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Hypertension in Women—Part II

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Abstract

In Part I, we reviewed the pathophysiology of hypertension in women This section focuses on the treatment of hypertension in special circumstances and special populations: pregnancy, preeclampsia, and lactation; hypertension in black women; and hypertension in the elderly.

Preeclampsia

Preeclampsia is more common in women with chronic hypertension than in those without, with an incidence of approximately 25%. Risk factors for superimposed preeclampsia include renal insufficiency, a history of hypertension of ≥4 years, and hypertension in a previous pregnancy. Prevention of preeclampsia relies on identification of high-risk women and close clinical and laboratory monitoring aimed at its early recognition and institution of intensive monitoring or delivery when indicated. Treatment of preeclampsia includes hospitalization for bed rest, control of blood pressure (BP), seizure prophylaxis in the presence of signs of impending eclampsia, and timely delivery. Of importance, many women with preeclampsia have previously been normotensive, so acute BP elevations even to modest levels (eg, 150/100 mm Hg) may cause significant symptomatology and require treatment. Treatment does not alter the underlying pathophysiology of the disease, but it may slow its progression and provide time for fetal maturation. preeclampsia rarely remits spontaneously and in most cases worsens with time.

While delivery may be appropriate therapy for the mother, it may compromise a fetus of fewer than 32 weeks' gestation. regardless of gestational age, delivery should be strongly considered when there are signs of fetal distress, intrauterine growth retardation, or maternal problems, including severe hypertension, hemolysis, elevated liver enzymes, low platelet count, deteriorating renal function, visual disturbance, headache, or epigastric pain. Vaginal delivery is preferable to Cesarean delivery to avoid the added stress of surgery.

Antihypertensive Drug Therapy

Antihypertensive therapy should be prescribed only for maternal safety; it does not improve perinatal outcomes and may adversely affect uteroplacental blood flow. selection of antihypertensive agents and route of administration depends on anticipated timing of delivery. if delivery is likely more than 48 hours away, oral methyldopa is preferred because of its safety record. Oral labetalol is an alternative, and other β-blockers and calcium antagonists are also acceptable on the basis of limited data. If delivery is imminent, parenteral agents are practical and effective (Table). Antihypertensives are administered before induction of labor if diastolic BP is persistently ≥105 to 110 mm Hg, aiming for levels of 95 to 105 mm Hg.

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Treating Hypertension During Lactation

Hypertensive mothers can usually breast-feed safely. However, all antihypertensive drugs that have been studied are excreted into human breast milk. Therefore, in mothers with stage 1 hypertension who wish to breast-feed for a few months, it might be prudent to withhold antihypertensive medication, with close monitoring of BP, and reinstitute antihypertensive therapy following discontinuation of nursing. No short-term adverse effects have been reported from exposure to methyldopa or hydralazine. Propranolol and labetalol are preferred if a β-blocker is indicated. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers should be avoided on the basis of reports of adverse fetal and neonatal renal effects. Diuretics may reduce milk volume and thereby suppress lactation. Breast-fed infants of mothers taking antihypertensive agents should be closely monitored for potential adverse effects.

Recurrence of Hypertension with Subsequent Pregnancy

Hypertension recurs in a large proportion (20%–50%) of subsequent pregnancies. Risk factors for recurrence include early onset of hypertension in the first pregnancy, a history of chronic hypertension, persistent hypertension beyond 5 weeks postpartum, and elevated BP early in pregnancy. Women with preeclampsia have a greater tendency to develop hypertension than those with normotension during pregnancy.

Hypertension in Older Women

Women constitute a significant proportion of the population older than 65 years, so consideration of hypertension in the elderly is essential. The challenges with treatment of hypertension in the elderly include underdiagnosis, undertreatment, difficulties with measurement, physiologic changes associated with aging, multiple comorbid conditions, and adverse effects of antihypertensive drugs.

Systolic BP increases with age, as does the proportion of hypertensive patients with isolated systolic hypertension (ISH). In contrast, diastolic BP increases in parallel with systolic BP until about age 55, after which it declines as a manifestation of age-related increases in central arterial stiffness. By age 60, about two-thirds of those with hypertension have ISH, and by age 75, almost all hypertensives have systolic hypertension and about three-fourths of hypertension cases are ISH. Currently, BP control rates (systolic BP <140 mm Hg and diastolic BP <90 mm Hg) are only about 20% in older persons with hypertension, largely due to poor control of systolic BP. ISH markedly increases cardiovascular risk; there is a 3- to 4-fold increase in cardiovascular disease (CVD) risk in older compared with younger individuals.

Treatment Outcomes in the Older Patients with Hypertension

In the Systolic Hypertension in the Elderly Program (SHEP), involving hypertensive patients older than 60 years with pretreatment systolic BP levels >160 mm Hg and diastolic BP levels >90 mm Hg, individuals treated with chlorthalidone (with or without a β-blocker) had reductions in the primary end point of stroke (36%), as well as heart failure events (54%), myocardial infarctions (27%), and overall CVD (32%) compared with the placebo group. Using a similar design and sample size, the Systolic Hypertension in Europe (Syst-Eur) study compared a regimen based on nitrendipine to placebo and found a significant reduction in stroke (41%) as well as overall CVD events (31%). A meta-analysis of 8 placebo-controlled trials in 15,693 elderly patients followed for 4 years found that active antihypertensive treatment reduced coronary events (23%), strokes (30%), cardiovascular deaths (18%), and total deaths (13%), with the benefit particularly great in those older than

70 years. Benefits of therapy have been demonstrated even in individuals older than 80 years.

Analyses of treatment trials in the elderly by the Hypertension Trialist Group have suggested that the choice of initial agent is less important than the degree of BP reduction achieved. Accurate and representative BP measurement can pose special problems in some older individuals. BP is more variable in the older patient, often because of stiff large arteries and age-related decreases in baroreflex buffering.

Exaggerated BP drops may occur in the elderly during postural change after meals and after exercise. Pseudohypertension, in which cuff BP overestimates the actual intra-arterial pressure because of relative inability of the BP cuff to compress a thickened, stiff, or calcified brachial artery, is an uncommon condition in older persons. But this condition should be strongly considered if usual treatment does not reduce BP, especially in those patients who complain of symptoms consistent with postural hypotension.

Treatment

Weight loss and reduced sodium intake are particularly beneficial in older individuals. In the Trial of Nonpharmacologic Interventions in the Elderly (TONE), reducing sodium to 80 mmol/d (2 g/d) reduced BP over 30 months, and about 40% of those on the low-salt diet were able to discontinue their antihypertensive medications. When weight loss was combined with salt reduction, an additional BP decrease was seen. Older persons should also be encouraged to avoid excessive alcohol intake and remain as physically active as feasible.

Use of specific drug classes in older individuals is largely similar to that recommended in the general algorithm and for individuals with compelling indications. Combination therapy with ≥2 drugs is generally needed to achieve optimal BP control. in routine practice, if the systolic BP goal is achieved, the diastolic BP goal will almost always be reached as well.

A significant number of elderly individuals have widely variable BP with exaggerated high and low extremes. Such individuals deserve consideration for a slow titration approach, as do individuals with a history of medication side effects and those with orthostatic hypotension. Unfortunately, the misperception that many elderly individuals have “brittle hypertension” has contributed to widespread inadequacy of drug titration and to poor BP control.

Hypertension in Black Women

The prevalence of stage 3 hypertension (>180/110 mm Hg) is 8.5% in blacks as compared with 1% in whites. BP in hypertensive black persons is on average 30/20 mm Hg higher than in normotensive persons, whereas in hypertensive whites, the difference is 23/15 mm Hg. Consequently, blacks have a 1.3 times greater rate of nonfatal stroke, 1.8 times greater rate of fatal stroke, 1.5 times greater rate of heart disease death, 4.2 times greater rate of end-stage kidney disease, and a 50% higher frequency of heart failure; overall, mortality due to hypertension and its consequences is 4 to 5 times more likely in blacks than in whites.

Hypertension-related end-stage renal disease, another common and critical consequence of hypertension, is most striking in young black persons aged 25 to 44, who are 20 times more likely than whites in that age group to develop hypertension-related kidney failure. The racial divergence is apparent even in childhood, as the Bogalusa Heart Study confirmed more reported elevations in BP before the age of 10 years in black children than in white children. The presence of risk factors such as obesity contributes to early vascular dysfunction in blacks. Recent preliminary observations suggest that obesity among

otherwise healthy black women is associated with impaired vascular function as measured by flow-mediated dilation, which is accounted for primarily by inflammation, body mass index, and oxidative stress.

A recent look at hypertension treatment patterns in primary care showed that in a population of patients (68% female; average age, 47±13 years) receiving therapy for known hypertension, only 37% had BP that was goal level. Such trends emphasize the need for more aggressive therapy to achieve goal BP values as recommended by the International Society on Hypertension in Blacks (ISHIB).

Treatment Considerations

There are no clinical trial data at present to suggest that lower than usual BP targets should be set for high-risk demographic groups such as blacks. Although the use of diuretics in black patients may be a logical first-line choice for BP reduction, ISHIB guidelines recognize that most patients will require combination therapy, much of it first-line, to reach appropriate BP goals. Black women with systolic BP levels >15 mm Hg and diastolic BP values >10 mm Hg above goal level should have therapy initiated with combination therapy. Follow-up using the ISHIB treatment algorithm should increase the proportion of patients in whom recommended BP targets are reached.

Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers both reduce angiotensin II-mediated stimulation of transforming growth factor-β1, which may be of clinical significance in the treatment of hypertension in blacks. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers may be less effective as monotherapy; combining these agents with low-dose diuretics or calcium antagonists may be particularly useful in blacks. although data suggest a solid association between visceral obesity in black women and sympathetic nervous system activity, β-blockers have also been shown to be somewhat less effective as monotherapy for hypertension in blacks.

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Table

Treatment of Acute Severe Hypertension in Preeclampsia

Hydralazine	5 mg IV bolus, then 10 mg every 20 to 30 min to a maximum of 25 mg; repeat in several hours as necessary
Labetalol (second-line)	20 mg IV bolus, then 40 mg 10 min later; 80 mg every 10 min for 2 additional doses to a maximum of 220 mg
	10 mg PO; repeat every 20 min to a maximum of 30 mg
Nifedipine (controversial)	Use caution when using nifedipine with magnesium sulfate; it can be associated with precipitous BP drops
	Short-acting nifedipine is not approved by the US Food and Drug Administration for management of hypertension
Sodium nitroprusside (rarely and when others fail)	0.25 μg/kg/min to a maximum of 5 μg/kg/min
	Fetal cyanide poisoning may occur if used for more than 4 hours

Abbreviations: BP, blood pressure; IV, intravenous; PO, by mouth.