Target Blood Pressure Goals for Treating Hypertension in Pregnancy
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Abstract

There are different clinical types of hypertensive disorders in pregnancy. The management mainly lies in the hands of an obstetrician; however, a physician’s role is often sought specially in chronic hypertension and when blood pressure (BP) remains uncontrolled. There is no doubt that severe hypertension ≥160/110 mm Hg will be treated expeditiously to prevent complications. It is in less severe hypertension, where the questions arise – what should be the cutoff to treat with medications, and what must be the goal of control that has to be achieved? The dilemma is due to the observations of increased incidence of small for gestational age newborns among those treated for mild hypertension. Research in the recent past has shown that strict control reduces severe hypertension though there was no significant benefit in terms of reduction in pregnancy loss, high-level neonatal care, or overall maternal complications. There is no clear consensus between various guidelines on indication to initiate medication for the control of hypertension and the target BP to be achieved. Considering the recent developments in the field, it appears prudent to control even mild-to-moderate hypertension effectively. Regardless of the type of hypertensive disorder of pregnancy, persistent BP ≥140/90 mmHg in clinic (or ≥135/85 mmHg at home) should be treated, aiming for a target BP of 110–140/85 mmHg in the office to reduce the likelihood of developing severe maternal hypertension, and other complications. However, in gestational hypertension and preeclampsia, strict surveillance to identify worsening of the condition so as to take appropriate interventions

Key words: Blood pressure; hypertension, pregnancy-induced, preeclampsia, pregnancy outcome

Introduction

With a prevalence of 10–15%, hypertension is one of the leading causes of maternal mortality and morbidity.\(^{1-3}\) Pregnancy-related hypertension has a unique pathogenesis unlike hypertension in the general population. The disease begins as a result of defective placentation, due to insufficient invasion of trophoblasts into the uterine spiral arterioles, thereby initiating a cascade of events leading to hypertension. Hypertension is just one of the manifestations of a far fetching placental disorder, which can also affect several organs such as kidneys, liver, eyes, brain, and the fetus.

The extensively researched subject continues to intrigue clinicians and researchers. The etiopathogenesis has a number of theories and hypothesis involving complex humoral and immunological factors, with the core problem of vasoconstriction, endothelial dysfunction, and resulting multiorgan impairment.

National High Blood pressure (BP) Education Program Working Group on High BP in pregnancy has suggested the following classification of hypertensive disorders in pregnancy:\(^4\)
- Chronic hypertension: Elevated BP in the mother that predated the pregnancy; can also be diagnosed in retrospect, when hypertension fails to normalize 12 weeks after delivery.
- Preeclampsia-eclampsia: Appearance of hypertension in pregnancy accompanied by new-onset proteinuria, defined as ≥300 mg per 24 h.
- Preeclampsia superimposed on chronic hypertension
- Gestational hypertension: De novo hypertension arising after mid-pregnancy and is distinguished from preeclampsia by the absence of proteinuria and severe complications related to hypertension

International Society for the Study of Hypertension in Pregnancy (ISSHP) Classification categorizes hypertension into two main categories as (1) hypertension known before
pregnancy or present in the first 20 weeks and (2) hypertension arising de novo at or after 20 weeks of pregnancy. It further adds white coat hypertension, masked hypertension, and transient gestational hypertension to the categories.\cite{5}

Definition of preeclampsia has also undergone modification due to the observations of severe complications even before the onset of proteinuria. Therefore, the latest definition adds “the presence of severe features with or without proteinuria” to the existing definition of preeclampsia.\cite{6}

### Chronic Hypertension

The goal of treatment of chronic hypertension would be (1) to prevent superimposed preeclampsia and (2) to minimize the devastating complications such as cerebral hemorrhage directly related uncontrolled hypertension per se.

It is well established that diastolic BP (DBP) ≥110 mm Hg is associated with fetoplacental complications such as placental abruption and fetal growth restriction. On the other hand, the systolic BP (SBP) ≥160 mm Hg is associated with maternal complications such as intracerebral hemorrhage. The degree of systolic hypertension is found to be the most important predictor of cerebral injury and infarction.\cite{7,8} Thus, there is no doubt about hypertension 160/110 mm Hg requiring to be controlled as an emergency.\cite{9,10} Here, the goal of pharmacologic treatment should be a DBP of <100–105 mm Hg and an SBP <160 mm Hg. Similarly, it is accepted beyond doubt that women with preexisting end-organ damage from chronic hypertension should have a lower threshold for starting antihypertensive medication.\cite{11}

There is dilemma regarding whether or not to treat the BP values at or just beyond the diagnostic cut off of 140/90 mm Hg; and if treatment is required what should be the target BP control. The guidelines as recently as 2010 recommended not to treat mild hypertension and to consider treatment only when BP was consistently above 150/100 mm Hg.\cite{12} This was well in line with the fact that prolonged antihypertensive treatment resulted in poor placental circulation thereby causing fetal growth restriction. Women with chronic hypertension, who received at least one antihypertensive in third trimester had a higher rate of intrauterine growth restriction (7.2% vs. 2.1%, respectively; adjusted odds ratio, 4.37; 95% confidence interval, 3.00–6.36; \(P < 0.001\)) compared to those who did not receive antihypertensive medication. They found similar observations between chronic hypertensive – no treatment group against non-hypertensives.\cite{13}

The Control of Hypertension in Pregnancy Study (CHIPS) trial including 987 women with non-proteinuric preexisting hypertension, or gestational hypertension with office DBP of 90–05 mm Hg (85–105 mm Hg if the woman was on antihypertensive medications) evaluated the benefits and risks of tight (85 mmHg) versus less tight (100 mmHg) DBP control. They observed that fewer women in the tight control group developed severe hypertension (27.5 vs. 40.6%). However, there was no significant between-group differences in the risk of pregnancy loss, high-level neonatal care, or overall maternal complications.\cite{14}

In the post hoc analysis of CHIPS data to determine whether clinical outcomes differed by occurrence of severe hypertension, it was found that severe hypertension was associated with perinatal loss or high-level neonatal care for >48 h, serious maternal complications, birth weight <10th percentile, preeclampsia, and delivery at <34 or <37 weeks, platelets <100 × 10^9/L, elevated liver enzymes with symptoms, and maternal length of stay ≥10 days.\cite{15}

These observations have led researchers to suggest tight control for minimizing the incidence of severe hypertension.

Further analysis of the data in CHIPS study, to find the role of gestational age at the time of randomization to “tight” control and “less tight” control groups, showed that there is no gestational age at which less tight (vs. tight) control is the preferred clinical option for women with chronic or gestational hypertension. Delaying the treatment to gestational age of beyond 24 weeks did show benefit in minimizing the small for gestation newborns; however, this benefit was countered by increase in severe hypertension and related premature delivery.\cite{16}

Meta-analyses including Cochrane review also inferred that antihypertensives in mild-to-moderate hypertension prevented development of severe hypertension. However, it had little or no influence on perinatal outcome in terms of fetal death, prematurity, small for gestation newborns, and neonatal complications; neither was there any significant effect on maternal outcome like preeclampsia/eclampsia.\cite{17,18}

Despite the recent observations, differences in guidelines prevail. In Ireland, clinical practice guidelines (2016, revised in 2019) recommend that for pregnant women with chronic hypertension without underlying medical problems, antihypertensive drug therapy should aim at BP below 150 /80–99 mm Hg and for those with underlying medical problems, such as diabetes or renal disease, tighter control with the goal of maintaining BP below 140/80–90 mmHg.\cite{19} ISSHP and National Institute for Health and Care Excellence (NICE) guidelines pragmatically recommend a common goal of 140/85 mm Hg 135/ 85 mm Hg, respectively, for control of BP for all types of hypertensive disorders in pregnancy.\cite{5,20}

ACOG Practice Guidelines 2019 recommendations for chr hypertension.\cite{21}

### Preeclampsia and Gestational Hypertension

Although gestational hypertension and preeclampsia are two different categories of pregnancy hypertension, their management in the absence of severe features is similar; and both require enhanced surveillance. Up to 50% of women with gestational hypertension will eventually develop proteinuria or other end-organ dysfunction consistent with the diagnosis of preeclampsia especially when hypertension is diagnosed at
<32 weeks of gestation. For all practical purposes, the two categories may be discussed as one entity.

Gestational hypertension and preeclampsia have placental origin; here, hypertension is due to increased vascular resistance secondary to increased sensitivity of the vasculature to angiotensin. Defective secondary wave of trophoblastic invasion of myometrial spiral arterioles during placentation results in failure of establishing a desired low resistance placental circulation, initiates the process of increased vascular resistance, endothelial damage, and platelet dysfunction all leading to maternal multiorgan dysfunction. On the fetoplacental side, vascular resistance causes poor perfusion. Initial response to this insult is brain-sparing adjustment by the fetus, at the cost of compromising other vital organs such as kidneys and liver. The fetus will become growth restricted; poor renal perfusion will result in oligohydramnios. The fetal effect may become evident much before high BP becomes evident on maternal side. Antihypertensive treatment will add to the already existing hypoperfusion at placental bed, especially when given for longer duration.

Similarly severe maternal complications may occur even without very high BP levels. Seizures can occur without other severe features of preeclampsia and with a normal BP; 15% of women with eclampsia have a DBP <90 mm Hg. The latest ACOG interim guidelines emphasize on intensive surveillance for women with gestational hypertension and preeclampsia with less severe BP and in the absence of severe features; the guidelines speak of antihypertensive medications only in case of severe hypertension. However, NICE and ISSHP recommend pharmacological treatment if BP remains above 140/90 mm Hg with an aim for BP of 135/85 mm Hg or less for preeclampsia, gestational hypertension, and preeclampsia with less severe BP and in the absence of severe features; in all cases, care should be taken to avoid reducing the BP below the lower limits (110/80 mmHg) which would lead to a risk of placental underperfusion.

Postpartum Management

Pregnancy hypertension is not just the problem of pregnancy; the risk extends even into the postpartum period. Community-Level Interventions for Pre-eclampsia trials in 27 geographical clusters in less-developed countries observed substantial proportion (40%) of pregnancy hypertension diagnosed postpartum. More dreaded are the complications of hypertension such as eclampsia and cerebrovascular events which are not uncommon after delivery; rather, 20–28% of eclampsia happens in postpartum period. Similarly, it is observed that preeclampsia/eclampsia was present in 57.5% of the patients with hemorrhagic stroke and 36% of the patients with ischemic stroke related to obstetrics. More interesting is that stroke associated with preeclampsia occurs most often in postpartum period.

This emphasizes the need to be vigilant in identifying postpartum hypertension and treating those who already had hypertension antepartum. After delivery, women with preeclampsia require ongoing close BP monitoring. As in antepartum management, BP 160/110 mm Hg should be treated with acute antihypertensive management. Persistent BP above 155/105 mm Hg will require oral antihypertensive treatment.

In case of chronic hypertension, persistent BP ≥ 140/90 mm Hg needs antihypertensive treatment with the goal of maintenance of BP at ≤140/90 mm Hg. Medications will be reduced as BP falls below 130/80 mmHg.

Summary Points

1. Regardless of the hypertensive disorder of pregnancy, severe hypertension (≥160/110 mmHg) requires urgent immediate acting antihypertensive agents.
2. BPs consistently ≥140/90 mmHg in clinic (or ≥135/85 mmHg at home) may be treated, aiming for a target DBP of 85 mmHg in the office (and SBP of 110–140 mmHg). However, in gestational hypertension and preeclampsia, intensive surveillance to identify proteinuria and/ or other features of end organ involvement needs to be emphasized.
3. Women with preexisting end-organ damage from chronic hypertension should have a lower threshold for starting antihypertensive medication and a strict control of BP.
4. Monitoring of BP and control of hypertension after delivery is not less important.

References

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