

Antihypertensive drug therapy

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Lifestyle measures plus antihypertensive drug therapy should be used to treat adults with hypertension (1-4). Adults with clinical cardiovascular disease (coronary heart disease, heart failure, and stroke) should have their blood pressure reduced below 130/80 mmHg for secondary prevention of recurrent cardiovascular disease events (4). The blood pressure should be reduced below 130/80 mmHg for primary prevention of cardiovascular disease in adults with an estimated 10-year risk of atherosclerotic cardiovascular disease $\geq 10\%$ (4,5). The blood pressure should be reduced below 140/90 mmHg for primary prevention of cardiovascular disease in adults with an estimated 10-year risk of atherosclerotic cardiovascular disease less than 10% (4,5). Initiate antihypertensive drug treatment with 2 first-line drugs from different classes either as separate drugs or in a fixed-dose combination in adults with a blood pressure of $\geq 140/90$ mmHg or with a blood pressure $>20/10$ mmHg above their blood pressure target (4).

The first antihypertensive drug administered to white and other non-black adults younger than 60 years of age with primary hypertension, should be an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (4,6). The second drug should be a thiazide diuretic (preferably chlorthalidone) or a calcium channel blocker. If a third antihypertensive drug is needed to control the hypertension, an ACE inhibitor or angiotensin receptor blocker plus a thiazide diuretic plus a calcium channel blocker should be administered (4,6). The first antihypertensive drug administered to white and other non-black adults aged 60 years of age and older with primary hypertension should be a thiazide diuretic (preferably chlorthalidone) or a calcium channel blocker (4,6). If a third antihypertensive drug is needed to control the hypertension,

a thiazide diuretic plus a calcium channel blocker plus an ACE inhibitor or angiotensin receptor blocker should be administered (4,6). The first antihypertensive drug administered to adult blacks with primary hypertension should be a thiazide diuretic (preferably chlorthalidone) or a calcium channel blocker (4,6). If a third antihypertensive drug is needed to control the hypertension, a thiazide diuretic plus a calcium channel blocker plus an ACE inhibitor or angiotensin receptor blocker should be administered (4,6).

Adults with hypertension and stable coronary heart disease should be treated with a beta blocker plus an ACE inhibitor or angiotensin receptor blocker (1,3,4,7-14). If a third antihypertensive drug is needed to control the hypertension, a beta blocker plus an ACE inhibitor or angiotensin receptor blocker plus a thiazide diuretic or a calcium channel blocker should be administered. If a fourth antihypertensive drug is required to adequately control the hypertension, an aldosterone antagonist should be administered (4). In persons with stable ischemic heart disease who have angina pectoris despite beta blocker treatment and persistent uncontrolled hypertension, a dihydropyridine calcium channel blocker should be added (1,3,4,7,8,15). The beta blockers that should be administered for treatment of hypertension in patients with coronary heart disease include carvedilol, metoprolol tartrate, metoprolol succinate, bisoprolol, nadolol, propranolol, and timolol (4). Atenolol should not be used (1,3,4,9,16,17). The nondihydropyridine calcium channel blockers verapamil and diltiazem are contraindicated if left ventricular systolic dysfunction is present (1,3,4). Carvedilol, metoprolol succinate, or bisoprolol are the beta blockers to be administered if left ventricular systolic dysfunction is present (1,3,4,8,9).

If patients with an acute coronary syndrome have hypertension after therapy with a beta blocker plus an ACE inhibitor or angiotensin receptor blocker, a long-acting dihydropyridine calcium channel blocker such as amlodipine or felodipine should be added to the therapeutic regimen (1,3). Aldosterone antagonists should be administered to patients treated with beta blockers plus ACE inhibitors or angiotensin receptor blockers after myocardial infarction with left ventricular systolic dysfunction and heart failure or diabetes mellitus if their serum potassium is below 5.0 meq/L and if their serum creatinine is ≤ 2.5 mg/dL in men and ≤ 2.0 mg/dL in women (1,3,4,18).

Patients with hypertension and heart failure with a decreased left ventricular ejection fraction should be treated with carvedilol, metoprolol succinate, or bisoprolol plus an ACE inhibitor or angiotensin receptor blocker or preferably an angiotensin receptor-neprilysin inhibitor plus a diuretic and if needed with an aldosterone antagonist (1,3,4,9,18,19). Nondihydropyridine calcium channel blockers are contraindicated in persons with heart failure and a reduced left ventricular ejection fraction (1,3,4,19,20).

Patients with hypertension and heart failure with a preserved left ventricular ejection fraction should have their volume overload managed with diuretics, their comorbidities treated, and their hypertension treated with a beta blocker plus an ACE inhibitor or angiotensin blocker plus an aldosterone antagonist (3,4,19,21,22).

Hypertensive adults with chronic kidney disease stage 3 or higher or stage 1 or 2 chronic kidney disease with albuminuria 300 mg and more per day should be administered an ACE inhibitor to slow progression of their chronic kidney disease (4,23-26). If an ACE inhibitor is not tolerated, these patients should be administered an angiotensin receptor blocker (4). Patients who have stage 1 or 2 chronic kidney disease without albuminuria may be administered usual first-line antihypertensive drugs (4). If 3 antihypertensive drugs are needed, these patients should be given an ACE inhibitor or angiotensin receptor blocker plus a thiazide diuretic plus a calcium channel blocker. After kidney transplantation, hypertension should be treated with a calcium channel blocker to improve glomerular filtration rate and kidney survival (4,27).

Hypertensive patients with a prior stroke or transient ischemic attack should be administered a thiazide diuretic or ACE inhibitor or angiotensin receptor blocker (4,28,29). If a third antihypertensive drug is needed, these patients should be given a thiazide diuretic plus an ACE inhibitor or angiotensin receptor blocker plus a calcium channel blocker.

Hypertensive patients with peripheral arterial disease should receive usual first-line antihypertensive drugs (4,30). There are no data showing that any one class of antihypertensive drugs is superior for treating hypertension in patients with peripheral arterial disease (4,30).

Thiazide diuretics, ACE inhibitors, angiotensin receptor blockers, and calcium channel blockers may be used as initial therapy in hypertensive diabetics (4,31-33). ACE inhibitors or angiotensin receptor blockers should be administered to hypertensive diabetics with persistent albuminuria (4,34). The ALLHAT study found that chlorthalidone was better than lisinopril, amlodipine, and doxazosin in reducing cardiovascular disease and renal outcomes in nondiabetics with hypertension and the metabolic syndrome (4,35).

Beta blockers are the preferred antihypertensive drugs in hypertensive patients with a thoracic aortic aneurysm (4,36). Beta blockers also improve survival in patients with type A and with type B acute and chronic thoracic aortic dissection (4,37,38). If thoracic aorta dissection develops, beta blockers are the initial drug of choice for decreasing blood pressure, ventricular rate, dP/dt, and stress on the aorta (36,39). Systolic blood pressure should be reduced to 100 to 120 mmHg and the ventricular rate decreased to lower than 60 beats/minute by intravenous propranolol, metoprolol, labetalol, or esmolol (36).

Pregnant women with hypertension should not be administered an ACE inhibitor, angiotensin receptor blocker, direct renin inhibitor, or atenolol because these drugs are fetotoxic (4,40,41). Pregnant women with hypertension should be treated with methyldopa, nifedipine, and/or labetalol (4,40,41).

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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