Management of Hypertension

Goals of Therapy

The primary goal of therapy of hypertension should be effective control of BP in order to prevent, reverse or delay the progression of complications and thus reduce the overall risk of an individual without adversely affecting the quality of life. Patients should be explained that the lifestyle modifications and drug treatment is generally lifelong and regular drug compliance is important.

Initiation of therapy

Having assessed the patient and determined the overall risk profile, management of hypertension should proceed as follows:

- In low risk patients, it is suggested to institute life style modifications and observe BP for a period of 2-3 months, before deciding whether to initiate drug therapy.
- In medium risk patients, institute life style modifications and initiate drug therapy after 2-4 weeks, in case BP remains above 140/90.
- In high and very high-risk groups, initiate immediate drug treatment for hypertension and other risk factors in addition to instituting life-style modification.

Targets of therapy

- Gradual reduction of BP is a prudent therapeutic approach except in stage 3 hypertension.

Table 8 : Lifestyle interventions for blood pressure reduction

Intervention	Recommendation	Expected systolic blood pressure reduction (range)
Weight reduction	Maintain ideal body mass index Below 23 Kg/m^2	5-20 mm Hg per 10 kg weight loss
DASH* eating plan	Consume diet rich in fruits, vegetables, low-fat dairy products with reduced content of saturated and total fat.	8-14 mm Hg
Dietary sodium Restriction	Reduce dietary sodium intake to <6 g salt or < 2.4 g sodium.	2-8 mm Hg
Physical activity	Engage in regular aerobic physical activity, for example, brisk walking for at least 30 min most days	4-9 mm Hg
Alcohol moderation	Men<60 ml per day, twice a week Women<30 ml per day, twice a week. Abstinence is preferred.	2-4 mm Hg
Tobacco	Total abstinence	

*DASH= Dietary Approaches to Stop Hypertension

Table 9 : Sodium content of foods per 100 gms[54,55]

<25 mg Low		25-50 mg Moderate	50-100 mg Moderately High	>100 mg High
Amla	Cow pea	Raisins	Cauliflower	Amaranth
Bitter gourd	Horse gram	Broad beans	Fenugreek	Bacon
Bottle gourd	Ragi	Carrots	Lettuce	Egg
Brinjal	Vermicelli	Reddish white	Field beans	Lobster
Cabbage	Semolina	Black gram dal	Beetroot	
Lady finger	Wheat	Green gram dal	Water melon	
Colocasia	Maida	Red gram dal	Bengal gram dal	
Cucumber	Milk	Lentil whole	Red gram tender	
French beans	Grapes	Bengal gram whole	Liver	
Peas	Sweetlime	Banana	Prawns	
Onion	Papaya	Pineapple	Beef	
Potato	Orange	Apple	Chicken	
Tomato ripe	Sapota	Mutton		
Yam				

Table 10 : Food items to be avoided in hypertensives[54,55]

A	B
Table salt	**Salt preserved foods**
Mono sodium glutamate (Ajinomoto)	Pickles and canned foods
Baking powder	Ketchup and sauces
Sodium bicarbonate	Prepared mixes
Fried foods	Ready to eat foods
Alcohol	**Highly salted foods**
	Potato chips, cheese, peanut butter, salted butter, papads
	Bakery products : Biscuits, cakes, breads and pastries

- In Hypertension Optimal Treatment (HOT) study (target diastolic pressure less than 90, 85 or 80 mm Hg) there was no increase in cardiovascular risk in patients randomized to the lowest target group (DBP<80 mm Hg).[31]
- Among diabetic patients participating in the HOT study, there was a significantly lower risk of coronary artery disease in patients with the lowest target DBP.[31]
- The results of United Kingdom Prospective Diabetes Study (UKPDS) demonstrated that a tight control of BP (average achieved : 144/82 mm Hg) in diabetic patients conferred a substantial reduction in the risk of Coronary Artery Disease compared to a less tight control of BP (average achieved: 154/87 mm Hg).[32]

Table 11 : Foods with high potassium[54,55]

Fruits		Vegetables	
Amla	Plums	Cabbage	Raddish white
Sapota	Lemons	Bitter gourd	Brinjal
Peaches	Sweetlime	Ladies finger	Pumpkin
Orange	Pineapple	Cauliflower	French beans
Papaya	Apple	Spinach	Colocasia
Banana	Watermelon	Potato	Tapioca
		Drumstick	

- The PROGRESS trial showed that in patients with a history of stroke or TIA, stroke risk was reduced not only in participants classified as hypertensive, but also among those classified as non-hypertensive, among whom the mean blood pressure at entry was 136/79 mm Hg.[33]
- In view of the above studies, it would seem desirable to achieve optimal or normal BP (<140/90 mHg) in the young and middle aged. In diabetic patients BP lowering to around 140 / 80 mm Hg is recommended. In patients who have survived stroke, a BP of around 130/85 mm Hg is suggested. In elderly patients a high normal BP around 140-145/90mm Hg should be taken as the target BP.[34]
- Initially the J-shaped hypothesis was accepted, and it was felt that lowering BP below a certain level (140/90 mmHg) would increase the risk of coronary events by lowering diastolic perfusion pressure in coronary circulation. Data from the HOT study and UKPDS study showed BP reduction to levels of 130/80 specially in high-risk individuals (diabetics, CKD, and CVA) was more beneficial. Hence, at the time of second guidelines it was suggested that the lower the better policy holds true for target BP in hypertension. More recent data (ADVANCE,ACCORD,INVEST) shows lowering of diastolic BP to below 70 mmHg can be deleterious, specially in patients with coronary artery disease.[115-117]
- As compared to the previous guidelines of 2007, we now realize that a relatively less aggressive approach towards achieving lower target BP is a reasonable goal, since as suggested above, recent data shows no additional benefit of lowering diastolic BP below certain levels in specific situations.

Management Strategy

- Recent evidence suggests that the level of SBP control correlates better with reduction of mortality than the level of DBP control.[28,35-42]
- Impressive evidence has accumulated to warrant greater attention to the importance of SBP as a major risk factor for CVDs. The rise in SBP continues throughout life, in contrast to DBP, which rises until approximately 50 years of age. It tends to level off over the next decade, and may remain the same or fall later in life. Diastolic hypertension predominates before 50 years of age, either alone or in combination with SBP elevation. DBP is a more potent cardiovascular risk factor than SBP until age 50; thereafter, SBP is more important.[2]
- Trials describe population averages for the purposes of developing guidelines, whereas physicians must focus on the individual patient's clinical responses.[43]

Non-pharmacologic Therapy

Life style measures should be instituted in all patients including those who require immediate drug treatment. These include:

- Patient education: Patients need to be educated about the various aspects of the disease, adherence to life style changes on long term basis and need for regular monitoring and therapy.
- Weight reduction: Weight reduction of even as little as 4.5 kg has been found to reduce blood pressure in a large proportion of overweight persons with hypertension.[44]
- Physical activity: Regular aerobic physical activity can promote weight loss, increase functional status and decrease the risk of cardiovascular disease and all-cause mortality. A program of 30-45 minutes of brisk walking or swimming at least 3-4 times a week could lower SBP by 7-8 mm Hg. Isometric exercises such as weight lifting should be avoided as they lead to pressor effects.
- Alcohol intake: Excess alcohol intake causes a rise in blood pressure, induces resistance to antihypertensive therapy and also increases the risk of stroke.[45,46] Alcohol consumption should be limited to no more than 2 drinks per day (24oz beer, 10oz wine, 3oz 80-proof whiskey) for most men and no more than 1 drink per day for women and lighter weight people.[2]
- Salt intake: Epidemiological evidence suggests an association between dietary salt intake and elevated blood pressure. The total daily intake of salt should be restricted to 6 gms (amounting to 3-4 gms of sodium), however, in hot summer this may be relaxed. Patients should be advised to avoid added salt, processed foods, and salt-containing foods such as pickles, papads, chips, chutneys and preparations containing baking powder. In the Indian context, salt restriction is more important as Indian cooking involves a high usage of salt.
- Smoking: Smoking or consumption of tobacco in any form is the single most powerful modifiable lifestyle factor for prevention of major cardiovascular and non-cardiovascular disease in hypertensives.[47-49] Cardiovascular benefits of cessation of smoking can be seen within one year in all age groups.[44]
- Yoga and Meditation: Yoga, meditation and biofeedback have been shown to reduce blood pressure.[50-53]
- Diet:
  - Vegetarians have a lower blood pressure compared to meat eaters.[54] This is due to a higher intake of fruit, vegetables, fibers coupled with a low intake of saturated fats and not due to an absence of intake of meat protein.[55]
  - Intake of saturated fats is to be reduced since concomitant hyperlipidaemia is often present in hypertensives.
  - Regular fish consumption may enhance blood pressure reduction in obese hypertensives.[56]
  - Adequate potassium intake from fresh fruits and vegetables may improve blood pressure control in hypertensives.[57]
  - Caffeine intake increases blood pressure acutely but there is rapid development of tolerance to its pressor

Table 12a : Guidelines for selecting the most appropriate first- line antihypertensive drugs

Class of drugs	Definite Indication/s	Possible indication/s	Definite contraindication/s	Relative contraindication/s
Diuretics	Heart failure Elderly patients Systolic hypertension	Diabetes	Gout	Dyslipidaemia
β –blockers	Angina Post-myocardial infarction Tachyarrhythmia Heart failure	Pregnancy Diabetes	Heart block	Dyslipidaemia Physically active Peripheral vascular disease Elderly persons > 50 years Asthma and chronic pulmonary disease (COPD)
CCBs	Metabolic syndrome Angina Elderly Systolic hypertension Diabetes	Peripheral vascular disease CVA	Heart block[a]	Congestive heart failure[a]
ACE inhibitors	Metabolic syndrome Heart failure Left ventricular dysfunction Post-myocardial Infarction Significant proteinuria Diabetes	CVA	Pregnancy and lactation Bilateral renal artery stenosis Hyperkalemia	Moderate renal failure (Creatinine levels >3 mg/dl)
Angiotensin II Receptor Blockers (ARBs)	Metabolic syndrome Diabetes mellitus Proteinuria LV dysfunction ACE inhibitor induced cough	Heart failure CVA	Pregnancy and lactation Bilateral renal artery stenosis Hyperkalemia	Moderate renal failure (Creatinine levels >3 mg/dl)

[a]Verapamil or diltiazem

Table 12b: Guidelines for other drugs

Class of drugs	Definite Indication/s	Possible indication/s	Definite contraindication/s	Relative contraindication/s
α blockers	Prostatic hypertrophy Chronic Kidney Disease	Glucose Intolerance Dyslipidemia	Orthostatic hypotension Congestive Heart Failure	
Centrally acting agents				
α methyldopa	Hypertension in Pregnancy	Resistant Hypertension	Acute or Chronic Liver Disease	
Clonidine	Resistant Hypertension	CKD	Pregnancy, Lactation	
Vasodilators	Resistant Hypertension Hypertension in Pregnancy			Coronary Artery Disease
Direct renin inhibitors				
liskiren	Resistant Hypertension		Pregnancy Lactation B/L Renal Artery Stenosis Hyperkalemia	Moderate Renal Failure (Creatinine > 3mg/dl)

effect. Epidemiological studies have not demonstrated a direct link between caffeine intake and high blood pressure.[58]

- Thus, the diet in hypertensives should be low calorie, low fat, and low sodium, with normal protein intake.[59,60]

Pharmacologic Therapy

Principles of drug treatment

- Over the past decade, the goals of treatment have gradually shifted from optimal lowering of blood pressure, which is taken for granted, to patient's overall well being, control of associated risk factors and protection from future target organ damage.[61]
- Achieve gradual reduction of blood pressure. Use low doses of antihypertensive drugs to initiate therapy.
- Five classes of drugs can be recommended as first line treatment for stage 1-2 hypertension[1,2] These include :1) ACE inhibitors, 2) angiotensin II receptor blockers, 3) calcium channel blockers, 4) diuretics and 5) newer β-blockers.
- The Blood Pressure Lowering Treatment Trialists' Collaboration concluded that treatment with any commonly used regimen reduces the risk of total major cardiovascular events and larger reductions in blood pressure produce larger reductions in risk.[62]
- Choice of an antihypertensive agent is influenced by age, concomitant risk factors, presence of target organ damage, other co-existing diseases, socioeconomic considerations, availability of the drug and past experience of the physician.
- Combining low doses of two or more drugs having synergistic effect is likely to produce lesser side effects. In

Table 13 : Anti-hypertensive drugs and their usual dosage

Class	Drug	Dosage (mg/day)	Dosing frequency/Day
Diuretics	Hydrochlorothiazide	6.25-12.5	1–2
	Chlorthalidone	6.25-12.5	1
	Indapamide	1.5-2.5	1
	Amiloride	5-10	1–2
	Triamterene	50-100	1–2
	Spironolactone	25-50	1–2
β -blockers	Metoprolol	25-100	1–2
	Bisoprolol	2.5-10	1
	Nebivolol	2.5 - 5	1
α + β Blocker	Carvedilol	3.125 – 50	2
	Labetalol	50 -200	2
CCBs	Amlodipine	2.5-20	1
	Cilnidipine	5 - 10	1
	Diltiazem	90-360	1
	Nifedipine (Long-acting)	10 - 40	1
	Verapamil	80-240	1-2
Racemic isomers	S-amlodipine	2.5 - 10	1
ACE inhibitors	Enalapril	2.5-20	1-2
	Lisinopril	2.5-20	1
	Ramipril	1.25-10	1-2
	Perindopril	2-8	1-2
	Quinapril	10-80	1-2
ARBs	Losartan	50-100	1-2
	Candesartan	8-32	1-2
	Valsartan	40-160	1
	Irbesartan	150-300	1
	Telmisartan	40-160	1
	Olmesartan	20 - 40	1
α -blockers	Prazosin	2.5-10	2-3
	Doxazosin	1-4	1
Centrally acting drugs	Clonidine	0.1-0.3	2
	Methyldopa	500-1500	2
	Moxonidine	0.2-0.4	1-2
Vasodilators	Hydralazine	25-100mg	2
	Minoxidil	2.5-5mg	1-2
Direct renin inhibitors	Aliskiren	150-300	1

60-70 % of patients, goal blood pressure will be achieved with two or more agents only.

- Use of fixed dose formulations should be considered to improve compliance.
- Drugs with synergistic effects should be combined pertinently to enhance BP lowering effect so as to achieve target BP.
- Use of long acting drugs that provide 24-hour efficacy with once daily administration ensures smooth and sustained control of blood pressure; which in turn is expected to provide greater protection against the risk of major cardiovascular events and target organ damage. Once daily administration also improves patient compliance.
- Although antihypertensive therapy is generally lifelong, an effort to decrease the dosage and number of antihypertensive drugs should be considered after effective control of hypertension (step-down therapy).
- Due to a greater seasonal variation of temperatures in India, marginal alterations in dosages of drugs may be needed from time to time.

Antihypertensive drugs

Angiotensin Converting Enzyme inhibitors (ACE inhibitors)

ACE inhibitors are effective in lowering blood pressure and are well tolerated. These are first line agents in post-MI patients, those with heart failure, diabetes, and in patients with other metabolic risk factors. In individuals with diabetes mellitus, they retard the onset and progression of renal disease (patients with microalbuminuria and early CKD). The HOPE trial (a primary prevention trial) showed that in high and average risk individuals, use of ramipril reduced overall mortality and cardiovascular endpoints, even with small reductions in blood pressure.[63] As a class, they are metabolically favorable. The most common side effect is dry cough. ACE inhibitors are contraindicated in pregnancy. Serum creatinine and potassium should be monitored in patients receiving ACE inhibitors. Ramipril and Perindopril have greater tissue ACE inhibition effect than other agents. Perindopril in combination with Indapamide has been particularly shown to reduce mortality in patients who have survived stroke (PROGRESS trial).[33]

Table 14:Adverse drug reactions for first-line drugs

Common side effects	ACE inhibitor	ARB	Calcium channel blocker	Diuretic	B-blocker
Headache	-	-	+	-	-
Flushing	-	-	+	-	-
Lethargy	-	-	-	-	+
Impotence	-	-	-	+	+
Dry cough	+	+/-	-	-	-
Gout	-	-	-	+	-
Oedema	-	-	+	-	-
Postural hypotension	+	+	-	+	-
Cold hands and feet	-	-	-	-	+
Hyperkalemia	+	+	-	-	-
Hyperglycemia				+	+
Dyslipidemia				+	+
Angioedema	+	+			

Angiotensin II Receptor Blockers (ARBs)

Angiotensin II receptor blockers block the angiotensin II AT-1 receptors, and thus prevent the action of angiotensin II. In the LIFE trial, losartan was better than atenolol in reducing the frequency of the primary composite endpoint of stroke, myocardial infarction and cardiovascular death; this was due to a significant reduction in stroke.[64] In the Valsartan Antihypertensive Long-term Use Evaluation (VALUE) trial, both valsartan and amlodipine reduced blood pressure in hypertensive patients at high cardiovascular risk, but the effects of the amlodipine-based regimen were more pronounced, especially in the early period.[65] These drugs have many features in common with ACE inhibitors, but do not cause an accumulation of bradykinin. Consequently, cough and angioedema are much less likely to occur than with ACE inhibitors.[9] Initially, some fears were raised regarding increase of coronary events with use of these agents, however, these have been disproved ever since. Also, one retrospective meta-analysis suggested increase in neoplasm with ARBs, however no prospective study has suggested this and is generally believed not to be a significant issue at present. In fact, the ONTARGET trial shows telmisartan (80mg OD) is as effective as ramipril (10mg OD) in reducing CV events in high-risk individuals in patients with vascular disease or high-risk diabetes. Also, the incidence of angioedema was less than with ramipril.[66] A combination of ACE and ARB should not be used due to increased risk of hypotension and hyperkalemia. In the recent randomized double blind ROADMAP[68] trial involving 4447 diabetic patients with olmesartan (40mg OD), the onset of microalbuminuria has been shown to be delayed in patients with type 2 diabetes.

Calcium Channel Blockers (CCBs)

The two subgroups of CCBs are dihydropyridines (amlodipine, felodipine, nifedipine, cilnidipine) and non- dihydropyridines (verapamil and diltiazem). Amlodipine is the most commonly used agent in this group. Besides blood pressure lowering effect, they also have antianginal effects and are devoid of metabolic side effects. CCBs are particularly recommended for elderly patients with isolated systolic hypertension. Verapamil and diltiazem reduce heart rate and have negative inotropic effects. In the Nordic trial,[67] diltiazem was shown to be as effective as treatment based on diuretics, β-blockers or both, in preventing the combined primary endpoints of stroke, myocardial infarction and cardiovascular deaths. The findings of the ASCOT-BPLA (Blood Pressure Lowering Arm) study show that an antihypertensive drug regimen starting with amlodipine (adding perindopril as required) is better than one starting with atenolol (adding thiazide as required) in terms of reducing the incidence of all types of cardiovascular events and all-cause mortality, and risk of subsequent new-onset diabetes.[37]

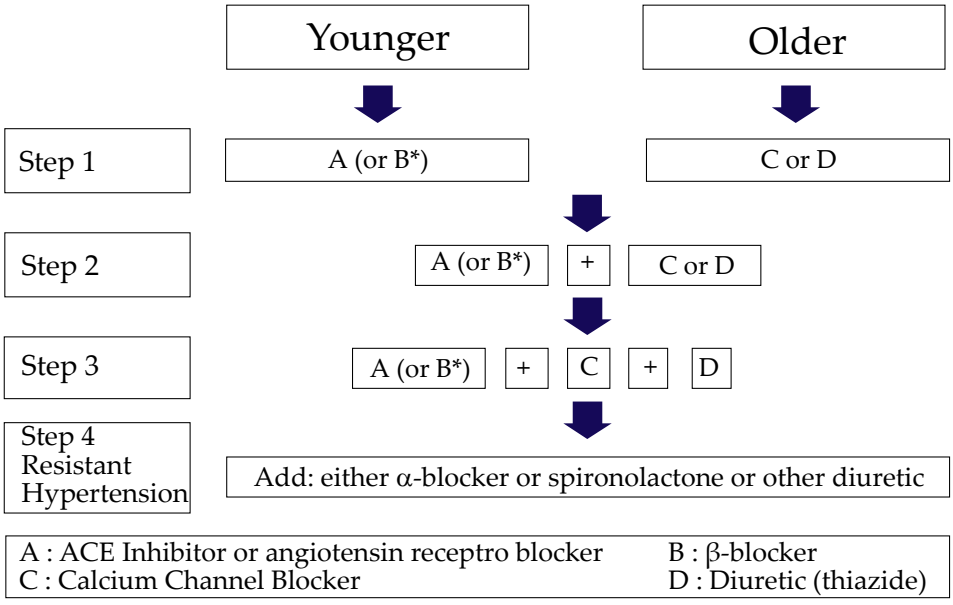
Short acting dihydropyridines (nifedipine) should be avoided. Amlodipine has no effect on heart rate and cardiac contractility, and has been shown to be safe even in the presence of congestive heart failure.[69]

Diuretics

Diuretics are widely used as first line agents. They are effective and inexpensive. Although high dose diuretic therapy was associated with side effects, currently recommended low dose diuretic therapy is generally well tolerated. Low dose diuretics have lesser metabolic side effects like worsening of glycemic control, hyperuricemia and dyslipidemia. Diuretics should be used in doses equivalent to 12.5 mg daily of chlorthalidone or hydrochlorothiazide to avoid adverse metabolic consequences. Chlorthalidone is preferred over hydrochlorothiazide as an antihypertensive.[70] Indapamide use has been shown to be associated with minimal metabolic side effects and is a useful agent. Combinations of thiazides and potassium-sparing diuretics are available and are effective options. Aldosterone antagonists (Spironolactone, Eplerenone) are being increasingly used as add-on agents to reduce BP in patients with resistant hypertension even without documenting hyperaldosteronemia. In cases of heart failure and/or renal failure, Furosemide (40-80mg), Torsemide (10-40mg), Metolazone (2.5-5mg) can be used as add-on therapy.

Newer β -blockers

Emerging evidence suggests that β-blockers are losing their pre-eminent place as first-line antihypertensive agents. This is based on the head to head trials where it was found that β-blockers are less effective than ACEIs or CCBs at reducing the risk of diabetes and stroke. This was particularly true in patients taking β-blockers and diuretics. In most of the studies, the β-blocker used was atenolol and in the absence of substantial data on other agents it would not be wise to apply this conclusion to all β-blockers. β - blockers reduce central aortic pressure to a lesser extent than other classes and this is additional reason for lack of mortality reduction with their use. They also have limitations in patients with dyslipidemia and impaired glucose tolerance. However, they are used in young hypertensives, those with stable and unstable angina and post-MI patients with hypertension. Agents with intrinsic sympathomimetic activity and highly selective β-blockers such as bisoprolol and nebivolol have lesser metabolic adverse effects. Labetalol is an



*Combination therapy involving B and D may induce more new onset diabetes compared with other combination therapies. Use β blockers only in special situations. B = Newer β blockers. Younger age: <55 years, Older: >55 years

Fig. 1 : Algorithm for recommended drug combination

α and β blocker and can be particularly used in hypertension in pregnancy.

Other drugs

α-blockers: Prazosin, terazosin and doxazosin - effectively reduce blood pressure both as monotherapy and in combination. They have a special place in the management of elderly hypertensives with benign prostatic hyperplasia (BPH) and CKD.[2,71,72] Since postural hypotension can occasionally occur, the dose of α-blockers should be carefully up-titrated. Data from the Antihypertensive and Lipid Lowering treatment to prevent Heart Attack Trial (ALLHAT) shows that patients in the doxazosin - based arm had 25% increase in the cardiovascular events and twice the risk of congestive heart failure.[73]

Centrally acting drugs : A-methyldopa, clonidine and moxonidine - have been in use for several years. In particular, methyldopa remains an important agent for the treatment of hypertension in pregnancy. Clonidine, though a potent antihypertensive agent, is infrequently used these days due to side effects such as postural hypotension and problem of withdrawal-related rebound hypertension. These agents are used in CRF patients with resistant hypertension.

Direct vasodilators : Hydralazine and minoxidil - are effective, but some of their side effects (such as tachycardia, headache, and retention of sodium and water) may make it difficult to use them in modern day treatment of hypertension.

Direct renin inhibitors: Aliskiren - has been evaluated and found to be effective. In the ALLAY trial, aliskiren was found to be as effective as losartan in regressing LVH.[74] In the more recent ACCELERATE trial,[75] combination of aliskiren and amlodipine was found to be more effective than monotherapy. It is a useful agent in resistant hypertension and also reduces the proteinuria in diabetes with hypertension.

Racemic forms: of calcium channel blockers and β-blockers are presently available. However, long-term studies regarding their efficacy and safety are not available.

Newer modalities: A novel baroreflex activation therapy has been evaluated recently. It stimulates baroreceptors through an implanted device and has been shown to reduce significant change in BP in patients with resistant hypertension. Renal sympathetic denervation therapy has been evaluated in which radiofrequency ablation of sympathetic plexus around renal arteries is performed. In the SYMPLICITY hypertension -2 trial,[76] it has been shown to reduce BP significantly over and above the pharmacological therapy. Presently, both these modalities are under evaluation for management of patients with resistant hypertension.

Table 12a and 12b presents guidelines for selecting the most appropriate antihypertensive drugs. Table 13 presents commonly used anti-hypertensive drugs and their usual dosage.

Table 14 lists some common side effects of these drugs.

Antihypertensive Drug Combinations

Combination therapy is gaining ground for effective control of hypertension since a majority of patients will require two or more drugs for sustained and effective control of blood pressure.[2,9]

One often needs to combine different classes of drugs with different mechanisms of action to achieve effective control of blood pressure with minimal side effects. Combinations with additive hypotensive effects will produce greater blood pressure reductions than those obtained with monotherapy. When a subject is in stage 2 or above, therapy can be initiated either with two drugs or as a fixed dose combination. The ACCOMPLISH trial has shown that combination of ACEIs with CCBs is better than a combination of ACEI with diuretic and should be the preferred combination.[77]

Younger individuals have high renin hypertension, hence ACE inhibitors/ARBs or newer β-blockers are preferred; while older individuals have low renin hypertension and hence diuretics or CCBs are preferred as first line agents.

In combination, one out of the two groups A [ACE inhibitor/

Table 15: Undesirable combinations

- B-blocker and ACE inhibitor
- B-blocker and centrally acting drugs
- B-blocker and verapamil/diltiazem
- ACE inhibitors and ARBs
- Two drugs from the same class

ARB] or B [β-blocker] is combined with C [calcium channel blocker] or D [thiazide diuretic] (step 2). In refractory patients, when 3 agents are to be used, A+C+D is a good choice (step 3).[9]

Drug Interactions

Since multiple drugs are used in hypertensive patients and often these patients have other co-existing conditions, certain common drug interactions should be kept in mind.

Maintenance and Follow-up of Therapy

Once therapy with particular antihypertensive drugs is instituted, patients need to be seen at frequent intervals during the period of stabilization in order to monitor changes in blood pressure and see whether non-drug measures are being strictly followed. At least once in a fortnight, blood pressure should be measured at the clinic or at home. Other CHD risk factors as well as co-existing diseases/conditions should be monitored. The overall risk category of a patient and the level of blood pressure decide the frequency of follow up visits to a large extent. The frequency can be reduced once blood pressure is stabilized and other risk factors are controlled. Tobacco avoidance and alcohol moderations must be promoted vigorously.

Associated Therapies

In order to reduce the overall risk, patients with hypertension need therapies for control of other risk factors for secondary prevention and now with recent available data even for primary prevention. Low dose aspirin should be prescribed to all hypertensives with cardiovascular disease and stroke (secondary prevention). All hypertensive patients with coronary, peripheral, or cerebrovascular disease with LDL levels >100 mg/dL should receive statins as secondary prevention strategies. Hypertensive patients without CV diseases but those in high-risk group should also receive statins for primary prevention.[79,80]

Table 16 : Drug interactions[78]

ACE inhibitors, diuretics and β-Blockers
NSAIDs including COX-2 inhibitors decrease efficacy of diuretics, β-blockers and ACE inhibitors
Calcium channel blockers
Verapamil increases the blood levels of several statins, such as atorvastatin, simvastatin and lovastatin
Nifedipine is broken down by hepatic CYP3A4 system. Cimetidine inhibits the CYP3A4 system and thus the breakdown of nifedipine also potentially increases blood levels and antihypertensive effects. Conversely, phenobarbital, phenytoin and rifampin induce the CYP3A4 system to metabolise nifedipine, so that blood levels should fall
Amlodipine should not be used with statins such as simvastatin, atorvastatin or lovastatin since both drugs are metabolised by hepatic CYP3A4 system
Cyclosporin levels are increased with diltiazem and verapamil
Diuretics
Steroids can worsen diuretic-induced hypokalemia. Steroids also produce sodium retention which antagonises the main effect of diuretics that is natriuresis.
Antiarrythmics of Class 1A (quinidine or procainamide) or Class III (sotalol, amiodarone) can prolong QT interval and may precipitate torsade de pointes in presence of diuretic-induced hypokalemia
ACEI or ARBs which retain potassium can counteract the potassium loss of diuretics. This is a favourable drug interaction
Combined use of ACE inhibitors or ARBs and potassium sparing diuretics may result in hyperkalemia
β blockers
Metoprolol and carvidelol metabolism is inhibited by paroxetine (Selective serotonin receptor blocker – antidepressant) and propoxyphene (opoid analgesic) resulting in increased antihypertensive effect
β blockers and non-dihydropyridine CCBs
Heart Blocks
α methyldopa
Concomitant use of tricyclic antidepressants with methyldopa is to be avoided