Control of Hypertension in Pregnancy — If Some Is Good, Is More Worse?
Caren G. Solomon, M.D., and Michael F. Greene, M.D.

Entering pregnancy with chronic hypertension is increasingly common. A nationwide study of deliveries in the United States revealed that the prevalence of chronic hypertension among pregnant women had increased significantly, from 0.9% in 1995–1996 to 1.5% in 2007–2008. The frequency of gestational hypertension (i.e., hypertension first detected during pregnancy) has also increased. Older maternal age at delivery and higher rates of obesity at least partially explain these increases. Chronic hypertension is an important risk factor for pregnancy complications, including, for the fetus or neonate, poor fetal growth, preterm birth, low birth weight, requirement for neonatal intensive care, and death, and for the mother, superimposed preeclampsia and eclampsia, acute renal failure, pulmonary edema, cesarean delivery, placental abruption, stroke, peripartum cardiomyopathy, and death.

There is consensus that treatment of hypertension in pregnancy is warranted if blood pressure is sufficiently high to pose a risk of stroke (i.e., ≥160 mm Hg systolic or either ≥105 mm Hg diastolic or ≥110 mm Hg diastolic) or if there is associated renal or cardiovascular disease. In the absence of those indications, there is considerable debate about the need for treatment of mild hypertension (i.e., hypertension below these thresholds) during pregnancy. Randomized trials of treatment of mild, chronic hypertension in pregnancy have consistently failed to show improvements in major complications; these trials have not been powered to detect potential reductions in maternal or perinatal mortality. Although treatment has been shown to reduce the risk of episodes of severely elevated blood pressure, it has not decreased the incidence of superimposed preeclampsia or other major maternal complications.

Moreover, some data have suggested that the risks of intrauterine growth restriction and low birth weight increase with zealous treatment of maternal hypertension, an observation that might be explained by reduced uteroplacental perfusion caused by excessive blood-pressure reduction. However, observational data supporting such associations are subject to confounding by indication (since the odds of intrauterine growth restriction with hypertension in pregnancy are two to three times the odds in women without hypertension). Randomized trials, which were not designed or powered to address this question, have yielded inconsistent results. The most recent Cochrane review concluded that there is “not enough evidence to show whether antihypertensive drug treatment for mild to moderate hypertension during pregnancy is worthwhile.”

In this issue of the Journal, Magee and colleagues report the results of an international, randomized trial comparing less-tight versus tight control of mild-to-moderate nonproteinuric hypertension in pregnancy (diastolic blood-pressure targets, 100 mm Hg and 85 mm Hg, respectively). In three quarters of study participants, hypertension antedated pregnancy, and slightly more than half the women were taking antihypertensive medication at enrollment, at a mean...
of approximately 24 weeks of gestation. There was no significant difference between groups in the frequency of the primary outcome, a composite of pregnancy loss or high-level neonatal care for more than 48 hours in the first 28 postnatal days (31.4% vs. 30.7%). The groups also did not differ significantly in the frequency of serious maternal complications, including development of preeclampsia, although severe hypertension (≥160/110 mm Hg) was significantly more common in the less-tight-control group. Results for women with chronic hypertension and for those with gestational hypertension appeared similar.

The proportion of infants with intrauterine growth restriction (birth weight below the 10th percentile for age) was slightly but not significantly lower in the less-tight-control group (16% vs. 20%). However, the study was not powered for this outcome, and the 95% confidence interval around the risk estimate cannot exclude a clinically important increase in risk.

Although larger than previous trials, this study was similarly not powered to detect differences in frequencies of fetal or maternal deaths. These events were uncommon; perinatal mortality was 2.8% in the less-tight-control group and 2.3% in the tight-control group, and there were no maternal deaths.

Although severe hypertension was more likely in the less-tight-control group than in the tight-control group, the difference was not accompanied by an increase in the serious complications of hypertension or transient ischemic attack or stroke. Pulmonary edema, renal failure, and placental abruptions were uncommon, and their frequencies, along with the frequency of emergency department visits or hospitalizations (other than for delivery), did not differ materially between groups.

The study protocol encouraged the use of labetalol when medication was needed to reach the target blood pressure, but this was a pragmatic trial, and one third of women requiring medication after randomization were not treated with this agent. Head-to-head trials of antihypertensive agents commonly used in pregnancy (labetalol, methyldopa, and nifedipine) have not shown significant differences in major fetal or maternal outcomes, but some — albeit inconsistent — evidence has suggested a reduced risk of severe hypertension and of an associated need for hospitalization in association with the use of labetalol versus methyldopa. The present report does not address whether outcomes vary according to the antihypertensive medication used.

In summary, the current study showed that tight control of hypertension conferred no apparent benefits to the fetus and only a moderate benefit (a lower rate of progression to severe hypertension) for the mother. It does, however, provide valuable reassurance that tight control, as targeted in this study, does not carry major risks for the fetus or newborn.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

From the Department of Obstetrics and Gynecology, Massachusetts General Hospital, Boston (M.F.G.).


DOI: 10.1056/NEJMe1414836
Copyright © 2015 Massachusetts Medical Society.