



REVIEW ARTICLE

Review on Hypertension

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Manuscript No: IJPRS/V3/I3/00390, Received On: 19/09/2014, Accepted On: 29/09/2014

ABSTRACT

Hypertension plays an important role in our health care system. It has a vital etiologic role in the development of various diseases and complications like cerebrovascular disease, ischemic heart disease, cardiac and renal failure and which leads to mortality and morbidity.

KEYWORDS

Hypertension, Etiologic, Complications, Mortality

INTRODUCTION

Hypertension (HTN) is a persistent increase in blood pressure. There are at least 970 million people worldwide who have hypertension. The World Health Organization (WHO) rates hypertension as among those diseases which causes premature death worldwide and the disease is still growing much bigger due to the present life style. In 2025 it is estimated there will be 1.56 billion adults living with high blood pressure.¹

Hypertension is an important topic in present medical and public health. The risk and occurrence of hypertension increases with increase age where more than 50 percent of the geriatric people are affected with maximum cases in those aged 70 years and above.² Blood pressure (BP) is the pressure exerted by the blood on the walls of the blood vessels. At normal condition heart beat is 60-70 times in a minute. When the heart beats, it pumps blood into the arteries.

Blood pressure when the heart beats during pumping the blood is called systolic blood pressure. In between the beats, when the heart is at rest, the blood pressure falls down which is called diastolic pressure.^{3,4}

HTN can be defined as a condition in which arterial blood pressure is elevated to an extent where clinical benefit is obtained from lowering of blood pressure.⁵ Normally the early stage of hypertension begin before developing sustained elevated blood pressure, and it can progress to organ damage often leading to morbidity and mortality. Hypertension plays an important etiologic role in the development of cerebrovascular disease, ischemic heart disease, cardiac and renal failure.⁶

Types of Hypertension

There are various types of hypertension namely,

Malignant Hypertension

It is also known as accelerated hypertension characterized by elevated blood pressure usually above 220/120 mm Hg, mostly associated with ongoing small blood vessels damage.⁵

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Primary or Essential Hypertension^{5,6,7,8}

Essential hypertension accounts for nearly 95% of all cases of hypertension where the cause cannot be identified. In patients with high BP, essential hypertension is diagnosed after secondary causes of hypertension are excluded.

Secondary Hypertension

Secondary hypertension has specific identified cause for the elevated blood pressure and is a potentially curable condition if the cause is eliminated.

Causes of Secondary Hypertension:

1. Renal diseases
2. Endocrine diseases: Conn's syndrome, Cushing syndrome, acromegaly, pheochromocytoma, etc.
3. Vascular causes: Renal artery stenosis, coarctation of the aorta, fibromuscular hyperplasia, renal artery atheroma, etc.
4. Drugs: Steroids, ciclosporin, NSAIDs, oestrogens, erythropoietin, etc.
5. Neurological causes: Guillain-Barre syndrome, Idiopathic, primary, or familial dysautonomia
6. Pregnancy induced hypertension
7. Increased intracranial pressure, Quadriplegia
8. Obstructive sleep apnea
9. Thyroid and parathyroid disorders
10. Alcoholism

Pseudo Hypertension

It mostly occurs in elderly patient. In this condition, the blood vessel become stiff and thicken due to calcification and resist compression from the bladder of the inflatable BP cuff.

White-coat Hypertension

It is the condition in which the patient's BP is consistently elevated when measured in a clinical environment in the presence of a health care professional. But when measured elsewhere, the BP is not elevated.

Hypertensive Crises

It is also known as hypertension emergency (with acute or progressive target organ damage) or urgency (without acute or progressive target organ damage). In this, the BP is markedly elevated above 180/110mm Hg. Hypertensive emergency requires immediate hospitalization.⁹

Pre-eclampsia

It is a pregnancy specific condition usually occurred after 20 weeks' gestation, consisting of hypertension with proteinuria.

Eclampsia

It is also a pregnant specific condition in which seizure occurs during pre-eclampsia.

Gestational Hypertension

In this, BP increased during pregnancy or in the first 24 hours and associated without proteinuria.⁹

Table 1: Blood Pressure Categories under JNC*7⁷

JNC 7	SBP (mmHg)		DBP (mmHg)
Normal	< 120	and	< 80
Pre-hypertension	120-139	Or	80-89
Hypertension			
Stage 1	140-159	or	90-99
Stage 2	≥160	or	≥ 100

*JNC= Joint National Committee

Risk Factors for Hypertension

High blood pressure has many risk factors which include:

Non Modifiable Risk Factors

Age, gender, race and genetic factors.

Modifiable Risk Factors

Overweight or obese, Alcohol intake, Physical activity, salt intake, Stress, Certain chronic conditions, etc.

Hypertension is an important worldwide public-health challenge because of its high frequency and concomitant risks of cardiovascular disease.¹⁰

Pathogenesis

Although the definitive cause of primary hypertension is unknown, it is believed those genes and the environment as well as their interactions play an important role. The major areas that involved are sympathetic nervous system (SNS) and renin-angiotensin system (RAS) and the kidney need to be reviewed.¹¹

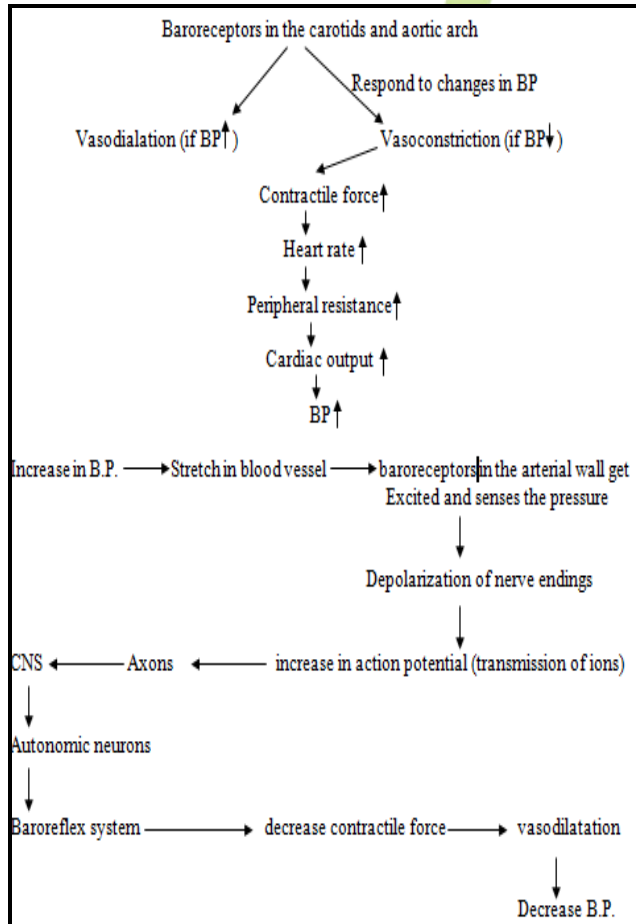
Blood pressure is proportional to cardiac output and peripheral resistance.

$$BP = \text{Cardiac output} \times \text{Total Peripheral resistance}^{12}$$

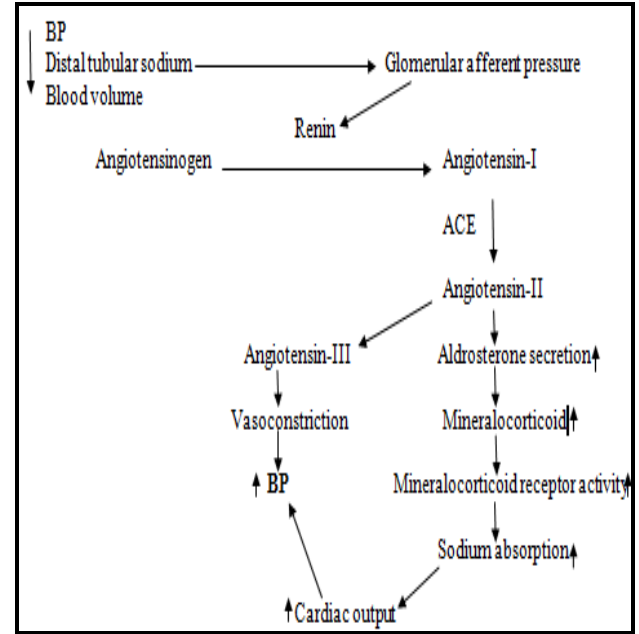
$$\text{Cardiac Output} = \text{Stroke volume} \times \text{Heart rate}$$

$$\text{Total Peripheral resistance} = \text{Vascular structure} \times \text{Vascular Function}$$

Sympathetic Nervous System



Renin Angiotensin – Aldosterone System



Complication of Hypertension¹³

As hypertension progresses, target-organ damage may appear. The primary organs involved are the heart, brain, kidney, eye, and peripheral blood vessels.

Cardiovascular events, cerebrovascular accidents, and kidney failure are the primary causes of morbidity and mortality in patients with hypertension.

Table 2: Target organ damage

	Target organ damage
Heart	Left ventricular hypertrophy Angina/prior myocardial infarction Prior coronary revascularization Heart failure
Brain	Stroke Transient ischemic attack Dementia
Kidney	Chronic kidney disease
Eyes	Retinopathy
Peripheral vasculator	Peripheral arterial disease

Management

Hypertension is termed the “silent killer” because patients with essential hypertension are usually asymptomatic. The primary physical finding is elevated BP. The diagnosis of hypertension cannot be made based on one elevated BP measurement.

The average of two or more measurements taken during two or more clinical encounters should be used to diagnose hypertension. Thereafter, this BP average can be used to establish a diagnosis and then to classify the stage of hypertension present.

Medical History and Physical Examination as per JNC IV¹⁴

Medical History

1. Duration and classification of hypertension
2. Patient history of CVD
3. Family history
4. Symptoms suggesting causes of hypertension
5. Lifestyle factors
6. Current and previous medications

Physical Examination

1. Blood pressure readings of minimum two times, including measurement in standing position
2. Verification in contralateral arm
3. Height, weight, and waist circumference
4. Fundoscopic examination for hypertensive retinopathy
5. Examination for any evidence of target organ damage

Goals of Therapy

The ultimate public health goal of antihypertensive therapy is the reduction of cardiovascular and renal morbidity and mortality. Hypertension associated complications are the primary causes of death in patients with hypertension.⁹

According to JNC 7

The BP goal is either < 140/90mm Hg in patients with hypertension associated with a decrease in CVD complications or < 130/80mm Hg in diabetes or renal disease associated hypertensive patients.

According to JNC 8

1. In patients of age 60 years and above; treatment starts if their BP is ≥ 150 mm Hg systolic or ≥ 90 mm Hg diastolic i.e. the goal is $\leq 150/90$ mm Hg
2. In patients below 60 years and ≥ 18 years with complication, treatment starts if their BP is ≥ 140 mm Hg systolic or ≥ 90 mm Hg diastolic i.e. the goal is $\leq 140/90$ mm Hg.

Non-Pharmacological Treatment

Adoption of healthy lifestyle by all hypertensive patients is critical for the prevention of elevated blood pressure. Lifestyle modifications lower blood pressure and should be encouraged for all patients with pre-hypertension. In patients who are overweight, reduction of weight is beneficial, regular exercise, control of diet like less salt intake, restriction in fat intake, consumption of more fruits and vegetables are advisable.⁵ These lifestyle modifications may be sufficient as initial therapy for patients with stage-1 hypertension. They are adjunctive therapy for those with severe hypertension.¹⁵

DASH Therapy: Dietary Approaches to Stop Hypertension

Diet rich in fruits, vegetables and low fat dairy products with a reduced content of saturated and total fat; dietary sodium is restricted to less than 2.3 gm sodium or 6gm sodium chloride; and encouraged physical activity like brisk walk, aerobic dance, etc; and decrease alcohol consumption.

Pharmacological Treatment

Pharmacological treatment of patients with hypertension is to reduce morbidity and mortality from cardiovascular diseases. An effective antihypertensive treatment can markedly reduce the risk of stroke, cardiac

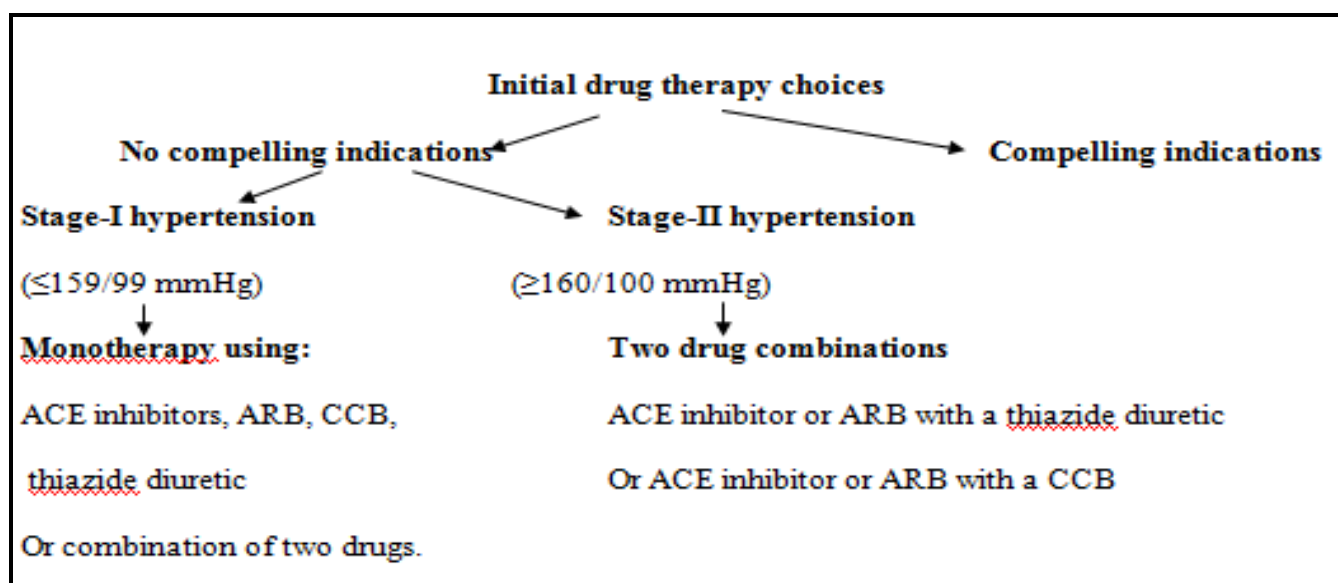
Lifestyle Modifications to Manage Hypertension

Modification	Recommendations	Approximate SBP reduction
Weight reduction	Maintain normal body weight (BMI 18.5 - 24.9)	5-20 mmHg/10 kg weight loss
Adopt DASH eating plan	Consume a diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated and total fat	8-14 mmHg
Dietary sodium	Reduce dietary sodium intake to no more than 2.4 g sodium or 6 g sodium chloride/day	2-8 mmHg
Physical activity	Engage in regular aerobic physical activity such as brisk walking (at least 30 minutes per day, most days of the week)	4-9 mmHg

Table 3: Anti-hypertensive drugs and their mechanism of action^{12,16}

Class	Examples	Mechanism of action	Common Side Effects
Diuretics	a) Thiazide diuretics: Chlorothiazide (250-500mg OD or bid), hydrochlorothiazide (12.5-50 mg), indapamide, etc. b) Loop diuretics: Furosemide (20-80mg), ethacrynic acid (25-100mg), torsemide, etc. c) Potassium sparing diuretics: Spironolactone (25-100mg), amiloride (5-10mg), triamterene, etc.	Reduction in plasma volume and cardiac output, reduction in total peripheral resistance	Hyponatremia, hypokalemia, hyperkalemia, hyperuricemia, hypercholesterolemia, dehydration, hyperglycemia, etc.
Angiotensin converting enzyme inhibitors (ACEIs)	Captopril (12.5-25 mg), enalapril (5-40mg), lisinopril (10-40mg), ramipril, benazepril, etc.	Inhibit the conversion of angiotensin I to angiotensin II	Cough, hypotension, angioedema, hyperkalemia, etc.
Angiotensin receptor Blockers (ARB)	Candesartan (8-32 mg), telmisartan (20-80 mg), Losartan, irbesartan, valsartan, etc.	Block the angiotensin II type I receptor and have similar effects as that of ACE	Diarrhea, dizziness, fatigue, angioedema, infection, etc.

Calcium channel blockers (CCBs)	<p>a) Benzodiazepine derivatives: Diltiazem (120-540mg)</p> <p>b) Diphenylalkylamine derivatives: Verapamil (120-480mg)</p> <p>c) Dihydropyridines: Amlodipine (2.5-10 mg), nifedipine, isradipine, felodipine, etc.</p>	Decrease peripheral resistance without compromising cardiac output	Bradycardia, oedema, flushing, palpitation, hypotension, constipation, etc.
Renin Inhibitors	Aliskiren (150-300 mg)	Decreased renin secretion thereby reduces RAAS activity.	Diarrhea, angioedema, etc.
β- Adrenergic Blockers	Propranolol (60-180 mg), atenolol (25-100mg), bisoprolol, acebutolol, carvedilol, metoprolol, pindolol, timolol, etc.	Decreased demand for myocardial energy, oxygen consumption, antagonist catecholamines, reduces plasma renin activity	Depression, bradycardia, fatigue, Congestive cardiac failure, etc.
Peripheral α-Adrenergic Blockers	Doxazosin (1-16mg), prazosin (2-20mg), terazosin (1-20mg), etc.	It blocks α action which constricts arterioles and veins	Dizziness, faintness, palpitation, syncope, etc.
Central sympatholytic or central α_2-receptor agonists	Clonidine (0.1-0.8mg), methyldopa (250-1000mg), guanfacine (0.5-2.0 mg), etc.	Decreases sympathetic outflow	Fluid retention, dry mouth, sedation, hypotension, etc.
Direct Vasodilators	Hydralazine (25-100mg), minoxidil (2.5-80mg), Diazoxide, etc.	Reduces total peripheral resistance	Tachycardia, fluid retention, hypotension, etc.
Adrenergic antagonist	Reserpine (0.1-0.5mg), guanethidine (10-50mg), guanadrel (10-74mg), etc.	Decreases sympathetic outflow	Nasal stuffiness, drowsiness, bradycardia, etc.



failure, renal insufficiency and other target organ damages due to hypertension.

Depending on the degree of elevated BP, the initial drug therapy is selected and also depends on the presence of any compelling indication(s).¹⁷

There can be six (6) major compelling indications with patients suffering from hypertension:

1. **Left ventricular dysfunction:** Diuretics with ACE inhibitors; then add β -blocker; then aldosterone antagonist or ARB
2. **Post myocardial infarction:** β -blocker; then add ACE inhibitor or ARB
3. **Coronary artery disease:** β -blocker; then add ACE inhibitor or ARB; later add CCB, diuretic
4. **Diabetes mellitus:** ACE inhibitor or ARB; then add diuretic and then CCB, β -blocker
5. **Chronic kidney disease:** ACE inhibitor or ARB
6. **Recurrent stroke syndrome:** Diuretic with ACE inhibitor

Special Populations⁵

1. Pediatric populations: Blood pressure of children varies according to age and

Physiological functions. In normal children, the normal blood pressure is as follows:

- a. 3-5 yrs old: SBP varies from 104 to 116 mm Hg and DBP varies from 63 to 74 mm Hg.
- b. 6-9 yrs old: SBP varies from 108 to 121 mm Hg and DBP varies from 71 to 81 mm Hg.
- c. 10-12 yrs old: SBP varies from 114 to 127 mm Hg and DBP varies from 77 to 83 mm Hg.

Dose adjustment is required for antihypertensive drug for children.

2. Geriatric population: Life style modification is required for geriatric patients. Elderly patients are very sensitive to medications that cause sympathetic inhibition. Decrease hepatic and renal function can increase the risk of adverse effects. Antihypertensive drugs should be started at half the recommended starting dose to decrease the adverse effects. Diuretics and β -blockers are effective in elderly patients.
3. Women: women taking oral contraceptives may have high BP. If hypertension develops as a result of oral contraceptives, alternative contraceptive method should be used. If hypertension is diagnosed before pregnancy, antihypertensives can be continued throughout the pregnancy except ACEIs and ARBs since they are teratogenic drugs. β -

blockers should be avoided during early phase (1st trimester) of pregnancy since there is risk of fetal growth retardation; but can be used in 2nd and 3rd trimesters. If hypertension is diagnosed during pregnancy, methyldopa is the choice of drug.

- Hypertension emergency/ malignant hypertension: immediate treatment with an intravenous antihypertensive agent is needed. The marked increased in BP can result in arteriolar fibrinoid necrosis, endothelial damage, platelet and fibrin deposition in smooth muscles, etc leading to end-organ ischemia, myocardial infarction, angina pectoris, pulmonary edema, stroke, etc. The choice of drug depends on clinical situation. Commonly, diazoxide, labetalol, hydralazine, nitroprusside, i.v. nitroglycerine, etc.
- Hypertension urgency: BP can reduce over 24hrs. Commonly captopril and clonidine are preferred.

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