

Medi Quest BRS Hospital

A monthly News letter from BRS Hospital

HYPERTENSION PRACTICE GUIDELINES

Part II

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TREATMENT OF HYPERTENSION

Life style modifications:- First line treatment for management of hypertension which includes

Salt reduction - Reduce salt added while preparing foods, and at the table. Avoid or limit consumption of high salt foods such as pickles, appalams, fast and processed foods including bread and cereals high in salt.

Healthy diet - diet rich in whole grains, fruits, vegetables, PUFA, dairy products and reducing food high in sugar, saturated fats and trans fats such as the DASH diet.

Moderation of alcohol consumption - Daily limit being for alcohol consumption is 2 standard drinks (90ml of 40% Alcohol by volume) for men and 1.5 standard drinks (67.5ml) for women. Binge drinking to be avoided. (Note: These are American guidelines, Japanese guidelines suggest 20-30ml for males and 10-20ml for females)

Weight reduction and regular physical activity- Abdominal obesity should be managed, ethnic specific cut offs for BMI and waist circumference should be used. Alternatively a waist-to-height ratio of <0.5 is recommended for all populations. Regular aerobic and resistance exercises may be beneficial for both the prevention and treatment of hypertension. Moderate intensity aerobic exercises 30mins on 5-7 days / week. Resistant

training exercise 2-3 days/week. Smoking cessation, stress reduction and induce mindfulness

Pharmacological treatment

Ideal characteristics of drug treatment

- Treatments should be evidence based in relation to morbidity/mortality prevention.
- Use a once-daily regimen which provides 24 hour blood pressure control.
- Affordable/ cost-effective relative to other agents.
- Treatments should be well tolerated.

Fig 1- General scheme of pharmacological treatment of hypertension

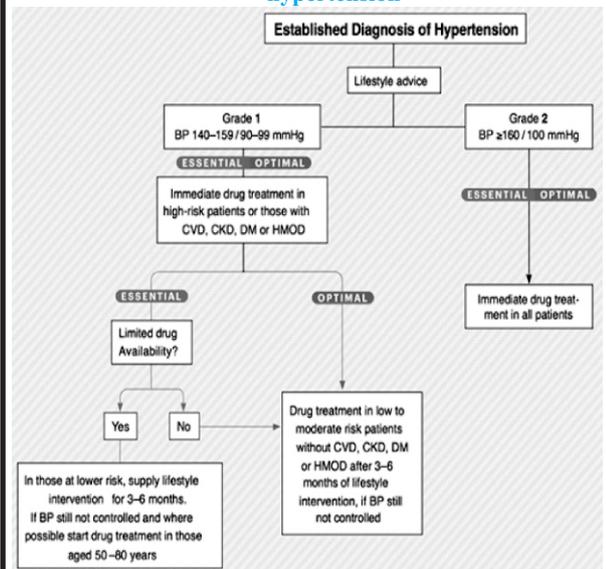
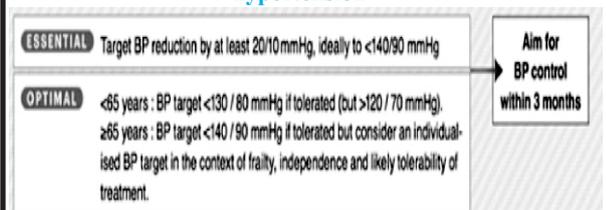


Fig 2 - Office blood pressure targets for treated hypertension



**Fig 3- International Society of Hypertension (ISH)
Core drug treatment strategy**

ESSENTIAL

- Use whatever drugs are available with as many of the ideal characteristics as possible.
- Use free combinations if SPCs are not available or unaffordable
- Use thiazide diuretics if thiazide-like diuretics are not available
- Use alternative to DHP-CCBs if these are not available or not tolerated (i.e. Non-DHP-CCBs: diltiazem or verapamil).

ESSENTIAL OPTIMAL

Consider beta-blockers at any treatment step when there is a specific indication for their use, e.g. heart failure, angina, post-MI, atrial fibrillation, or younger women with, or planning pregnancy.

OPTIMAL

Step 1 Dual low-dose# combination	A + C^{a,b,c}
Step 2 Dual full-dose combination	A + C^{a,b}
Step 3 Triple combination	A + C + D
Step 4 (Resistant Hypertension) Triple Combination + Spironolactone or other drug*	A + C + D Add Spironolactone (12.5 – 50 mg o.d.)^d

Ideally Single Pill Combination Therapy (SPC)

a) Consider monotherapy in low risk grade 1 hypertension or in very old (≥80 yrs) or frailer patients.
b) Consider A + D in post-stroke, very elderly, incipient HF or CCB intolerance.
c) Consider A + C or C + D in black patients.
d) Caution with spironolactone or other potassium sparing diuretics when estimated GFR <45 ml/min/1.73m² or K⁺ >4.5 mmol/L.

A = ACE-Inhibitor or ARB (Angiotensin Receptor Blocker)
C = DHP-CCB (Dihydropyridine -Calcium Channel Blocker)
D = Thiazide-like diuretic

Supportive references: A + C,^{68,70} Spironolactone,⁷¹ Alpha-blocker,⁷² C + D⁷³.

* Alternatives include: Amiloride, doxazosin, eplerenone, clonidine or beta-blocker.

low-dose generally refers to half of the maximum recommended dose

RCT-based benefits between ACE-I's and ARB's were not always identical in different patient populations. Choice between the two classes of RAS-Blockers will depend on patient characteristics, availability, costs and tolerability.

Common and other comorbidities and complications of Hypertension

Hypertension and coronary artery disease - A strong epidemiological interaction exists between CAD and hypertension that accounts for 25% to 30% of acute myocardial infarctions.

Lifestyle changes, Target BP- < 130/80mm Hg (<140/80mm Hg in elderly). Drugs - RAS Blockers, beta-blockers irrespective of BP levels with or without CCBs are first line drugs in hypertensive patients. Anti

platelet therapy with aspirin and lipid lowering treatment with an LDL-C < 55mg/dl.

Hypertension and previous stroke - Target BP < 130/80 mmHg (<140/80 mmHg in elderly)

Drugs - RAS blockers, CCBs, diuretics are first line drugs. Lipid lowering with an LDL-C target < 70mg/dl in ischemic stroke. Anti-platelet treatment in case of ischemic stroke, and should be carefully considered in patients with hemorrhagic stroke only in the presence of a strong indication.

Hypertension and Heart failure - Hypertension is a risk factor for the development of both HF with reduced ejection fraction (HFrEF) as well as HF with preserved EF (HFpEF).

Target- < 130/ 80mm Hg but > 120/70 mm Hg. Drugs- RAS Blockers, beta-blockers, mineralocorticoid antagonists, are all effective in HFrEF; whereas for diuretics evidence is limited to symptomatic improvement. CCBs are indicated in case of poor BP control. ARNIs (Angiotensin receptor - neprilysin inhibitor)- sacubitril-valsartan is indicated for the treatment of HFrEF as an alternative to ARBs and ACE inhibitors. The same treatment strategy applies for HFpEF though optimal strategy is unknown.

Hypertension and Chronic Kidney Disease- Hypertension is a major risk factor for the development and progression of albuminuria and any form of CKD. Target - < 130/80 mm Hg (<140/80 mm Hg in elderly patients). Drugs- RAS inhibitors are first-line drugs because they reduce albuminuria in addition to BP control. CCBs and diuretics can be added (loop diuretics if eGFR < 30ml/min/1.73m²).

Hypertension and COPD - Hypertension is the most frequent comorbidities in patients with COPD. Target- < 130/80mm Hg (elderly < 140/ 80mm Hg). Drugs- ARBs, CCBs, diuretics while beta blockers may be used in selected patients.

Diabetes - Target - < 130/80 mmHg (< 140/80mm Hg in elderly). Drugs- RAS inhibitor(and a CCB+ thiazide-like diuretic). Statin therapy if LDL > 70mg/dl in diabetes with target organ damage or uncomplicated diabetes > 100mg/dl.

Lipid disorders - BP should be lowered preferentially with RAS Inhibitors. Statins are the lipid lowering treatment of choice with or without ezetimibe or PCSK9 inhibitor . Serum triglyceride lowering

should be considered if >200mg/dl particularly in patients with hypertension and diabetes.

RESISTANT HYPERTENSION

Resistant hypertension is defined as seated office BP >140/90 mmHg in a patient treated with three or more antihypertensive medications at optimal (maximally tolerated) doses including a diuretic and after excluding pseudo resistance (poor BP measurement technique, white coat effect, non adherence and suboptimal choices in anti hypertensive therapy) as well as the substance/ drug-induced hypertension and secondary hypertension. It affects around 10% of hypertensive individuals, increases the risk of CAD, Chronic HF, ESRD and all cause mortality. Approximately 50% of patients diagnosed with resistant hypertension have pseudo resistance rather than true resistant hypertension.

Management - Optimize the current treatment regimen including health and behaviour changes and diuretic-based treatment (maximally tolerated doses of diuretics, and optimal choice of diuretic: use of thiazide-like rather than thiazide diuretics and an initiation of loop diuretics for eGFR < 30ml/min/1.73m² or clinical volume overload). Add a low dose spironolactone as the 4th line of agent in those whose serum potassium is <4.5mEq/L and whose eGFR is >45ml/min/1.73m² to achieve BP targets. If spironolactone is contraindicated or not tolerated, amiloride, doxazosin, eplerenone, clonidine, and beta-blockers are alternatives or any other available anti hypertensive class not already in use.

HYPERTENSIVE EMERGENCIES AND SPECIFIC CIRCUMSTANCES

Emergency - Severely elevated BP associated with acute hypertension mediated organ damage. Requires immediate BP lowering with intravenous therapy

Neurological end organ damage - Hypertensive encephalopathy, CVA, Sub-arachnoid haemorrhage, IC bleed.

Cardiac - Acute MI, myocardial ischemia, Acute LV dysfunction, Acute pulmonary edema, Aortic dissection

Other systems - Acute renal failure, retinal haemorrhage, eclampsia and Microangiopathic hemolytic anemia (MAHA).

Urgency - Severely elevated BP without Hypertension mediated organ damage (HMOD) can be managed with oral anti hypertensive

agents.

Handling Hypertensive emergencies and urgencies

The fundamental principle in dealing with such cases in Emergency department depends upon the presence and absence of end organ damage. Primary goal of the ED Physician is to determine which patients with acute hypertension are exhibiting signs and symptoms of end organ damage and require immediate intravenous therapy. In contrast, patients presenting with acutely elevated BP (SBP > 200mm Hg or diastolic BP >120mm Hg) without symptoms and whose BP stays significantly elevated to this level on discharge should have initiation of medical therapy and close follow-up in the outpatient setting, with BP reduction over hours or days.

Commonly used drugs

LABETALOL - Is an alpha and beta blocking agent preferred in hypertension in acute dissection, and those with end stage renal disease. Initial bolus of 20mg IV over 2 minutes, then 40-80mg IV q10min; total dose not to exceed 300mg
Alternatively - 1 to 2 mg/min by continuous IV infusion; total dose of 300mg. Available as Inj. LABLOL 20mg/4ml

NITROGLYCERIN - Initial 5mcg/min, then titrate by 5mcg/min at 3-5min intervals; if no response is seen at 20mcg/min, incremental increase of 10-20mcg/min may be used.
Available as Inj. NITROPLUS 25mg/ml

Guidelines recommendations

Admit adults with a hypertensive emergency to an ICU for continuous monitoring of BP and target organ damage, as well as for parenteral administration of an appropriate medication. For adults with a compelling condition (i.e. aortic dissection, severe preeclampsia or eclampsia, or pheochromocytoma crisis), lower SBP to below 140mmHg during the first hour and to below 120mm Hg in aortic dissection. For adults without a compelling condition, reduce SBP to a max of 25% within the first hour; then if the patient is clinically stable, lower the BP to 160/100-110mmHg over the next 2-6 hours and then cautiously to normal over the following 24-48 hours.

Fig 4 - Hypertensive emergencies requiring immediate BP lowering

Clinical presentation	Timeline and target BP	1st line treatment	Alternative
Malignant hypertension with or without TMA or acute renal failure	Several hours, MAP – 20 % to – 25 %	Labetalol Nicardipine	Nitroprusside Urapidil
Hypertensive encephalopathy	Immediate, MAP – 20 % to – 25 %	Labetalol Nicardipine	Nitroprusside
Acute ischemic stroke and BP > 220 mmHg systolic or >120 mmHg diastolic	1 h, MAP – 15 %	Labetalol Nicardipine	Nitroprusside
Acute ischemic stroke with indication for thrombolytic therapy and BP > 185 mmHg systolic or > 110 mmHg diastolic	1 h, MAP – 15 %	Labetalol Nicardipine	Nitroprusside
Acute hemorrhagic stroke and systolic BP >180 mmHg	Immediate, systolic BP < 130 < BP < 180 mmHg	Labetalol Nicardipine	Urapidil
Acute coronary event	Immediate, systolic BP < 140 mmHg	<u>Nitroglycerine</u> Labetalol	Urapidil
Acute cardiogenic pulmonary edema	Immediate, systolic BP <140 mmHg	Nitroprusside or <u>Nitroglycerine</u> (with loop diuretic)	<u>Urapidil</u> (with loop diuretic)
Acute aortic disease	Immediate, systolic BP <120 mmHg and heart rate <60 b.p.m.	Esmolol and Nitroprusside or <u>Nitroglycerine</u> or Nicardipine	Labetalol or Metoprolol
Eclampsia and severe pre-eclampsia/HELLP	Immediate, systolic BP < 160 mmHg and diastolic BP < 105 mmHg	Labetalol or Nicardipine and Magnesium sulphate	

BLOOD PRESSURE REDUCTION TARGETS IN DIFFERENT SCENARIOS

HYPERTENSIVE ENCEPHALOPATHY- Reduce MAP to 25% over 8 hours. Labetalol, nicardipine, esmolol are preferred.

ACUTE ISCHEMIC STROKE- preferred medications are labetalol and nicardipine. Withhold antihypertensive medications unless the SBP is above 220 mm Hg or the DBP is over 120 mm Hg, UNLESS the patient is eligible for IV tissue plasminogen activator (tPA); then, the goal is a gradual reduction of BP with a goal SBP of less than 185 mm Hg and a DBP below 110 mm Hg before initiating thrombolytic therapy. After initiating drug therapy but before administering tPA, the SBP should be maintained at less than 180 mm Hg and the DBP below 105 mm Hg for 24 hours.

ACUTE INTRACEREBRAL HEMORRHAGE -the preferred medications are labetalol, nicardipine, and esmolol; avoid nitroprusside and hydralazine. The treatment is based on clinical/radiographic evidence of increased intracranial pressure (ICP). If there are signs of increased ICP, maintain the MAP just below 130 mm Hg (or SBP < 180 mm Hg) for the first 24 hours after onset. In patients without increased ICP, maintain the MAP below 110 mm Hg (or SBP < 160 mm Hg) for the first 24 hours after

symptom onset. In adults with acute intracerebral hemorrhage who present with an SBP above 220 mm Hg, continuous IV drug and close BP monitoring is reasonable to lower SBP. Note that it may be harmful to immediately lower SBP to below 140 mm Hg in adults with spontaneous intracerebral hemorrhage who present within 6 hours of the acute event and have an SBP between 150 and 220 mm Hg.

SUB ARACHNOID HEMORRHAGE- In subarachnoid hemorrhage, nicardipine, labetalol, and esmolol are also the preferred agents; again, nitroprusside and hydralazine should be avoided. Maintain the SBP below 160 mm Hg until the aneurysm is treated or cerebral vasospasm occurs.

ACUTE HEART FAILURE - In acute heart failure, the preferred medications are IV nitroglycerin or sublingual nitroglycerin and IV enalaprilat. Treat with vasodilators (in addition to diuretics) for a SBP of 140 mm Hg.

ACUTE CORONARY SYNDROME - For acute coronary syndrome, beta blockers and nitroglycerin are the preferred drugs. Treatment is indicated if the SBP is above 160 mm Hg and/or the DBP is over 100 mm Hg. Reduce the BP by 20%-30% of baseline. Note that thrombolytics are contraindicated if the BP is above 185/100 mm Hg.

PERIOPERATIVE HYPERTENSION - The ACC/AHA defines perioperative hypertension as a BP of 160/90 mm Hg or higher or an SBP elevation of at least 20% of the preoperative value that persists for longer than 15 minutes. Nitroprusside, nitroglycerin, clevidipine, nicardipine, and esmolol are preferred. Target the perioperative BP to within 20% of the patient's baseline pressure, except if there is the potential for life-threatening arterial bleeding. Perioperative beta blockers are the first choice in patients undergoing vascular procedures or in patients with an intermediate or high risk of cardiac complications.

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