

Pharmacological and non- pharmacological treatment of hypertension: A review article

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Abstract

BACKGROUND: Hypertension is a worldwide epidemic disease. It is more common and more severe in elderly persons. Various studies however have estimated 41.9 million men and 27.8 million women to have prehypertension. Diagnosis and early treatment of prehypertension are of utmost importance. Although hypertension is usually divided into 2 general categories of essential (primary) and secondary hypertension, the initial treatment for hypertension often depends on its stage which is determined by systolic and diastolic blood pressure. Lifestyle modification is the first step in treating stage one hypertension. Pharmaceutical treatments including diuretics, angiotensin converting enzyme (ACE) inhibitors, calcium blockers, beta blockers, and angiotensin receptor blockers will be recommended if lifestyle modification fails to control blood pressure.

METHODS: The PubMed database was searched by a number of keywords including hypertension, pharmaceutical treatment, and non-pharmaceutical treatment. The results were limited by determining a date range of 2008-11.

RESULTS: High blood pressure causes major health problems for many people around the world. It should be controlled because of its high mortality and morbidity. However, in order to select an appropriate treatment modality, it is initially important to diagnose the kinds and stages of hypertension. Pharmaceutical or non-pharmaceutical treatments can then be employed to control this serious disease.

CONCLUSION: Treating hypertension depends on the kinds and stages of this disease. Several tips should be considered when selecting a method of treatment.

Keywords: Hypertension, Pharmacological treatment, Non-pharmacological treatment

ARYA Atherosclerosis Journal 2012, 8(Special Issue in National Hypertension Treatment): S217-S221

Date of submission: 09 Jan 2012, *Date of acceptance:* 04 Jun 2012

Introduction

Blood pressure

Hypertension is often called the silent killer because in the initial stages it presents with no symptoms. Blood pressure is the force of blood against the walls of arteries. As hypertension does not cause symptoms, the consequences of high blood pressure are realized only after an organ in the body is irritated or damaged. It is one of the most common diseases worldwide. Approximately 50 million people in the United States are affected by hypertension and approximately 30% of adults are still unaware of their hypertension. Up to 40% of people with hypertension are not receiving treatment and of treated patients, up to 67% do not have their blood pressure controlled to less than 140/90 mmHg.^{1,2} Because of the associated morbidity and mortality and the cost imposed on the society, hypertension is an important public health challenge. The researchers believe that an appropriate treatment needs to know the pathophysiology of

blood pressure and diagnose the stage of the disease.

Acute coronary syndrome events, such as heart attacks, are still the most common result of hypertension. Hypertension is also related to increased severity of atherosclerosis, stroke, nephropathy, peripheral vascular disease, aortic aneurysms, and heart failure.³

Classification of blood pressure

Defining abnormal high blood pressure is extremely difficult. Furthermore, the relationship between systolic arterial pressure and morbidity appears to be quantitative rather than qualitative. Since the risk to an individual patient may correlate with the severity of hypertension, a classification system is essential for making decisions about aggressiveness of treatment or therapeutic intervention.

Base on previous studies, the classification of blood pressure for adults aged 18 years or older is as follows:

- Normal blood pressure: Less than 120/80 mmHg.

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- Prehypertension: Systolic blood pressure of 120-139 mmHg or diastolic blood pressure of 80-90 mmHg (Patients with prehypertension are at risk for progression to hypertension and lifestyle modification is an important preventive strategy.);

- Stage 1 hypertension: Systolic blood pressure 140-159 mmHg or diastolic blood pressure 90-99 mmHg;

- Stage 2 hypertension: Systolic blood pressure equal to or more than 160 mmHg or diastolic blood pressure equal to or more than 100 mmHg.

Severe cases of hypertension may be further categorized. Severe and urgent hypertension are defined as blood pressure above 180/110 mmHg without symptoms and with mild, end organ effects such as headache and dyspnea, respectively. Moreover, emergency hypertension is blood pressure of 220/140 mmHg or greater with life-threatening end-organ dysfunction.

Hypertensive emergencies encompass a spectrum of clinical presentations in which uncontrolled blood pressure leads to progressive or impending end-organ dysfunction. Blood pressure should be lowered aggressively over minutes to hours. Acute end-organ damage in the setting of a hypertensive emergency may include the following:

- Neurologic damage: Hypertensive encephalopathy, cerebrovascular accident or cerebral infection, subarachnoid hemorrhage, and intracranial hemorrhage;

- Cardiovascular complications: Myocardial ischemia or infarction, acute left ventricular dysfunction, acute pulmonary edema, and aortic dissection;

- Other damages: Acute renal failure or insufficiency, retinopathy, eclampsia, microangiopathy.^{1,4-6}

Hypertension can also be categorized as either essential (primary) or secondary. Essential hypertension means high blood pressure with no obvious medical cause while secondary hypertension is caused by a disease such as polycystic kidney and hyperaldosteronism.⁵ In this article, only essential hypertension is emphasized.

Pathophysiology

The pathogenesis of essential hypertension is multifactorial and highly complex. Multiple factors modulate blood pressure for adequate tissue perfusion. These factors include humoral mediators, vascular reactivity, circulating blood volume, vascular caliber, blood viscosity, cardiac output, blood vessel elasticity, and neural stimulation.

In a proposed pathogenesis of essential

hypertension, several factors including genetic predisposition, excessive dietary salt, and adrenergic tone have been suggested to interact to produce hypertension. Although genetics appears to contribute to essential hypertension, the exact mechanism has not been established.^{7,8}

One mechanism of hypertension has been described as high-output hypertension which in turn results from decreased peripheral vascular resistance and concomitant cardiac stimulation by adrenergic hypertension and altered calcium homeostasis. A second mechanism manifests with normal or reduced cardiac output and elevated systemic vascular resistance due to increased vasoactivity. Another mechanism is increased salt and water reabsorption (salt sensitivity) by the kidney which increases the circulating blood volume.

As it was mentioned earlier, hypertension needs to be first classified and then treated. Based on a recent clinical trial, new recommended treatment goals are as follows:

- 1) Reducing blood pressure to less than 140/90 mmHg for people with typical diastolic hypertension who are not at risk.

- 2) For elderly people with isolated systolic hypertension, caution should be taken to avoid reducing the diastolic pressure to less than 65-70 mmHg. Less than optimal lowering of the systolic pressure should be accepted in order to avoid reducing the diastolic pressure.

- 3) For high-risk patients with diastolic hypertension, more aggressive therapy to reduce the diastolic pressure to 80 mmHg or less should be considered. In these cases, the goal is to reduce blood pressure to 130/80 mmHg or less to reduce the risk of cardiac disease in diabetics and to 125/75 mmHg or less to slow the progression of kidney disease in patients with renal insufficiency.⁴

Discussion

According to the pathophysiology and kinds of hypertension we can choose the type of treatment:

Non-pharmacological treatment

Life style modification is an important first step for lowering blood pressure especially in patients with prehypertension and stage 1 hypertension. Current guidelines recommend that people should exercise at rest 30 minutes a day, maintain normal weight, reduce sodium (salt) intake, increase potassium intake, avoid alcohol consumption, use low-fat diets rich in fruits and vegetables, and quit smoking. According to DASH, hypertensive individuals need to limit sodium intake, reduce saturated fat and select

monounsaturated oils, choose fresh fruits and vegetables, use potassium- and fiber-rich foods (30 g daily) and protein sources (18% total daily calories), and limit carbohydrates to 55% of daily calories and dietary cholesterol to 150 mg.

Diet

Low salt and high potassium

Scientists believe that high salt intake is associated with high blood pressure. Therefore, a potassium-rich diet is important for reducing blood pressure. Potassium-rich foods include bananas, oranges, pears, prunes, tomatoes, nuts, potatoes, and avocados. However, patients who take medications that limit the ability of kidneys to excrete potassium, such as angiotensin-converting-enzyme (ACE) inhibitors and digoxin or potassium-sparing diuretics, should not take potassium supplements. They need to watch excessive potassium in their diet.

Fiber

Increasing fiber in diet may help reduce blood pressure levels.

Fish oil and omega 3 fatty acids

Omega 3 fatty acids, which are found in fish oil, may have specific benefits for many medical conditions including heart disease and hypertension. They appear to keep blood vessels flexible and may help protect the nervous system.

Calcium

Calcium regulates the tone of blood vessels of smooth muscles lining. Studies have found that people with sufficient dietary calcium have lower blood pressure. In addition, hypertension itself increases calcium loss from the body.

Weight loss

Weight loss in overweight people, particularly in the abdominal area, can immediately lower blood pressure. Weight loss, especially when accompanied by salt restriction, may allow patients with prehypertension to safely reduce or go off medication.

Exercise

Regular exercise (at least 30 minutes a day) improves the elasticity of arteries, even in older people, which in turn ensures blood flow and normal blood pressure. High-intensity exercise may not lower blood pressure as effectively as moderate intensity exercise and may be dangerous in people with hypertension.

Good sleep habits

Certain sleep disorders, especially sleep apnea, are associated with hypertension. Insufficient sleep may raise blood pressure in patients with hypertension and place them at increased risk of heart disease and death. Moreover, increased levels of adrenalin hormone due to sleeplessness can activate the

sympathetic nervous system.

Stress reduction

Patients can use relaxation techniques such as meditation for reducing stress.⁹⁻¹²

Pharmacological treatment

If high blood pressure cannot be controlled by non-pharmacological treatment, it should be treated by pharmacological treatment. At first, patients should be treated by one drug (monotherapy). If the first drug is insufficiently effective or poorly tolerated, it will be changed with another single drug and then with a third if necessary. If three or more attempts of monotherapy fail, the next step will be trying combination therapy with two or more drugs. Drugs which are useful in controlling blood pressure are as follow:

Diuretics

Diuretics help the kidneys get rid of excess salt and water. They are the main step of antihypertensive therapy and are often the first kind of drug selected for most people with hypertension. They are also especially helpful for treating patients with heart failure, patients with isolated systolic hypertension, the elderly, and diabetics. Diuretics are often used in combination with other antihypertensive drugs. Results of long term studies have suggested that diuretics work just as well as other drugs in lowering blood pressure and are more effective in preventing heart failure, heart attack, and stroke.

The three main types of diuretics which are useful for controlling hypertension include:

1. Thiazide diuretics (like hydrochlorothiazide);
2. Loop diuretics (like furosemide) which act faster than other diuretics and are more potent. Therefore, it is important to avoid dehydration and potassium loss;
3. Potassium-sparing diuretics (like spironolactone)

Beta blockers

Beta blockers such as carvedilol, can reduce heart rate and the force of heart contraction by affecting the nervous system. So they can control hypertension by these two actions. They are usually used in combination with other drugs such as ACE inhibitors and diuretics. Beta blockers are more likely to be used to treat hypertension in patients with angina, previous heart attack, arrhythmias with fast heart rates, or migraine headaches. With careful use, they can also be beneficial for patients with heart failure.

ACE inhibitors

ACE inhibitors such as captopril can block the enzyme that converts angiotensin I to angiotensin II. Without angiotensin II, the vessels cannot constrict. Therefore, blood vessels will be dilated and the heart workload will be decreased. They treat high blood pressure and can also help protect the heart and

kidneys. Patients with heart failure or an enlarged left ventricle, previous heart attack, diabetes or kidney disease are considered particularly good candidates for ACE inhibitors as part of treatment for high blood pressure. However, it is so important to know that ACE inhibitors can increase potassium levels, particularly in patients with kidney disease.

Angiotensin-receptor blockers (ARBs)

ARBs, also known as angiotensin II receptor antagonists (like Losartan), are similar to ACE inhibitors in their ability to widen blood vessels and lower blood pressure. They may have fewer or less severe side effects than ACE inhibitors. In general, they are used when patients cannot tolerate or did not respond to ACE inhibitors.

Calcium-channel blockers (CCBs)

CCBs or calcium antagonists such as diltiazem help the dilation of blood vessels. Along with diuretics, CCBs may work better than other drug classes for lowering blood pressure. Recent research has indicated that newer types of drugs (CCBs combined with ACE inhibitors) may be a better treatment option for some patients than older drugs like beta blockers.

Alpha blockers

Alpha blockers (like prazosin) help the dilation of small blood vessels. As the injection form of these drugs are available and they can reduce blood pressure rapidly, they can be used in emergency hypertension.

Vasodilators

Vasodilators such as hydralazine are usually used in combination with a diuretic or a beta blocker. They are rarely used alone.¹³

Aliskiren

In 2007, the US Food and Drug Association (FDA) approved aliskiren for treatment of high blood pressure. This drug inhibits renin enzyme. Aliskiren can be taken either alone or in combination with other blood pressure medications. It should not be used during pregnancy as it can cause injury or death to the fetus.

Most patients with high blood pressure should be treated immediately. They should also be followed step by step to control their response to treatment. Figure 1 shows the treatment steps in these patients according to their responses to treatments.

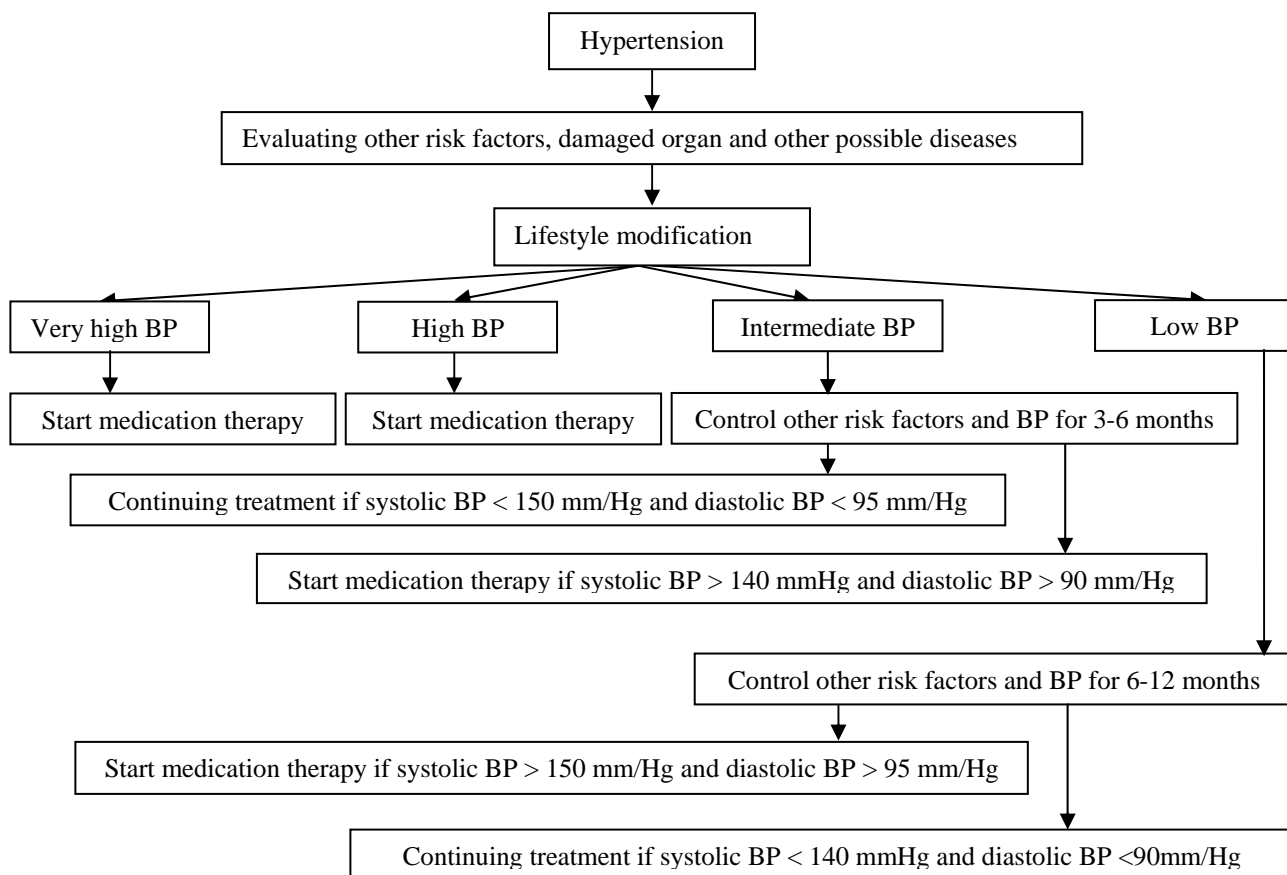


Figure 1. Hypertension Treatment steps
BP: Blood pressure

We should also know that low response to treatment has various reasons including fluid excess due to hypernatremia, treatment with non-diuretic anti-hypertensive drugs, or secondary impairment of kidney function, inadequate drug dose, drug antagonists, and secondary hypertension

Conclusion

Treating hypertension depends on the kinds and stages of this disease. A number of tips should be considered when using each treatment modality. Moreover, patients should be followed according to their responses to the treatment.

Conflict of Interests

Authors have no conflict of interests.

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How to cite this article: Seyedmazhari M. **Pharmacological and non-pharmacological treatment of hypertension: A review article.** *ARYA Atherosclerosis Journal* 2012; 8(Special Issue in National Hypertension Treatment): S217-S221.