

SMFM Statement: benefit of antihypertensive therapy or mild-to-moderate chronic hypertension during pregnancy remains uncertain

SMFM Publications Committee



Chronic hypertension is present in up to 5% of pregnant women and constitutes a major cause of maternal and neonatal morbidity and mortality.¹⁻⁴ To mitigate these sequelae, antihypertensive treatment is often prescribed. The purpose of this document is to summarize the current recommendations regarding use of antihypertensive medications during pregnancy for women with mild-to-moderate chronic hypertension in the setting of the recently published Control of Hypertension in Pregnancy Study (CHIPS).⁵

The most updated recommendations regarding management of pregnant women with hypertension are found from the American Congress of Obstetricians and Gynecologists Task Force on Hypertension in Pregnancy, which are endorsed by the Society of Maternal-Fetal Medicine (SMFM).¹ For women with persistent chronic hypertension with systolic blood pressure (BP) ≥ 160 mm Hg or diastolic BP > 105 mm Hg, antihypertensive therapy is recommended. Treatment benefit for mild-to-moderate hypertension (defined as systolic BP ≥ 140 mm Hg but < 160 mm Hg or diastolic BP ≥ 90 mm Hg but < 110 mm Hg) is less clear and thus it is suggested these women not be treated with pharmacologic antihypertensive therapy. These recommendations result from the lack of data confirming maternal or perinatal benefit of treatment

Chronic hypertension is present in up to 5% of pregnant women and constitutes a major cause of maternal and neonatal morbidity and mortality. The purpose of this document is to summarize the current recommendations regarding use of antihypertensive medications during pregnancy for women with mild-to-moderate chronic hypertension in the setting of the recently published Control of Hypertension in Pregnancy Study (CHIPS). The recently published CHIPS trial was a multicenter international randomized controlled trial comparing "less tight control" to "tight control" of blood pressure for pregnant women with hypertension. The most updated recommendations regarding management of pregnant women with hypertension are found from the American Congress of Obstetricians and Gynecologists Task Force on Hypertension in Pregnancy, which are endorsed by the Society of Maternal-Fetal Medicine (SMFM). SMFM recommends that clinicians continue to follow existing guidelines for management of pregnant women with mild-to-moderate chronic hypertension due to the fact that the benefits and risks of pharmacologic treatment for these women remain uncertain, and adequately powered randomized controlled trials are needed to address the less common but clinically significant nonsurrogate perinatal outcomes.

Key words: antihypertensive treatment during pregnancy, chronic hypertension during pregnancy, mild-to-moderate chronic hypertension during pregnancy

as well as concerns that treatment may impair fetal growth. Until now, limited data from several small randomized controlled trials (RCTs) demonstrated that treatment of mild-to-moderate hypertension in pregnancy is associated with a 50% reduction in progression to severe maternal hypertension (occurring in approximately 10-20% without treatment). However, no reduction in key adverse maternal and perinatal outcomes, including superimposed preeclampsia, has been demonstrated.⁶⁻⁹ Metaanalyses have suggested that lowering BP with antihypertensive therapy during pregnancy may be associated with a 1.5- to 2-fold increased risk of SGA and lower birthweight.^{10,11}

The recently published CHIPS trial was a multicenter international RCT comparing "less tight control" to "tight control" of BP for pregnant women with hypertension.⁵ The study reported outcomes for 987 women who were enrolled at 14-33 weeks of gestation; participants

had either chronic (75%) or gestational (25%) nonproteinuric hypertension. Women with diastolic BP 90-105 mm Hg (85-105 mm Hg if already on antihypertensive medication) were randomized to either less tight control (target diastolic BP 100 mm Hg) or tight control (target diastolic BP 85 mm Hg) during pregnancy. The primary outcome of pregnancy loss or need for high-level neonatal care for ≥ 48 hours did not differ between groups (31.4% vs 30.7%). As expected, the frequency of severe hypertension was higher with less-tight control (40.6% vs 27.5%; adjusted odds ratio [aOR] 1.8; range, 1.3-2.4). The increased risk of severe hypertension in the less-tight group was not associated with any adverse pregnancy outcome such as preeclampsia (48.9% vs 45.7%), abortion (2.3% vs 2.2%), or composite of "serious maternal complications" (3.7% vs 2.0%). The overall risk of SGA (< 10 th percentile) was not different between groups (16.1% vs 19.7%; aOR

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0.78; range, 0.56–1.08). In the subgroup with chronic hypertension, the risk of SGA was one third lower with less-tight control (13.9% vs 19.7%; aOR 0.66; range, 0.44–1.00), although CHIPS was underpowered to examine subgroup differences.⁵

Of note, among CHIPS trial participants, >56% in each group were kept on antihypertensive therapy at randomization (10–12% on at least 2 drugs), 14% had prior severe hypertension, and only 35% were enrolled <21 weeks of gestation. Although the study was well conducted and has strong interval validity, its findings are not generalizable to the management of women with mild-to-moderate chronic hypertension for 2 main reasons: (1) a small percentage of women were enrolled <20 weeks of gestation with mild-to-moderate hypertension; and (2) over half of subjects in each group stayed on their antihypertensive medications at randomization; therefore, there was not an adequate comparison of outcomes between women with and without therapy. In addition, while CHIPS had adequate power to assess the selected primary outcome, the sample size was not adequate to address other key pregnancy outcomes that are likely to be influenced by treatment such as rate of small-for-gestational-age infants and indicated preterm birth. Finally, the CHIPS trial only provided short-term outcomes; thus the potential longer-term benefits and risks and benefits of giving or withholding antihypertensive therapy during pregnancy remain unknown.

For these reasons, SMFM recommends that clinicians continue to follow existing guidelines for management of pregnant women with mild-to-moderate chronic hypertension due to the fact that the benefits and risks of pharmacologic treatment for these women remain uncertain, and adequately powered RCTs

are needed to address the less common but clinically significant nonsurrogate perinatal outcomes. A large multicenter National Institutes of Health (National Heart, Lung, and Blood Institute)–funded RCT (clinicaltrials.gov NCT02299414) that is planned to start in 2015 in the United States will address some of these questions.

Therefore, until additional information becomes available, SMFM supports current guidance from the Task Force on Hypertension in Pregnancy that states pregnant women with mild-to-moderate chronic hypertension (without end-organ damage) should not be treated with pharmacologic antihypertensive therapy.¹ For women starting pregnancy already on medication with BP controlled in the mild-to-moderate range, the task force states that although decision-making must be individualized, it is reasonable practice to discontinue medications during the first trimester and restart them if BP approaches the severe range.¹ ■

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