the following situations:

In the presence of visible herpetic rashes

If a woman with herpes experiences prodrome symptoms before giving birth

If herpes appeared for the first time at the end of the 3rd trimester (when the virus is expected to spread from the cervical canal during childbirth)

If there are no visible rashes and prodromes, even if there is a repeated course of the disease, the risk is low and birth through the birth canal is possible. In asymptomatic cases, even serial virological studies of cultures do not help to determine the risk of transmission. If a woman has recurrent herpes during pregnancy but has no other risk factors for contracting it, labor can be induced to ensure delivery between relapses. During natural childbirth, cervical and neonatal examination is performed for herpes virus. Taking acyclovir (oral and topical) during pregnancy is not dangerous.

Antibiotics

The use of antibacterial agents should be avoided during pregnancy unless there is reliable evidence of bacterial infection. The use of any antibiotic during pregnancy should be based on the benefits and risks, which vary by trimester (see the table "Some drugs with adverse effects during pregnancy" for specific side effects). The severity of the infection and other possible treatments should also be considered.

During pregnancy, aminoglycosides can be used to treat pyelonephritis and chorioamnionitis, but treatment should be carefully monitored to avoid harm to the mother or fetus.

Cephalosporins are generally considered safe.

Levomecetin, even in large doses, is harmless to the fetus; however, newborns cannot adequately metabolize chloramphenicol and high blood levels can cause circulatory failure (gray baby syndrome). Chloramphenicol is rarely used in the United States.

Fluoroquinolones are not used during pregnancy; they have a high affinity for bone and cartilage tissue and therefore may cause musculoskeletal side effects.

A macrolide is generally considered safe.

The use of metronidazole in the 1st trimester is generally considered controversial; however, several studies have not found it to be teratogenic or mutagenic.

Nitrofurantoin is not known to cause birth defects. Its use in the early stages is contraindicated, as it can cause hemolytic anemia in newborns.

Penicillin is generally considered safe.

Sulfonamides are generally safe during pregnancy. However, long-acting sulfonamides cross the placenta and can displace bilirubin from binding sites. Because of the risk of kernicterus in newborns, these drugs are often not prescribed after 34 weeks of pregnancy.

Tetracyclines pass through the placenta and accumulate in the bones and teeth of the fetus, they bind to calcium and prevent the development of the fetus (see the table: "Some drugs that have negative effects during pregnancy");

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