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Recent Advances in the Management of Hypertension; Relevant to General Practice

by

Dr. M.R. Mubarak, MBBS, MD
Consultant Cardiologist
Lanka Hospitals, Colombo
mubarakmr@yahoo.co.uk

Converted to CPD print format by
Dr Jayantha Thambar
MBBS, DFM, FRACGP, MRCGP (INT)

Lets remind ourselves that….

Hypertension is one of the most preventable causes of premature morbidity and mortality worldwide. It is a major risk factor for stroke, myocardial infarction, heart failure, chronic kidney disease, peripheral vascular disease, cognitive decline and premature death.

Untreated hypertension is associated with progressive rise in blood pressure which is resistant to treatment due to associated vascular and renal damage.

Hypertension 'battle' is largely fought by Family Physicians who are in the front line of primary care. It is the number one diagnosis for office visits of primary care physicians in USA.

The following discussion is based on the latest 2013 ESH/ ESC guidelines for the management of arterial hypertension.

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DEFINITION AND CLASSIFICATION

Category	Systolic		Diastolic
Optimal	<120	and	<80
Normal	120 –129	and/or	80 –84
High normal	130 –139	and/or	85–89
Grade 1 hypertension	**140** –159	and/or	**90** –99
Grade 2 hypertension	160 –179	and/or	100 –109
Grade 3 hypertension	≥180	and/or	≥110
Isolated systolic hypertension	≥140	and	<90

All guidelines define the first stage of hypertension as Systolic blood pressure of 140 mmHg and Diastolic blood pressure of 90 mmHg. Therefore an Office BP of 140/90 is required to start a pharmacological treatment.

Blood pressure measurement

Preparation

- BP measurement is done manually by using brachial pressure cuff and auscultation of brachial artery to identify the appearance and disappearance of Koratkoff's sounds.
- A quite, comfortable location at normal room temperature is required.
- Patient should not have the need to pass urine, not recently eaten, smoked or taken caffeine or exercised.
- Allow to rest at least 3-5 minutes before measuring.
- Usually the BP is measured in the non-dominant arm.
- Arm out stretched in line with mid sternum and supported by a table or some other means.
- BP tends to increase if arm is lowered.

Measurement

- Take two readings 1-2 mins apart. Take additional readings if the first two readings are quite different.
- Correctly wrap the cuff containing appropriate size bladder.
- Palpate the brachial pulse in the antecubital fossa.
- Rapidly inflate the cuff to 20mmHg above the point where the pulse disappears.
- Deflate the cuff and note the pressure at which the pulse reappears. This is the approximate Systolic BP.
- Re inflate the cuff to 20 mmHg above the point at which the brachial pulse disappears.
- Using one hand place the Stethoscope over the brachial artery, ensuring complete skin contact with no clothing in between.
- Slowly deflate at 2-3mmHg per second while listening for Koratkoff's sound.
- When the sound disappears, quickly deflate the cuff.
- A difference of < 10mmHg between the right and left arm is normal.
- A difference of > 20mmHg is usually associated with underlying vascular disease.
- Therefore it is advised to take readings in both arms at the initial visit. Then use the arm with higher reading for subsequent measurements.
- BP tends to increase as the patient moves from supine to standing position.
- Traditionally the BP is measured while the patient is seated.
- Significant lowering of BP when standing is called postural hypertension. It is measured at least 1-3 mins after standing and blood pressure fall of more than 20mmHg when standing is significant.
- We need to review the medication to find the cause for postural drop.
- Blood pressure measurement is influenced by disease states, fullness of bladder, pain, shock and dehydration
- It also depends on temperature, altitude, time of day, posture, emotion, exercise, meals and drugs.

Equipment

- Modern cuffs consist of an inflatable cloth-enclosed bladder.
- Recommended bladder width 40% and length 80% of arm circumference
- When bladder is too small (under cuffing), it over estimates the BP
- Over cuffing and consequent under estimation, is of smaller magnitude.

White Coat Hypertension (WCH)

- It occurs in as many as 15-30% of the people.
- It is commonly seen in pregnancy and increasing age.
- Some patients can have atypically very high readings.
- White Coat Hypertension is defined when a patient has persistently elevated office BP and normal, home or ambulatory BP.
- A difference of 10/5 mmHg has been reported.
- **'White coat effect'** occurs in patients with diagnosed Hypertension who are either treated or untreated. Here office BP readings are disproportionately greater than their home or ambulatory BP readings but their home or ambulatory BP averages are in the hypertensive range. This is called 'white coat effect'.

Masked Hypertension

- This is seen in patients with normal office BP but raised out-of-office BP.
- They are found to have high CV risk. Look for dysmetabolic risk factors and organ damage at diagnosis and during follow-up.
- Lifestyle measures and antihypertensive drug treatment should be considered.

Ambulatory BP Monitoring (ABPM)

- ABPM involves cuff & bladder connected to an electronic sensor which detects changes in cuff pressure which is measured oscillometrically.
- These devices can automatically measure BP at regular intervals, eg: every 30mins from 8am to 10pm (awake) and at lesser frequencies in the night(sleep).
- We can calculate the average readings over a 24 hour period.
- These BP devices should be validated to international standards.

Home BP monitoring (HBPM)

- This is done by automated devices which use oscillometric method.
- Frequent measurements can give average values which are reproducible and reliable.
- White coat effect, systematic errors, terminal digit preference, observer prejudice can be removed by home BP monitoring.
- It can improve treatment compliance.
- In some, home BP monitoring can cause anxiety or obsessive self interest.
- It is recommended to use internationally validated devices.
- When monitoring BP at home, for each BP recording two consecutive measurements are taken at least 1 min apart and while the person is seated. BP is recorded twice daily in the morning and evening and continue recording for at least 4 days, ideally 7 days.
- Then discard the measurements taken on the 1st day and use the average measurements to confirm a diagnosis of HT.

DIAGNOSIS OF HYPERTENSION USING OFFICE AND OUT OF OFFICE BP

Category	**Systolic BP (mmHg)**		**Diastolic BP (mmHg)**
Office BP	≥140	and/or	≥90
Ambulatory BP			
Daytime (or awake)	≥135	and/or	≥85
Nighttime (or asleep)	≥120	and/or	≥70
24-hour	≥130	and/or	≥80

Clinical indications for HBPM or ABPM
• Suspicion of white-coat hypertension
- Grade I hypertension in the office
- High office BP in individuals without asymptomatic organ damage and at low total CV risk
• Suspicion of masked hypertension
- High normal BP in the office
- Normal office BP in individuals with asymptomatic organ damage or at high total CV risk
• Identification of white-coat effect in hypertensive patients
• Considerable variability of office BP over the same or different visits
• Autonomic, postural, post-prandial, siesta- and drug-induced hypotension
• Elevated office BP or suspected pre-eclampsia in pregnant women
• Identification of true and false resistant hypertension

*HBPM-Home blood pressure monitor

* ABPM –Ambulatory blood pressure monitor

PRIMARY HYPERTENSION

90% of people with sustained high BP in clinical practice have no obvious identifiable cause.

SECONDARY HYPERTENSION

In 10% of hypertensive patients a specific cause for hypertension can be determined. Therefore a detailed clinical examination is essential in all hypertensive patients.

COMMON CAUSES OF SECONDARY HYPERTENSION

	Clinical indications			Diagnostics	
Common causes	**Clinical history**	**Physical examination**	**Laboratory investigations**	**First-line test(s)**	**Additional/ confirmatory test(s)**
Renal parenchymal disease	History of urinary tract infection or obstruction, haematuria, analgesic abuse; family history of polycystic kidney disease.	Abdominal masses (in case of polycystic kidney disease).	Presence of protein, erythrocytes, or leucocytes in the urine, decreased GFR.	Renal ultrasound	Detailed work-up for kidney disease.
Renal artery stenosis	Fibromuscular dysplasia: early onset hypertension (especially in women). Atherosclerotic stenosis: hypertension of abrupt onset, worsening or increasingly difficult to treat; flash pulmonary oedema.	Abdominal bruit	Difference of >1.5 cm in length between the two kidneys (renal ultrasound), rapid deterioration in renal function (spontaneous or in response to RAA blockers).	Renal Duplex Doppler ultrasonography	Magnetic resonance angiography, spiral computed tomography, intra-arterial digital subtraction angiography.
Primary aldosteronism	Muscle weakness; family history of early onset hypertension and cerebrovascular events at age <40 years.	Arrhythmias (in case of severe hypokalaemia).	Hypokalaemia (spontaneous or diuretic-induced); incidental discovery of adrenal masses.	Aldosterone–renin ratio under standardized conditions (correction of hypokalaemia and withdrawal of drugs affecting RAA system).	Confirmatory tests (oral sodium loading, saline infusion, fludrocortisone suppression, or captopril test); adrenal CT scan; adrenal vein sampling.
Uncommon causes					
Pheochromocytoma	Paroxysmal hypertension or a crisis superimposed to sustained hypertension; headache, sweating, palpitations and pallor; positive family history of pheochromocytoma.	Skin stigmata of neurofibromatosis (café-au-lait spots, neurofibromas).	Incidental discovery of adrenal (or in some cases, extra-adrenal) masses.	Measurement of urinary fractionated metanephrines or plasma-free metanephrines.	CT or MRI of the abdomen and pelvis; 123 I-labelled meta-iodobenzyl-guanidine scanning; genetic screening for pathogenic mutations.
Cushing's syndrome	Rapid weight gain, polyuria, polydipsia, psychological disturbances.	Typical body habitus (central obesity, moon-face, buffalo hump, red striae, hirsutism).	Hyperglycaemia	24-h urinary cortisol excretion	Dexamethasone-suppression tests

Signs suggesting secondary hypertension
• Features of Cushing syndrome.
• Skin stigmata of neurofibromatosis (pheochromocytoma).
• Palpation of enlarged kidneys (polycystic kidney).
• Auscultation of abdominal murmurs (renovascular hypertension).
• Auscultation of precordial or chest murmurs (aortic coarctation; aortic disease; upper extremity artery disease).
• Diminished and delayed femoral pulses and reduced femoral blood pressure compared to simultaneous arm BP (aortic coarctation; aortic disease; lower extremity artery disease).
• Left–right arm BP difference (aortic coarctation; subclavian artery stenosis).

AFTER DIAGNOSIS

1. Assess total cardiovascular risk

The following table shows the stratification of total CV risk in categories of low, moderate, high and very high risk according to SBP and DBP and prevalence of risk factors

Other risk factors, asymptomatic organ damage or disease	Blood Pressure (mmHg)			
	High normal SBP 130–139 or DBP 85–89	Grade 1 HT SBP 140–159 or DBP 90–99	Grade 2 HT SBP 160–179 or DBP 100–109	Grade 3 HT SBP ≥180 or DBP ≥110
No other RF		Low risk	Moderate risk	High risk
1–2 RF	Low risk	Moderate risk	Moderate to high risk	High risk
≥3 RF	Low to Moderate risk	Moderate to high risk	High Risk	High risk
OD, CKD stage 3 or diabetes	Moderate to high risk	High risk	High risk	High to very high risk
Symptomatic CVD, CKD stage ≥4 or diabetes with OD/RFs	Very high risk	Very high risk	Very high risk	Very high risk

2. Assess organ damage by Clinical and laboratory investigations

Signs of organ damage
• Brain: motor or sensory defects.
• Retina: fundoscopic abnormalities.
• Heart: heart rate, 3rd or 4th heart sound, heart murmurs, arrhythmias, location of apical impulse, pulmonary rales, peripheral oedema.
• Peripheral arteries: absence, reduction, or asymmetry of pulses, cold extremities, ischaemic skin lesions.
• Carotid arteries: systolic murmurs.

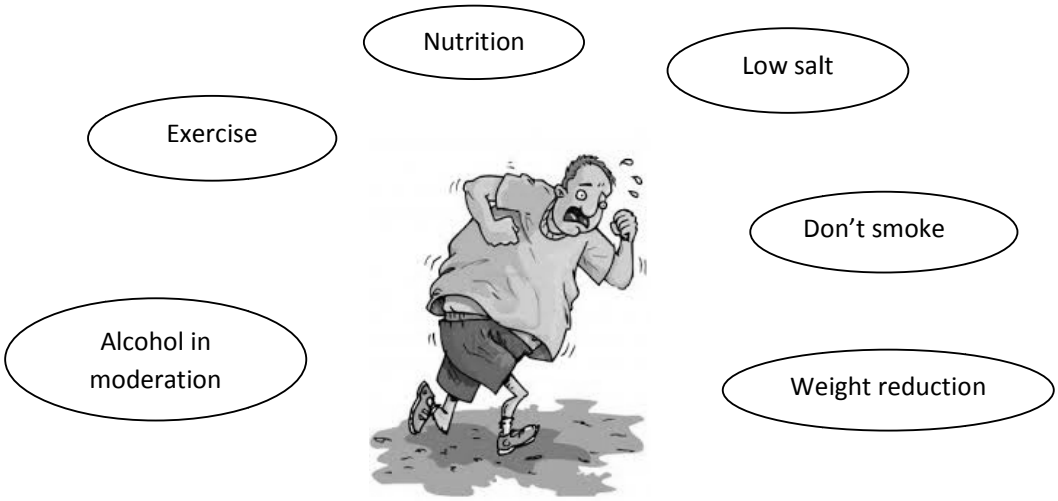
Routine tests
• Haemoglobin and/or haematocrit.
• Fasting plasma glucose.
• Serum total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol.
• Fasting serum triglycerides.
• Serum potassium and sodium.
• Serum uric acid.
• Serum creatinine (with estimation of GFR).
• Urine analysis: microscopic examination; urinary protein by dipstick test; test for microalbuminuria.
• 12-lead ECG.

Additional tests, based on history, physical examination, and findings from routine laboratory tests
• Haemoglobin A_{1c} (if fasting plasma glucose is >5.6 mmol/L (102 mg/dL) or previous diagnosis of diabetes).
• Quantitative proteinuria (if dipstick test is positive); urinary potassium and sodium concentration and their ratio.
• Home and 24-h ambulatory BP monitoring.
• Echocardiogram.
• Holter monitoring in case of arrhythmias.
• Exercise testing.
• Carotid ultrasound.
• Peripheral artery/abdominal ultrasound.
• Pulse wave velocity.
• Ankle-brachial index.
• Fundoscopy.

3. Management of Hypertension

Other risk factors, asymptomatic organ damage or disease	Blood Pressure (mmHg)			
	High normal SBP 130–139 or DBP 85–89	Grade 1 HT SBP 140–159 or DBP 90–99	Grade 2 HT SBP 160–179 or DBP 100–109	Grade 3 HT SBP ≥180 or DBP ≥110
No other RF	• No BP intervention	• Lifestyle changes for several months • Then add BP drugs targeting <140/90	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
1–2 RF	• Lifestyle changes • No BP intervention	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
≥3 RF	• Lifestyle changes • No BP intervention	• Lifestyle changes for several weeks • Then add BP drugs targeting <140/90	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
OD, CKD stage 3 or diabetes	• Lifestyle changes • No BP intervention	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90
Symptomatic CVD, CKD stage ≥4 or diabetes with OD/RFs	• Lifestyle changes • No BP intervention	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • BP drugs targeting <140/90	• Lifestyle changes • Immediate BP drugs targeting <140/90

DON'T FORGET! LIFESTYLE INTERVENTIONS



DRUG TREATMENT

Drug	Action	Adverse effects	Contra Indications	Common drugs
Thiazide Diuretics	Vasodilatation, Moderate diuresis	Gout,Hypocalcaemia, Hyponatreamia, increase risk of T2DM		Hydrochlorothiazide, Bendroflumethiazide, Chlorthalidone, Indepamide
Potassium sparing diuretics	vasodilatation, moderate diuresis	Gynaecomastia, hyperkalaemia	if serum k+ >4.5 in renal impairment	Spironolactone, Amiloride
Beta blockers	Negative inotropic and chronotropic effect, suppress plasma rennin, drugs with beta and alpha activity cause vasodilatation. Used in resistant cases, in women of child bearing age, potential, angina, post-MI and HF.	Lethargy, depression, sleep disturbance, can increase risk of type 2 DM	Bronchial Asthma, heart block, bradycardia	Atenolol, Metaprolol, Bisoprolol, Nebivalol, Carvedilol
Calcium channel	vasodilatation and natriuresis	Initial headache,palpitati	Caution with HF and with	Dihydropyridines ; Amlodipine,Felodipine, Nifedepine, Rate-limiting

blockers		on ,facial flushing, ankle swelling Verapamil(constipation),Diltiazem(skin rash)	betablockers	CCB Verapamil, Diltiazem
ACE Inhibitors	Inhibition of ACE and reduce angiotensin-II production	Side effects-Persistent dry cough, rash, loss of taste and rarely angiooedema	Monitor K+ levels & renal function in renal impairment Contraindicated in pregnancy	Captopril, Enalapril, Ramipril, Imidapril,Peridopril
Angiotensin Receptor blockers	Selective inhibition of AT-1 receptor	Careful monitoring of K+ and renal function in renal impairment.	pregnancy	Losartan.Candesartan, Irbesartan, Olmersartan, Valsartan, Telmisartan
Alpha blockers	Antagonist of alpha-1 receptor Use full in Resistant HT, Benign Prostatomegaly	initial dizziness, postural hypotension, headache, flushing, nasal congestion, fluid retention, ankle swelling, tachycardia, can worsen stress incontinence in women		Doxazocin, Prazocin, Terazocin

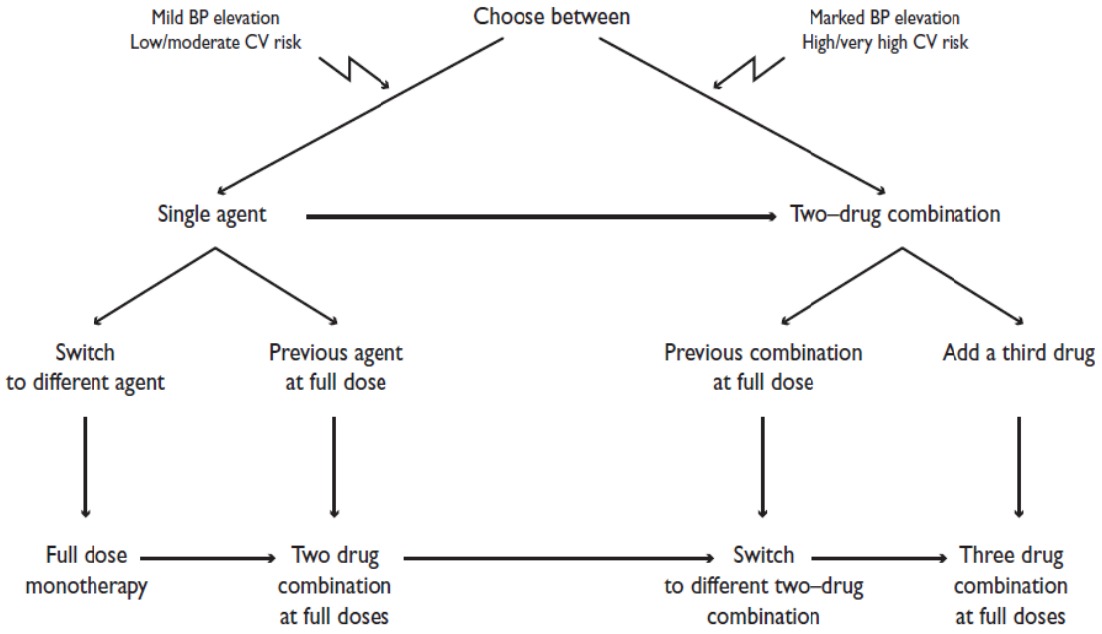
Preferred anti-hypertensive drugs in specific clinical conditions

Condition	Drug
Asymptomatic organ damage	
LVH	ACE inhibitor, calcium antagonist, ARB
Asymptomatic atherosclerosis	Calcium antagonist, ACE inhibitor
Microalbuminuria	ACE inhibitor, ARB
Renal dysfunction	ACE inhibitor, ARB
Clinical CV event	
Previous stroke	Any agent effectively lowering BP
Previous myocardial infarction	BB, ACE inhibitor, ARB
Angina pectoris	BB, calcium antagonist
Heart failure	Diuretic, BB, ACE inhibitor, ARB, mineralocorticoid receptor antagonists
Aortic aneurysm	BB
Atrial fibrillation, prevention	Consider ARB, ACE inhibitor, BB or mineralocorticoid receptor antagonist
Atrial fibrillation, ventricular rate control	BB, non-dihydropyridine calcium antagonist
ESRD/proteinuria	ACE inhibitor, ARB
Peripheral artery disease	ACE inhibitor, calcium antagonist
Other	
ISH (elderly)	Diuretic, calcium antagonist
Metabolic syndrome	ACE inhibitor, ARB, calcium antagonist
Diabetes mellitus	ACE inhibitor, ARB
Pregnancy	Methyldopa, BB, calcium antagonist
Blacks	Diuretic, calcium antagonist

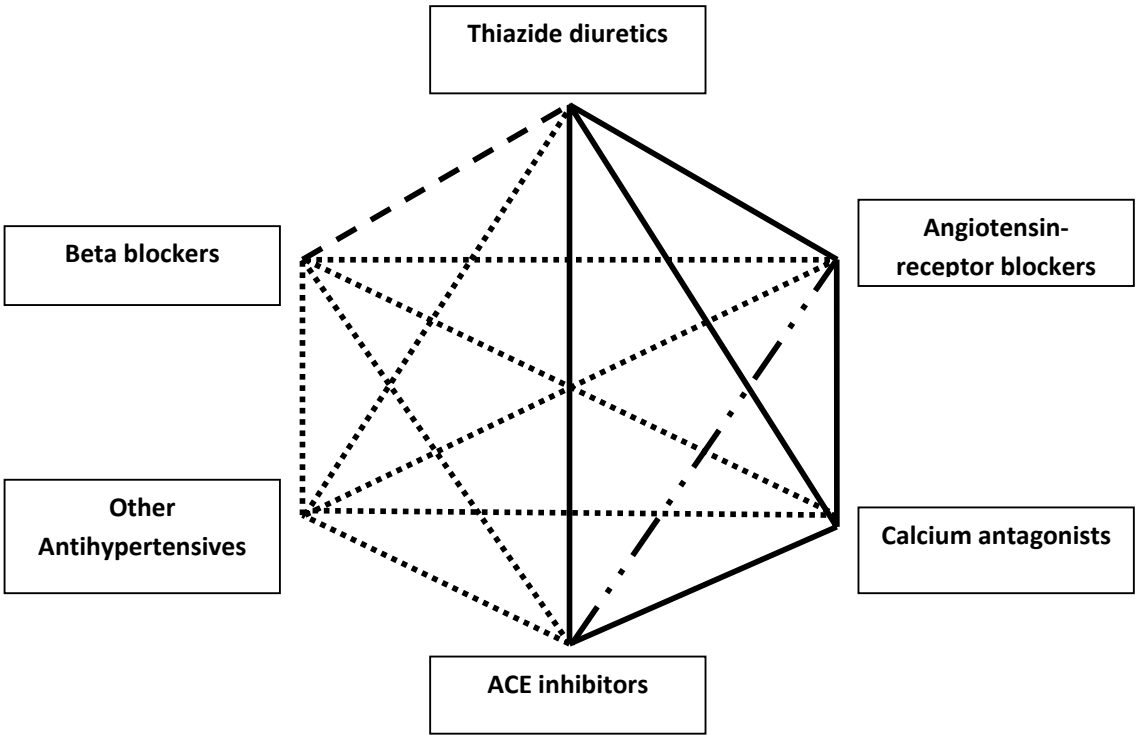
Clinical conditions where certain anti-hypertensive drugs are contra-indicated

Drug	Compelling	Possible
Diuretics (thiazides)	Gout	Metabolic syndrome Glucose intolerance Pregnancy Hypercalcaemia Hypokalaemia
Beta-blockers	Asthma A–V block (grade 2 or 3)	Metabolic syndrome Glucose intolerance Athletes and physically active patients Chronic obstructive pulmonary disease (except for vasodilator beta-blockers)
Calcium antagonists (dihydropyridines)		Tachyarrhythmia Heart failure
Calcium antagonists (verapamil, diltiazem)	A–V block (grade 2 or 3, trifascicular block) Severe LV dysfunction Heart failure	
ACE inhibitors	Pregnancy Angioneurotic oedema Hyperkalaemia Bilateral renal artery stenosis	Women with child bearing potential
Angiotensin receptor blockers	Pregnancy Hyperkalaemia Bilateral renal artery stenosis	Women with child bearing potential
Mineralocorticoid receptor antagonists	Acute or severe renal failure (eGFR <30 mL/min) Hyperkalaemia	

Anti-hypertensive drug combinations are recommended to achieve target BP



Possible combinations of anti-hypertensive drugs



Continuous line: preferred combination
Dashed line: useful combination
Dotted line: possible but less well tested combination
Dot and dash line: not recommended combination

RESISTANT HYPERTENSION

- Here BP remains repeatedly above 140/90 on treatment with three anti-hypertensive drugs including a diuretic. It is defined as "resistant hypertension". Really resistant cases are small in number (10-15%)
- Check patient compliance to treatment.
- Check BP using ambulatory techniques.
- Strict control of risk factors.
- Try a small dose of an aldosterone antagonist.
- Catheter based technique of renal denervation (RDN) is a promising mode of treating resistant hypertension.

REFERRALS

Urgent

- Accelerated HT is detected (BP usually > 180/100 mmHg with signs of papilloedema /or retinal haemorrhages)
- Suspected Phaeochromocytoma (Labile or postural hypotension, headache, palpitation, pallor and diaphoresis)
- If signs and symptoms suggesting a secondary cause for HT

Consider a specialist referral in following conditions

- Age <40 years
- Evidence of end organ damage
- Evidence of secondary cause.
- CV disease, Diabetes