New Developments in the Management of Hypertension

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The management of hypertension has evolved over the past decade. Isolated systolic blood pressure elevation, the most common form of uncontrolled hypertension, is recognized as a significant risk factor for vascular complications in patients with hypertension. Nutritional management of hypertension has moved beyond simply restricting sodium intake to ensuring that patients consume adequate amounts of the major food groups, particularly those containing calcium, potassium, and magnesium. Selective aldosterone receptor blockers are a new class of antihypertensive medication, and the angiotensin-receptor blocker class has several new additions. However, the mainstay of treatment remains a diuretic or a combination of a diuretic and either a beta blocker or an angiotensin-converting enzyme inhibitor. Hypertension is a significant risk factor for vascular complications of diabetes, and the target blood pressure in patients with diabetes or chronic renal disease and hypertension should be lower than that in patients with hypertension alone. Controlling hypertension in elderly patients can reduce their complications at least as much as it does those of younger patients with hypertension. (Am Fam Physician 2003;68:853-8,865-6. Copyright© 2003 American Academy of Family Physicians.)

A patient information handout on dietary control of high blood pressure, written by Clarissa Kripke, M.D., is provided on page 865.

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See page 785 for definitions of strength-of-evidence levels.

Hypertension is the most common problem for which patients visit physicians.[1] More than one half of all persons older than 65 years have hypertension, often isolated systolic hypertension.[2] Improved control of hypertension has contributed to reductions of nearly 60 percent in stroke-related deaths and 53 percent in deaths from ischemic heart disease since 1972. However, in the United States, only 70 percent of patients with hypertension are aware of their condition, only 59 percent are receiving treatment, and only 34 percent have achieved adequate control.[3] Recommendations to identify and treat hypertension are nearly universal,[4] although some physicians accept inappropriately high blood pressure measurements, especially systolic pressure, as adequate control in their patients.[5]

Basic evaluation and management of hypertension have been reviewed recently in the seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) and are summarized in *Table 1*.[3] Advances in the management of hypertension have refined our understanding of systolic blood pressure, nutrition, medication selection, and hypertension in special populations.

Systolic Blood Pressure

Although physicians traditionally have emphasized management of diastolic blood pressure,[4] systolic blood pressure and pulse pressure (the difference between systolic and diastolic pressures) correlate more strongly with cardiovascular disease risk than does diastolic blood pressure, and treatment of isolated systolic blood pressure reduces vascular complications.[6] [Evidence level B, clinical cohort study] This finding is especially important because most patients with uncontrolled hypertension have isolated elevation of systolic blood pressure.[7-9] Thus, persistent isolated elevation of systolic blood pressure should be treated to

Isolated systolic hypertension should be treated to achieve blood pressures of less than 140 mm Hg.

achieve a normal range (less than 140 mm Hg), even in the presence of normal diastolic blood pressure.

Diastolic blood pressure is still important, however, because it may be a clinical marker for hypertensive urgency or emergency. In hypertensive urgencies, elevated blood pressure (diastolic pressure usually greater than 120 mm Hg) that is not associated with new or progressive end-organ damage may be lowered over hours to days in an outpatient setting. Hypertensive emergencies, however, require immediate lowering of blood pressure through intensive inpatient care and parenteral medications to limit or prevent progressive end-organ damage.

NUTRITION

Sodium restriction is an effective nutritional therapy in patients with hypertension.[3,10,11] Calcium supplementation also may help to reduce blood pressure.[12,13] Supplementation with potassium or magnesium has been suggested, but this step does not consistently lower blood pressure.[14]

However, patients with hypertension can now try a new and effective whole-food approach known as the DASH (Dietary Approaches to Stop Hypertension) diet *(see patient information handout for more information on the DASH diet)*.[15] The DASH diet is high in fruits, vegetables, nuts, whole grains, fish, poultry, and low-fat dairy products, which results in a diet high in calcium, potassium, and magnesium. The diet is low in red meat, sugar, fat, and cholesterol. The DASH diet lowers blood pressure more than sodium restriction alone.[15] [Evidence level A, randomized controlled trial (RCT)] Furthermore, a combination of the DASH diet and sodium restriction lowers blood pressure more in patients with hypertension than in those without hypertension. Thus, it seems that patients with hypertension should follow the DASH diet in addition to reducing sodium intake.[3] [Evidence level C, expert guidelines]

Among patients on the DASH diet at the lowest sodium intake levels, the mean decrease in systolic blood pressure was 8.9 mm Hg, when compared with the high-sodium phase of the control diet.[15] Although the DASH diet is not a weight-loss plan, it can be adapted for patients who need to restrict calories to lose weight.

The current epidemic of obesity in the United States is another contributing factor to hypertension. Having a body mass index of 27 or more, as well as truncal obesity, is associated with elevated blood pressure.[3] Blood pressure can be reduced by losing as little as 4.5 kg (10 lb) of body weight.[13,16] According to the JNC 7 report, patients with hypertension should be prescribed an individualized, monitored weight-reduction program.[3] In fact, increasing average body mass index contributed to 2 percent of the 3.6-percent increase in hypertension prevalence from the 1988-1991 National Health and Nutrition Examination Survey to the survey conducted in 1999-2000.[17]

TABLE 1
Stages of Hypertension and Treatment Strategies as Recommended by JNC 7

Blood pressure stages	*Treatment strategies*
Prehypertension (120 to 139/80 to 89 mm Hg)	Lifestyle modification* Drug therapy in patients with diabetes mellitus or chronic kidney disease
Stage 1 (140 to 159/90 to 99 mm Hg)	Consider coexisting conditions Thiazide-type diuretics for most patients
Stage 2 (≥160/≥100 mm Hg)	Consider coexisting conditions Two-drug combination for most patients

JNC = Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.

**—Lifestyle modification includes diet, exercise, and weight reduction.*

Information from Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report [Published erratum in JAMA 2003;290:197]. JAMA 2003; 289:2560-72.

NEWER MEDICATIONS

Hypertension is the most common condition for which Americans take prescription medication.[18] Physicians are currently prescribing fewer diuretics and beta blockers, the recommended first-line agents for hypertension, and more angiotensin-converting enzyme (ACE) inhibitors and calcium channel blockers (CCBs).[19] Although ACE inhibitors reduce rates of morbidity and mortality in patients with

cardiovascular disease, the same cannot be said for CCBs, for which no similar morbidity/mortality data exist.[19-21] Short-acting dihydropyridine CCBs should be avoided in the treatment of hypertension, and other CCBs should be added to the regimen only if control is not achieved with a beta blocker, diuretic, and/or ACE inhibitor.[22] [Evidence level A, meta-analysis]

The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) involved 33,357 men and women older than 55 years with hypertension and at least one other risk factor for ischemic heart disease.[23] Participants were randomized to treatment with a CCB (amlodipine), a diuretic (chlorthalidone), or an ACE inhibitor (lisinopril), with a mean follow-up time of 4.9 years. The results demonstrated that the thiazide diuretic chlorthalidone was superior to the other medications in preventing nonfatal myocardial infarction (MI), stroke, and heart failure, and was significantly less expensive.[23] [Evidence level A, RCT]

ACE inhibitors may be a preferred second drug to add to diuretics if necessary to achieve blood pressure control. Investigators in the African American Study of Kidney Disease and Hypertension trial found that ACE inhibitors were more effective than beta blockers or dihydropyridine CCBs in preventing progression of hypertensive nephrosclerosis in blacks.[24] [Evidence level A, RCT] Although blacks do not respond to monotherapy with beta blockers, ACE inhibitors, or ARBs as well as the rest of the population, combination therapy with a diuretic largely eliminates the differential response.

An earlier ALLHAT publication suggested that alpha blockers such as doxazosin may increase the risk of stroke and congestive heart failure when used to treat hypertension, and the alpha-blocker arm of the ALLHAT trial was discontinued.[25] The American College of Cardiology suggests that the use of alpha blockers as initial therapy should be reassessed, except in patients who require alpha-blocker therapy for benign prostatic hypertrophy.[26]

A relatively new class of antihypertensives is the angiotensin-II receptor blockers (ARBs). ARBs do not cause cough because, unlike ACE inhibitors, ARBs do not lead to accumulation of bradykinin, the purported cause of cough occurring with ACE inhibitors.

The results of long-term trials of morbidity and mortality in the treatment of hypertension with select ARBs are now becoming available.[27] The largest study to date—the Losartan Intervention for Endpoint Reduction in Hypertension study—demonstrated a reduction in the incidence of stroke, but no difference in mortality from any cause; the ARB losartan was compared with atenolol in patients with hypertension and left ventricular hypertrophy, with similar reductions in blood pressure.[28] [Evidence level A, RCT] In trials of patients with heart failure, ARBs appear to be a safe and effective alternative for those unable to tolerate ACE inhibitors.[29]

Eplerenone should not be used in patients with hyperkalemia or renal insufficiency.

Also recently approved for the treatment of hypertension is eplerenone (Inspra), the first agent in a new class of antihypertensives called selective aldosterone receptor antagonists. Interest in these medications is focused primarily on their use in patients with heart failure or as an add-on to other antihypertensives. However, one study[30] showed eplerenone to be as effective as amlodipine in the treatment of systolic hypertension, with the added advantage of a reduction in microalbuminuria in the patients with this condition at baseline. Cardiovascular morbidity and mortality outcome data are not yet available with this agent.

The most common side effect of eplerenone is hyperkalemia. Selective aldosterone receptor antagonists are contraindicated in patients with hyperkalemia (serum potassium level greater than 5.5 mEq per L [5.5 mmol per L]), elevated serum creatinine levels (1.8 mg per dL [160 mmol per L] in women, 2.0 mg per dL [180 mmol per L] in men), and in those with a creatinine clearance of less than 50 mL per minute (0.8 mL per second). Significant drug interactions include potassium supplements or potassium-sparing diuretics, and inhibitors of cytochrome P450 3A4, such as ketoconazole (Nizoral) and itraconazole (Sporanox). Caution should be used when combining selective aldosterone receptor antagonists with ACE inhibitors or ARBs.

Most patients with hypertension will require two or more agents to achieve their blood pressure goal. Initial combination therapy is suggested by JNC 7 for patients whose blood pressure is more than 20/10 mm Hg above their goal blood pressure.[3] Initial combination therapy should consist of a thiazide diuretic (in most cases) in combination with an ACE inhibitor or beta blocker.[3]

Hypertension and Diabetes

The prevalence of hypertension is about twice as high among patients diagnosed with type 2 diabetes as it is among persons without diabetes, and hypertension further contributes to the higher rate of cardiovascular mortality and renal failure that occurs in patients with diabetes.[31] The rate at which glomerular filtration decreases in patients with diabetic nephropathy is directly related to diastolic and, to a lesser degree, systolic blood pressure.[32]

Effective treatment of hypertension in patients with diabetes may reduce the cerebrovascular and cardiovascular complications more than tight control of hyperglycemia does.[33,34]

In addition, patients with coexistent hypertension and diabetes or chronic renal disease (creatinine level greater than 1.5 mg per dL [132.6 μmol per L] in men or greater than 1.3 mg per dL [114.9 μmol per L] in women) or the presence of albuminuria (greater than 300 mg per day or 200 mg albumin per g of creatinine) should be treated until they reach a target blood pressure of 130/80 mm Hg.[3]

Most patients with diabetes and hypertension require two or more medications to control hypertension.[35-37] An emerging consensus suggests that one of the two medications should be an ACE inhibitor or an ARB,[37,38] because the benefits of ACE inhibitors exceed those of blood pressure control alone in preventing cardiovascular disease[38] and because both ACE inhibitors and ARBs prevent the progression of renal disease.[39,40]

Hypertension in the Elderly

Hypertension becomes more prevalent with increasing age, most likely because of reduced arterial compliance. As many as 90 percent of normotensive elderly adults develop stage 1 hypertension.[41] Reducing blood pressure in older adults prevents stroke, MI, heart failure, and renal failure,[42] and drug therapy in elderly patients with hypertension has become a universal recommendation.[3] Lifestyle modifications, such as reduced salt intake, regular exercise, and controlling body weight, may not be effective in reducing complications of hypertension in elderly adults.[43]

Elderly patients with hypertension have a higher absolute risk of cardiovascular events than younger persons with hypertension and are more likely to have higher systolic blood pressure, a higher pulse pressure (increasingly recognized as an independent risk factor for cardiovascular events[44]), and isolated systolic hypertension. Both borderline (defined as systolic blood pressure of 140 to 159 mm Hg and diastolic blood pressure of up to 90 mm Hg) and true isolated systolic hypertension (systolic blood pressure of at least 160 mm Hg and diastolic blood pressure up to 90 mm Hg) have received more attention in the past decade after large European and North American trials consistently demonstrated the value of treating these conditions. JNC 7 recommends similar treatment for hypertension and isolated systolic hypertension for younger and older patients.[3]

Reduced rates (relative reductions) of complications are substantial, including stroke (30 percent), ischemic heart disease events (23 percent), all cardiovascular events (26 percent), and cardiovascular deaths (18 percent).[45] [Evidence level A, meta-analysis] Despite these reductions, undertreatment of isolated systolic hypertension has been called "the major problem for the lack of hypertension treatment and control in the United States today."[46]

If an elderly patient has no concomitant conditions for

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which an alternative medication might be helpful, diuretics are most effective and have the least expense and minimal side effects.[47] Other classes of drugs should be added and tailored for coexisting disease.[3,48] Patients with a history of MI or angina should start with beta-blocker and ACE-inhibitor therapy. Patients with chronic renal disease should start with an ACE inhibitor or ARB. Patients with diabetes should start with an ACE inhibitor, ARB, thiazide diuretic, or beta blocker. Nondihydropyridine CCBs may be chosen for use in patients with supraventricular tachyarrhythmia, angina, or heart failure from diastolic dysfunction. Recent evidence suggests that, compared with diuretics, ACE inhibitors produce better outcomes in elderly patients, especially in men.[49] However, it is difficult to directly compare these data with information from other trials such as ALLHAT.

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