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Approach to the Patients with Hypertension

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Person who is detected as high blood pressure should have complete history and physical examination to confirm the diagnosis of hypertension & also screen for other cardiovascular disease risk factor, secondary causes of hypertension, consequences of hypertension, complications of hypertension and associated comorbidities and lastly determine the potentials for proper therapeutic or surgical intervention to control the hypertension.

The patients with raised blood pressure are asymptomatic, but some patient complaints of headache which occur in the morning and localised to occipital region, other nonspecific symptoms like dizziness, palpitations early fatigability and impotence. These symptoms are usually related to causes of secondary hypertension. History taking should be excellent & include family history of hypertension and other CVS diseases, DM, dietary & psychosocial history weight gain, dyslipidaemia, smoking, physical inactivity. The renal disease, change in physical appearance, muscle weakness, excessive sweating, palpitation, tremors, erratic sleep and snoring, hypo or hyperthyroidism and drug consumption favour secondary hypertension. History taking will determine the type of hypertension primary or secondary hypertension.

The physical examination includes measurement of BMI to exclude metabolic and endocrine causes. The pulse rate, rhythm, volume and equal pulses in upper and lower extremities gives idea of AF, coarctation, hyper dynamic circulation (anemia, hyperthyroid & aortic incompetence, hypokalemia, shock, CCF) etc.

The technique of BP measurement should be accurate. Now days BP machine are replaced with aneroid oscillometric devices. These devices should be calibrated periodically and accuracy should be confirmed and maintained. Patient's position is very important; patient should be seated in quiet room in a chair with feet on floor for five minutes. The temperature of room should be normal, patient should not exercise, consume tea, coffee any drug prior to measurement of blood pressure. Two BP reading should be taken.

The centre of cuff should be at heart level. The width of bladder cuff should equal at least 40% of the arm circumference and length of the cuff bladder should encircle at least 80% of arm circumference. The bladder cuff and stethoscope placement should be proper. The bladder cuff should be inflated till patients pulse disappear and it should be raised 20 mm/Hg above then deflate the cuff 2mm of Hg/sec, the systolic BP is first two regular tapping sounds (Korotkoff) & diastolic BP is point at which regular Korotkoff sound is disappear.

Now days 24 hours ambulatory BP monitoring is more reliably predict cardiovascular disease risk. In suspected white coat hypertension, resistant hypertension, symptomatic hypotension, autonomic failure or episodic hypertension it is more useful.

The blood pressure should be measure in supine, sitting and standing position for evidence of postural hypotension. The neck should be examined for enlargement of thyroid gland for exclude hypothyroidism or hyperthyroidism.

The examination of blood vessels may provide underlying vascular disease like atherosclerotic diseases. The second heart sound is due to closure of aortic valves and S_3 gallop attributed to atrial contraction against non-complaint left ventricles. The LVH may be detected as sustained and laterally displaced apical impulse. The abdominal bruit throughout systole into diastole gives clue to renovascular hypertension. Palpable kidneys suspect polycystic or obstructed kidneys due to stone, stricture either unilateral or bilateral. The sign of CHF gives clue to heart enlargement and reduced pump (LVEF) action. Neurological examination shows evidence of TIA, embolic phenomenon and neurodeficit.

INVESTIGATION

(CBC, urine analysis, ECG, Funduscopy, X-ray chest and USG Abdomen pelvis).

CBC-shows type of anaemia type, renal function, electrolytes, fasting and Post meal blood sugar & lipid to rule out secondary causes of hypertension. Special investigation like MR angiogram is to localise the site of lesion in hypertension.

MANAGEMENT OF HYPERTENSION

Implementation of lifestyle as a first step in hypertension management is for prevention and treatment of hypertension. The impact of lifestyle interventions i.e. weight reduction, salt restriction is more pronounced in persons with hypertension. It prevents development of hypertension, avoids hypertensive complication as well as drug therapy in early or prehypertensives.

Dietary modification like weight reduction, salt reduction and increase potassium and morning brisk walk with 5 days a week, effectively lower blood pressure, reduced obesity and metabolic complications & increase insulin

Table 1 : Patient's Relevant History

- Duration of hypertension
- Previous therapies: responses and side effects
- Family history of hypertension and cardiovascular disease
- Dietary and psychosocial history
- Other risk factors: weight change, dyslipidemia, smoking, diabetes, physical inactivity.
- Evidence of secondary hypertension: history of renal disease; change in appearance; muscle weakness; spells of sweating, palpitations, tremor; erratic sleep, snoring, daytime somnolence; symptoms of hypo-or hyperthyroidism; use of agents that may increase blood pressure
- Evidence of target organ damage: history of TIA, stroke, transient blindness; angina, myocardial infarction, congestive heart failure; sexual function
- Other comorbidities

Abbreviation: *TIA, transient ischemic attack.*

sensitivity. Average BP reduction 6.3/3.1mm of Hg with reduction in mean body weight 9.2kg. Many long terms prospective trials have reported that reduction in salt intake reduces cardiovascular events. Ideally BMI should be maintained at or below < 25Kg/m^2 for reducing the risk related to hypertension. In patients with advance renal disease, dietary protein restriction may have modest effect in mitigating renal damages by reducing the intra renal transmission of systemic arterial pressure. DASH (Dietary approaches to stop hypertension) trial convincingly shown that over 8 weeks period diet high in fruits, vegetables, low fat dairy products lower BP in mild hypertensive and further salt reduction 4-6 gm/day augment this effect on blood pressure. Fruits & vegetables are rich sources of potassium, magnesium, fibre and diary product for calcium.

PHARMACOLOGICAL THERAPY

Drug therapy is recommended for persons who follow life style modification and having blood pressure more than 140/90mm of Hg.

Systolic BP reduction by 10-12 mm of Hg & diastolic blood pressure by 5-6mm of Hg confer the risk reductions of 35-40% stroke, 12-16% for CHD & heart failure 50% within 5 yrs of treatment. The reduction of blood pressure is single most factors for slowing the rate of progression of hypertension related kidney disease.

Most of available drug reduces SBP 7-13mm of Hg & DBP 4-8mm of Hg. Proper combination of these antihypertensive agents augment BP reduction and reach goal BP. Selection of drug should be based on age, severity of BP, risk factors, associated comorbid conditions, practically affordable cost for masses, less side effects and frequency of drug dosing.

THIAZIDE DIURETICS

Inhibit Na+/Cl in distal convoluted tubules so it increases sodium execretion. In long term use they act as vasodilators. It is safe, effective and low cost. They provide additive BP reduction when combine with B blocker, ACE, ARB, while with CCB it is less effective. Dose 6.25-50mg/day. Higher doses it increases potassium loss (hypokalaemia), insulin resistance and increase cholesterol but it is short acting (half life 9-15hrs).

Chlorthalidone is a diuretic structurally; similar to hydrochloride blocks sodium-chloride in the early distal tubule. Chlorthalidone has a longer half-life (40-60 h vs.9-15h) an antihypertensive potency ~1.5-2.0 times that of hydrochlorothiazide. Potassium loss is also greater with chlorthalidone. These agents are weak antihypertensive agents but may be used in combination with a thiazide to protect against hypokalemia. The main pharmacologic target for loop diuretics is the Na+, - K+ - 2Cl- cotransporter in the thick ascending limb of the loop of Henle. Loop diuretics generally are reserved for hypertensive patients with reduced glomerular filtration rates. Serum Creatinine (>2.5mg/dL)CHF or sodium retention and edema for some other reason, potent vasodilator, e.g., minoxidil. Blockers of the **Renin-Angiotensin system**: ACEIs decrease the production of angiotensin II, increase bradykinin levels, and reduce sympathetic nervous system activity. ARBs provide selective blockade of AT1 effect of angiotensin II on unblocked AT2 receptors may augments their hypotensive effect& reduce the risk of developing diabetes in high-risk hypertensive patients. ACE1/ARB combinations are less effective in lowering blood pressure. In patients with high risk of diabetes, combination ACE1/ARB therapy has been associated with more adverse events (e.g cardiovascular death, myocardial infarction, stroke, and hospitalization for heart failure) without increase in benefit.

Side effects of ACEs and ARBs include efferent renal arteriolar dilation in a kidney with stenotic lesion of the renal artery. Additional predisposing conditions to renal insufficiency induced by these agents are dehydration, CHF, and non-steroidal anti-inflammatory drugs. Dry cough and angioedema occurs in <1%. Angioedema occurs most commonly Asian origin and more commonly in African Americans. Hyperkalemia due to hypoaldosteronism is an occasional side effect of both ACE and ARBs.

Blockade of the rennin-angiotensin system is more complete with renin inhibitors than with ACEIs or ARBs. Monotherapy with aliskiren seems to be as effective as an ACEI or ARB lowering blood pressure.

Aldosterone antagonists

Spironolactone particularly effective agent in patients with low-renin primary hypertension, resistant hypertension and primary aldosteronism. In patients with CHF, low-dose spironolactone reduces mortality and hospitalizations for heart failure when given in addition to conventional therapy with ACEIs, digoxin, and loop diuretics. Spironolactone side effects may include gynecomastia, impotence, and menstrual abnormalities. Eplerenone selective.

Table 2 : Examples of Oral Drugs Used in Treatment of Hypertension

Drug class	Examples	Usual Total Daily Dose (Dosing Frequency/Day)	Other Indications	Contraindications/ Cautions
Diuretics				
Thiazides	Hydrochlorothiazide Chlorthalidone	6.25-50mg (1-2) 25-50 mg (1)		Diabetes, dyslipidaemia, hyper-uricemia, gout, hypokalemia
Loop diuretics	Furosemide Ethacrynic acid	40-80 mg (2-3) 50-100mg (2-3)	CHF due to systolic dysfunction, renal failure	Diabetes, dyslipidaemia, hyper-uricemia, gout, hypokalemia
Aldosterone antagonists	Spironolactone Eplerenone	25-100mg (1-2) 50-100mg (1-2)	CHF due to systolic dysfunction, primary aldosteronism	Renal failure, Hyperkalemia
K+ retaining	Amiloride Triamterene	5-10 mg (1-2) 50-100mg (1-2)		Renal failure, Hyperkalemia
Beta Blockers				
Cardioselective	Atenolol	25-100mg (1)	Angina, CHF due to systolic dysfunction, post-MI, sinus tachycardia, ventricular tachyarrhythmias	Asthma, COPD, 2nd-or 3rd-degree heart block, sick-sinus syndrome.
Nonselective	Metoprolol Propranolol Propranolol LA	25-100mg (1-2) 40-160mg (2) 60-180 (1)		
Combined alpha/beta	Labetalol Carvedilol	200-800mg (2) 125-50mg (2)	?Post MI, CHF	
Alpha antagonists				
Selective	Prozosin Doxazosin Terazosin	2-20 ,g (2-3) 1-16 mg (1) 1-10mg (1-2)	Prostatism	
Nonselective	Phenoxybenzamine	20-120mg (2-3)	Pheochromocytoma	
Sympatholytics				
Central	Clonidine Clonidine patch Methyldopa Reserpine Guanfacine	0.1-0.6mg (2) 0.1-0.3mg (1/week) 250-1000mg (2) 0.05-0.25mg (1) 0.5-2mg (1)		
ACE inhibitors	Captopril Lisinopril Ramipril	25-200mg (2) 10-40mg (1) 2.5-20mg (1-2)	Post-MI, coronary syndromes, CHF with low ejection fraction, nephropathy	Acute renal failure, bilateral renal artery stenosis, pregnancy, Hyperkalemia
Angiotension II antagonists	Losartan Valsartan Candesartan	25-100mg (1-2) 80-320 mg (1) 2-32mg (1-2)	CHF with low ejection fraction, nephropathy, ACE Inhibitor cough	Renal failure, bilateral renal artery stenosis, pregnancy Hyperkalemia

Contd...

Table 2 : Examples of Oral Drugs Used in Treatment of Hypertension

Drug class	Examples	Usual Total Daily Dose (Dosing Frequency/Day)	Other Indications	Contraindications/ Cautions
Renin inhibitors	Aliskiren	150-300mg (1)	Diabetic nephropathy	Pregnancy
Calcium antagonists				
Dihydropyridines Nondihydropyridines	Nifedipine (long-acting)	30-60mg (1)	Post-MI, supraventricular tachycardias, angina	2nd- or 3rd-degree heart block
	Verapamil (long-acting)	120-360mg (1-2)		
	Diltiazem (long-acting)	180-420mg (1)		
Direct vasodilators	Hydralazine Minoxidil	25-100 mg (2) 2.5-80 mg (1-2)		Severe coronary artery disease

*At the initiation of therapy, lower doses may be preferable for elderly patients and for select combinations of antihypertensive agents. ***Abbreviations:*** ACE, angiotension- converting enzyme; CHF, congestive heart failure, COPD, chronic obstructive pulmonary disease, MI, myocardial infarction.

Betablockers

β-Adrenergic receptor blockers lower blood pressure by decreasing cardiac output, reduction of heart rate and contractility. Central nervous system effect and inhibition of rennin release, beta blockers are particularly effective in hypertensive patients by co administration with a diuretic.

Beta blockers without intrinsic sympathomimetic activity decrease the rate of sudden death, overall mortality and recurrent myocardial infarction. In patients with CHF, beta blockers reduce the risk of hospitalization and mortality. Beta blockers remain appropriate therapy for hypertensive patients with concomitant heart disease. Carvedilol and labetalol block both B receptors and peripheral a-adrenergic receptors. Nebivolol represents another class of cardioselective beta blockers that has additional vasodilator actions related to enhancement of nitric oxide activity.

Alpha blockers are also effective in treating lower urinary tract symptoms in men with prostatic hypertrophy.

Sympatholytic agents centrally acting alpha 1625 2 sympathetic agonists decrease peripheral resistance by inhibiting sympathetic outflow. They may be particularly useful in patients with autonomic neuropathy. Drawbacks include somnolence, dry mouth and rebound hypertension on withdrawal. Although they are potentially effective antihypertensive agents, their usefulness is limited by orthostatic hypotension, sexual dysfunction. Rebound hypertension is another concern with abrupt cessation of drugs with a short half-life.

CALCIUM CHANNEL BLOCKERS

Reduce vascular resistance through L-channel blockade, which reduces intracellular calcium and blunts vasoconstriction. Three classes of calcium channel blocker are Phenylalkylamines (Verapamil), benzothiazepines (diltiazem) and 1,4-dihydropyridines (Nifedipine-like) effectively lowers Blood pressure. There are used in combination with ACEI and ARBs. The side effects are flushing; headache and edema with dihydropyridine use are related to their potencies as arterioliar dilator. Edema is due to an increase in transcapillary pressure gradient, and not due to net salt and water retention.

Direct Vasodilators

They decrease peripheral resistance via sympathetic nervous system. Minoxidil is a particularly potent agent and is used most frequently in patients with renal insufficiencies that are refractory to all other drugs. Side effects of minoxidil include hypertrichosis, pericardial effusion. Intravenous nitroprusside can be used to treat malignant hypertension and life-threatening left ventricular heart failure associated with elevated arterial pressure.

COMPARISON OF ANTIHYPERTENSIVES

On average, standard doses of most antihypertensive agents reduce blood pressure by 8-10/4-7 mmHg; however, there may be subgroup differences in responsiveness. Younger patients may be more responsive to beta blockers and ACEIs, over age 50 may be more responsive to diuretics and calcium antagonists. Patients with high-renin hypertension may be more responsive to ACEIs and ARBs patients with low-renin hypertension are more responsive to diuretics and calcium antagonists. ACEIs and ARBs A meta-analysis of more than 30 randomized trials of blood pressure-lowering therapy indicates that reduction in blood pressure, the major drug classes seem to produce similar overall net effects on total cardiovascular events. ALLHAT trial demonstrated that the occurrence of CHD and nonfatal myocardial infarction, overall mortality, was virtually identical in hypertensive patients treated with either an ACEI (lisinopril) a diuretic (Chlorthalidone) & Calcium antagonist. ACEI and ARBs decrease intraglomerular pressure and paroteninuria and may retard the rate of progression of renal insufficiency.

In patients with type 2 diabetes, treatment with an ACEI, and ARB, or aliskiren decreases proteinuria and delays the progression of renal disease. Among African Americans with hypertensionrelated renal disease, ACEIs appear to be more effective than beta blockers or dihydropyridine calcium channel blockers in slowing, although not preventing, the decline of glomerular filtration rate. In most patients with hypertension and heart failure due to systolic, diastolic dysfunction, the use of diuretics, ACEIs or ARBs, and beta blockers is recommended to improve survival. Independent of blood pressure, in both hypertensive and normotensive individuals, ACEIs attenuate the development of left ventricular hypertrophy, improve symptomatology and risk of sudden death from CHF, & reduce morbidity and mortality in post-myocardial infarction patients. The use of ACEIs provide better coronary protection than do calcium channel blockers, whereas calcium channel blockers provide more stroke protection than do either ACE1 of beta blockers. Combination treatment with an ACEI (benazepril) plus a calcium antagonist was superior to treatment with ACEI plus a diuretic in reducing the risk of cardiovascular events and death among high-risk patient with hypertension. Combination of an ACEI, diuretic recently been shown to produce major reductions in morbidity and mortality in the very elderly.

After a stroke, combination therapy ACEI and a diuretic, but not with ARB reduce the rate of recurrent stroke. There is a recent resurgence of interest in two nonpharmacologic, antihypertensive therapies which interrupt sympathic outflow (1) device-based cartotid baroreflex activation by electrical stimulation of the carotid sinus; (2) endovascular radiofrequency ablation of the renal sympathetic nerves. Whereas renal denervation is a minimally invasive procedure, both interventions inhibit sympathetic drive and decrease blood pressure by increasing the capacity of the kidney to excrete sodium and by decreasing renin release. Experience with these interventions is limited. In the short term, blood pressure is lowered in 75-80% of patients, and the magnitude of the blood pressure reduction is similar for both procedures. Most impressive results have been observed in patients with "resistant" hypertension and with obesity-related hypertension.

BLOOD PRESSURE GOALS OF ANTIHYPERTENSIVE THERAPY

Maximum protection against combined cardiovascular endpoints is achieved with pressures <135-140mmHg for systolic blood pressure and <80-85 mmHg for diastolic blood pressure. In diabetic patients, effective blood pressure control reduces the risk of cardiovascular events and death as well as the risk for micro vascular disease (nephropathy, retinopathy). Hypertension control have recommended more aggressive blood pressure targets <130/80 in patients with diabetes, CHD, chronic kidney disease patients with diabetes and coronary heart disease, "tight control" of systolic blood pressure is not associated with improved cardiovascular outcomes. The concept "J-curve" suggest that the risk of CVS events increases at BP that are either too high or too low. Too low BP may exceed auto regulatory capacity of cerebral, coronary and renal blood flows. Caution should be exercised in lowering blood pressure <130/80 mmHg in patients with diabetes, CHD, and other high risk patients. Patient with renal insufficiency may show Serum creatinine concentration. In older patient isolated systolic hypertension, further lowering of diastolic blood pressure does not result in harm. However, gradual blood pressure reduction to a less aggressive target level of control may be appropriate. Three or more drugs frequently required in patients with diabetes and renal insufficiency to control the blood pressure. For most agent reduction of blood pressure at half-standard dose is only ~20% less than at standard doses. Appropriate combinations of agents at these lower have additive or almost additive effects on blood pressure with a lower incidence of side effects.

The term resistant hypertension refers to patients with blood pressures persistently >140/90 mm/Hg despite taking three or more antihypertensive agents, including a diuretic. Resistant or difficult to-control hypertension is more common in patients >60 years than younger patients. Resistant hypertension may be related to "pseudo resistance" (high office BP and low home BP), non-adherence therapy, identifiable causes of hypertension (Including obesity excessive alcohol intake) and use of any non-prescription drugs. Rarely older patient pseudo hypertension may be related to the inability to measure blood pressure accurately in severely sclerotic arteries. This condition is suggested if the Radial pulse remains palpable despite occlusion of the bronchial artery by the cuff. The actual blood pressure can be determined direct intra-arterial measurement. The resistance hypertension may be evaluated by measuring of home and office blood pressure or ambulatory blood pressure monitoring.

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