Therapy of Hypertension

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Therapy of Hypertension

Classification:

1. **Essential or primary hypertension:**

- **Most common (~ 90% of patients).**
- **Unknown etiology.**
- **Can NOT be cured, but it can be controlled.**

2. **Secondary hypertension:**

- **A small percentage of patients (< 10% of patients).**
- **Specific cause.**
- **Can be relieved or potentially cured.**

Secondary Hypertension

Secondary Hypertension:

- **A co-morbid disease or a drug is responsible for elevating BP.**

Causes:

1. **Chronic kidney disease**
2. **Cushing's syndrome**
3. **Coarctation of the aorta**
4. **Obstructive sleep apnea**
5. **Primary hyperparathyroidism**
6. **Pheochromocytoma**
7. **Primary aldosteronism**

Secondary Hypertension

8. Renovascular disease.
9. Thyroid disease (both hypo- and hyper-thyrodism)
10. Drugs:

a) Amphetamines.

b) Antivascular endothelial growth factor agents (Bevacizumab, ranibizumab and aflibercept). May increase vascular tone due to inhibition of VEGF-mediated vasodilation.

c) Corticosteroids.

d) Calcineurin inhibitors (cyclosporine, tacrolimus).

Secondary Hypertension

e) Decongestants (pseudoephedrine, phenylephrine)

f) Ergot alkaloids (bromocriptine, methysergide, dihydroergotamine).

g) Erythropoiesis-stimulating agents (erythropoietin, darbepoetin). May increase response to circulating vasoconstrictors.

h) Estrogen-containing oral contraceptives.

i) Nonsteroidal anti-inflammatory drugs.

j) β-blocker withdrawal.

k) Tryamine-containing foods.

Secondary Hypertension

l) **Street drugs and other products: Cocaine and cocaine withdrawal; Ephedra alkaloids (Ma huang), "herbal ecstasy" ; Nicotine and withdrawal, anabolic steroids, narcotic withdrawal, ergot-containing herbal products; St. John's wort.**

m) **Food substances: Sodium, Alcohol drinking (by increasing levels of endothelin and angiotensin II), Licorice (aldosterone-like action).**

n) **Others…**

Secondary Hypertension

- **When a secondary cause is identified, removing the offending agent or treating/correcting the underlying co-morbid condition should be the first step in management.**

Classification of Hypertension

- **2020 International Society of Hypertension Global Hypertension Practice Guidelines**

https://www.ahajournals.org/doi/epub/10.1161/HYPERTENSIONAHA.120.15026

Table 1 Blood pressure classification in the ACC/AHA and ESC/ESH guidelines

ACC/AHA				ESC/ESH			
Category	SBP		DBP	Category	SBP		DBP
Normal	< 120	and	< 80	Optimal	< 120	and	< 80
Elevated	120–129	and	< 80	Normal	120–129	and/or	80–84
Stage 1 hypertension	130–139	or	80–89	High-normal	130–139	and/or	85–89
Stage 2 hypertension	≥ 140	or	≥ 90	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

Reference:

New American (JNC8) and European Hypertension Guidelines, Reconciling the Differences. Cardiol Ther (2019) 8:157–166. https://doi.org/10.1007/s40119-019-0144-3

Classification of Hypertension

- **Hypertensive crises are clinical situations where there are extreme BP elevations, typically greater than 180/120 mm Hg.**
- **They are categorized as either:**

1. **Hypertensive emergency: extreme BP elevations that are accompanied by acute or progressing end-organ damage.**
2. **Hypertensive urgency: extreme BP elevations without acute or progressing end-organ injury.**

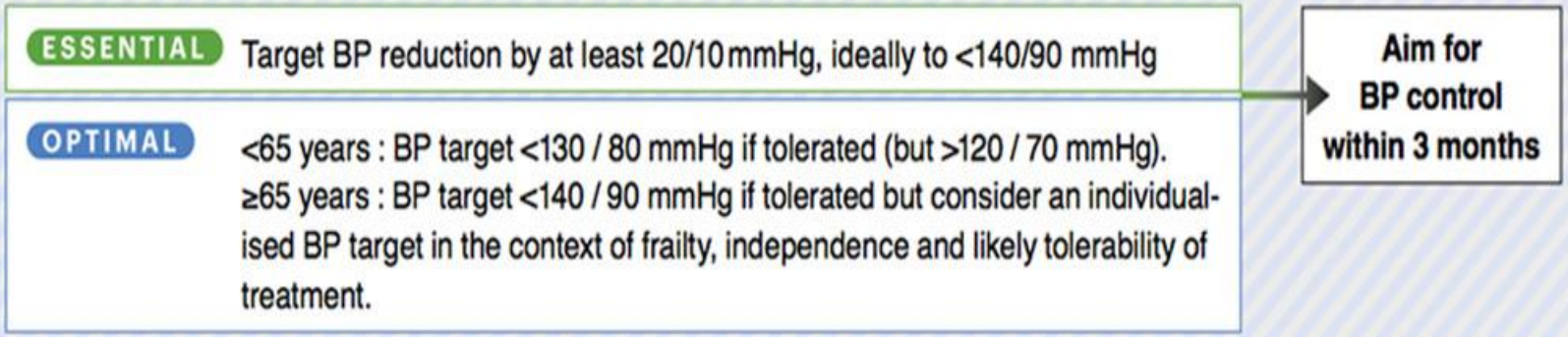
Therapy of Hypertension

Overall Goal of Treatment:

- **The overall goal of treating hypertension is to reduce associated morbidity and mortality from cardiovascular (CV) events (coronary events, cerebrovascular events, heart failure, kidney disease).**
- **Therefore, the specific selection of antihypertensive drug therapy should be based on evidence demonstrating CV event reduction.**

Therapy of Hypertension

- **Guidelines recommend a goal BP of < 130/80 mm Hg for the management of hypertension in most patients. (American guidelines).**



Reference is in slide 8

Therapy of Hypertension

- **Treating patients to lower BP goals may lead to hypotension, syncope, electrolyte abnormalities, and acute kidney injury or failure.**
- **BP control rates are poor. The main reason is "Clinical Inertia" which is defined as a clinic visit at which NO therapeutic move was made to lower BP in a patient with uncontrolled hypertension.**
- **During visits, treatment can be initiated, titrated, and/or changed.**

Therapy of Hypertension

General Approach to Treatment:

- **Most patients should be placed on both life-style modifications and drug therapy concurrently after the diagnosis of hypertension.**
- **Life-style modification alone is appropriate for most patients with pre-hypertension.**
- **Life-style modifications alone may NOT adequately lower BP in hypertensive patients.**

Therapy of Hypertension

- **Patients with additional CV risk factors or those with hypertension-associated complications need antihypertensive drug therapy in addition to life-style modifications.**
- **The choice of initial antihypertensive drug therapy depends on the degree of BP elevation and presence of compelling indication.**

Therapy of Hypertension

1. **Most patients with stage 1 hypertension should be initially treated with a first-line drug or the combination of two.**

- **Monotherapy: ACEi, ARB, CCB or a thiazide diuretic.**
- **Two-drug combination: ACEi or ARB + CCB or thiazide diuretic.**

Therapy of Hypertension

2. **For patients with stage 2 hypertension, combination drug therapy is recommended, using preferably two first-line antihypertensive drugs.**

- **ACEi or ARB + CCB.**
- **ACEi or ARB + thiazide.**

Therapy of Hypertension

Non-pharmacologic Therapy:

- **All patients with pre-hypertension and hypertension should follow life-style modifications.**
- **Life-style modifications should never be used as a replacement for antihypertensive drug therapy.**
- **They can provide small-to-moderate reductions in SBP.**
- **Strict adherence with life-style modification can decrease the progression to hypertension in patients with pre-hypertension.**

Life-style Modifications

Modification	Recommendation
Weight loss	Maintain normal body weight (body mass index, 18.5-24.9 kg/m^2), reduce wt gradually
Diet	A diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated and total fat
Reduced salt intake	Reduce daily dietary sodium intake as much as possible, (1.5 g/day sodium, or 3.8 g/day sodium chloride)
Aerobic physical activity	3 to 4 sessions/wk, lasting an average of 40 min/session, and involving moderate- to vigorous-intensity physical activity
Moderation of alcohol intake	Limit consumption to ≤2 drink equivalents per day in men and ≤1 drink equivalent per day in women and lighter-weight persons

Therapy of Hypertension

Pharmacotherapy:

- **An ACE-inhibitor, an angiotensin II receptor blocker (ARB), a calcium channel blocker (CCB), or a thiazide diuretic are preferred first-line antihypertensive agents for most patients.**
- **They should be used to treat the majority of patients with hypertension because of evidence demonstrating cardiovascular event reduction.**

Therapy of Hypertension

- **β-Blocker therapy should be reserved to either treat a specific compelling indication or used in combination with one or more of the first-line antihypertensive agents for patients without a compelling indication.**
- **A β-blocker can be used as a first-line antihypertensive agent when an ACEi, ARB, CCB, or thiazide can NOT be used as the first-line agent.**

Therapy of Hypertension

- **Alternative antihypertensive drug classes may be used in select patients after first-line agents:**
  Loop diuretics, potassium sparing diuretics, β-blockers, α_1-blockers, central α_2-agonists, direct renin inhibitors, and direct arterial vasodilator (hydralazine).

Therapy of Hypertension

Patients with Compelling Indications:

- **Compelling indications represent specific co-morbid conditions where evidence supports using specific antihypertensive classes to treat both the compelling indication and hypertension.**
- **In these cases, drug therapy consists of drug combination.**

Therapy of Hypertension

Heart Failure with Reduced Ejection Fraction:

- **Systolic heart failure associated with decreased cardiac output.**
- **The following are indicated: An ACEi or ARB plus diuretic therapy, followed by the addition of a β-blocker (bisoprolol, carvedilol, or metoprolol) and possibly an aldosterone receptor antagonist.**
- **An ACEi or ARB should be started with low doses, especially in patients with acute exacerbation.**

Therapy of Hypertension

- **Heart failure induces a compensatory high-renin condition, and starting an ACEi or ARB can cause a profound first-dose effect and possible orthostatic hypotension.**
- **Diuretics provide symptomatic relief of edema.**
- **Loop diuretics are often needed, especially for patients with more advanced heart failure and/or CKD.**

Therapy of Hypertension

- **A β-Blocker must be started in very low doses, much lower than that used to treat hypertension, and titrated slowly to higher doses based on tolerability.**
- **Bisoprolol, carvedilol, and sustained-release metoprolol are the only β-blockers proven to be beneficial.**
- **The addition of an aldosterone antagonist (spironolactone or eplerenone) can reduce cardiovascular morbidity and mortality.**

Therapy of Hypertension

Post-Myocardial Infarction:

- **β-Blockers (without intrinsic sympathomimetic activity) and ACEi or ARB are first choice to decrease cardiac adrenergic stimulation.**
- **They reduce the risk of a subsequent MI or sudden cardiac death.**
- **ACEi treatment improves cardiac remodeling and cardiac function and reduces cardiovascular events post-MI.**
- **β-blockers should be used first.**

Therapy of Hypertension

Coronary Artery Disease:

- **Chronic stable angina and acute coronary syndrome (unstable angina and acute MI) are the most common hypertension-associated complications.**
- **β-Blocker therapy is a standard of care for treating these conditions in patients with hypertension.**
- **They are first-line therapy in chronic stable angina and have the ability to reduce BP and improve ischemic symptoms by decreasing myocardial oxygen consumption and demand.**

Therapy of Hypertension

- **Long-acting CCBs (the non-dihydropyridines diltiazem and verapamil) are alternatives to β-blockers.**
- **Dihydropyridine CCBs are considered as add-on therapy in chronic stable angina for patients with ischemic symptoms.**
- **For acute coronary syndromes (ST-elevation MI and unstable angina/non-ST-segment MI), first-line therapy should consist of a β-blocker and ACEi or ARB.**

Therapy of Hypertension

- **Once ischemic symptoms are controlled with β-blocker and/or CCB therapy, other antihypertensive drugs (ACEi or ARB) can be added to provide additional cardiovascular risk reduction.**
- **Thiazides can be added thereafter to provide additional BP lowering and to further reduce cardiovascular risk, but they do NOT provide anti-ischemic effects.**

Therapy of Hypertension

Diabetes Mellitus:

- **The primary cause of mortality in diabetes is cardiovascular disease, and hypertension management is a very important risk reduction strategy.**
- **ACEi or an ARB have been shown to reduce CV events in patients with diabetes.**
- **These agents provide nephro-protection due to vasodilation in the efferent arteriole.**

Therapy of Hypertension

- **CCBs are the most appropriate add-on agents for BP control for patients with diabetes.**
- **A thiazide (?), used in low doses, is recommended add-on therapy to lower BP and provide additional cardiovascular risk reduction.**

Therapy of Hypertension

- β-Blockers (especially non-selective) can mask the signs and symptoms of hypoglycemia in patients with tightly controlled diabetes because most of the symptoms of hypoglycemia (tremor, tachycardia, and palpitations) are mediated through the sympathetic nervous system.
- Sweating, a sympathetic-cholinergic function, still occurs during a hypoglycemic episode despite β-blocker therapy.
- Patients may have a delay in hypoglycemia recovery time because compensatory recovery mechanisms need catecholamine input which is antagonized by β-blockers.
- Unopposed α-receptor stimulation during the acute hypoglycemic recovery phase (due to endogenous epinephrine release intended to reverse hypoglycemia) may result in acutely elevated BP due to vasoconstriction.
- Despite these potential problems, β-blockers (selective) can be used for patients with diabetes.

Therapy of Hypertension

Chronic Kidney Disease (CKD):

- **ACEi or ARB therapy reduces intraglomerular pressure, which slows progression of CKD in diabetics and nondiabetics.**
- **Patients may experience a rapid and profound drop in BP or acute kidney failure when given an ACEi or ARB, especially in patients with bilateral renal artery stenosis or a solitary functioning kidney with stenosis.**
- **Start with low dose and measure serum creatinine soon after starting the drug to minimize this risk.**

Therapy of Hypertension

Recurrent Stroke Prevention:

- **Ischemic stroke and transient ischemic attack are complications of hypertension.**
- **A thiazide is a reasonable choice.**
- **It can be combined with an ACEi or an ARB.**
- **Antihypertensive drug therapy should only be implemented after the patient has stabilized following an acute cerebrovascular event.**

Therapy of Hypertension

Alternative Drug Treatments:

- **Include: direct renin inhibitors, α-blockers, central α_2-agonists, adrenergic inhibitors, and arterial vasodilators.**
- **These agents are effective in lowering BP, but they may NOT reduce morbidity and mortality in hypertension, or have poor tolerability and adverse effects that significantly limit their use.**
- **Alternative agents may be used for patients with resistant hypertension, or as add-on therapy with multiple other first-line antihypertensive agents.**

Therapy of Hypertension

Hypertension in elderly patients:

- **Hypertension may present as isolated systolic hypertension in the elderly.**
- **This population is at high risk for hypertension-associated complications.**
- **Many elderly patients with hypertension are either NOT treated, or treated but NOT controlled.**
- **Thiazides and long-acting dihydropyridine CCBs reduce cardiovascular morbidity and mortality in these patients.**

Therapy of Hypertension

- Elderly patients are more sensitive to volume depletion and sympathetic inhibition than younger patients → orthostatic hypotension.
- This can increase the risk of falls due to the associated dizziness.
- Centrally acting agents and α_1-blockers should be avoided because they are frequently associated with dizziness and orthostatic hypotension.

Therapy of Hypertension

- **A thiazide, ACEi, or ARB provide significant benefits and can safely be used in the elderly, at smaller-than-usual initial doses.**
- **To minimize risks, dosage should be titrated over a longer period of time.**
- **Standard SBP goals of <140 mm Hg should be considered for elderly patients.**

Therapy of Hypertension

Patients at Risk of Orthostatic Hypotension:

- **The risk of orthostatic hypotension is increased in older patients, those with isolated systolic hypertension, those with long-standing diabetes, severe volume depletion, baroreflex dysfunction, autonomic insufficiency, and on concomitant venodilators (α-blockers, mixed α-/β-blockers, nitrates, and phosphodiesterase inhibitors).**
- **Antihypertensive agents should be started in low doses, especially a thiazide, ACEi or ARB.**

Therapy of Hypertension

Hypertension in Children and Adolescents:

- Hypertensive children often have a family history of high BP, and many are overweight predisposing them to insulin resistance and associated cardiovascular disease.
- Secondary hypertension is more common in children and adolescents, thus, we need to find the cause.
- Kidney disease (pyelonephritis, glomerulonephritis) is the most common cause of secondary hypertension in children.
- Coarctation of the aorta can also produce secondary hypertension.

Therapy of Hypertension

- **Medical or surgical management of the underlying disorder usually normalizes BP.**
- **Weight loss is the cornerstone of therapy.**
- **An ACEi, ARB, β-blocker, CCB, and thiazide are all acceptable choices in children.**
- **Like adults, selection of initial agents should be based on the presence of compelling indications or concurrent conditions that may warrant their use (ACEi or ARB for diabetics or CKD).**

Therapy of Hypertension

Pulmonary Disease:

- **Nonselective β-Blockers should be avoided in hypertensive patients with reactive airway disease (asthma or COPD) due to a fear of inducing bronchospasm.**

Peripheral Arterial Disease:

- **β-Blockers decrease peripheral blood flow secondary to unopposed stimulation of α_1-receptors that results in vasoconstriction, and should be avoided.**
- **β-blocker with α_1-blocking properties (carvedilol) can be used.**

Monitoring of Therapy

Ongoing monitoring, in all patients treated with antihypertensive drugs, is required to assess:

1) **The desired effects of antihypertensive therapy (BP goal).**
2) **Drug adverse effects.**
3) **Disease progression.**

Monitoring of Therapy

Monitoring of antihypertensive therapy

Class	Parameters
Aldosterone antagonists	BP; BUN/serum creatinine; serum potassium
ACEis & ARBs	BP; BUN/serum creatinine; serum potassium
Calcium channel blockers	BP; heart rate
Thiazides	BP; BUN/serum creatinine; serum electrolytes (potassium, magnesium, sodium); uric acid, glucose.
β-Blockers	BP; heart rate

Adherence and Persistence

- Poor adherence is frequent.
- Only 50% of patients with newly diagnosed hypertension are continuing treatment at 1 year.
- Identification of nonadherence should be followed up with appropriate patient education, counseling, and intervention.
- Once-daily regimens are preferred in most patients to improve adherence.

Resistant Hypertension

- **Failure to achieve goal BP with the use of three or more antihypertensive drugs indicates resistant hypertension.**
- **It affects ~ 12% of patients.**
- **Pseudo-resistance should also be ruled out by assuring adherence with prescribed therapy.**

Causes of Resistant Hypertension

1. Improper BP measurement.
2. Volume overload:
- Excess sodium intake.
- Volume retention from kidney disease.
- Inadequate diuretic therapy.
3. Drug-induced (2◦) (mentioned before)
4. Other causes:
- Nonadherence.
- Inadequate antihypertensive doses.
5. Associated conditions:
- Obesity, excess alcohol intake, obstructive sleep apnea.

Hypertensive Urgencies and Emergencies

- **Hypertensive urgencies and emergencies (hypertensive crises) are characterized by very elevated BP (> 180/120 mm Hg).**
- **The difference is that emergencies are associated with acute or immediately progressing end-organ injury.**
- **Urgencies are NOT associated with acute or immediately progressing end-organ injury.**

Hypertensive Urgencies and Emergencies

- **Acute end-organ injury include encephalopathy, intracranial hemorrhage, retinopathy, nephropathy, acute left ventricular failure with pulmonary edema, dissecting aortic aneurysm, unstable angina, and eclampsia or severe hypertension during pregnancy.**

Hypertensive Urgency

- **A common error with hypertensive urgency is aggressive antihypertensive therapy.**
- **Hypertensive urgencies are ideally managed by adjusting maintenance therapy:**

1) **adding a new antihypertensive.**
2) **increasing the dose of a present medication.**

- **This provides a more gradual reduction in BP.**

Hypertensive Urgency

- **Very rapid reductions in BP to goal values should NOT be attempted because autoregulation of blood flow in patients with hypertension occurs at a much higher range of pressure than in normotensive persons.**
- **The risks of reducing BP too rapidly include cerebrovascular accidents, MI, and acute renal failure.**

Hypertensive Urgency

- **Hypertensive urgency requires BP reductions with oral antihypertensive agents to stage 1 over a period of several hours to days.**
- **All patients with hypertensive urgency should be reevaluated within, and NOT later than, 7 days (preferably after 1 to 3 days).**

Hypertensive Urgency

- Administration of a short-acting oral antihypertensive (captopril, clonidine, labetalol) followed by careful observation for several hours to assure a gradual reduction in BP is an option.
- For patients with hypertensive rebound following withdrawal of clonidine, 0.1-0.2 mg can be given initially, followed by 0.05-0.1 mg hourly until the DBP falls below 110 mm Hg or a total of 0.7 mg clonidine has been administered.

Hypertensive Urgency

- **A single dose may be all that is necessary.**
- **Labetalol can be given in a dose of 200 to 400 mg, followed by additional doses every 2 to 3 hours.**
- **Oral or sublingual immediate-release nifedipine is dangerous, should never be used for hypertensive urgencies due to risk of causing severe adverse events (MI, stroke).**

Hypertensive Emergency

- Hypertensive emergencies require immediate BP reduction to limit new or progressing end-organ damage.
- They require parenteral therapy, at least initially.
- Do NOT lower BP to < 140/90 mm Hg.
- The initial target is a reduction in MAP of up to 25% within minutes to hours. [MAP = {SBP + 2 (DBP)}/ 3]
- When the patient is stable, DBP can be reduced to 100 - 110 mm Hg within the next 2 - 6 hours.

Hypertensive Emergency

- **Precipitous drops in BP may lead to end-organ ischemia or infarction.**
- **If patients tolerate this reduction well, additional gradual reductions toward goal BP values can be attempted after 24 to 48 hours.**
- **The exception to this guideline is for patients with an acute ischemic stroke where maintaining an elevated BP is needed for a longer period of time.**

AHA/ASA Recommendations for BP Management in Acute Ischemic Stroke

1. Patients eligible for treatment with intravenous thrombolytics or other acute reperfusion intervention and SBP >185 mm Hg or DBP >110 mm Hg should have BP lowered before the intervention. A persistent SBP of >185 mm Hg or a DBP >110 mm Hg is a contraindication to intravenous thrombolytic therapy. After reperfusion therapy, keep SBP <180 mm Hg and DBP <105 mm Hg for at least 24 hours.
2. Patients who have other medical indications for aggressive treatment of BP should be treated.
3. For those not receiving thrombolytic therapy, BP may be lowered if it is markedly elevated (SBP >220 mm Hg or DBP >120 mm Hg). A reasonable goal would be to lower BP by approximately 15% during the first 24 hours after onset of stroke.
4. In hypotensive patients, the cause of hypotension should be sought. Hypovolemia and cardiac arrhythmias should be treated and in exceptional circumstances, vasopressors may be prescribed in an attempt to improve cerebral blood flow.

Hypertensive Emergency

- **The clinical situation should dictate which IV medication is used to treat hypertensive emergencies.**
- **Therapy should be provided in a hospital or emergency room setting with intra-arterial BP monitoring.**

Hypertensive Emergency

1. **Sodium nitroprusside was drug of first choice in the past.**
2. **IV nitroglycerin is ideal for the management of hypertensive emergency in the presence of myocardial ischemia.**

- **IV nitroglycerin is associated with tolerance when used over 24 to 48 hours and can cause severe headache.**

Hypertensive Emergency

3. **Fenoldopam is a D_1-receptor agonist. It can improve renal blood flow and may be especially useful for patients with renal insufficiency.**
4. **Nicardipine and clevidipine provide arterial vasodilation and can treat cardiac ischemia similar to nitroglycerin, and may provide more predictable reductions in BP. (use with caution)**

Hypertensive Emergency

Sodium nitroprusside:

- **Dose: 0.25-10 µg/kg/min IV infusion (requires special delivery system).**
- **Onset: immediate.**
- **Duration: 1-2 min.**
- **Adverse effects: Nausea, vomiting, muscle twitching, sweating, thiocyanate and cyanide intoxication.**
- **Special indications: Most hypertensive emergencies.**
- **Caution with high intracranial pressure, azotemia, or in chronic kidney disease.**

Hypertensive Emergency

Nitroglycerin:

- **Dose: 5-100 µg/min IV infusion.**
- **Onset: 2-5 min.**
- **Duration: 5-10 min.**
- **Adverse effects: Headache, vomiting, methemoglobinemia, tolerance with prolonged use.**
- **Special indications: Coronary ischemia.**

Hypertensive Emergency

Clevidipine:

- **Dose: 1-2 mg/h (32 mg/h maximum).**
- **Onset: 2-4 min.**
- **Duration 5-15 min.**
- **Adverse effects: Headache, nausea, tachycardia, hypertriglyceridemia.**
- **Special indications: Most hypertensive emergencies except acute heart failure; caution with coronary ischemia.**
- **Contraindications: soy or egg allergy, defective lipid metabolism, and severe aortic stenosis.**

Hypertensive Emergency

Nicardipine:

- **Dose: 5-15 mg/h IV.**
- **Onset: 5-10 min.**
- **Duration: 15-30 min, may exceed 4 hours.**
- **Adverse effects: Tachycardia, headache, flushing, local phlebitis.**
- **Special indications: Most hypertensive emergencies except acute heart failure.**
- **Caution with coronary ischemia.**

Hypertensive Emergency

Enalaprilat:

- **Dose: 1.25-5 mg IV every 6 hours.**
- **Onset: 15-30 min.**
- **Duration: 6-12 hours.**
- **Adverse effects: Precipitous fall in pressure in high-renin states; variable response.**
- **Special indications: Acute left ventricular failure.**
- **Avoid in acute myocardial infarction, eclampsia.**

Hypertensive Emergency

Esmolol:

- **Dose: 250-500 µg/kg/min IV bolus, and then 50-100 µg/kg/min IV infusion; may repeat bolus after 5 minutes or increase infusion to 300 µg/min**
- **Onset: 1-2 min.**
- **Duration: 10-20 min.**
- **Adverse effects: Hypotension, nausea, asthma, first-degree heart block, heart failure.**
- **Special indications: Aortic dissection; perioperative.**
- **Avoid in patients already on β-blocker, bradycardic, or decompensated heart failure.**

Hypertensive Emergency

Fenoldopam:

- **Dose: 0.1-0.3 µg/kg/min IV infusion.**
- **Onset: <5 min.**
- **Duration: 30 min.**
- **Adverse effects: Tachycardia, headache, nausea, flushing.**
- **Special indications: Most hypertensive emergencies.**
- **Caution with glaucoma.**

Hypertensive Emergency

Hydralazine:

- **Dose: 12-20 mg IV; 10-50 mg intramuscular.**
- **Onset: 10-20; 20-30 min, respectively.**
- **Duration: 1-4; 4-6 hours, respectively.**
- **Adverse effects: Tachycardia, flushing, headache vomiting, aggravation of angina.**
- **Special indications: Eclampsia.**

Hypertensive Emergency

Labetalol:

- **Dose: 20-80 mg IV bolus every 10 minutes; 0.5-2 mg/min IV infusion.**
- **Onset: 5-10 min**
- **Duration: 3-6 hours.**
- **Adverse effects: Vomiting, scalp tingling, bronchoconstriction, dizziness, nausea, heart block, orthostatic hypotension.**
- **Special indications: Most hypertensive emergencies except acute heart failure or heart block.**