Management of Hypertension: Focus On Current Treatment Algorithms

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Abstract : One of the main obstacles in the treatment of hypertension is the largely asymptomatic nature of the disease, even with marked elevation in systemic blood pressure. This disconnect between symptoms and long term adverse consequences has earned hypertension the designation, "silent killer". Fortunately, the number and spectrum of agents available to treat patients with hypertension have expanded dramatically over the past 2 decades. Current treatment algorithms recognize that any given drug will likely have effect on more than one of the interrelated systems that regulate circulatory functions.[Choudhary R et al NJIRM 2013; 4(3) : 133-137]

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Introduction: Hypertension is the most common cardiovascular disease. The prevalence varies with age, race, education and many other variables. According to some studies, 60-80% of both men and women will develop hypertension by age 80. Sustained arterial hypertension damages blood vessels in kidney, heart and brain and leads to an increased incidence of renal failure, coronary disease, heart failure and stroke. Effective pharmacologic lowering of blood pressure has been shown to prevent damage to blood vessels and substantially reduce morbidity and mortality rates. Knowledge of several antihypertensive drugs, along with their antihypertensive mechanisms and sites of action allows accurate prediction of efficacy and toxicity. As a result, rational use of these agents, alone or in combination, can lower blood pressure with minimal risk of serious toxicity in most patients[1].

Measurement of Blood Pressure: Blood pressure should be measured at least on 2-3 different occasions and every time in 2-3 different positions (recumbent, sitting and standing) and then diagnosis should be made. Both the systolic and diastolic BP is important and rise in either has deleterious effect. Systolic BP is due to circulatory volume and heart rate while diastolic BP is due to peripheral vascular resistance[2].

Categories of hypertension: According to Joint National Committee (JNC) VII on hypertension (2003), the normal and degree of hypertension have been categories as follows:

Category	BP (mmHg)	
	Systolic	Diastolic
Normal	<120	<80
Prehypertension	120-139	80-89
Hypertension stage I	140-159	90-99
Hypertension stage II	≥160	≥100

Note : If diastolic BP is more than 120mmHg it is hypertensive crises and further subdivided into hypertensive urgency if there is no evidence of organ damage and the hypertensive emergency, if there is evidence of organ damage, respectively.

Types of Hypertension:

Primary/Essential/ Idiopathic: In most of the patients (≥90%), the cause of hypertension is not detected. These cases are not curable but they are well controlled throughout the life with proper drug treatment and non pharmacological measures.

Secondary hypertension: In small number of patients (≥10%) there is persistent rise in BP secondary to certain disease. The cause is cardiovascular including anomalies like coarctation of aorta, renal, endocrine and other causes.

If cause is known the definite treatment (often curative) is treatment of the cause apart from symptomatic treatment for short duration.

Uncontrolled hypertension: Prolonged uncontrolled hypertension may lead to complications, even if it is not severe. These complications lead to damage to various organs and increases mortality.

Resistant hypertension: Monotherapy as a rule is less efficacious and most of the patients with hypertension require two or more drugs, preferably acting by different mechanisms[3].

Pulmonary hypertension : It is more common in females than males. May be associated with tricuspid valve disease, due to increased COP as in cirrhosis of liver, Raynauld's disease etc.

Lifestyle Modifications: It is beneficial for both non hypertensive and hypertensive individuals. Risk factors such as hyperlipidemia, obesity and diabetes and in all groups of patient's life style changes are more important[4].

"Maintaining a diet low in salt and saturated fats, high in fresh fruits and vegetables with low fat dairy products (DASH diet)" plus

- 30-60 min of moderate intensity dynamic exercise, 4-7 days of the week will lower blood pressure.
- Weight reduction in overweight individuals.
- Smoking cessation to reduce global cardiovascular risk.
- Discouraging of alcohol consumption.

Principles Of Drug Therapy: There are three general approaches to the pharmacological treatment of essential hypertension: The first involves the use of diuretics to reduce the blood volume.

The second employs drug that interfere with the RAAS (Renin-Angiotensin-Aldosterone System).

The third approach is aimed to the drug-induced reduction in PVR, COP or both. A reduction in PVR can be achieved directly by vasodilators and calcium cannel blockers or indirectly by modifying adrenergic mechanisms. In the latter category, the drugs are : beta blockers, alpha blockers and alpha+ beta blockers, and drugs which reduce central sympathetic outflow and ganglionic blockers[5]. (Table-1)

Table : 1 Antihypertensive drugs in use

Beta blockers	K+ sparing
Propranolol	Spironolactone
Metorpolol	Triamterene
Atenolol etc.	Amiloride, etc.
Beta+ alpha blockers	ACE inhibitors
Labetalol	Enalapril
Carvedilol, etc	Lisinopril
Alpha blockers	Ramipiril, etc.
Prazosin	AT1, antagonists
Terazosin	Losartan
Doxasozin	Candesartan
Phenoxybenzamine, etc.	Irbesatan, etc.
Central sympatholytics	Ca++ channel blockers
Clonidine	Verapamil
Metylolopa	Diltiazem
Ganglion blockers	Nifedipine
Trimetharphan	Amlodipine
Diuretics	Felodipine, etc.
Thiazides	Vasodilators
Hydrochlorozide	Arteriolar
Chlorthalidone	Hydralazine
Indapamide, etc.	Diazoxide
High ceiling	Fenoldopam
Furosemide, etc	Arteriolar + venous dilators
	Sodium-nitroprusside

Monotherapy and Stepped Care : Monotherpay is often sufficient to normalize blood pressure in patients with mild hypertension; this approach may improve patient compliance and avoid the risk of potential drug interactions. Thiazide diuretics, ACE-I, AT1, antagonists, Beta antagonists and calcium channel blockers have been shown to be similar in terms of efficacy in lowering blood pressure, in 30-50% of patients.

In the treatment of hypertension, it refers to the progressive, step by step addition of drugs to a therapeutic regimen combination therapy is based on the use of agents with distinct mechanism of action; it also emphasizes the use of sub maximal doses of drugs in an attempt to minimize potential adverse effects and toxicities. Current treatment algorithms recognize that any given drug will likely have effects on more than one of the interrelated systems that regulate circulatory function.

Furthermore pharmaceutical advances have allowed for novel drug formulation that can alter the kinetics of drug metabolism and eliminations[6].

Hypertensive Crisis: Hypertensive crises include hypertensive emergencies and urgencies.

Table : 2 Relative indications and contraindications for anti hypertensive agents

Drug class	Indications	Contraindications
Diurectics	Heart failure systolic hypertension	Gout
Beta antagonists	Coronary artery disease, Heart failure, Migraine, tachyarrhythmias	Asthma, Heart block
Alpha antagonist	Prostatic hypertrophy	Heart failure
Calcium channel blockers	Systolic hypertension	Heart block
ACE inhibitors	Diabetic or other nephropathy Heart failure, previous MI	Bilateral renal artery stenosis, Hyperkalemia, pregnancy
AT1, antagonists	ACE inhibitors-associated cough, Diabetic or other nephropathy, Heart failure	Hyperkalemia, pregnancy

Hypertensive Emergencies: Are situations with very high BP (210/120mmHg) associated with target organ damage. They may be life threatening conditions like malignant hypertension, hypertensive encephalopathy, acute myocardial infarction, dissecting aneurysm of aorta, acute LVF with pulmonary edema, etc. They require treatment in ICU with constant monitoring of BP.

Hypertensive Urgencies: Are conditions with highly elevated BP but no target organ damage. They require gradual reduction of BP over about 24 hours. Parenteral drugs are preferred in the treatment of hypertensive crises[7]. (Table -3). BP should be constantly monitored because drugs like sodium nitroprusside can bring down BP suddenly which results in hypoperfusion of vital organs.

Table : 3 Drugs in hypertensive emergencies

Drug	Dose	Duration of action
Sodium nitroprusside	0.5to10µg/kg/min IV infusion	1-2 min
Nifedpine	10mg sublingual	2-3hrs
Nitroglycerine	5to100µg/min IV infusion	3-5min
Fenoldapam	0.1to1.6µg/kg/min IV infusion	15-30min
Hydralazine	10to20mg IV bolus or 10-50mg IM	4-8hrs
Esmolol	50to300µg/kg/min IV infusion	10-15min
Labetalol	20to80mg IV every 10 min (max 300mg)	3-6hrs

Table : 4: Therapeutic combinations for treating hypertension

Indications	**Initial therapy**	**Second line therapy**	**Notes**
Isolated systolic hypertension without other compelling indications	Thiazide diuretics, ARBs, or long acting dihydropyridine CCBs	Combination of first-line drugs	Hypokalemia should be avoided in people who are prescribed diuretics
Diabetes mellitus with nephropathy	ACE inhibitors or ARBs	Addition of one or more thiazide diurectics, cardio selective beta blocker, long acting CCBs or use of	

		an ARB/ACE inhibitor combination	
Diabetes mellitus without nephropathy	ACE inhibitors, ARBs, or thiazide diurectics or long acting dihydropyridine CCBs	Combination of first line drugs or addition of cardio selective beta blockers and/or long acting CCBs	
Angina Pectoris	Beta blockers (strongly consider adding ACE inhibitors)	Long acting CCBs	Avoid short acting nifedipine
Prior myocardial infarction	Beta blockers and ACE inhibitors (ARBs if ACE intolerant)	Combinations of additional agents	
Heart failure	ACE inhibitors (ARBs if ACE inhibitor intolerant), beta blocker, spironolactone in selected patients	Hydralazine/ isosorbide dinitrate; thiazide or loop diuretics as additive therapy	Avoid nondihydropyridine CCBs
Past cerebrovascular accident or TIA	ACE inhibitor/ diuretic combination		Blood pressure reduction reduces recurrent cerebrovascular events
Chronic kidney disease	ACE inhibitor (diurectics as additive therapy)	Combinations of additional agents (ARBs if ACE inhibitor intolerant)	Avoid ACE inhibitors and ARBs if bilateral renal artery stenosis
Left ventricular hypertrophy	ACE inhibitors, ARBs, CCBs, thiazide diuretics (beta-blocker for patients under 60 years)		Avoid Hydralazine and minoxidil
Peripheral arterial disease	Does not affect treatment recommendation		Avoid beta-blockers with severe disease

Conclusion: The hemodynamic consequences of long term treatment with antihypertensive agents, provide a rationale for potential complementary effects of concurrent therapy with two or more drugs. Concurrent use of drugs from different classes is a strategy for achieving effective control of blood pressure while minimizing dose related adverse effects (Table-4). Lastly, genome wide scanning may lead to identification of novel genes that are significant clinically8. Likewise, treatment may benefit from an increased understanding of the molecular and genetic bases of hypertension.

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