

Continuing Education for Pharmacists

Volume XXIV, No. 6

Management of Hypertension: Lifestyle Modifications and Drug Therapy

Thomas A. Gossel, R.Ph., Ph.D.
Professor Emeritus
Ohio Northern University
Ada, Ohio

and

**J. Richard Wuest, R.Ph.,
Pharm.D.**
Professor Emeritus
University of Cincinnati
Cincinnati, Ohio

Goals. The goals of this lesson are to define hypertension, and discuss current management guidelines and reasons for non-compliance.

Objectives. At the conclusion of this lesson, successful participants should be able to:

1. define hypertension and its prevalence;
2. list lifestyle modifications to reduce the risk of onset and maximize reduction of elevated blood pressure;
3. recognize appropriate drug therapy and monitoring parameters; and

This continuing education activity is supported by an educational grant from GlaxoSmithKline.



Gossel



Wuest

4. identify barriers to patient adherence and reasons for non-compliance.

Hypertension is the most common primary diagnosis in America. Approximately 50 million individuals in the United States (i.e., one in four adults) and one billion worldwide have elevated arterial pressures. Prevalence will increase further as the population ages unless widespread, effective preventive measures are implemented. At present, individuals with normal blood pressure at age 55 have a 90 percent lifetime risk for developing hypertension.

Hypertension is asymptomatic, readily detectable, and oftentimes manageable. Less than one-third of patients with hypertension, however, actually achieve optimal blood pressure control because of their non-adherence to lifestyle modification and/or drug therapy. Based on the National Health and Nutrition Examination Survey, the elderly have the poorest rates of achieving blood pressure control. This is especially problematic since high blood pressure can lead to other medical complications and may be fatal if not treated.

This lesson discusses current guidelines for therapy of hypertension based on the Seventh Report of the Joint National Committee on

Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7). It also lists barriers to patient adherence to lifestyle modifications and therapy.

Classification of Blood Pressure and Health Benefits of Reducing It

Table 1 summarizes blood pressure values for the normal state and various levels of pathology for persons 18 years and older, according to JNC 7. Classification is based on the average of two or more blood pressure readings, for each of two or more physician office visits. New to the current classification is a category designated *prehypertension*. Persons with prehypertension have an increased risk for advancement to clinical hypertension. Moreover, Stage 3 hypertension, from the previous classification system, has been combined with Stage 2 in the current classification. Individuals with blood pressure 130-139/80-89 mmHg are at twice the risk of developing hypertension as those with lower pressures.

The correlation between blood pressure and risk of adverse cardiovascular events continues throughout life. The higher the pressure, the greater the risk for developing heart failure, myocardial infarction (MI), stroke, and kidney disease. For individuals 40 to 70 years of age, each 20 mmHg increase in systolic or 10 mmHg in diastolic blood pressure doubles the risk of adverse cardiovascular events across the blood pressure range from 115/75 to 185/115 mmHg. The classification *prehypertension* acknowledges this correlation, thereby affirming the need for increased patient education by all members of the health care team.

Table 1
Classification of Blood Pressure for Adults ≥ 18 Years of Age*

Blood Pressure**	Systolic Pressure	Diastolic Pressure
Normal	<120 mmHg	and <80 mmHg
Prehypertension	120-139 mmHg	or 80-89 mmHg
Stage 1 hypertension	140-159 mmHg	or 90-99 mmHg
Stage 2 hypertension	≥ 160 mmHg	or ≥ 100 mmHg

*The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7)

**When systolic and diastolic pressures fall into different categories, the higher category should be selected to classify the individual's blood pressure status.

Antihypertensive drug therapy (Table 2) has been demonstrated to reduce the incidence of MI by 20 to 25 percent, heart failure by >50 percent, and stroke by 35 to 40 percent. In patients with Stage 1 hypertension along with additional cardiovascular risk factors, blood pressure lowering of 12 mmHg systolic sustained over 10 years will prevent one death for every 11 patients treated.

Systolic Versus Diastolic Blood Pressures

Systolic blood pressure normally increases with age until the eighth or ninth decade of life. Diastolic pressure, in contrast, increases only until middle age and then either levels off or decreases slightly. The Framingham Heart Study showed that there was a gradual shift from diastolic to systolic blood pressure with increasing age as a predictor of cardiovascular risk. Diastolic pressure was a stronger predictor in patients <50 years of age; age 50 to 59 years was a transition period when both systolic and diastolic pressures were comparable predictors. From 60 years and over, however, coronary heart disease risk correlated positively with systolic pressure, more so than with diastolic pressure. Other studies have confirmed the greater reliability of systolic pressure over diastolic pressure as a predictor of cardiovascular morbidity and mortality.

Effective blood pressure control can be achieved in many hypertensive patients, but most will require two or more antihypertensive drugs to bring them to goal. Effective

control requires adequate drug doses, appropriate drug combinations, and lifestyle modifications if blood pressure treatment goals are to be met.

Goals of Therapy

The ultimate goal of therapy is to reduce cardiovascular and renal morbidity and mortality. Most persons with hypertension, especially those ≥ 50 years of age, will reach diastolic pressure goals once systolic pressure is under control. Therefore, the primary day-by-day goal is to achieve the systolic pressure goal. Treating systolic pressure and diastolic pressure to targets suggested in Table 1 will result in fewer cardiovascular complications.

Lifestyle Modifications

The adoption of healthy lifestyles is critical for all persons in order to reduce the risk for onset of hypertension, as well as to maximize reduction of elevated pressure. Major lifestyle modifications known to lower blood pressure are summarized in Table 3. Lifestyle modifications lower blood pressure, enhance antihypertensive drug efficacy, and decrease the risk for adverse cardiovascular events. These include dietary restrictions with weight reduction in persons who are overweight or obese, cessation of smoking, moderation in alcohol consumption, and programmed physical activity. Restricting sodium intake to 1,600 mg/day or less, for example, is equivalent to single antihypertensive drug therapy. Combining two (or more)

Table 2
Antihypertensive Drug Classification*

Diuretics

- Thiazides (hydrochlorothiazide, etc.)
- Loop diuretics (furosemide, etc.)
- K⁺-sparing diuretics (spironolactone, etc.)

Sympatholytics

- Beta-blockers (metoprolol, etc.)
- Alpha-blockers (doxazosin, etc.)
- Mixed adrenergic blockers (carvedilol, etc.)
- Centrally acting agents (methyldopa, etc.)
- Adrenergic neuron blocking agents (guanadrel, etc.)

Calcium Channel Blockers (nifedipine, etc.)

Angiotensin Converting Enzyme Inhibitors (lisinopril, etc.)

Angiotensin-II Receptor Antagonists (losartan, etc.)

Vasodilators

- Arterial (hydralazine, etc.)
- Arterial & venous (nitroprusside)

**The Pharmacological Basis of Therapeutics, 11th edition*

lifestyle modifications can achieve even better results.

Approach to Drug Therapy

The aim of therapy is to use antihypertensive drugs, alone or in combination, to return arterial pressure to target levels with minimal adverse effects. Ideally, the drug would correct the underlying defect that causes the elevated pressure (e.g., use of spironolactone to treat primary aldosteronism). As knowledge of the underlying mechanisms in hypertension increases, specific drug programs to achieve this goal will be made available. Such programs presumably will result in normalization of blood pressure with fewer adverse effects. Meanwhile, an empirical approach to treatment is used, which takes into consideration efficacy, safety, impact on quality of life issues, compliance, ease of use, and economics. Most hypertensive patients will require multiple drugs to reach goal pressure. Drugs used in combination should be chosen from different classes.

Table 3
Lifestyle Modifications to Manage Hypertension*

Modification	Recommendation	Approximate SBP Reduction (Range)
Weight reduction	maintain normal body weight (body mass index 18.5-24.9 kg/m ²)	5-20 mmHg/10kg weight loss
DASH [†] eating plan	consume a diet rich in fruits, vegetables, and low fat dietary products with a reduced content of saturated and total fat	8-14 mmHg
Dietary sodium reduction	reduce dietary sodium intake to no more than 2.4 g Na or 6 g NaCl	2-8 mmHg
Physical activity	engage in regular aerobic physical activity such as brisk walking, at least 30 min/day, 5 to 6 days a week	4-9 mmHg
Moderation of alcohol consumption	limit consumption to no more than 2 drinks/day [‡] in men, and 1 drink/day in women and persons of lighter weight	2-4 mmHg

*The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7). For overall cardiovascular risk reductions, stop smoking. Effects of implementing these modifications are dose and time dependent, and could be greater for some individuals.

[†]DASH, Dietary Approaches to Stop Hypertension

[‡]Two drinks = 1 oz or 30 mL ethanol; e.g., 24 oz beer, 10 oz wine, or 3 oz 80-proof whiskey

If low doses of two drugs do not achieve blood pressure control, the primary agent should be increased to full dose. If the goal pressure is still not attained, a search for a secondary cause of hypertension is indicated. If none is found, a detailed assessment of dietary habits may reveal an aggravating inciter, e.g., excessive sodium intake. In this case, if dietary modification with reduced sodium intake fails to lower the pressure, a third agent should be added.

If with addition of a third agent the pressure is controlled, a stepwise reduction in the dose and/or withdrawal of one or both of the previous drugs may be undertaken to determine the minimal drugs and doses to maintain blood pressure at goal values. More than 95 percent of patients should be adequately controlled at this point. For failures, a reason for the

therapeutic failure (Table 4) should be sought. If none can be identified, an additional agent(s) should be added. When blood pressure is controlled, previous drugs may be withdrawn sequentially to determine the minimum number that will maintain a normal blood pressure.

Pharmacologic Treatment

If non-drug treatment is ineffective in reducing blood pressure, the choice of drug therapy is determined by its efficacy and safety. When efficacy and safety are equal, choice of pharmacotherapy should ideally be based on drugs with the lowest cost. JNC 7 recommends drug therapy at $\geq 140/90$ mmHg for otherwise healthy patients and $\geq 130/80$ mmHg for patients with heart and kidney disease or diabetes mellitus.

Thiazide diuretics have been the mainstay of antihypertensive

therapy in most clinical trials to date. In these trials, including the landmark Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), diuretics have been unsurpassed in preventing onset of the adverse cardiovascular events associated with hypertension. Diuretics enhance the antihypertensive efficacy of multidrug regimens and are more affordable than many other antihypertensive agents. Their use today, in controlling hypertension is, however, underutilized.

Thiazide diuretics should be used as initial therapy for most patients with hypertension, either alone or in combination with one of the other antihypertensive drug classes. Table 5 lists specific indications that require use of alternative antihypertensive drugs as initial therapy due to the alternative drugs' demonstrated efficacy in those conditions. If a drug's adverse effects are excessive or a drug is contraindicated, one of the agents from an alternative class that is proven to reduce adverse cardiovascular events should be used instead.

As noted earlier, most hypertensive patients will require multiple antihypertensive medications to achieve their blood pressure goal. Blood pressure that is more than 20/10 mmHg above goal may be treated initially with two drugs, either as separate prescriptions or in fixed-dose combinations. Initiation of therapy with multiple drugs may increase the likelihood of achieving the goal pressure in a more timely fashion, but puts the patient at increased risk for adverse effects.

Follow-up

After antihypertensive drug therapy is initiated, follow-up with medication(s) adjustment is indicated for most patients at monthly intervals until the pressure goal is reached. Patients with Stage 2 hypertension and those with comorbid conditions should be evaluated more frequently until reduced pressures are stabilized.

Table 4
Reasons for Poor Therapeutic Response in Patients with Hypertension*

- Inadequate patient compliance
- Volume expansion, caused by
 - excessive sodium
 - nondiuretic antihypertensive drug
 - renal damage
- Excessive weight gain
- Inadequate doses
- Drug antagonism
- Sympathomimetic drugs (e.g., cold remedies)
- Oral contraceptives (estrogens)
- Adrenal steroids
- Secondary forms of hypertension

*Principles of Internal Medicine, 16th edition

Serum potassium and creatinine should be monitored one to two times a year. When blood pressure reaches goal and is stable, follow-up visits at three- to six-month intervals should be adequate. Comorbidities increase the need for more frequent visits. Other cardiovascular risk factors should be treated to their respective goals, and smoking cessation should be vigorously promoted. Low-dose aspirin therapy can be considered, but only after blood pressure has been controlled, since aspirin increases the risk of hemorrhagic stroke in persons with uncontrolled hypertension.

Patient Adherence with Antihypertensive Drug Therapy

The most effective therapy will control hypertension only if the patient is motivated to comply with the physician's instructions including maintaining a healthy lifestyle. In studies of elderly hypertensive patients designed to assess adherence with antihypertensive drug therapy, the average patient failed to refill prescriptions more than 50 percent of the time. Moreover, only one patient in five exhibited compliance with physicians' instructions sufficient to achieve therapeutic benefit. Adherence decreased even more with multiple drug regimens and treatment periods extending

Table 5
Compelling Indications for Individual Drug Classes*

Compelling Indication [‡]	Recommended Drugs [†]					
	DIU	BAB	ACE	ARB	CCB	ANT
Heart failure	X	X	X	X		X
Postmyocardial infarction		X	X			X
High coronary disease risk	X	X	X		X	
Diabetes	X	X	X	X	X	
Chronic kidney disease			X	X		
Recurrent stroke prevention	X		X			

*The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7).

[†]DIU = diuretic; BAB = beta-adrenergic blocker; ACE = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker; CCB = calcium channel blocker; ANT = aldosterone antagonist

[‡]Compelling indications for antihypertensive drugs are based on benefits from outcome studies or existing clinical guidelines; the compelling indication is managed in parallel with the blood pressure.

beyond one year. Reasons why patients fail to comply with therapy include:

- increased misunderstanding of the condition or treatment;
- denial of illness due to lack of symptoms or perception of drugs as symbols of ill health;
- lack of patient involvement in the care plan;
- unexpected adverse effects of medications;
- cost of medications;
- complexity of care (i.e., transportation, patient difficulty with polypharmacy, difficulty in scheduling appointments, etc.); and
- life's competing demands.

Pharmacists need to be aware of opportunities for patient interventions, e.g., when patients seek OTC products that may interfere with blood pressure control. The pharmacist can encourage hypertensive patients to avoid adding any new OTC product(s) without first discussing it with their physician or pharmacist. For example, non-steroidal anti-inflammatory drugs (NSAIDs) can cause salt retention or drug interactions. Thiazide diuretics, beta-blockers, ACE inhibitors, and alpha-blockers are less effective in some patients who use NSAIDs. Decongestants may elevate blood pressure.

Summary

Tight control of blood pressure at normal values is important to reduce the risk of adverse cardiovascular events. While control of blood pressure is often achieved with currently available antihypertensive therapies, too many patients fail to maintain lowered pressures. A major contributing reason is non-adherence with instructions.

JNC 7 guidelines indicate that the most effective therapy prescribed will control hypertension only if patients are motivated to follow instructions. Positive experiences with and trust in their health professionals have shown to improve patient motivation.