



PATHOPHYSIOLOGY OF HYPERTENSION: TREATMENT, DIAGNOSIS, RISK AND ETIOLOGY

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ABSTRACT

Hypertension basically does not show any major symptoms initially, but persistent hypertension over time is a major risk factor for hypertensive heart disease, stroke, coronary artery disease, peripheral artery disease, aortic aneurysm, and chronic kidney disease. Hypertension is further classified as either primary hypertension or secondary hypertension. Most of the cases, about 90–95% of cases are categorized as primary hypertension, defined as high blood pressure with no noticeable underlying cause. The remaining 5–10% of cases are categorized as secondary hypertension, defined as hypertension due to an restricted cause, such as chronic kidney disease, narrowing of the aorta or kidney arteries, or an endocrine disorder such as excess cortisol, aldosterone, or catecholamine. The simply way to know whether you have high blood pressure is to get it measured. The medical doctor will measure your blood pressure with an instrument called sphygmomanometer. Earlier the normal blood pressure reading was approximately 120/80 mm Hg, but as per the WHO guideline now a day it is considered as 130/90 mm Hg. There are several types of drugs used to treat high blood pressure, like Beta-blockers, Angiotensin-converting enzyme inhibitors, Angiotensin II receptor blockers (ARBs), Calcium channel blockers, Alpha-blockers, Diuretics, Alpha-agonists and Renin inhibitors etc.

Key words: Hypertension, treatment, diagnosis, risk, etiology

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INTRODUCTION

Blood pressure is spoken by two measurements, the systolic and diastolic pressures, which are the maximum and minimum pressures, respectively, in the arterial system. The systolic pressure takes place when the left ventricle is most contracted; the diastolic pressure occurs when the left ventricle is relaxed prior to the subsequent contraction. Normal blood pressure at rest is within the range of 100–140 mm Hg systolic and 60–90 mmHg diastolic. Hypertension is present if the blood pressure is determinedly at or above 140/90 millimeters mercury (mm Hg) for most adults; but some different criteria may apply to children [1-2].

Hypertension mainly does not cause symptoms initially, but sustained hypertension over time is a major risk factor for hypertensive heart disease, coronary artery disease, stroke, aortic aneurysm, peripheral artery disease, and chronic kidney disease.

Hypertension is classified as primary hypertension or secondary hypertension. About 90–95% of cases are categorized as primary hypertension, which may be

defined as high blood pressure with no obvious underlying cause. The remaining 5–10% of cases is categorized as secondary hypertension, defined as hypertension due to an identifiable cause, such as chronic kidney disease, narrowing of the aorta or kidney arteries, or an endocrine disorder such as excess aldosterone, cortisol, or catecholamine [2-4]. Dietary and lifestyle changes can improve blood pressure control and decrease the risk of health complications, although treatment with medication is still often necessary in people for whom lifestyle changes are not enough or not effective [3]. The treatment of moderately high arterial blood pressure (defined as >160/100 mmHg) with medications is associated with an improved life expectancy. The benefits of treatment of blood pressure that is between 140/90 mmHg and 160/100 mmHg are less clear, with some reviews finding no benefit and other reviews finding benefit [1-3]. Hypertension, also referred to as high blood pressure, is a condition in which the arteries have persistently elevated blood pressure. Every time the human heart beats, it pumps blood to the whole body through the arteries [5].

Blood pressure is the force of blood pushing up against the blood vessel walls. The higher the pressure the harder the heart has to pump [4].

Hypertension can lead to damaged organs, as well as several illnesses, such as renal failure (kidney failure), aneurysm, heart failure, stroke, or heart attack. Researchers from UC Davis reported in the Journal of the American Academy of Neurology that high blood pressure during middle age may raise the risk of cognitive decline later in life. The normal level for blood pressure is below 120/80, where 120 represents the systolic measurement (peak pressure in the arteries) and 80 represents the diastolic measurement (minimum pressure in the arteries). Blood pressure between 120/80 and 139/89 is called pre hypertension (to denote increased risk of hypertension), and a blood pressure (table 1) of 140/90 or above is considered hypertension [6-8].

Hypertension may be classified as essential or secondary. Essential hypertension is the term for high blood pressure with unknown cause. It accounts for about 95% of cases. Secondary hypertension is the term for high blood pressure with a known direct cause, such as kidney disease, tumors, or birth control pills. Kidneys act as filters to rid the body of waste. High blood pressure can narrow and thicken the blood vessels of the kidneys [3,5-8].

The kidneys filter less fluid and waste builds up in the blood. The kidneys may fail altogether. To measure a patient's blood pressure, the patient should be seated quietly for at least 5 minutes in a chair rather than on an examination table, with feet on the floor and arm supported at heart level. A sphygmomanometer with an appropriate-sized cuff (cuff bladder encircling at least 80% of the arm) should be used to ensure accuracy. At least 2 measurements should be made for confirmation the blood pressure [6-8].

Laboratory Routine Tests [4-9]

- Electrocardiogram
- Urinalysis
- Blood glucose,
- Serum potassium, creatinine, or the corresponding estimated GFR, and calcium

- Lipid profile, after 9- to 12-hour fast that includes high-density and low-density lipoprotein cholesterol, and triglycerides.
- **Optional tests:** Measurement of urinary albumin excretion or albumin/creatinine ratio. More extensive testing for identifiable causes is not generally indicated unless BP control is not achieved.

Incidence in India [4-9]

- 25% of urban population and 10 % of rural population suffer from hypertension
- 70% of all hypertensive patients are stage I hypertension.
- 12% of all hypertensive suffer from isolated systolic hypertension.

High blood pressure or hypertension increases the risk of heart disease and stroke. Hypertension risk factors include obesity, drinking too much alcohol, smoking, and family history. Beta-blockers are a common treatment for hypertension. Some 70 million adults in the United States are affected by hypertension.

Risk of Hypertension Disease [6-10]

There are several known factors that increase the risk of hypertension. These include -

Age: On an average, people above 40 years of age have a higher risk of developing hypertension.

Family history: If you have a family member with high blood pressure, you're also likely to suffer.

Stress: Several studies have linked stress with high blood pressure. Hormones released by the body under stress affect the blood vessels and blood flow, causing a temporary rise in BP.

High salt intake: Salt contains sodium that causes fluid retention in the body, leading to increased blood pressure.

Smoking: Smoking causes narrowing of the arteries, thereby increasing the pressure exerted by blood flowing through them. Here are 25 things that happen inside your body when you smoke.

Heavy alcohol intake: Heavy drinking generally has a known bad effect on crucial organs like liver, kidneys and the heart. It also affects the blood pressure.

Chronic diseases: While hypertension is a risk factor for chronic diseases like heart disease and kidney disease, chronic diseases can also lead to hypertension.

Table 1: Blood Pressure Classification

BP Classification	SBP mmHg	DBP mmHg
Normal	<120	<80
Pre hypertension	120-139	80-89
Stage 1 Hypertension	140-159	90-99
Stage 2 Hypertension	≥160	≥100

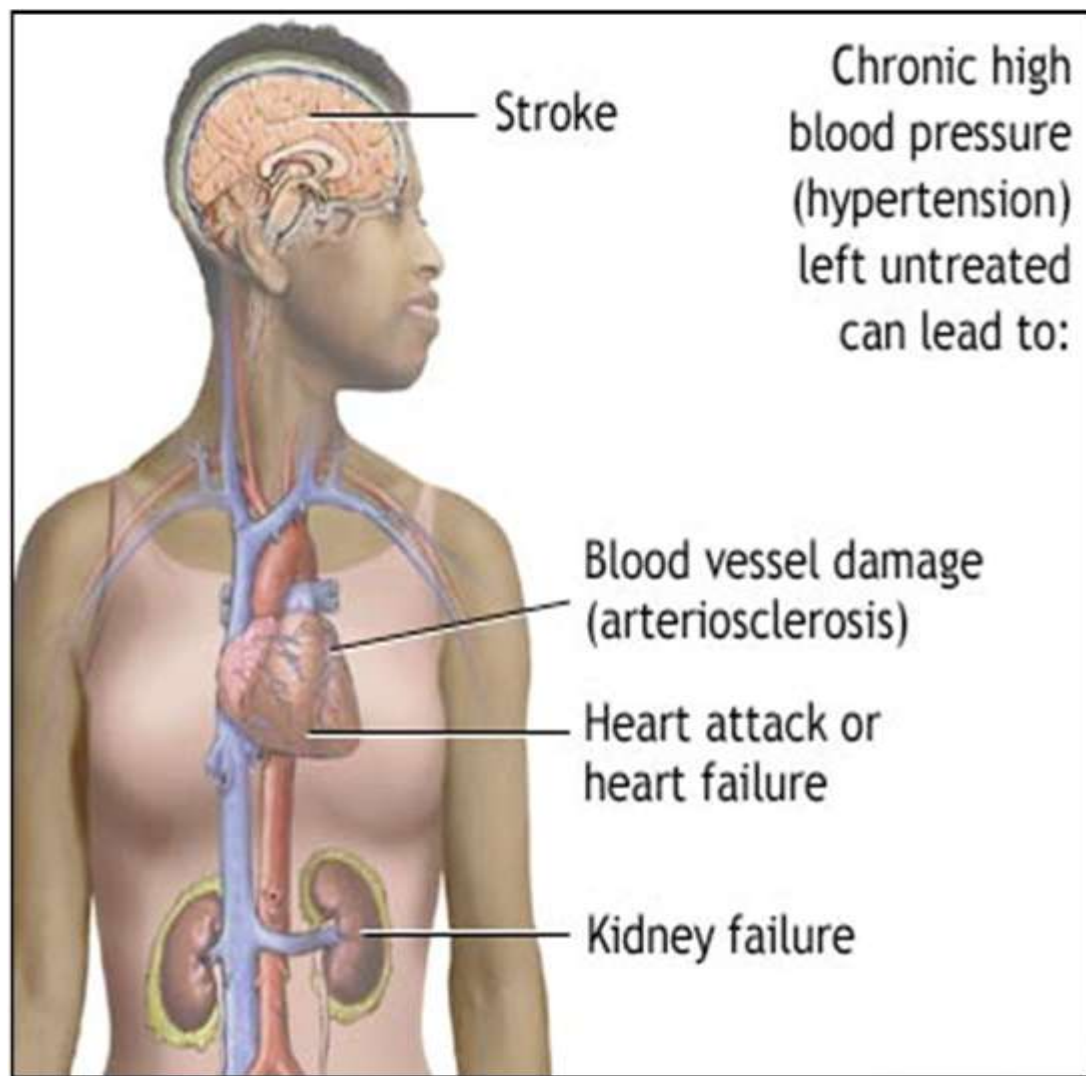


Figure 1: Risk of Hypertension

ETIOLOGY OF HYPERTENSION

High blood pressure is a major risk factor for heart attack. The arteries bring oxygen-carrying blood to the heart muscle. If the heart cannot get enough oxygen, chest pain, can occur. If the flow of blood is blocked, a heart attacks results. The heart is unable to pump enough blood to supply the body's needs. High blood pressure is the most important risk factor for stroke.

Very high pressure can cause a break in a weakened blood vessel, which then bleeds in the brain. This can cause a stroke. If a blood clot blocks one of the narrowed arteries, it can also cause a stroke. Though the exact causes of hypertension are usually unknown, there are several factors that have been highly much alcohol consumption (more than 1 to 2 drinks associated with the condition [7-11]. These include:

- Smoking
- Obesity or being overweight
- Being obese/ overweight as a child - a research team at the Indiana University School of Medicine found that obese/overweight children are much more likely to suffer from hypertension during adulthood.
- Diabetes
- Sedentary lifestyle
- Lack of physical activity

- High levels of salt intake (sodium sensitivity). According to the American Heart Association (AHA), sodium consumption should be limited to 1,500 milligrams per day, and that includes everybody, even healthy people without high blood pressure, diabetes or cardiovascular diseases. AHA's chief executive officer, some researchers said "Our recommendation is simple in the sense that it applies to the entire U.S population, not just at-risk groups. Americans of all ages, regardless of individual risk factors, can improve the heart health and reduce their risk of cardiovascular disease by restricting their daily consumption of sodium to less than 1,500 milligrams" [9].
- Insufficient calcium, potassium, and magnesium consumption
- Vitamin D deficiency
- High levels of alcohol consumption
- Stress
- Aging
- Medicines such as birth control pills
- Genetics and a family history of hypertension - In May 2011, scientists from the University of Leicester, England, reported in the journal *Hypertension* that some genes in the kidneys may contribute to hypertension.
- Chronic kidney disease Adrenal and thyroid problems or tumors.

PATHOPHYSIOLOGY OF HYPERTENSION

There is still much uncertainty about the pathophysiology [8, 11-15] of hypertension. A small number of patients (between 2% and 5%) have an underlying renal or adrenal disease as the cause for their raised blood pressure. In the

remainder, however, no clear single identifiable cause is found and their condition is labelled "essential hypertension". A number of physiological mechanisms are involved in the maintenance of normal blood pressure, and their derangement may play a part in the development of essential hypertension.

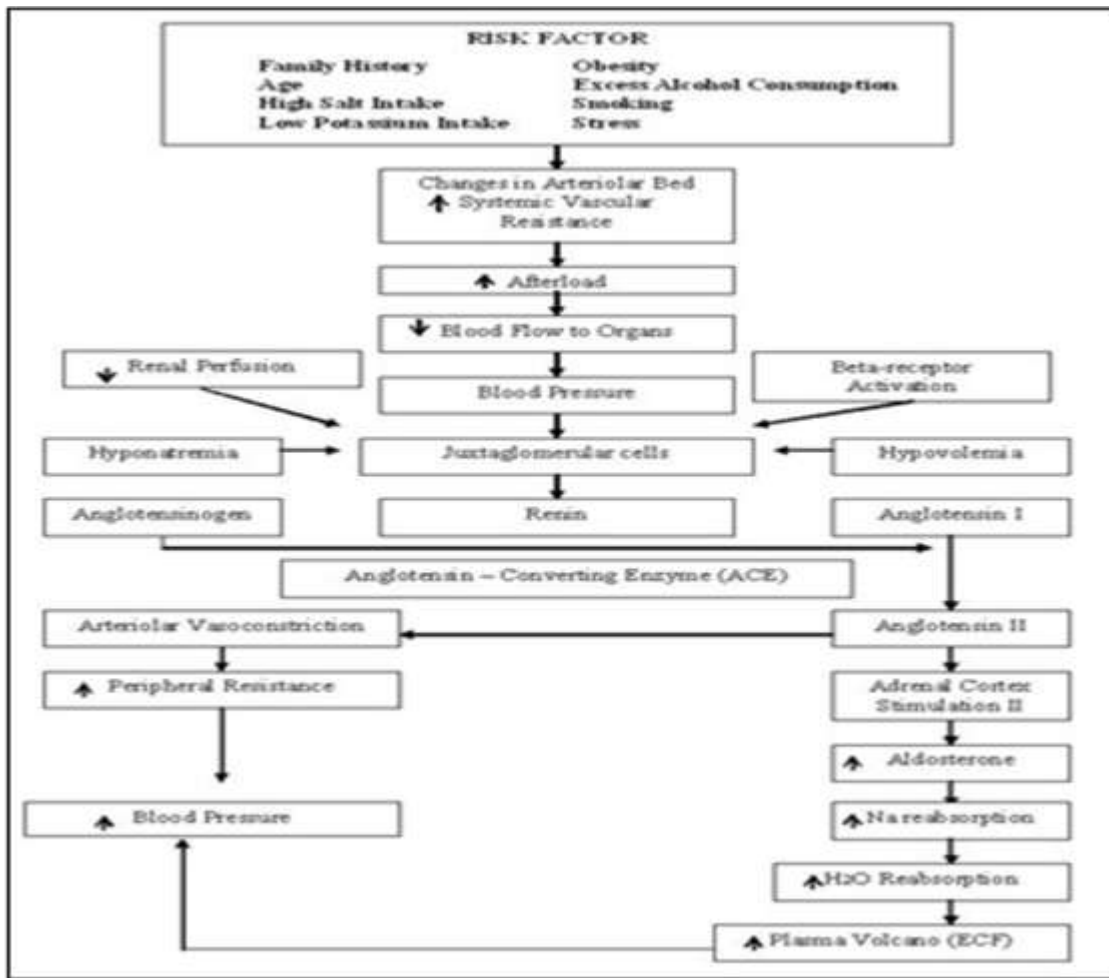


Figure 2: Risk factors and treatment of hypertensive patients.

Physiological mechanisms involved in development of essential hypertension [11-15]

- Cardiac output
- Peripheral resistance
- Renin-angiotensin-aldosterone system
- Autonomic nervous system

Other factors:

- Bradykinin
- Endothelin
- EDRF (endothelial derived relaxing factor) or nitric oxide
- ANP (atrial natriuretic peptide)
- Ouabain

Cardiac output and peripheral resistance [12-14]

Maintenance of a normal blood pressure is dependent on the balance between the cardiac output and peripheral vascular resistance. Most patients with essential

hypertension have a normal cardiac output but a raised peripheral resistance.

Peripheral resistance is determined not by large arteries or the capillaries but by small arterioles, the walls of which contain smooth muscle cells. Contraction of smooth muscle cells is thought to be related to a rise in intracellular calcium concentration.

Manifestation of hypertension [12-16]

One of the most dangerous aspects of hypertension is that you may not know that you have it. In fact, nearly one-third of people who have high blood pressure don't know it. The only way to know if your blood pressure is high is through regular checkups. This is especially important if you have a close relative who has high blood pressure. If your blood pressure is extremely high, there may be certain symptoms to look out for, including:

- Severe headache
- Fatigue or confusion
- Vision problems
- Chest pain

- Difficulty breathing
- Irregular heartbeat
- Blood in the urine
- Pounding in your chest, neck, or ears

If you have any of these symptoms, see a doctor immediately. You could be having a hypertensive crisis that could lead to a heart attack or stroke.

People often do not seek medical care until they have symptoms arising from the organ damage caused by chronic (ongoing, long-term) high blood pressure.

The following types of organ damage are commonly seen in chronic high blood pressure:

- Heart attack
- Heart failure
- Stroke or transient ischemic attack (TIA)
- Kidney failure
- Eye damage with progressive vision loss
- Peripheral arterial disease causing leg pain with walking (claudication)
- Outpunching of the aorta, called aneurysm

About 1% of people with high blood pressure do not seek medical care until the high blood pressure is very severe, a condition known as malignant hypertension.

- In malignant hypertension, the diastolic blood pressure (the lower number) often exceeds 140 mm Hg.
- Malignant hypertension may be associated with headache, lightheadedness, nausea, vomiting, and stroke like symptoms.
- Malignant hypertension requires emergency intervention and lowering of blood pressure to prevent brain hemorrhage.

Diagnosis of Hypertension [14-17]

The only way to know whether you have high blood pressure is to get it measured. The physician will measure your blood pressure with an instrument called sphygmomanometer. The normal blood pressure reading is 120/80 mmHg.

The first number is the measure of pressure exerted on the walls of arteries when the heart contracts and pushes blood in the arteries. This is called systolic blood pressure. Normal systolic blood pressure is below 120 mmHg. Read about how your heartbeat affects your BP.

The second number is the diastolic pressure or the pressure exerted on the walls of the arteries when the heart is at rest between beats. The normal diastolic blood pressure is less than 80 mmHg.

Recently, new guidelines released by the U.S. revised the normal range of blood pressure to 150/90 for people above 60 years of age. Read more about the guideline - 150/90 is the new 'normal BP' for people over 60.

TREATMENT OF HYPERTENSION

Drugs to Treat High Blood Pressure

There are several types of drugs used to treat high blood pressure, including:

- Angiotensin-converting enzyme (ACE) inhibitors
- Angiotensin II receptor blockers (ARBs)
- Diuretics
- Beta-blockers

- Calcium channel blockers
- Alpha-blockers
- Alpha-agonists
- Renin inhibitors
- Combination medications

TREATMENTS AND DRUGS [3, 6-8, 12-17]

Alpha blockers

Alpha blockers, also called alpha-adrenergic antagonists, treat several conditions, such as high blood pressure and enlarged prostate. Find out more about these medications. Ex-Prazosin, Terazosin, Doxazosin.

Prazosin

This prototype selective alpha 1 agonist dilates both resistance and capacitance vessels; effect on the former predominating. The haemodynamic effects, viz reduction in t.p.r. and mean BP accompanied by minor decrease in venous return and c.o. are similar to that produced by a direct acting vasodilator. However, unlike hydralazine, there is little reflex cardiac stimulation and rennin release during long term therapy. Tachycardia does not compensate for the fall in BP, because release inhibitory alpha 2 receptors are not blocked: auto regulation of NA release remains intact. It probably decreases central sympathetic tone also.

Advantages of Prazosin are:-

- Does not impair carbohydrate metabolism; suitable for diabetic, but not if neuropathy is present, because postural hypotension is accentuated.
- Has a small but favorable effect on lipid profile: lowers LDL cholesterol and triglycerides, increases HDL.

Terazosin, Doxazosin

These are long acting congeners of prazosin with similar properties but suitable for once daily dosing study doxazosin monotherapy has doubled the incidence of CHF; but this can occur with any alpha 1 blocker. A higher incidence of stroke relative to patients receiving a thiazide diuretic was also noted. Their status in hypertension is similar to that of prazosin.

Angiotensin II receptor blockers

Angiotensin II receptor blockers, sometimes called angiotensin II inhibitors, treat a variety of conditions, such as high blood pressure, heart failure and scleroderma. In a dose of 50mg/day losartan is an effective antihypertensive. Action manifests early and progresses to peak at 2-4 weeks. Addition of 12.5 mg/day hydrochlorothiazide further enhances the fall in BP. The newer ARBs -valsartan, candesartan, irbesartan and telmisartan have been shown to be as effective antihypertensive as ACE inhibitors, while losartan may be somewhat weaker than high doses of ACE inhibitors related cough is not encountered. Angioedema, urticaria and taste disturbance are also rare. Though effects of ACE inhibitors and ARBs are not identical, the latter have all the metabolic and prognostic advantages of ACE inhibitors.

Angiotensin-converting enzyme (ACE) inhibitors

ACE inhibitors treat a variety of conditions, such as high blood pressure, scleroderma and migraines. Find out more about this class of medication.

Mechanism of Action

The ACE inhibitors are one of the first choice drugs in all grades of essential as well as reno vascular hypertension. Most patient require relatively lower doses which are well tolerated. They are the most appropriate antihypertensive in patient with diabetes, left ventricular hypertrophy, CHF, angina and post MI cases. They appear to be more effective in younger hypertension than in the elderly. Dry persistent cough is the most common side effect requiring discontinuation of ACE inhibitors.

Beta blockers

Beta blockers treat a variety of conditions, such as high blood pressure, glaucoma and migraines. Find out more about dosing and side effects. They are mild hypertensive; do not significantly lower BP in normotensive. Used alone they suffice in 30-40% patients-mostly stage 1 cases. Additional BP lowering may be obtained when combined with other drugs. The hypotensive response to B blockers develops over 1-3 weeks and is then will sustained. Despite short and differing plasma half lives, the antihypertensive action of most B blockers is maintained over 25 hr with a single daily dose.

All B blockers, irrespective of associated properties, exert similar antihypertensive effect. A drug with intrinsic sympathomimetic activity (ISA) causes no reduction of HR and cardiac output, but it may lower vascular resistance by beta 2 agonism. Nebivolol reduces t.p.r. by generating NO. The nonselective B blockers slightly reduce renal blood flow and g.f.r., but this is minimal in the beta 1 selective blockers and in those with ISA.

There are several contraindications to beta blockers, including cardiac, pulmonary and peripheral vascular disease. The nonselective beta blockers have an unfavourable effect on lipid profile. They have also fared less well on quality of life parameters like decreased work capacity, fatigue, loss of libido and subtle cognitive effects, nightmares and increased incidence of antidepressant use. Beta blockers and ACE inhibitors are the most effective drugs for preventing sudden cardiac death in post infarction patient.

Calcium channel blockers

Calcium channel blockers, also called calcium antagonists, treat a variety of conditions, such as high blood pressure, migraines and Raynaud's disease.

Mechanism of Action

Calcium channel blockers are another class of first line antihypertensive drug. All 3 subgroups of CCBs, are dihydro pyridines. Phenyl alkylamine and benzithiazepine and these are most efficacious anti hypertensive. They lower BP by decreasing peripheral resistance without compromising c.o. Despite vasodilatation, fluid retention is insignificant.

Other advantages of CCBs are:

1. Do not compromise with haemodynamics.

2. No sedation or other CNS effects; cerebral perfusion is maintained.
3. Not contraindicated in asthma, angina and PVD patients: may benefit these conditions.
4. Do not impair renal perfusion.
5. Do not affect male sexual function.
6. No deleterious effect on plasma lipid profile, uric acid level and electrolyte balance.
7. Shown to have minimal effect on quality of life.
8. No adverse fetal effects; can be used during pregnancy.

Central-acting agents

Central-acting agents, also called central adrenergic inhibitors, treat conditions such as high blood pressure and drug or alcohol withdrawal by affecting your nervous system.

Choosing blood pressure medications

Choosing the right high blood pressure medication can be tricky. Find out when the various drug options are appropriate.

Diuretics

Diuretics, sometimes called water pills, treat a variety of conditions, such as high blood pressure and edema. Find out more about this class of medication. Ex- Thiazide, High ceiling diuretics, Potassium sparing diuretics.

Thiazide

These are the diuretic of choice for uncomplicated hypertension; have similar efficacy and are dose to dose equivalent. All mega trials have been carried out with these two only. Chlorthalidone is longer acting than hydrochlorothiazide and may have better round the clock action. Indapamide is also mainly used as antihypertensive, and is equally effective.

High Ceiling Diuretics

Furosemide, the prototype of this class, is a strong diuretic, but the antihypertensive efficacy does not parallel diuretic potency.

Furosemide is a weaker antihypertensive than thiazides: fall in BP is entirely dependent on reduction in plasma volume and c.o. The explanation of this paradox may lie in its brief duration of action.

The natriuretic action lasting only 4-6 hr after the conventional morning dose is followed by compensatory increase in proximal tubular reabsorption of Na deficient state in vascular smooth muscle may not be maintained round the clock? The t.p.r. and vascular responsiveness is not reduced. The high ceiling diuretics are more liable to cause fluid and electrolyte imbalance, weakness and other side effects.

Potassium Sparing Diuretics

Spironolactone, eplerenone and amiloride but not triamterene themselves lower BP slightly. However, they are used only in conjunction with a thiazide diuretic to prevent K loss and to augment the antihypertensive action. Spironolactone is not favored because of its hormonal side effects.

Serotonin syndrome

Serotonin syndrome is caused by mixing some antidepressants and other medications and that can be life-threatening if left untreated.

Vasodilators

Vasodilators treat a variety of conditions, including high blood pressure. Find out more about this class of medication.

Mechanism of Action:

Hydralazine/ Dihydralazine

It is a directly acting arteriolar vasodilator with little action on venous capacitance vessels; causes greater decreases in diastolic than in systolic BP. Reflex compensatory mechanisms are evoked which cause tachycardia, increase in c.o. and rennin release –increased aldosterone-Na and water retention. The mechanism of vascular smooth muscle relaxant action of hydralazine is not clearly known. Interference with Ca release, opening of certain K channels and no generation may be involved.

Sodium nitropruside

It is a rapidly and consistently acting vasodilator, has brief duration of action so that vascular tone can be titrated with the rate of i. v. infusion. Nitropruside improve ventricular dilatation and c.o. mainly by reducing aortic impedance, but also by lowering arterial filling pressure.

Alternative Remedies

Hypertension or high blood pressure is a chronic condition in which the arterial blood pressure is elevated (normal blood pressure is 120/80 mm Hg). Although antihypertensive medications are available to treat high blood pressure, they are usually associated with many side-effects.

Hence, hypertensive individuals prefer natural alternatives instead of conventional medications as they are not only effective but are comparatively safe. Some of the widely used alternative measures for lowering high blood pressure are –

Dietary changes

The DASH diet includes eating foods with potential antihypertensive activity like fresh fruits and vegetables (amla juice, beetroot garlic and radish), whole grains, milk, etc and lowering the intake of salt and processed foods. Read about 10 fruits and vegetables that are good for people with hypertension.

Exercise

Regular physical activity of 30 to 60 minutes lowers your blood pressure level by 4 – 9 mm Hg. Read about top 8 reasons to start exercising today

Natural herbs

The commonly used natural remedies with antihypertensive property include garlic, custard apple, celery, ajwain, carrot, flaxseeds (alsi), tomato, drumsticks, basil (tulsi), and pomegranate, sesame (til), cocoa bean, wheat bran, black plum and ginger. Read about herbal remedies for hypertension

Stress management

Stress is one of the key factors responsible for hypertension. The various relaxation techniques used to relieve stress and lower high blood pressure are controlled breathing, reiki, acupuncture and meditation.

Yoga

Sitting and supine positions that place the spine in a horizontal position, and exert less strain on the heart can be therapeutic. Some recommended yoga *asanas* are sukhasana, bhramari pranayama, janusirsasana, paschimotanasana, shavasana, setubandhasana, pawanmuktasana and shishuasana.

Probiotics

Probiotics, which contain good bacteria, were known to promote a healthy digestive system in addition to improving immunity. But research studies have shown that these 'helpful bacteria' exert antihypertensive potential by improving lipid profile, function of the enzyme renin (responsible for normal blood pressure) and insulin resistance in the body.

Prevention & Maintenance of Hypertension

Below are some changes you could make to your lifestyle to reduce high blood pressure. Some of these will lower your blood pressure in a matter of weeks, others may take longer.

- **Cut your salt intake to less than 6g (0.2oz) a day.** Find out how you can reduce the amount of salt in your diet.
- **Eat a healthy, low-fat, balanced diet**, including plenty of fresh fruit and vegetables. Get tips on eating more healthily.
- **Be active:** being physically active is one of the most important things you can do to prevent or control high blood pressure. Get tips on being more active.
- **Cut down on alcohol:** Get tips on cutting down, download a drinks diary and keep track of your drinking.
- **Lose weight:** Find out what your ideal weight is using the BMI healthy weight calculator.
- **Stop smoking:** Smoking greatly increases your chances of getting heart and lung diseases. Get help quitting.
- **Drink less coffee, tea or other caffeine-rich drinks such as cola.** Drinking more than four cups of coffee a day may increase your blood pressure.

You can take these steps today, regardless of whether or not you're taking blood pressure medication. You don't need a doctor to prescribe lifestyle changes.

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