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### HYPERTENSION: MANAGING THE SILENT KILLER

Mohana. M. Nair\*<sup>1</sup>, M. R. Anithalekshmi<sup>1</sup>, L. lekshmi<sup>1</sup>, Linku abraham<sup>1</sup>, Neema aniyani<sup>1</sup>, Nikhila. M. Nair<sup>1</sup>, Rinu varghese<sup>1</sup>, A. Shajan<sup>1</sup>

<sup>1</sup>\* Department of Pharmaceutics, Nazareth College of Pharmacy, Othara P.O, Thiruvalla, Kerala- 689546, India.

#### ABSTRACT

High blood pressure (BP) is a major public health problem and its prevalence is rapidly increasing among urban and rural populations. Hypertension puts strain on the heart, which leads to hypertensive heart disease and coronary artery disease if not been treated and becomes major risk factor for stroke, aneurysms of arteries, peripheral arterial disease and is a cause of chronic kidney disease. Cardiovascular risk can be decreased by reducing systolic and diastolic blood pressure and this can be achieved by non-pharmacological (lifestyle measures) and pharmacological means. Lifestyle changes should be the initial approach for management of hypertension and include dietary interventions (reducing salt, increasing potassium, alcohol avoidance), weight reduction, cease tobacco use, physical exercise, and stress management. The pharmaceutical agents which are available for initial treatment of high BP include older molecules like Thiazide diuretics and beta-blocking agents and newer molecules, dihydropyridine calcium channel blockers (CCB), angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARB). Comprehensive management of hypertension focuses on reducing overall cardiovascular risk by lifestyle management, BP lowering and lipid management and should be the preferred initial treatment approach, although drug treatment is still necessary in patients for whom lifestyle changes are not enough or not effective.

#### KEYWORDS

Hypertension, Diuretic, Angiotensin Receptor Blocker, Systolic and Diastolic.

#### Author for Correspondence:

Mohana. M. Nair,  
Department of Pharmaceutics,  
Nazareth College of Pharmacy,  
Othara P. O, Thiruvalla, Kerala, India.

**Email:** mohananair90@gmail.com

#### INTRODUCTION

Hypertension is a major public health issue throughout the world because of its high prevalence and its association with increased risk of cardiovascular disease that contributes significantly to cardiovascular mortality. This risk reduction is steeper in younger subjects than in the older subjects. The increasing prevalence of hypertension is attributed to population growth, age and behavioural risk factors, such as unhealthy diet, harmful use of alcohol, lack of physical activity,

excess weight and persistent stress. Advances in the diagnosis and treatment of hypertension have played a major role in decreasing coronary heart disease and stroke mortality in industrialized countries.

In 2008, worldwide, approximately 40 percentage of adults aged 25 and above were diagnosed with hypertension; now the number of people with the condition has been roused from 600 to above 1 billion. Globally cardiovascular disease accounts for approximately 17 million deaths a year, one by third of the total. Of these, complications of hypertension account for 9.4 million deaths worldwide every year. Hypertension causes at least 45% of deaths due to heart disease and 51% of deaths due to stroke. It contributes to the burden of heart disease, stroke and kidney failure and premature mortality and disability<sup>1</sup>.

### **Hypertension**

(HTN) or high blood pressure, sometimes called arterial hypertension, is a chronic medical condition in which the blood pressure in the arteries is persistently elevated exceeding 140 over 90mm Hg or high blood pressure is defined as a systolic blood pressure of 140 mm Hg or greater and a diastolic blood pressure of 90 mm Hg or greater. The measure of the force applied on the artery walls when the heart is contracting or beating is called the Systolic blood pressure. The force applied on the walls of artery when the heart is relaxed or in between beats. Blood pressure is measured in millimeters of mercury (mm Hg) is called the Diastolic blood pressure<sup>2</sup>. High blood pressure can occur in people of any age, but is more common in adults over the age of 35. Hypertension is a silent, invisible killer that rarely causes symptoms in the early stages and many people remain undiagnosed. Those who are diagnosed may not have access to treatment and may not be able to successfully control their illness over the long term the damage it does to the arteries and organs can lead to considerable suffering and healthcare costs. Hypertension is the most important modifiable risk factor for coronary heart disease (which leads to premature death) and stroke (the third leading cause). It is also an important cause of congestive heart failure and chronic kidney disease so there is a

significant health and economic gain related to the early detection, adequate treatment and a good control of hypertension. Hence this has 'earned' hypertension a name as the 'silent killer', making it a key priority for prevention, detection and control, and one of the most important challenges facing public health today<sup>3</sup>.

### **RISK FACTORS FOR HYPERTENSION<sup>2,4</sup>**

Obesity (abdominal circumference  $\geq 102$  cm for men and  $\geq 88$  cm for women) C-reactive protein  $\geq 1$  mg/dL

Family history of high blood pressure

High dietary salt or sodium intake

Sedentary lifestyle

Smoking

High stress environment

Unhealthy diet

Other risk factors

Diabetes mellitus: plasma glucose  $\geq 126$  mg/dL (fasting)

Plasma glucose  $\geq 200$  mg/dL (postprandial)

Cerebrovascular disease

Heart disease (angina, myocardial infarction, heart failure)

Renal disease (diabetic nephropathy, serum creatinine  $>1.5$  mg in men,  $>1.4$  mg in women, proteinuria  $>300$  mg/24 hours)

Peripheral vascular disease

Advanced retinopathy (haemorrhage, papilloedema)

### **Prevention of hypertension<sup>2,4</sup>**

Stop smoking

Lose weight, if overweight

Increase in physical activity to improve cardiac fitness

Reduce sodium intake to  $<2.4$  g of sodium or  $< 6$  g of salt per day (1 1/4 teaspoon of salt)

Reduce intake of dietary saturated fat and cholesterol

Reduce alcohol intake (one to two drinks per day)

Adequate calcium, potassium, magnesium, and protein intake

Management of stress

### **Signs and symptoms of hypertension<sup>2,4</sup>**

There is a common misconception that people with hypertension always experience symptoms, but in reality most hypertensive people have no symptoms

at all. Sometimes hypertension causes symptoms such as,

Headache  
Shortness of breath  
Dizziness  
Chest pain  
Palpitations of the heart  
Nose bleeds  
Fatigue  
Vision changes  
Nausea  
Vomiting  
Anxiety  
Confusion  
Pale skin or redness of skin

It can be dangerous to ignore these symptoms, but neither can they be relied upon to signify hypertension. Hypertension is a serious warning sign for which significant lifestyle changes are required. The condition can be a silent killer and it is important for everybody to know their blood pressure reading.

#### **Diagnosis of hypertension<sup>5</sup>**

Uncomplicated hypertension is usually asymptomatic and many of these symptoms lead to hypertension such as headache, tinnitus, dizziness and fainting are probably psychogenic in origin. They may indicate hyperventilation, induced by anxiety over the diagnosis of a lifelong disease that threatens well-being and survival. But recent data indicate that, a person's general sense of well-being often improves during initiation of medical treatment of hypertension. These new data suggest that hypertension may not be as asymptomatic as was previously assumed. Even if not totally asymptomatic, hypertension can go unrecognized for years because overt signs and symptoms generally coincide with the onset of target organ damage. Therefore, proper technique of blood pressure measurement is required for hypertension detection. This can be achieved with the help of the following guidelines.

#### **Blood pressure measurement**

For Clinic BP, patients should be,  
Seated for at least 5 mins, without smoking, meal, caffeine intake or physical exercise for at least 30 mins

Seated position in a quiet room, back supported, arm supported (for example, resting on the Table)  
Seated with legs uncrossed, not talking and relaxed  
The correct cuff bladder must be placed at heart level

For home measurements, besides the above;  
A minimum measurement for 3 days and ideally 7 days should be performed

Should be done at about the same time once in the morning and evening

Morning (before drug intake if treated) and evening (before meal) readings

Should be taken with two measurements per occasion (1-2 mins apart)

The results must be immediately recorded in a specific logbook or stored in device memory

#### **Number of readings**

Take at least two readings separated by as much time as is practical. If readings vary by more than 5 mm Hg, take additional readings until two or more are close. Multiple measurements should be taken in patients with irregular pulse and in older patients with systolic hypertension.

For diagnosis, obtain at least two sets of readings at least a week apart. Although it is traditional to average blood pressure measurements at a given visit, recording individual blood pressure measurements with the lowest reading in any position (including standing) to be considered as the "blood pressure taken at that visit".

Initially, take pressure in both arms. If pressure differs by >10/5 mm Hg, use arm with higher pressure.

#### **Recordings**

Note the pressure, patient position, the arm used and cuff size (e.g. 140/90, seated, right arm, large adult cuff).

Office blood pressure measurements taken by trained professionals should be the blood pressure used for diagnosing and treating hypertension in all but a few special situations.

#### **TYPES OF HYPERTENSION<sup>6-9</sup>**

##### **Pre-hypertension**

Pre-hypertension is defined as SBP of 120 to 139 or DBP 80 to 89 mm Hg, based on 2 or more seated BP readings on each of 2 or more clinic visits. The

term “pre-hypertension” replaces former categories “high-normal” (130-139/85-89 mmHg) and “above optimal” (120-129/80-84 mm Hg). The term “Borderline Hypertension” is discouraged from use as it is imprecise and inconsistently defined.

Patients with pre-hypertension are at increased risk for progression to hypertension. Pre-hypertension tends to cluster with other CVD risk factors such as dyslipidaemia, glucose abnormalities and obesity. However, the weight of evidence suggests that pre-hypertension itself is an independent CVD risk factor

#### **Management of pre-hypertension**

Patients should be managed with non-pharmacologic interventions or lifestyle modifications to lower blood pressure..

There should be a 6-12 monthly follow-up in patients with pre-hypertension to detect and treat hypertension as early as possible.

Decision regarding pharmacological treatment should be based on the individual patient’s global CV risk. In Diabetes mellitus with proteinuria or patients with chronic kidney disease (with proteinuria >1g/day), medical treatment is required if BP is above 130/80. This also applies to other high risk subjects such as those with Previous CVA or CAD.

All patients with pre-hypertension should have full cardiovascular risk assessment. There is an inadequate evidence for pharmacological intervention in pre-hypertensive patients CV risk.

#### **Essential hypertension**

Also called primary hypertension or idiopathic hypertension) is the most common type of hypertension that accounts for 95% of cases of hypertension. No specific underlying cause but thought to be result from a genetic predisposition in addition to the cumulative effects of various lifestyle factors such as diet and exercise play important roles. The prevalence of essential hypertension increases with age and individuals with relatively high blood pressure at younger ages are at increased risk for the development of hypertension and it makes them suffer a lot. Hypertension increases the risk of cerebral, cardiac and renal events.

#### **Secondary hypertension**

Accounts for up to 5% of cases and is high blood pressure which is caused from an underlying disorder. Following are the examples:

Narrowing of certain arteries

Adrenal gland disorders

Kidney disorders

Use of medications, drugs or other chemicals, including over-the-counter medications like ibuprofen (Motrin, Advil) and pseudoephedrine (Afrin, Sudafed).

Pregnancy

The use of oral contraceptives, antihistamines, steroids, antidepressants or non-steroidal anti-inflammatory drugs.

Other related disorders and syndromes include airway obstruction during sleep, diseases of the adrenal glands, hormone abnormalities, thyroid disease, and too much salt or alcohol in the diet.

A good news is that if the cause is found, hypertension can often be controlled.

#### **Gestational**

Gestational hypertension occurs during pregnancy and usually returns to normal following childbirth. Hypertension in pregnancy is defined as a systolic blood pressure greater than or equal to 140mm Hg or diastolic pressure greater than or equal to 90mm Hg (with the patient seated and at rest). Hypertension in pregnancy is a risk factor for eclampsia, placental abruption and premature delivery.

#### **Additional hypertension types: Isolated systolic, Malignant and Resistant**

Isolated systolic hypertension, malignant hypertension and resistant hypertension are all recognized hypertension types with specific diagnostic criteria.

#### **Isolated systolic hypertension**

As people age, their arteries tend to lose elasticity and become less able to accommodate surges of blood. The damage created in the blood vessel lining when blood flows through the arteries at high pressure can accelerate plaque build up. Eventually, plaque deposits lead to atherosclerosis (hardening of the arteries). Atherosclerosis can elevate systolic blood pressure, while diastolic pressure stays in the normal range. A systolic pressure of 140 or greater

coupled with a diastolic reading of 89 or below is called isolated systolic hypertension. The systolic pressure is much more important than the diastolic pressure when it comes to the risk of cardiovascular disease for an older person. Changing patterns of BP occur with increasing age. The rise in Systolic blood pressure continues throughout life in contrast to Diastolic blood pressure, which rises until approximately age 50, tends to level off over the next decade, and may remain the same or fall later in life. Diastolic hypertension predominates before age 50, either alone or in combination with SBP elevation. The prevalence of systolic hypertension increases with age, and above 50 years of age, systolic hypertension represents the most common form of hypertension. DBP is a more potent cardiovascular risk factor than SBP until age 50; thereafter, SBP is more important. This is the most common form of high blood pressure in the elderly (over the age of 65).

#### **Malignant or accelerated hypertension**

A very high or rapidly rising blood pressure which threatens end-organ damage and requires urgent or emergency treatment. If your diastolic pressure goes over 130, you may have malignant hypertension. This is a medical emergency and should be treated in a hospital. Symptoms include numbness in the arms and legs, blurred vision, confusion, chest pain, and headache. About 1% of those with essential hypertension develop malignant hypertension. It is more common in younger adults.

#### **Resistant hypertension**

If the doctor has prescribed three different types of antihypertensive medications and your blood pressure is still too high, you may have resistant hypertension. Resistant hypertension may occur in 20 to 30% of high blood pressure cases. Resistant hypertension may have a genetic component and is more common in people who are older, obese, female, African American, or have an underlying illness, such as diabetes or kidney disease.

#### **Descriptive hypertension terms**

White coat hypertension and labile hypertension are terms that have been used interchangeably to describe hypertension types that come and go. These forms could indicate a higher risk for developing hypertension, or they could just be a

normal response. The term "labile" means blood pressure that changes over time—a pretty common occurrence for almost everyone.

"White coat hypertension" - patients may have high blood pressure when they see a doctor or nurse but have normal blood pressure when taken at home. Studies show this type of high blood pressure may affect as many as 30 percent of the population. In these subjects the clinic BP is persistently above 140/90 mm Hg but the home or 24-hour ambulatory systolic/diastolic BP measurements are lower than 130/80 mmHg. Because blood pressure can vary, your blood pressure must be documented at least three different times to accurately diagnose hypertension. Another suggestion is to repeat high blood pressure readings after 5 to 10 minutes. See your doctor regularly and make sure you know what your blood pressure is—your doctor can then figure out which of the hypertension types you have. It is still debatable whether isolated office hypertension is an innocent phenomenon or whether it carries an increased cardiovascular risk.

#### **Masked hypertension**

Patients with masked hypertension have normal clinic blood pressure but elevated 24 hour ambulatory or home blood-pressure load ( $\geq 135/85$  mmHg). Prognosis of masked hypertension is worse than isolated office hypertension. For both isolated office and masked hypertension, once diagnosed, first-line therapeutic interventions should be non-pharmacological and aim at lifestyle changes. However, drug treatment is indicated, particularly when the patient's cardiovascular risk profile is elevated or when target-organ damage (TOD) is detected.

The classification of blood pressure of adults is shown in Table No.1.

### **TREATMENT OF HYPERTENSION**

#### **Non pharmacological treatment<sup>5,10</sup>**

Dietary management; reduce salt, saturated fat and cholesterol in take

Stress management; reduce stress or look for ways to handle stress

Exercise; thirty minutes of moderate physical activity daily is recommended

Weight loss, if necessary

Your doctor may prescribe medication to control blood pressure

Non-pharmacological management (therapeutic lifestyle modification) plays an important role in the management of hypertension and in improving overall cardiovascular health. When recommending lifestyle modification, it is important to know that these interventions require a concerted effort from both the patient and the doctors.

#### **Weight reduction**

Weight-reducing diets in overweight hypertensive persons can result in modest weight loss in the range of 3-9% of body weight and are associated with blood pressure reduction of about 3-6 mm Hg for every kilogram of weight loss. It is advisable for overweight hypertensive patients to lose at least 5% of their weight. The blood pressure lowering effect of weight reduction may be enhanced by a simultaneous increase in physical exercise. Thus, sedentary patients should be advised to take up modest levels of aerobic exercise on a regular basis such as brisk walking for at least 30 minutes per day, most days of the week. However, isometric exercise such as heavy weight-lifting can have pressor effect and should be avoided. When hypertension is poorly controlled, and always for severe hypertension, heavy physical exercise should be discouraged or postponed until appropriate drug treatment has been instituted and found to be effective.

#### **Sodium intake**

Reducing dietary sodium intake to no more than 100 mEq/L (2.4 g sodium or 6 g sodium chloride a day is recommended) which is equivalent to <1¼ teaspoonfuls of salt or 3 teaspoonfuls of monosodium glutamate reduces the blood pressure by an average of 4-6 mmHg. Patients should be advised to avoid added salt, to avoid obviously salted food (particularly processed foods) and to eat more meals cooked directly from natural ingredients containing more Potassium. Hypertensive patients should also be advised to eat more fruit and vegetables, to eat more fish and to reduce their intake of saturated fat and cholesterol. This is well achieved by adoption of the Dietary Approach to Stop Hypertension (DASH) eating plan. The DASH diet is rich in fruits, vegetables and low-fat dairy

foods including whole grains, poultry, fish and nuts, and is reduced in fats, red meat, sweets and sugar-containing beverages. It contains reduced amounts of total and saturated fat and cholesterol, and increased amounts of potassium, calcium, magnesium, dietary fibre and protein. Fruits and vegetables, including nuts, are responsible for at least half of the total effect of the DASH diet. Moreover, the DASH diet is reasonably low in cost. The combined effects on blood pressure of low sodium intake and the DASH diet are greater than the effects of either alone and are substantial.

#### **Avoidance of alcohol intake**

There is a linear relationship between alcohol consumption, blood pressure levels and prevalence of hypertension in populations. High levels of alcohol consumption are associated with a high risk of stroke, particularly so for binge drinking. Alcohol attenuates the effects of antihypertensive drug therapy. Heavy drinkers may also experience a rise of blood pressure after acute alcohol withdrawal. Hypertensive patients who drink alcohol should be advised to stop drinking. If they insist on continuing to drink they should be advised, in any case, not to consume more than 30 ml of ethanol (the equivalent of two drinks per day) in men and no more than 15 ml of ethanol (one drink per day) in women and lighter-weight persons. (One drink is 360 ml of beer, 150 ml of wine and 45 ml of 80%-proof liquor). The only way to reduce these patients' BP effectively is by reducing or stopping their alcohol intake.

#### **Regular physical exercise**

Aerobic exercise is more effective than resistance training (e.g., weight lifting). Exercise like walking-jogging can result in a reduction of 13/18 mm Hg in SBP/DBP. More recent evidence showed that resistant exercise is effective in lowering blood pressure among normotensives and pre-hypertensives but not among hypertensives. General advice on cardiovascular health would be for modest exercise, such as brisk walking for a total of at least 150 mins per week.

#### **Diet**

A diet rich in fruits, vegetables and low fat dairy products with reduced saturated and total fat can substantially lower BP (11/6 mmHg in hypertensive

patients and 4/2 mm Hg in patients with high normal BP). More recently, following DASH diet and diet with high in L-Arginine has been shown to be able to reduce BP.

#### **Cessation of smoking**

Smoking can raise BP acutely. However the effect of chronic smoking on BP is less clear. Never the less smoking cessation is important in reducing overall cardiovascular risk.

#### **Relaxation therapy**

Relaxation interventions for eg. yoga, meditation etc. Are shown to be associated with statistically significant reductions in systolic and diastolic blood pressure of about 3 mm Hg. However, another systematic review of studies on the effect of stress reduction on blood pressure found small and non-significant effect on blood pressure. It is not recommended for routine provision in primary care.

#### **Others**

These include micro nutrient alterations, caffeine reduction and dietary supplementation with fish oil, potassium, calcium, magnesium and fibre. However the evidence for its beneficial effect is limited. In summary while weight reducing diet, regular exercise, alcohol and salt restriction have been consistently shown to be beneficial in reducing BP in patients, the evidence thus far has not been consistent for relaxation the rapies and supplementations with calcium, magnesium or potassium.

### **PHARMACOLOGICAL MANAGEMENT<sup>5,13,14</sup>**

#### **General guidelines**

Initiate pharmacologic treatment depends on the total cardiovascular risk. It is the reduction of BP which provides the main benefits in the general hypertensive population. The choice of drug should be individualized.

#### **Initiating Treatment**

As a first principle, chemical therapy should be coupled with lifestyle modifications (maintaining ideal body weight, engaging in aerobic physical exercise, having a healthy diet low in saturated and total fats, limiting sodium intake and reducing alcohol intake). Patients should be counseled on smoking cessation, lipid reduction and diabetic management. For patients with Stage I hypertension

with low cardiovascular risk, advice should be given on lifestyle modification for a period of three to six months. The patient should be seen two to three times during this period to assess the efficacy of the above intervention. Each of these lifestyle modifications has been shown to reduce blood pressure modestly. These modifications are inexpensive and pose very little risk. Compliance remains the primary trouble with these methodologies Stage I patients with medium or higher risk should be offered drug treatment upon diagnosis (Figure No.1).

#### **Best initial therapy for the newly diagnosed hypertensive patient**

If the lifestyle modification does not rectify the situation, then one should move to diuretics-particularly thiazide diuretics. If the diuretic is not fully successful, then a sympatholytic such as a beta-blocker must be added. Thereafter, vasodilators such as calcium-channel blockers, ACE inhibitors, or ARB's are instituted. Thiazide diuretics or beta-blockers are considered by many as first line agents in the treatment of hypertension because they are in expensive and have proven efficacy in reducing overall mortality. Unfortunately, the side effects of these drugs trouble some patients, and this may decrease compliance. Due to this reason, many patients are started early on more expensive drugs like ACE inhibitors. The long-term effects on morbidity and mortality are still being determined, and is considered "firstline therapy" which is likely to be a moving target in the coming years. The concept of stepped care is very important in the treatment of hypertension. If one therapy fails to achieve the targeted blood pressure, one adds an additional therapy (Table No.2). In general, giving small doses of two or more antihypertensives from different classes can cause additive or synergistic effects on blood pressure while minimizing side effects. In most cases this is preferable to giving a larger dose of a single drug.

### **Rational pharmacotherapy of hypertension**

#### **Reduce LV systolic performance (reduce the ESPVR)**

Negative inotropes (betablockers (metoprolol, atenolol and propranolol) and calcium channel blockers (verapamil, diltiazem).

#### **Reduce blood volume and thus drop LVEDV**

Diuretics (thiazide - hydrochlorothiazide, loop diuretics - furosemide, bumetanide and potassium sparing diuretics - spironolactone, amiloride, triamterene).

#### **Reduce venous tone and thus venous return**

Central sympatholytics such as clonidine act to reduce overall sympathetic tone.

#### **Reduce arterial tone (i.e. resistance) and thus reduce Ea**

Effective arterial dilators include angiotensin converting enzyme inhibitors (ACE inhibitors - lisinopril, captopril), angiotensin receptor blockers (ARB's - valsartan, losartan), calcium channel blockers (nifedipine, amlodipine), potassium channel openers (minoxidil), nitric oxide donors (nitroprusside), alpha1 blockers (prazosin, terazosin, doxazosin) and mixed alpha and beta-blockers.

### **Major Antihypertensive Drug Classes**

Diuretics (thiazide, loop, and potassium-sparing diuretics).

Thiazide diuretics such as hydrochlorothiazide and chlorthalidone are the most commonly used drugs for treating hypertension. They inhibit reabsorption of Na and Cl in the distal tubule and lose effectiveness when GFR is low. Their initial effects are said to be mediated by decreasing intravascular volume, however most untreated hypertensives have contracted intravascular volume. Diuretics cause peripheral vascular resistance to fall through an unknown mechanism. Unfortunately thiazide diuretics have a number of undesirable metabolic effects such as hypercalcemia, hypokalemia, hyponatremia, hyperglycemia, hyperlipidemia, and hyperuricemia. These side effects often dictate which drugs to use. When thiazide diuretics are used in low doses, their side effects seem to be minimized.

Loop diuretics such as furosemide inhibit the Na/K/Cl cotransporter in the ascending limb of the

loop of Henle. They cause a very brisk diuresis, but their anti-hypertensive effects are actually not that strong. Acute intravenous administration of furosemide can cause venodilation by an unknown mechanism. Loop diuretics are often part of treatment for malignant hypertension and hypertension with hypervolemia (e.g., renal insufficiency). The metabolic derangements produced by these drugs (particularly hypokalemia, and hypocalcemia) can be profound. This class is not recommended as initial monotherapy for hypertension.

Potassium-sparing diuretics such as spironolactone, amiloride, and triamterene are not as efficacious as thiazides or loop diuretics in reducing blood pressure, however, they do correct the potassium loss associated with thiazide and loop diuretics. Amiloride and triamterene inhibit the Na/proton exchanger in the distal and collecting tubules. Spironolactone inhibits the Na/K exchanger affected by aldosterone, and it is particularly effective in the face of hyperaldosteronism. If potassium-sparing diuretics are given to patients on ACE inhibitors, particular care must be taken since both classes cause elevations in serum potassium.

#### **Sympatholytics**

(beta-blockers, mixed alpha and beta-blockers, alphablockers and central sympatholytics).

#### **Beta adrenergic blockers**

Such as propranolol, metoprolol or atenolol are typical first-line agents for treating hypertension. They have negative chronotropic and negative inotropic effects. The acute effect of blocking beta-2 receptors is an increase in SVR, however chronic administration can decrease peripheral resistance, probably by decreasing plasma renin and angiotensin II. Unfortunately beta-blockers can elevate triglycerides and reduce HDL. In addition, they can produce glucose intolerance, impotence, and depression. In patients prone to bronchospasm (i.e., asthmatics), non-selective beta-blockers can theoretically worsen the problem, although the risks are somewhat overplayed. These side effects often dictate drug choices for the hypertensive patient.

#### **Alpha-1 adrenergic blockers**

Such as prazosin, terazosin and doxazosin are effective at reducing sympathetic vasoconstriction



and thereby reducing vascular resistance. These drugs are also useful for men who have benign prostatic hypertrophy because they can reduce bladder outlet obstruction. Unlike the beta blockers and thiazide diuretics, the alpha blockers have not been shown to decrease mortality. In fact, doxazosin caused an increase in congestive failure in the ALLHAT trial. Thus, the indications for these drugs in hypertension are currently unclear, and they are not considered first line treatments. Non-selective alpha blockers such as phenoxybenzamine and phentolamine are not used for hypertension because they produce an excessive amount of reflex tachycardia. However, the profound alpha blockade possible with the non-competitive antagonist, phenoxybenzamine, has proven very useful in the treatment of pheochromocytoma. These patients are usually given alpha-blockade first and then beta-blockade to control the reflex tachycardia.

#### **Central sympatholytics**

Such as clonidine stimulate central alpha-2 receptors and thereby reduce sympathetic outflow. These drugs are effective in decreasing heart rate, contractility and vasomotor tone, however, they cause sedation and are usually not first line therapies.

#### **Mixed alpha and beta antagonists**

Such as labetalol. And carvedilol block both alpha receptors and beta receptors, so the reduction in blood pressure is usually not associated with reflex tachycardia. Labetalol is a very effective intravenous antihypertensive, but it is less frequently used chronically in its oral form. Carvedilol has had its primary use in the treatment of chronic congestive heart failure.

#### **Vasodilators**

(Calcium-channel blockers, direct arterial vasodilators, and sodium nitroprusside).

#### **Calcium channel blockers**

Such as verapamil, diltiazem, nifedipine and amlodipine block L-type calcium channels and are effective arterial vasodilators. The dihydropyridine agent's nifedipine and amlodipine act primarily as vasodilators and have minimal direct effects on the heart. In contrast, verapamil and diltiazem act principally as negative inotropes and negative chronotropes, and thus decrease heart rate,

contractility and cardiac conduction speed. In addition, they reduce vascular resistance. There is controversy over the use of short-acting dihydropyridines in patients with angina because they can cause reflex sympathetic activation and worsen ischemia. When using verapamil or diltiazem one has to expect a reduction in LV systolic function as well as a reduction in cardiac conduction. Thus, in patients with congestive heart failure of the systolic type or in those with a significant conduction defect, these drugs should be avoided. Verapamil and diltiazem are synergistic with beta-blockers and the combination can cause severe bradycardia, heart block or pump dysfunction.

#### **Direct arterial vasodilators**

Such as minoxidil and hydralazine have relatively limited use. Neither has much effect on tone. The mechanism of action of hydralazine is not known. Minoxidil appears to increase potassium conductance in vascular smooth muscle, and the resultant hyperpolarization reduces calcium entry. Both drugs can cause reflex tachycardia (particularly minoxidil) and fluid retention. These side effects can be managed with the addition of a beta-blocker and/or a diuretic. Neither drug is effective for sustained periods. They are usually reserved for the short-term treatment of refractory hypertension, especially in patients with renal failure. Each of these drugs has a unique side effect: hydralazine can cause a lupus-like syndrome (Drug Allergy case), and minoxidil can produce hair growth (and is sold for the purpose).

#### **Sodium nitroprusside**

Breaks down non-enzymatically to form nitric oxide. It is an extremely potent arteriolar and venous dilator that is used intravenously for rapid control of hypertensive crises and for blood pressure control during operations. Reflex increases in heart rate and contractility usually require treatment with beta blockers.

#### **Renin-angiotensin system (RAS) blockers**

Comprise two broad categories: angiotensin converting enzyme inhibitors (ACE inhibitors) and angiotensin type 1 receptor blockers (ARB's).

### **ACE inhibitors**

Like captopril, enalapril, and lisinopril decrease the conversion of angiotensin I to angiotensin II (ATII). This reduces peripheral vascular resistance and promotes both natriuresis and hyperkalemia, since a reduction in ATII leads to a reduction in aldosterone. ACE also breaks down bradykinin, so inhibiting this enzyme can increase bradykinin levels and cause more vasodilation. ACE inhibitors have been shown to reduce morbidity (and possibly mortality - see below), and their relatively benign side-effect profile makes them frequent choices for first-line or monotherapy. Of note, ACE inhibitors are associated with a definite improvement in renal function in patients with diabetes and it has been shown that renal injury due to long-standing diabetes is reduced. ACE inhibitors are associated with a 5-10% incidence of dry cough, probably caused by the elevated bradykinin levels. For patients who have reduced renal perfusion pressure (e.g., renal artery stenosis), ACE inhibitors can cause renal dysfunction or renal failure. (Patients with bilateral renal artery stenosis have high levels of endogenous angiotensin II which is used to maintain glomerular filtration and ACE inhibitors disrupt that compensatory process.) Finally, ACE inhibitors are associated with a rare, but potentially fatal, angioedema of the airway.

### **Angiotensin receptor blockers (ARB's)**

Like losartan and valsartan cause arteriolar vasodilation by blocking the effects of angiotensin II at the angiotensin Type I receptor. Since the mechanism is essentially the same as for the ACE inhibitors, the indications and contraindications are the same. The blockade is downstream, so bradykinin is not elevated, and this class of drugs is not associated with a cough.

### **Demographic factors**

Elderly Patients are said to respond quite favorably to diuretics and calcium-channel blockers. However, due to their frequent conduction system disease, many of these patients need to be watched carefully when they are introduced to beta-blockers. Beta-blockers and diuretics reduce mortality in patients with isolated systolic hypertension (very common in the elderly).

### **Hypertensive crisis (malignant hypertension)**

This is an uncommon form of acute severe hypertension that can rapidly progress to stroke, MI, renal failure, or encephalopathy. These patients are admitted to the Intensive Care Unit for invasive hemodynamic monitoring and careful reduction of their blood pressure with fast-acting potent vasodilators such as sodium nitroprusside.

### **Disease processes which are affected by anti-hypertensive drugs**

#### **Diabetes**

Beta-blockers and thiazide diuretics may make glycemic control difficult. ACE inhibitors can protect the kidney.

#### **Coronary Artery Disease**

Beta-blockers offer a mortality benefit (in general). Short-acting calcium channel blockers can worsen ischemia.

#### **Congestive Heart Failure**

(Compensated vs. un-compensated) - Beta-blockers offer a mortality benefit as do ACE inhibitors. Beta-blockers should not be used in uncompensated CHF.

#### **Hyperlipidemia**

Beta-blockers and thiazide diuretics may affect lipid profile unfavorably.

#### **COPD/Asthma**

Beta-blockers need to be used with caution.

#### **Peripheral Vascular Disease**

(With Symptoms) - Beta-blockers need to be used with discretion.

#### **Renal Artery Stenosis**

(Bilateral vs. unilateral) - ACE inhibitor or ARB's are relatively contraindicated.

#### **Cardiac Conduction Defects**

Beta-blockers, diltiazem and verapamil can exacerbate conduction defects.

#### **Benign Prostatic Hypertrophy**

Alpha-1 blockers can provide symptomatic improvement.

#### **Depression**

Beta-blockers may exacerbate.

#### **Raynaud's Syndrome**

Beta-blockers may exacerbate.

#### **Renal Failure**

ACE inhibitors may cause a reduction in renal performance.

**Pregnancy**

ACE inhibitors and ARB's are contraindicated.

**Aortic Stenosis**

Vasodilators need to be introduced with caution.

**Hyperuricemia**

Gout) - Thiazide diuretics may increase uric acid levels.

ARB = angiotensin receptor blocker, ACEI = angiotensin-converting enzyme inhibitor, CCB = calcium channel blocker, DRI = direct renin inhibitor.

**Table No.1: Classification of Blood Pressure for Adults**

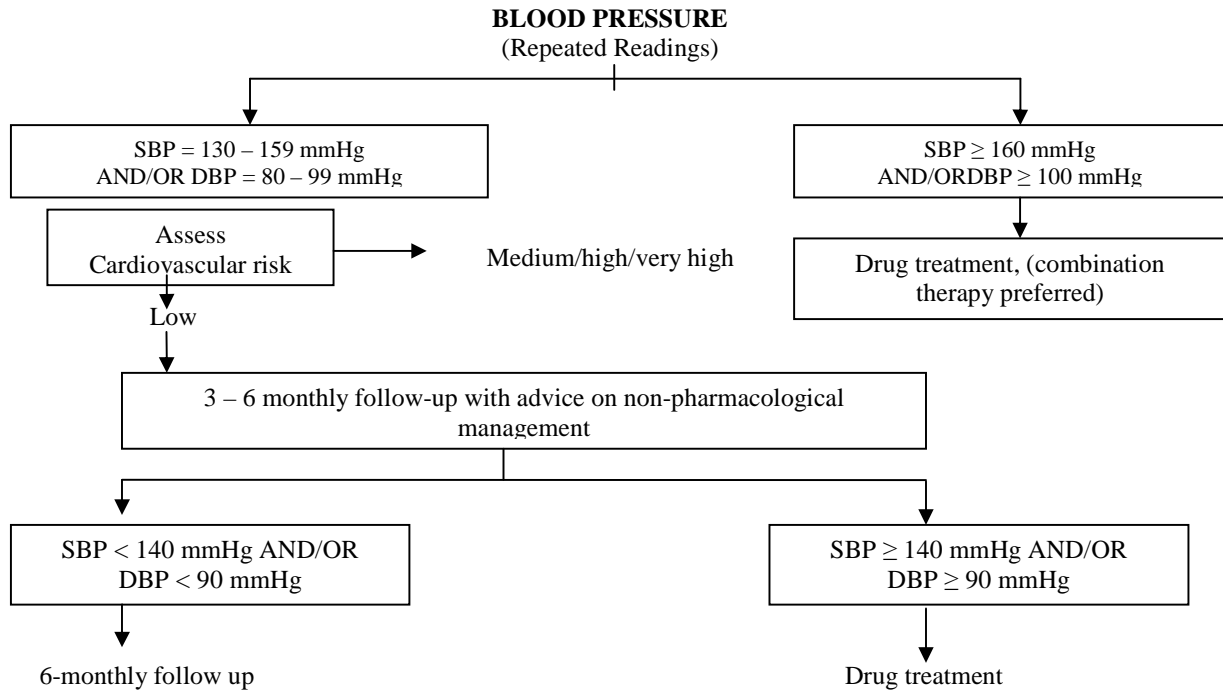
S.No	Category	Systolic BP (mm Hg)	and/ or	Diastolic BP (mm Hg)
1	Optimal	<120	and	<80
2	Normal	120-129	and	80-84
3	High normal	130-139	or	85-89
4	Hypertension	>140	or	>90

**Table No.2: Drug Combinations in Hypertension**

**Preferred (based on outcome trials)**  
 ACEI / thiazide or thiazide-like diuretics  
 ARB / thiazide diuretics  
 ACEI / CCB  
 β-Blocker / thiazide diuretics  
 Thiazide diuretics / K<sup>+</sup> sparing diuretics

**Acceptable (no outcome trial evidence yet)**  
 ARB / CCB  
 β-Blocker / thiazide-like diuretics  
 DRI/diuretic

ARB = angiotensin receptor blocker  
 ACEI = angiotensin-converting enzyme inhibitor  
 CCB = calcium channel blocker  
 DRI = direct renin inhibitor



**Figure No.1: Algorithm for the Management of Hypertension**

## CONCLUSION

Hypertension is a silent disease which is a major problem and the most prevalent chronic disease among which the majority of cases in the country remains undiagnosed. Most of the subjects have mild to moderate hypertension and the initial strategies for management involve lifestyle changes focussing on reduction of dietary salt, fat and alcohol and increase in potassium and fruits and vegetables. Blood pressure should be measured at every chance encountered. Weight management and reduction in obesity, regular physical exercise, tobacco cessation and stress management are important. Pharmacological treatment should be initiated after lifestyle interventions and choice of drug depends on age, the overall cardiovascular risk and co-morbidities. Every effort should be made to achieve target blood pressure. Target blood pressure depends on specific patient groups. Combination therapy is often required to achieve target and may be instituted clearly in patients with stage II hypertension and in high risk stage I hypertension. Management should focus on comprehensive risk reduction for better prognosis.

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## CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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