The Pathophysiology and Pharmaceutical Treatment of Hypertension

Release Date: 12/30/2011
Expiration Date: 12/30/2013

FACULTY:
J Dufton, MD

FACULTY AND ACCREDITOR DISCLOSURE STATEMENTS:

Mr. Dufton has no actual or potential conflict of interest in relation to this program.

ACCREDITATION STATEMENT:

Pharmacy
PharmCon Inc is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.
Program No.: 0798-0000-11-103-H01-P
Credits: 2 contact hour, 0.2 CEU

Nursing
Pharmaceutical Education Consultants, Inc. has been approved as a provider of continuing education for nurses by the Maryland Nurses Association which is accredited as an approver of continuing education in nursing by the American Nurses Credentialing Center's Commission on Accreditation.
Program No.: N-720
Credits: 2 contact hour, 0.2 CEU
TARGET AUDIENCE:

This accredited program is targeted nurses and pharmacists practicing in hospital and community pharmacies. Estimated time to complete this monograph and posttest is 120 minutes.

DISCLAIMER:

PharmCon, Inc does not view the existence of relationships as an implication of bias or that the value of the material is decreased. The content of the activity was planned to be balanced and objective. Occasionally, authors may express opinions that represent their own viewpoint. Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and their own professional development. The information presented in this activity is not meant to serve as a guideline for patient or pharmacy management. Conclusions drawn by participants should be derived from objective analysis of scientific data presented from this monograph and other unrelated sources.

Program Overview:

To provide nurses and pharmacists with an understanding of the prevalence and incidence of hypertension, its pathophysiology, primary symptoms and main risk factors, and be able to identify the most commonly used pharmaceuticals and their potential side effects.

OBJECTIVES:

After completing this program, participants will be able to:

- Understand the prevalence and incidence of hypertension
- Understand the pathophysiology, primary symptoms and main risk factors of hypertension
- Identify the most commonly used pharmaceuticals and their potential side effects
Pathophysiology

Hypertension, or high blood pressure, is a chronic and often asymptomatic medical condition in which systemic arterial blood pressure is elevated beyond normal. As such, the heart is forced to work harder to overcome the increased systemic pressure in order to deliver blood to tissues, which puts strain on the heart and arteries. Over time, the additional strain leads to cardiovascular dysfunction and is a primary contributing cause of potentially deadly sequelae such as congestive heart failure, myocardial infarction, pulmonary embolism, cerebral aneurysm and kidney failure.1

Abnormally high blood pressure is generally divided into two main categories: essential hypertension and secondary hypertension. Essential or primary hypertension is the most prevalent type, affecting between 90-95 percent of patients diagnosed with hypertension.2 The cause of essential hypertension has not been directly identified, but its pathophysiology is assumed to be multifactorial. Many causal factors have been linked to essential hypertension including a sedentary lifestyle, tobacco smoking, excessive stress, visceral obesity, hypokalemia (potassium deficiency), high sodium intake and other poor dietary habits, sodium sensitivity, alcohol consumption, vitamin D deficiency, and obesity.3,4,5 In fact, more than 85 percent of patients diagnosed with essential hypertension have a body mass index (BMI) greater than 25.6 Increased risk of essential hypertension has been associated with advancing age, inherited genetic mutations, family history of hypertension, low birth weight, insulin resistance, elevated levels of renin (a kidney hormone), and sympathetic nervous system over-activity.7,8 The sympathetic nervous system is responsible for the “flight or fight” response, which causes vasoconstriction of certain arteries and the release of adrenalin and other hormones and neurotransmitters. Chronic stress / anxiety, over-consumption of caffeine, kidney disease, and cerebral and glandular tumors all contribute to sympathetic overstimulation.

Essential hypertension can be further subcategorized as stage I or stage II (depending on progression and symptomatology), isolated systolic hypertension (where diastolic readings are considered normal), or as medication resistant hypertension if pharmaceutical intervention does not make a significant impact on blood pressure readings. Exercise-related hypertension is defined as excessively high blood pressure during intense exercise, although the normal range of systolic pressures during exercise is between 200 and 230 mmHg.9 Those people who exhibit exercise-related hypertension may be at risk of developing essential hypertension while at rest.

The remaining 5-10 percent of hypertension cases are classified as secondary hypertension. Secondary hypertension results from an identifiable cause, usually a disease that affects hormone synthesis and excretion. Secondary hypertension is approached differently than essential hypertension, in that the underlying cause of the elevated blood pressure is treated and managed. In contrast, essential hypertension is treated directly with medications that affect vasoconstriction of arteries and with lifestyle modifications. Secondary hypertension often results as a consequence of a compromise or imbalance of the hormone-dependent endocrine system, which is responsible for regulating blood volume and heart function. Common disease conditions that lead to secondary hypertension include atherosclerosis, diabetes, kidney disease, adrenal gland tumors, Cushing's syndrome, hyperthyroidism, hypothyroidism, obesity, metabolic disorders, preeclampsia during pregnancy, sleep apnea, congenital defects of the aorta and heart, alcoholism, and toxicity from prescribed and illicit drugs, especially cocaine and methamphetamines.10

While the causes of secondary hypertension are generally well understood and involve proven therapeutic protocols, the causes of essential hypertension are far less understood. What has been observed with essential hypertension is that cardiac output increases early in the disease course while total peripheral vascular resistance remains normal. But as time progresses, cardiac output drops to normal levels and
peripheral resistance increases. The three theories proposed to explain this phenomenon include: 1) the kidneys are unable to properly excrete sodium, which results in natriuretic factors (such as Atrial Natriuretic Factor) being over-secreted to promote salt excretion, leading to increased peripheral resistance as a side effect; 2) an overactive renin-angiotensin system leads to vasoconstriction and retention of excessive sodium and water, which increases blood volume and leads to hypertension; and 3) an overactive sympathetic nervous system, due to a variety of factors mentioned above, leads to increased stress responses that involve excessive secretion of hormones that affect blood vessel diameter and blood pressure. In addition to these theories and postulated mechanisms, it is recognized that essential hypertension appears to be highly heritable and a few candidate genes have already been postulated for its etiology.

More recently, the association between essential hypertension and arterial endothelial damage has gained popularity among scientists and researchers. A large body of evidence indicates that patients with essential hypertension are characterized by endothelial dysfunction mediated by impaired nitric oxide availability secondary to oxidative stress production. Nitric oxide is essential for vasodilation, which reduces systemic blood pressure, and free radicals from oxidation are very damaging to the endothelium of the inner lumen of blood vessels. Decreased levels of nitric oxide combined with increased production of vasoconstrictors like angiotensin-II creates an environment that allows the development of atherosclerosis. Damaged and poorly functioning endothelium is an early marker in the development of atherosclerosis, which is characterized by lipid deposition, inflammation, fibrosis and the formation of fibrolipid plaques. As the plaques grow in size, arterial lumen diameter decreases, which eventually increases systemic blood pressure.

Vascular reactivity tests represent the most widely used methods in the clinical assessment of the endothelial function of arteries. Several methodologies have been developed to study microcirculation (resistance arteries and arterioles) and macrocirculation (conduit arteries), both in coronary and peripheral regions. Endothelial dysfunction in the coronary and peripheral circulation of hypertensive patients is associated with organ damage, and it is predictive of cardiovascular events. Some antihypertensive drugs can improve endothelial dysfunction, especially calcium channel antagonists in the microcirculation, and ACE-inhibitors and AT1-receptor antagonists in conduit arteries. Some beneficial effects on endothelium are also seen with the use of nebivolol and various statin-type drugs. Future studies are needed to confirm whether the improvement in endothelial dysfunction is associated with better cardiovascular prognosis in hypertension. Further, it still remains somewhat unclear if endothelial changes precede the development of hypertension or whether such changes are mainly due to chronically elevated blood pressure.

**Diagnosing Hypertension**

Blood pressure is classified based on the combined systolic and diastolic pressures of the vascular system. Systolic blood pressure is the pressure in arterial vessels during a heartbeat. Diastolic blood pressure is the pressure in the arterial vessels between heartbeats. Consistent and repeated systolic or diastolic blood pressure measurements higher than the accepted normal values for age and gender are classified as either prehypertension or hypertension. Normal blood pressure is generally thought to be 120/80 mmHg or slightly lower for most individuals (particularly younger adults), where the first number represents systolic pressure and the later diastolic pressure. According to the vast majority of medical sources, abnormally high blood pressure is anything consistently measured above 140/90 mmHg during restful states, although the age of the patient must also be considered. Consequently, prehypertension is usually defined as being measured between 120-139 / 80-89, whereas clinically significant hypertension is often defined as readings greater than 140/90.
Gender differences exist for blood pressure. Studies using 24-hour ambulatory blood pressure monitoring have shown that blood pressure is higher in men than in women of the same race at similar ages. After menopause, however, blood pressure increases in women to levels even higher than in men. Further, hormone replacement therapy in most cases does not significantly reduce blood pressure in postmenopausal women, suggesting that the loss of estrogens may not be the only component involved in the higher blood pressure in women after menopause. In contrast, androgens may decrease only slightly, if at all, in postmenopausal women. As such, it may be the androgens that increase blood pressure by impacting the renin-angiotensin system, which promotes oxidative stress and leads to the production of vasoconstrictor substances and the reduction of available nitric oxide.

Age differences in blood pressure also exist. In general, blood pressure increases with age for both genders, so the minimum and maximum systolic and diastolic values considered normal and healthy also change with age. For example, according to the medical literature, a healthy 25-year-old should have a systolic blood pressure near 122 mmHg (with a minimum of 108 mmHg and a maximum of 133 mmHg) and an average diastolic pressure near 80 mmHg (with a minimum of 76 mmHg and a maximum of 84 mmHg). In contrast, a 55-year-old is considered healthy if their average systolic pressure is 136 mmHg (with a minimum of 117 mmHg and a maximum of 146 mmHg) and their average diastolic pressure is 86 mmHg (with a minimum of 82 mmHg and a maximum of 90 mmHg). This can be confusing for doctors and patients alike because terms like “average” and “normal” may not always mean healthy for certain individuals. Additionally, it is not clearly understood if mildly increased blood pressure with age is always a sign of disease that should be combated with medication, or if it is a healthy adaptive response that is beneficial overall. As such, diagnosis of hypertension often entails multiple visits to the physician's office and should include a complete history, lifestyle assessment, and physical examination.

Hypertension is diagnosed on the basis of persistently high blood pressure readings taken by a physician or qualified medical personnel. Usually this requires at least three separate sphygmomanometer measurements at least one week apart; although, if the elevation is extreme (≥180/110 mmHg or ≥130 mmHg diastolic pressure) or if symptoms of organ damage are present, then a diagnosis may be made and treatment started immediately. Organ damage from severe hypertension involves cerebrovascular disease, hypertensive retinopathy, coronary artery disease, kidney disease and peripheral vascular issues. Patients with diabetes mellitus or chronic kidney disease (glomerular filtration rate less than 60 mL/min) are often diagnosed with hypertension immediately if systolic pressure is 140 mmHg or higher and/or if their diastolic pressure is 90 mmHg or higher.

The diagnosis of hypertension can be further qualified as mild, moderate, or severe depending on the average pressures of multiple readings. Mild hypertension is usually defined as systolic blood pressure between 140 and 160 mmHg and diastolic pressure between 90 and 100 mmHg. Moderate hypertension is usually defined as systolic blood pressure between 160 and 200 mmHg and diastolic pressure between 100 and 120 mmHg. Severe hypertension is usually defined as systolic blood pressure above 200 mmHg and diastolic pressure greater above 120 mmHg.

Once the diagnosis of hypertension is made, physicians will attempt to identify the underlying cause based on risk factors and other symptoms. Secondary hypertension is more common in preadolescent children (and often caused by renal disease), whereas essential hypertension is much more common in adolescents and adults. Laboratory tests can also be performed to identify possible causes of secondary hypertension, and to determine whether hypertension has caused damage to the heart, eyes and kidneys. Additional tests for diabetes and high cholesterol levels are usually performed because they are additional risk factors for hypertension and the development of heart disease. Common tests include urinalysis, creatinine testing, blood chemistry, serum TSH (thyroid-stimulating hormone), fasting blood glucose, total cholesterol, HDL and LDL cholesterol, triglycerides, electrocardiogram, and chest radiographs.
Measuring Blood Pressure

Blood pressure measurements should be taken with a sphygmomanometer (blood pressure cuff) known to be accurate or a recently calibrated electronic device. The cuff should be placed so that the lower edge is about 1.5 inches above the elbow crease with the bladder centered over the brachial artery. The patient should be resting comfortably for at least 5 minutes in the seated position with appropriate back support. The arm should be bare and supported with the blood pressure cuff at heart level, because a lower position will result in erroneously high systolic and diastolic blood pressures.18 The patient should not talk, and his or her legs should not be crossed. At least three measurements should be taken in the same arm with the patient in the same position. The first reading should be discarded and the latter two averaged. Blood pressure also should be assessed after 2 minutes of standing (with arm supported) and at times when patients report symptoms suggestive of postural hypotension. Blood pressure measurements taken in the supine position may also be helpful in the assessment of elderly and diabetic patients.

When inflating the cuff, the pressure should be increased rapidly to 30 mmHg above the level at which the radial pulse is extinguished. The diaphragm of the stethoscope should be positioned gently and steadily over the brachial artery at the elbow. The control valve near the pump should be opened so that the rate of deflation of the cuff is approximately 2 mmHg per heartbeat. A cuff deflation rate of 2 mmHg per beat is necessary for accurate systolic and diastolic estimation. The first appearance of a clear tapping sound (phase I Korotkoff) represents the systolic pressure, while the diastolic pressure is the point at which the tapping sound disappears (phase V Korotkoff). In the case of arrhythmia, additional readings may be required to estimate the average systolic and diastolic pressure. Leaving the cuff partially inflated for too long will congest the venous system and make sounds difficult to hear. To avoid venous congestion, it is recommended that at least 1 minute should elapse between readings. Blood pressure should be taken in both arms on at least one visit, and if one arm has a consistently higher pressure, that arm should be subsequently used for blood pressure measurement and interpretation.

Signs and Symptoms

It is important to note that mild-to-moderate essential hypertension is usually asymptomatic, which is why it is sometimes called the “silent killer.” Accelerated and severe hypertension is associated with signs and symptoms that include headache, drowsiness, confusion, blurred vision, nausea and vomiting. These symptoms are collectively called hypertensive encephalopathy, which is caused by reversible small blood vessel congestion and brain swelling.17 Some additional hormone-related signs that suggest hypertension is likely include abdominal obesity, fat accumulation on the upper thoracic spine (“buffalo hump”) and wide purple scars on the abdomen known as striae. A hormone disorder known as Cushing’s syndrome is also highly correlated with hypertension. Other causes of secondary hypertension are accompanied by additional symptoms specific to these diseases. For example, hyperthyroidism causes hypertension, but also weight loss, tremors, heart rate abnormalities and increased sweating.

Hypertension during pregnancy is one symptom of preeclampsia. Preeclampsia can progress to a life-threatening condition called eclampsia, which is the development of protein in the urine, generalized swelling and severe seizures. Eclampsia occurs when substances from the placenta cause endothelial dysfunction in the maternal blood vessels of susceptible women. Kidney and liver damage can ensue, which causes the release of vasoconstrictive factors in the blood and increased blood pressure. However, a slight increase in blood pressure is often considered normal during the later stages of pregnancy because cardiac output and blood volume is increased to provide sufficient circulation in the utero-placental arterial bed.20
Severe, uncontrolled hypertension eventually leads to tissue and organ damage as noted above. Specific symptoms of organ damage includes ischemic stroke and paralysis, intracerebral hemorrhage and CNS insult, subarachnoid hemorrhage, vascular dementia, retinopathy, left ventricular dysfunction, myocardial infarction, angina pectoris, congestive heart failure, renal failure, albuminuria, and intermittent claudication.\(^{17}\)

**Prevalence and Incidence**

In the year 2000 it was estimated that about 26 percent of the adult population had hypertension worldwide.\(^{21}\) Hypertension is common in both developed and undeveloped countries, although incidence rates vary markedly in different regions with rates as low as 3.4 percent for men and 6.8 percent for women in rural India to as high as 68.9 percent for men and 72.5 percent for women in Poland.\(^{22}\) In 1995 it was estimated that almost 24 percent of American adults had hypertension or were taking antihypertensive medication, although by 2004 that figure had risen to 29 percent.\(^{23}\) Rates of hypertension are similar in Canada, with an estimated 27 percent of Canadians between the ages of 35 and 64 years living with the condition.\(^{18}\)

In the U.S., hypertension is more common in African Americans and Native Americans and less in Caucasians and Mexican Americans.\(^2\) Incidence rates of hypertension are greatest in the southeastern region of the U.S., and they increase with age, as noted above. Hypertension is more prevalent in men (though menopause tends to decrease this difference) and those of low socioeconomic status, which is often directly related to dietary habits. Between 90 and 95 percent of adult hypertension is diagnosed as essential hypertension, with the other 5-10 percent divided between secondary and exercise-related hypertension.\(^9\)

In children, including American and other nationalities, the prevalence of high blood pressure is increasing.\(^{24}\) Most childhood hypertension (especially preadolescents) is secondary to an underlying disorder, with kidney disease being the most common primary cause. Adolescents usually have essential or exercise-related hypertension, which accounts for 85–95 percent of cases.\(^{25}\)

The World Health Organization attributes hypertension as the leading cause of cardiovascular mortality, which takes a huge financial toll on government health care programs and economic production. In 2002, the National Heart, Lung, and Blood Institute estimated that hypertension cost the U.S. $47.2 billion.\(^{26}\) Hypertension is the most common chronic medical problem prompting visits to primary health care providers, although only 34 percent of Americans diagnosed with hypertension have their blood pressure at or below 140/90 mmHg.\(^{27}\) Moderately elevated arterial blood pressure leads to shortened life expectancy because it increases rates of atherosclerosis, heart disease, peripheral vascular disease, and strokes. Thus, lowering blood pressure significantly reduces the risk of death due to cardiovascular complications, the development of other debilitating conditions, and the cost associated with advanced medical care.\(^{27}\) Dietary and lifestyle changes can control blood pressure and decrease the risk of associated health complications, although drug treatment may prove necessary in patients for whom lifestyle changes prove ineffective or insufficient.

**Prevention**

The degree to which hypertension can be prevented depends on a number of features including base-line blood pressure, sodium/potassium balance, sodium sensitivity, detection and removal of environmental toxins, health status of target organs, the number of risk factors for cardiovascular disease, and age.\(^{20}\) Ideally, the patient is alerted to the risk of developing hypertension by a physician who provides a thorough assessment and takes multiple blood pressure readings over at least three separate visits,
Dietary modification is an important lifestyle change that can help prevent the development of hypertension or potentially combat and reduce high blood pressure. Lowering sodium intake (especially from table salt) reduces excessive water retention, which helps maintain normal blood pressure.\(^28\) Further, sodium chloride in table salt is toxic and damaging to arteries and other tissues in large amounts, which may initiate atherosclerosis and lead to hypertension secondarily. Adopting a high potassium diet helps rid the renal system of excess sodium and restore sodium/potassium balance. Additional dietary changes beneficial to reducing blood pressure include adopting the DASH diet (which is rich in fruits, vegetables, fish, whole grains and low-fat dairy products), reducing consumption of refined sugar and heavily processed food, reducing caffeine intake, and limiting alcohol consumption.\(^29\) In fact, simply limiting alcohol intake to less than 2 standard drinks per day can reduce systolic blood pressure by between 2 and 4 mmHg.

Other strategies that are effective at reducing blood pressure include weight reduction and regular aerobic exercise such as walking. Weight loss reduces the resistance burden on the vascular system, and regular exercise improves blood flow and helps to reduce resting heart rate and blood pressure. Discontinuing tobacco use has also shown to lower blood pressure, which is related to its nicotine content as well as various toxins. Abstaining from cigarette smoking reduces the risks of stroke and heart attack associated with hypertension. Stress reduction from practicing meditation, yoga, biofeedback, paced breathing, and other mind-body relaxation techniques can also lower blood pressure.\(^30\)

**Natural Remedies**

There are a number of natural remedies that can make a positive impact on high blood pressure as well. Niacin (vitamin B3) affects receptors on smooth muscle cells primarily in small arteries directly underneath the skin, which leads to vasodilation and harmless “flushing” of the skin. Niacin’s immediate effect on systemic blood pressure is only slight, but long-term use may safely lower blood pressure by 10-15 percent.\(^31\) Niacin also impacts lipid metabolism and reduces cholesterol and triglycerides in the blood, which reduces the risk of atherosclerosis. Atherosclerosis is a major cause of secondary hypertension. Niacin can make the effects of blood pressure medications stronger, leading to the risk of hypotension. Some physicians take advantage of this and combine lower dosages of medication with supplemental niacin, in efforts to minimize drug side effects.

Increasing dietary consumption of omega-3 fatty acids may also help reduce hypertension. A rich source of omega-3 fatty acids is fish oil, which is able to reduce blood pressure somewhat by increasing the excretion of sodium and excess water.\(^32\) Other remedies commonly used to combat hypertension that have some scientific validation include coenzyme Q10, supplemental garlic, hawthorn extract, and folic acid (vitamin B9). However, more research is need before specific recommendations can be made.

**The Pharmaceutical Treatment of Hypertension**

Pharmaceutical treatment for hypertension has been associated with reductions in stroke (reduced an average of 35 to 40 percent), heart attacks (reduced 20 to 25 percent), and heart failure (reduced more than 50 percent) according to research.\(^33\) Specifically, a reduction in diastolic blood pressure of only 6 mmHg produces a 42 percent reduction in incidence of stroke.\(^34\) There are several types of drugs used to treat hypertension including thiazide diuretics, angiotensin-converting enzyme (ACE) inhibitors, beta-blockers, calcium channel blockers, angiotensin-II receptor blockers (ARBs), alpha-blockers, and renin...
inhibitors. The aim of treatment should be to reduce blood pressure to less than 140/90 mmHg for most individuals, and closer to 120/80 mmHg for individuals with diabetes or kidney disease.

1) Thiazide Diuretics

The first-line antihypertensive medication supported by the best evidence is a low-dose thiazide diuretic. Thiazide diuretics (sometimes called water pills) are recommended as a first-line therapy for hypertension because of their effectiveness and ability to vasodilate arteries. Diuretics help the kidneys eliminate excess sodium and water from the body's tissues and blood, which reduces systemic pressure. Loop diuretics and potassium sparing diuretics are also used for hypertension, but thiazide diuretics such as epitizide, hydrochlorothiazide, chlorothiazide and bendroflumethiazide work quickly and are often cheaper. Despite thiazides being cheap, effective, and recommended by many experts, they are not prescribed as often as some newer drugs because they have been associated with increased risk of hyperglycemia and type-2 diabetes. Furthermore, thiazides reduce the clearance of uric acid and are therefore to be used with caution in patients with gout or hyperuricemia. As such, thiazides are more popular for use in patients over 65 where the risk of diabetes and gout are outweighed by the benefits of reducing high systolic blood pressure. Other side effects include an increased need to urinate and a higher risk of sexual dysfunction.

2) ACE Inhibitors

For younger adults and those with diabetes, ACE inhibitors are a popular choice for hypertension. ACE inhibitors inhibit the activity of angiotensin-converting enzyme, which is responsible for the conversion of angiotensin-I into angiotensin-II, a potent vasoconstrictor. As a consequence, ACE inhibitors lower arteriolar resistance and increase venous capacity, cardiac output, and stroke volume, while leading to increased excretion of sodium in the urine. ACE inhibitors may be especially important in treating hypertension in people with coronary artery disease, heart failure or kidney failure. ACE inhibitors don't work as well in African-Americans when prescribed alone, but they are effective when combined with a thiazide diuretic. Frequently prescribed ACE inhibitors include captopril, enalapril, lisinopril and ramipril. Common adverse reactions to ACE inhibitors include hypotension, dizziness, hyperkalemia, coughing, headache, fatigue, nausea. and renal impairment. ACE inhibitors are not recommended during pregnancy, and some evidence suggests that they might increase inflammation-related pain.

3) Beta-blockers

Beta-blockers work by reducing the workload on the heart and vasodilating blood vessels, which lead to slower and less forceful heartbeats. Specifically, they block the action of catecholamines (such as adrenaline and noradrenaline) on beta-adrenergic receptors, which mediate the “fight or flight” response of the sympathetic nervous system. Although beta-blockers reduce blood pressure, they are not as effective or do not have as many positive effects as some other antihypertensives. As such, beta-blockers such as atenolol are no longer recommended as a first-line treatment for hypertension due to relative adverse risk of stroke and type-2 diabetes when compared to other medications. They do have an important role in the prevention of myocardial infarcts in people who have already experienced one, but the 2006 guidelines of the National Institute for Health and Clinical Excellence in the U.K. downgraded the role of beta-blockers to second-line hypertension treatments. When prescribed alone, beta-blockers don't work as well in African-Americans or the elderly, although they are more effective when combined with thiazide diuretics (which is similar to ACE inhibitors). Further, beta-blockers generally are not prescribed for people with asthma because they can increase muscle spasms in the lungs. However, a meta-analysis of trials of diuretics and beta-blockers found that they effectively lowered the risk of stroke.
by approximately 40 percent. Possible side effects of beta-blockers include fatigue, sleep disturbance, slowed heart rate and poor circulation in hands and feet.

4) Calcium Channel Blockers

Calcium channel blockers work by blocking voltage-gated calcium channels in cardiac muscle and blood vessels, which decreases intracellular calcium leading to reduced muscle contraction. In the heart, a decrease in calcium results in reduced contractility. In blood vessels, a decrease in calcium results in less contraction of the vascular smooth muscle and therefore an increase in arterial diameter, or vasodilation. Calcium channel blockers may work better for African-Americans and the elderly than do ACE inhibitors or beta-blockers alone. Despite the effectiveness, calcium channel blockers have a high mortality rate over an extended dosage period and have a high rate of side effects. Common side effects include dizziness, headache, rosacea, edema, rapid heart rate, slow heart rate, constipation and gingival overgrowth. The two main classes of calcium channel blockers are dihydropyridines (numerous types) and non-dihydropyridines (verapamil, diltiazem). It should be noted that grapefruit juice interacts with some calcium channel blockers, increasing blood levels of the medication and causing more side effects.

5) ARBs

ARBs block the activation (not the formation) of angiotensin-II AT1 receptors, which directly causes vasodilation and reduces the secretion of vasopressin and the production and secretion of aldosterone, among other actions. The combined effect reduces blood pressure. Like ACE inhibitors, ARBs are often useful for people with coronary artery disease, heart failure, and kidney failure. ARBs are usually chosen for treatment of hypertension when a patient is intolerant of ACE inhibitor therapy. ARBs do not inhibit the breakdown of bradykinin or other kinins, and are thus only rarely associated with the persistent dry cough and angioedema that limit ACE inhibitor therapy. ARBs irbesartan and losartan have proven to be of benefit to hypertensive patients with type-2 diabetes and may delay the progression of diabetic nephropathy. ARBs also display a negative association with Alzheimer's disease. A retrospective analysis discovered that patients taking ARBs for hypertension were 35-40 percent less likely to develop Alzheimer’s disease than those using other antihypertensives. However, some studies suggest ARBs can increase the risk of myocardial infarction.

6) Combination Therapy

Sometimes combining antihypertensive medications achieves the best results for those with high blood pressure. Commonly combined medications include an ACE inhibitor and a calcium channel blocker (such as perindopril and amlodipine), the efficacy of which has been demonstrated in individuals with glucose intolerance or metabolic syndrome. Another common example is combining a thiazide-based diuretic and an ARB. However, combining an ACE inhibitor or ARB with a thiazide-based diuretic and a nonsteroidal anti-inflammatory (including selective COX-2 inhibitors and over-the-counter drugs such as ibuprofen) should be avoided whenever possible due to a high documented risk of acute kidney failure.

7) Contraindicated Prescription Drugs

Some prescription drugs on their own can induce or aggravate hypertension, including all types of nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids and anabolic steroids, oral contraceptive and sex hormones, vasoconstricting decongestants, calcineurin inhibitors (cyclosporin, tacrolimus), erythropoietin and analogues, monoamine oxidase inhibitors, and midodrine.
Strategies to Improve Patient Adherence to Therapy

According to the 2010 Canadian Hypertension Education Program recommendations for the management of hypertension, there are some strategies for the physician and pharmacist to employ in order to assist the patient to adhere to pharmaceutical therapy. 29

1) Tailor pill-taking to fit patient’s daily habits.

2) Simplify medication regimens to once-daily dosing.

3) Replace multiple-pill antihypertensive combinations with single-pill combinations.

4) Use unit-of-use packaging (of several medications to be taken together).

5) Improve adherence to an antihypertensive prescription through a multidisciplinary team approach.

6) Encourage greater patient responsibility/autonomy in monitoring his or her blood pressure and adjusting prescriptions.

7) Educate patients and patients’ families about his or her disease and treatment regimens.

8) Encourage adherence with therapy by out-of-office contact (either by phone or mail), particularly during the first three months of therapy.

9) Coordinate with work-site health care givers to improve monitoring of adherence with pharmacological and lifestyle modification prescriptions.

10) Use electronic medication compliance aids.
References


