CHAPTER

139 Hypertension Urgencies & Emergencies

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INTRODUCTION

Hypertension is defined as the level of blood pressure beyond which the vascular risk has increased in general population.Over the last few decades the cut off limit of normal blood pressure has changed considerably.Last JNC guideline suggests the upper limit of normal blood pressure is 140/90mmHg below the age of 60years. As the prevalence of the hypertension is increasing for the last 3decades the hypertensive crisis is also increasing. It has been estimated globally that 1 -2 % of hypertensive populations suffer from hypertension urgencies & emergencies which parallels the distribution of primary hypertension. Uncontrolled hypertension beyond 180/120 mmHg can be classified as hypertensive urgency or emergency depending upon the end organ damage. The prompt recognition of hypertensive emergency & urgency with proper diagnostic test and triage may lead to prevention of end organ damage and fatal outcomes like myocardial infarction, stroke, renal failure, Coma and death.

HISTORY

In 1914 The clinician Franz Volhard and pathologist Theodor Fahr coined the term malignant hypertension which we recognize today as hypertensive urgency.They described individuals with severe hypertension along with renal failure, retinopathy with papilledema,fibrinoid necrosis and death.

In 1921 - Keith and Wagener identified similar patients having papilledema with retinopathy but no renal insufficiency. They introduced the term "Accelerated Hypertension".

In 1928 Oppenheimer & Fishberg described hypertensive encephalopathy in the back ground of Accelerated Hypertension.

Currently it is defined as –

1. Accelerated HTN – Severely elevated BP more than 179/109 mmHg associated with ocular hemorrhages,exudates but no papilledema (Grade III Kimmel Stiel – Wilson retinopathy)
2. Malignant HTN - Severely elevated BP more than 179/109 mmHg associated with ocular hemorrhages, exudates with papilledema (Grade IV Kimmel Stiel – Wilson retinopathy)

DEFINITION

The hypertensive crisis and its outcome depends on

1. Degree of BP elevation
2. The briskness /rapidity of increase of BP
3. The length of time of Hypertensive crisis
4. The degree of end organ damage.

Therefore Hypertensive crisis is classified into two types

1. Hypertensive Urgency – defined as the elevated blood pressure more than 180/120 in the presence of target end organ damage
2. Patients may present with non progressive symptoms of headache, shortness of breath, epistaxis,pedal edema
3. Hypertensive emergency defined as severe HTN more than 220/140 mmHg with end organ damage. It may lead to acute MI, Hypertensive encephalopathy, intracranial hemorrhage, dissecting aneurysm, acute renal failure, pulmonary edema and so on. In case of pregnant females BP more than 169/109 mmHg is considered as hypertensive emergency

EPIDEMIOLOGY

Hypertensive emergencies are common and occur 1% to 2% of hypertensive population. Hypertensive crisis affects 5 lakhs Americans every year. Zampaglione et al evaluated the prevalence of hypertensive crisis in emergency department for 1 year and frequency of end organ damage during the 1st 24 hours after presentation. They observed that the frequency of the hypertensive urgencies was 76% and hypertensive emergencies was 24%. They also found that the hypertensive crisis was more common in patients of renal disease.

It is more prevalent in the elderly and men are affected 2 times more often than woman. It is also common in lower socioeconomic status and among those who are non-compliant.

In South East Asia region 36% of adults have hypertension. In India, review of epidemiological studies suggest that the prevalence of hypertension has increased in both urban and rural subjects and presently 25% of the urban adults and 10 to 15% of rural adults are hypertensive. Among all Indian hypertensive 1 to 2 % present with hypertensive crisis.

ETIOLOGY

Common causes of Hypertensive Crisis

1. Medication Noncompliance

Table 1: Hypertensive Crises According to the Plasma Renin Level

1	Disorders with high renin	Malignant hypertension
2	Medium to high renin states	Unilateral renovascular hypertension Renal vasculitis (scleroderma, lupus, polyarteritis) Renal trauma Renin secreting tumors Adrenergic crises: pheochromocytoma, cocaine abuse, clonidine
3	Probable medium to high renin states (PRA ≥ 0.65 ng/mL/h)	Hypertension with cerebral hemorrhage Hypertension with (impending) stroke Hypertension with pulmonary edema Hypertension with acute myocardial infarction or unstable angina Dissecting aortic aneurysm Perioperative hypertension
4	Sodium-volume overload, low renin states: PRA ≤ 0.65 ng/mL/h	Acute tubular necrosis Acute glomerulonephritis Urinary tract obstruction Primary aldosteronism Low renin essential hypertension Preeclampsia/eclampsia

2. Antihypertensive drug withdrawal
3. Renal Parenchymal disease
4. Reno vascular disease
5. Drugs (i.e. cocaine, PCP)
6. Collagen Vascular diseases
7. Cushing disease
8. Pheochromocytomas
9. Preeclampsia and eclampsia
10. Postoperative state

The most common cause of Hypertensive crisis is chronic hypertension with its acute exacerbation. The followings drugs can precipitate hypertensive crisis in normotensive or hypertensive individuals.

1. Oral contraceptives
2. Cocaine
3. Phencyclidine
4. MAO inhibitor with tiramine
5. Linezolid
6. NSAIDS
7. Amphetamines

Secondary causes of hypertension that leads to hypertensive crisis

1. Renal Disease
2. Endocrine Disorders-

a. Cushing Syndrome

b. Primary Hyperaldosteronism

c. Pheochromocytoma

4. Cerebro Vascular accident
5. Cardiac & Spinal Surgery
6. Spinal cord and Head injuries
7. SLE
8. TTP-HUS
9. Pregnancy

Associated risk factors

1. Lack of a primary care physicians
2. Lack of resources & medical insurance
3. Smoking
4. Diabetes
5. Obesity

PATHOPHYSIOLOGY (FIGURE 1)

Precise mechanism of hypertensive crisis is not known. Two general theories, Pressure hypothesis and Humoral hypothesis suggest that pathologic events of hypertensive crisis develop when there is critical imbalance of pressure and humoral factors. In severe hypertension –

1. Amplification of RAS →Damage to endothelium of blood vessel and deposition of fibrin thrombi,
2. High vascular reactivity and elevated levels of vasoactive agents such as norepinephrine, angiotensin II and vasopressin → Natriuresis → Hypovolemia → More elevation of vasoactive agents → arteriolar fibroid necrosis → Endothelial damage → Plate late deposition and micro angiopathic hemolatic anemia. It leads to ischemia and further release of vasoactive agents.Thus the cycle continues
3. Elevation of asymmetric dimethyle arginine,endogenous NO synthase inhibitors.It is observed in preeclampsia.

CLINICAL PRESENTATION

Hypertension urgencies and emergencies may present asymptomatically. Silent HTN crisis has been found commonly in young black men.

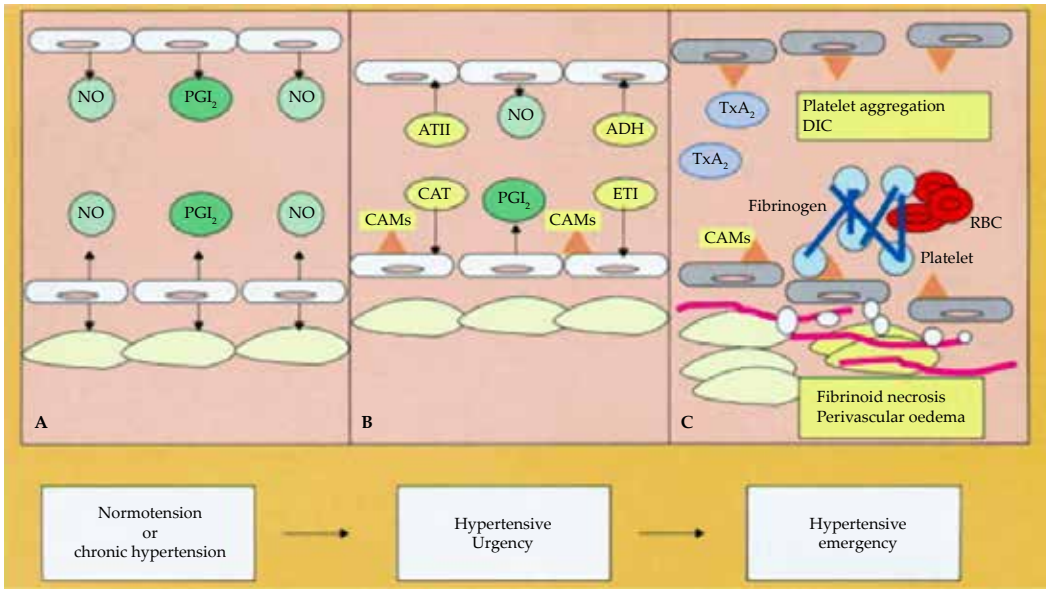

Fig. 1: Pathophysiology of Hypertensive emergencies

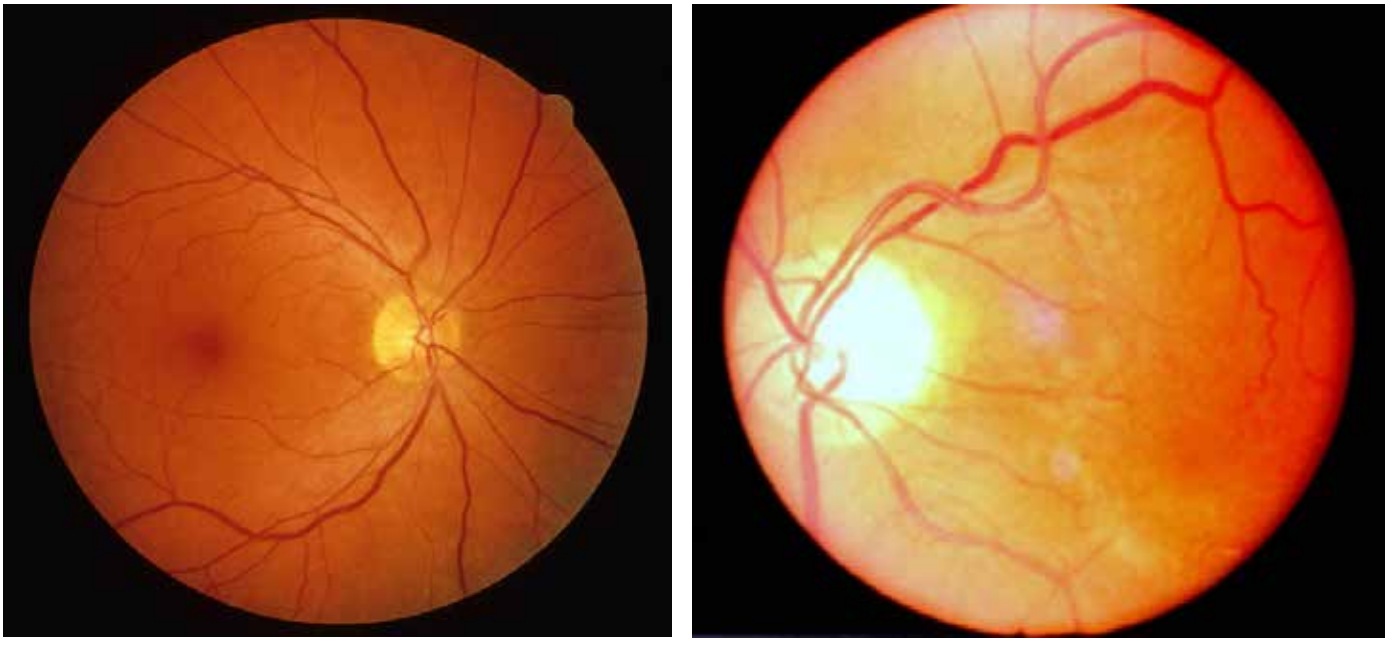

Fig. 2: Grade 1 : Hypertensive Retinopathy

Signs and symptoms of hypertensive urgency

1. Headache --- 22%
2. Epistaxis ----17%
3. Faintness ---- 10%
4. Psychomotor agitation ---- 10%
5. Chest pain --- 9%
6. Dyspnea ---- 9%
7. Less Common symptoms are arrhythmias and paresthesias.

Signs and symptoms of hypertensive emergency

1. Chest pain ---- 27%
2. Dyspnea --- 22%
3. Neurologic deficits ---21%

End organ damage

1. Cerebral infarction --- 24%
2. Acute pulmonary edema --- 22%
3. Hypertensive encephalopathy --- 16%
4. Congestive heart failure --- 12%
5. Less common presentation are intracranial heamorrhage, acute aortic dissection, acute MI, acute kidney injury and eclampsia.

Single organ involvement is observed in 83 % of patients

Two organ involvement is observed in 14% of patients

Multi organ involvement (> 3 organs) is observed in 3% of patients.

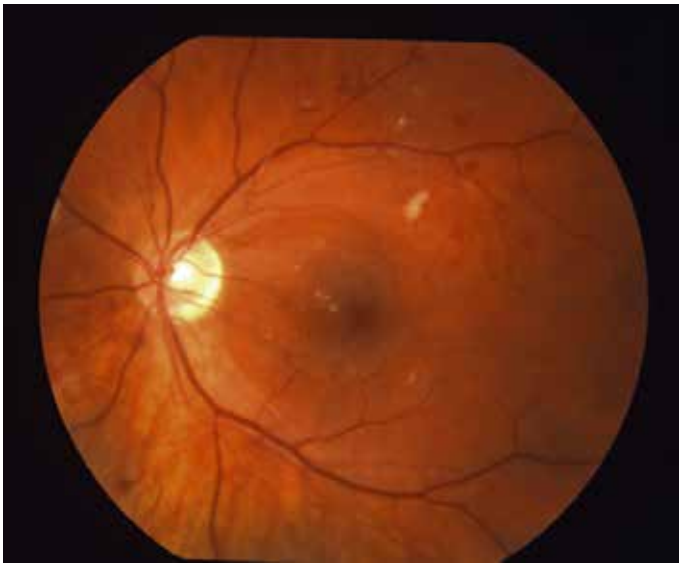

Fig. 3A

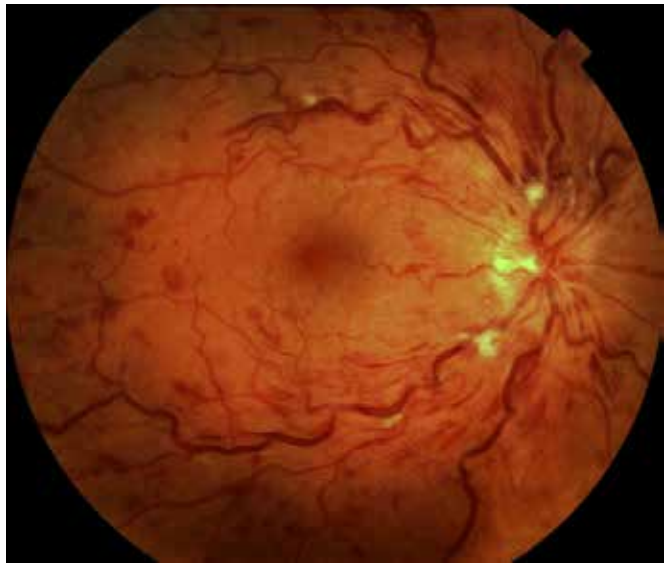

Fig. 3B

Grade 3 KWB Retinopathy

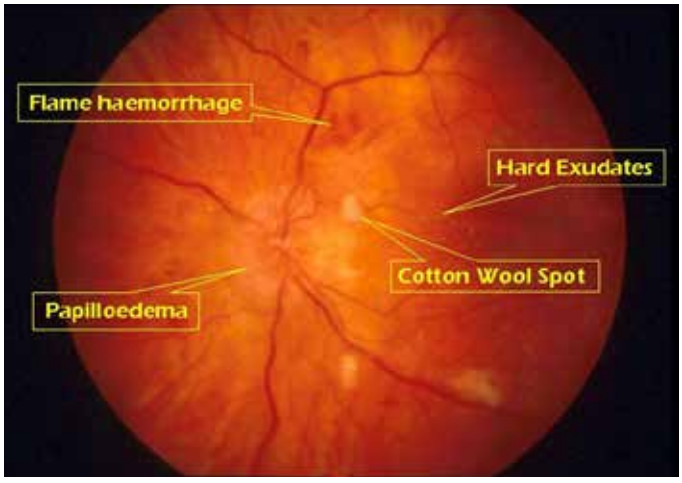

Fig. 4: Hypertensive Retinopathy Grade 4

FUNDOSCOPIC EXAMINATION

- Lost art
- Keith-Wagener-Barker Classification

Keith-Wagener-Barker Classification

- Grade 1 (Figure 2)
- Mild narrowing of the arterioles
- "Copper Wire"
- Grade 2
- Moderate narrowing - Copper wire and AV nicking
- Changes associated with long standing essential hypertension
- Grade 3 (Figure 3A & 3B)
- Severe Narrowing - Silver wire changes, hemorrhage, cotton wool spots, hard exudates
- Grade 4 (Figure 4)
- Grade 3 + Papilledema
- Grade 3 and 4 highly correlated with progression to end organ damage and decreased survival

DIAGNOSIS

Clinical examination should include thorough history taking, physical examination and relevant investigation. History should include duration and severity of hypertension, previous BP records prior organ damage associated symptoms, recreational drug and alcohol use. Thorough auditing of list of medications particularly antihypertensive drugs and their dosing compliance with antihypertensive regimen.

A. Relevant Symptoms

1. Headache and chest pain
2. Dyspnea,edema and acute fatigue
3. Epistaxis
4. Seizures
5. Change in the level of consciousness
6. Palpitation, Diaphoresis and tremors suggestive of pheochromocytoma
7. Weight gain and thinning of skin suggestive of cushing's syndrome.

B. History of comorbid condition

Diabetes, smoking, hyperlipidemia, chronic kidney disease

C. Medication and addiction

D. Physical Examination

1. Fell all peripheral pluses including uperlimbs, carotids, femoral and lower extremities
2. Measure the blood pressure using appropriate technique and proper BP cuff
3. Measure blood pressure both arms and at least one leg.

Table 2: differences in Management of HTN Urgency & Emergency

	Goal	Admission to Hospital	Route of Medication	Selecting Drug	Choice of Drugs	Precaution	Discharge & follow up
Hypertensive Urgency	Gradual BP control over 12-48 Hrs. reduce BP to 160/100 mmHg over hours	Observation to general ward IPD admission for those having comorbidities like Diabetes,stroke, IHD or noncompliant to drugs	Oral Medication	Low dose short acting drugs	Labetalol captopril extended release Nifedipine Clonidine, Prazosin, Amlodepine	BP Should not be lowered rapidly to their normal base line. Parenteral route & high dose to be avoided to protect hypoperfusion of major arterial beds	Can be discharged to be followed up after 48Hrs. at OPD
Hypertensive Emergency	BP should be reduced effectively within minutes to one hour Goal is to reduce BP <25% within 2-6 Hrs. & stabilized to 160/100 mmHg then 25% within 48 Hrs.	Immediate admission to ICU for prompt BP control once stabilized patient may be shifted to general ward	Parenteral titrable agents with continuous monitoring of BP, Neurological status,Urine output	Rapid acting antihypertensive agents	Labetalol, Esmolol, Nicardipine Nitroglycerine, Fenoldapam, Hydralazine **Less Use** Enalapril Phentolamine **New Drug** Clevidipine	Aggressive reduction of BP may aggravate Hypoperfusion &worsening of end organ damage. However in patient of aortic dissection rapid reduction of BP <120/80mmHg should be achieved within 5-10mines initially with B blockers	

4. BP reading in supine and sitting and standing positions are required to measure volume status.
5. A comprehensive cardiovascular examination is of value.
6. Elevated jugular venous pressure, Pedal edema, third heart sound, gallop, crepitations, provide the evidences of heart failure
7. A prominent and displaced apical impulse or a harsh intrascapular murmur is suggestive of coarctation of aorta.
8. Auscultation of carotids and abdominal bruits.
9. Fundoscopic examination – Presence of hemorrhages, exudates, papilledema – confirms hypertensive emergency.
10. Neurological examination – to assess stroke, somnolence, stupor, visual loss, focal neurological deficits, seizures or coma.
11. Check for mental status.
12. Look for target organ damage.

E. Relevant Investigation

1. Initial evaluation

a. Electrocardiogram – ST, T wave changes, evidence of LVH, ischemia, arrhythmia

b. Hematocrit, total leucocyte count and peripheral blood smear

c. Renal function test

d. Urinalysis with microscopic examination-hematuria and proteinuria

e. Chest radiograph – cardiomegaly and pulmonary congestion

f. Thyroid function test

g. Non contrast CT of head

h. Echocardiogram (LV

Table 3: Drugs for hypertensive urgencies

Agent	Dose	Onset of action	Comment
Captopril	12.5-25 mgPO	15-60 min	Can precipitate acute renal failure in patients with bilateral renal artery stenosis
Nifedipine (extended release)	10-20 mgPO	20 niin	Avoid short-acting or sublingual nifedipine due to risk of sudden hypotension, stroke, cardiac event
Labetalol	200-400 mg PO	20 120 min	Heart failure, bradycardia, bronchospasm
Clonicline	0.1-0.2 mgPO	30-60 min	Rebound hypertension due to abrupt withdrawal
Prazosin	l-2 mgPO	2-4 h	First-dose hypotension, syncope, tachycardia
Amlodipine	5-10 mg	30-50 min	Headache, tachycardia, flushing

Table 4: Parenteral Agents used in the Management of Various Hypertensive Crises

Primary Condition	Therapy
Acute aortic dissection	Labctalol or nicardipine + esmolol, nitroprusside + esmolol
Hypertensive encephalopathy	Labetalol, nicardipine, fenoldopam, clevidipine
Acute myocardial ischemia	Nitroglycerin ± esmolol, fenoldopam, labetalol
Congestive heart failure	Enalaprilat, loop diuretic
Eclampsia	Hydralazine, nicardipine, labetalol
Pheochromocytoma	Phentolamine, labetalol
Acute pulmonary edema	Sodium nitroprusside. nicardipine, fenoldopam. loop diuretic, nitroglycerin
Acute ischemic stroke/ intracerebral bleed	Nicardipine, fenoldopam, labctalol, clevidipine
Acute renal failure/ MAHA	Nicardipine, fenoldopam

Adapted from Varon et al.[47] MAHA indicates microangiopathic hemolytic anemia.

dysfunction, valve abnormalities, wall motion abnormalities)

i. Lipid profile

F. Tests to be done once the patients is stabilized

1. Renal artery imaging – Renal artery stenosis
2. Urinary VMA /Metanephrines/ 5 HIAA – Pheochromocytoma
3. Plasma cortisol and dexamethasone suppression test – Cushing's syndrome.

The differences in management of hypertensive emergencies and urgency are given in Table 2.

MANAGEMENT

Proper management of hypertensive crisis is essential to prevent end organ injury of brain, heart, kidneys & vascular system. Understanding of treatment goal appears to be of parament importance (Tables 3, 4 & 5).

PROGNOSIS

Studies have shown that patients are not being evaluated properly at the emergency room during the time of hypertensive crisis. Fundoscopic examination is the most neglected clinical examination in emergency setting and studies revealed that 2/3rd of patients evaluated for hypertensive crisis did not have fundoscopic examination done. Serum biochemistry is not properly obtained along with other investigation.

Data regarding the outcome of hypertensive crisis is very poor.In a study of 315 patients of malignant hypertension,40% were alive after 33months. The most common causes of death were renal failure (39.7%), stroke (23.8%), MI (11.1%) & heart failure (10.3%).

The main predictors of survival in hypertensive crisis were found to be known duration of HTN & procuring the serum level at presentation. In one study 1year, mortality rate has been found 79% in untreated hypertensive emergences and 5years survival rate in all treated hypertensive crisis is 74%.This study indicates categorically the benefits of managing hypertensive crisis effectively.

CONCLUSION

Physicians should be prompt enough to perform –

1. Complete evaluation of patients of hypertensive crisis including fundoscopic examination & suggestive proper laboratory investigation.
2. To manage effectively to reverse the crisis
3. To correct underlying trigger, so that such event should not happen in future.
4. To improve long-term outcome.

Table 5: Drugs for hypertensive emergencies

Labetalol

Dose: 10-80 mg IV bolus every 10 min to a maximum dose of 300 mg

Infusion: 0.5-2 mg/min

Onset/ : 5-10 min duration /3-6 h

Comments

- Combined α- and β-blockade
- Bradycardia, bronchospasm
- Avoid in congestive heart failure (CHF). bronchial asthma
- Commonly used in pregnancy-induced hypertension

Esmolol

Dose: 500 mcg/Kg IV bolus can be repeated after 5 min

Infusion: 50-200 mcg/Kg/min

Onset/duration of action after discontinuation: 1-5 min/15-30 min

Comments

- Avoid in patients with heart block, CHF, asthma
- Short-acting cardioselective β-blocker
- Bradycardia. CHF, heart block, may precipitate bronchospasm

Nicardipine

Dose: 5 mg/h IV infusion; titrate up by 2.5 mg/h every 20 min up to maximum dose of 15mg/h

Onset/duration of action after discontinuation: 15-30 min/1-4 h

Comments

- Dihydropyridine calcium channel blocker
- Reflex tachycardia
- Avoid in acute heart failure
- Useful in subarachnoid hemorrhage

Fenoldopam

0.1 mcg/Kg/min IV infusion, titrate up every 15 min to a maximum of 0.8 mcg/Kg/min Onset/duration of action after discontinuation: 3-5 min/30 min

Comments

- Selective peripheral dopamine-1 receptor agonist
- Arterial vasodilator
- Improves renal perfusion, useful in patients with hypertensive emergencies with renal failure
- Contraindicated in glaucoma

Nitroglycerine

Dose: 5-100 mcg/min IV infusion

Onset/duration of action after discontinuation: 2-5 min/5-15 min

Comments

- Mostly venodilator with modest arterial dilation
- Headache, tachycardia, flushing, vomiting
- Develops tolerance with prolonged use
- Methemoglobinemia
- Useful in emergencies with cardiac failure or ischemia

Hydralazine

Dose: 10-20 mg IV holus may be repeated every 30 min till goal BP is reached or unacceptable tachycardia develops

Onset/duration of action after discontinuation: 10-30 min/2-4 h

Comments

- Direct arteriolar vasodilator
- Reflex tachycardia, flushing
- Avoid in patients with increased ICP, ischemic heart disease, and aortic dissection (without β-blockade)

Sodium nitroprusside

Dose: 0.25-10 mcg/Kg/min IV infusion

Onset/duration of action after discontinuation: seconds/2-3 min

Comments

- Arterial and venodilaior with rapid onset and offset of action
- Preferred agents for most hypertensive emergencies
- Titrate to goal BP
- Infusion bag and delivery set must be light resistant or covered
- Nausea, vomiting, muscle twitching on prolonged use (>24-48 h)
- Thiocyanate/cyanide intoxication, metabolic acidosis in patients with renal impairment
- Thiocyanate level >10 mg/dL should be avoided

Phentolamine

Dose: 5-15 mg IV bolus, repeat every 5-15 min Infusion: 0.2-5 mg/min

Onset/duration of action after discontinuation: 1-2 min/10-30 min

Comments

- Pure α-blockade
- Reflex tachycardia, orthostatic hypotension
- Used in syndromes with excess catecholamine (pheochromocytoma)

Enalapril

Dose: 1.25 mg every 6 h

Onset/duration of action alter discontinuation: 15-30 min/6-12 h

Comments

- Mainly afterload reduction
- Contraindicated in pregnancy, renal artery stenosis
- Useful in patients with CHF

Ref: ICU protocols, A Step wise approach, ISCCM –Chawla and Todi.