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A Diagnostic and Clinical Approach to the Practical Management of Hypertensive Crisis-Clearing the Haze in Critical Clinical Context

Pradnya Brijmohan Bhattad[1], Vinay Jain[2]

1 *Resident, Department of Internal Medicine, East Tennessee State University, Tennessee (TN), USA*

2 *Attending Radiologist, Department of Radiology, James H. Quillen Veterans Affairs Medical Center, Mountain Home, Tennessee (TN), USA*

Abstract

Severe hypertension is the systolic blood pressure of 180 mmHg or above and/or diastolic blood pressure of 120 mmHg or above. Hypertensive urgency is defined as severe hypertension in the absence of any signs or symptoms of acute or ongoing end-organ damage. Hypertensive emergency is defined as the presence of severe hypertension with evidence of acute, life-threatening end-organ damage. Signs of end-organ damage include acute renal failure or malignant sclerosis, acute aortic dissection, acute pulmonary edema, acute coronary syndrome, retinal hemorrhages, papilledema, subarachnoid or intracerebral hemorrhage, and hypertensive encephalopathy. Patients with a hypertensive emergency need to be treated with intravenous antihypertensive agents for rapid titration and aggressive control of blood pressure. Patients with hypertensive urgency can be treated with oral antihypertensive medications to gradually lower the blood pressure over several hours to days.

Keywords: Hypertensive crisis, Hypertensive urgency, Hypertensive emergency, Severe hypertension, End-organ damage.

INTRODUCTION

Hypertensive crisis is a potentially life-threatening situation due to elevated blood pressure (BP). Hypertensive crisis usually includes two different diagnoses, hypertensive urgency, and hypertensive emergency [1,2]. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure (JNC – 7) defines a hypertensive emergency as "severe elevations in BP >180/120mmHg, complicated by evidence of impending or progressive target organ dysfunction." The JNC-7 defined hypertensive urgency as "situations associated with severe elevations in blood pressure without progressive target organ dysfunction." [1].

Hypertensive emergencies require a rapid lowering of BP, within one hour to avoid end-organ damage. Hypertensive urgencies should be corrected within 24 hours of presentation [1-3]. Severe hypertension with pre-existing chronic organ damage without any acute manifestations does not constitute an emergency. It is important to differentiate hypertensive emergency from hypertensive urgency to determine the need for immediate parental antihypertensive treatment in a monitored setting such as the intensive care unit to minimize the end-organ damage and complications [3-5].

Pseudo-emergencies are acute elevation in BP due to some physiological triggers such as pain, hypoxia, hypercarbia, anxiety, or hypoglycemia leading to catecholamine surge. It is important to differentiate pseudo-emergencies from two hypertensive crises because the management differs greatly. Treatment for pseudo-emergencies is directed at the underlying trigger and may not include antihypertensive therapy [3,5-7].

***Corresponding author:**
Dr. Pradnya Brijmohan Bhattad
Resident, Department of Internal Medicine, East Tennessee State University, Tennessee (TN), USA
Email:
pradnyabhattad20@gmail.com

Etiology

Table 1: Precipitating factors for hypertensive crisis

Precipitating factors for the hypertensive crisis: [Ref: 3,5-8,10-13, 21-23,32]
Essential hypertension which may be undiagnosed or poorly controlled hypertension
Renovascular disease
Noncompliance to antihypertensive therapy
Pheochromocytoma
Obstructive sleep apnea
Preeclampsia, eclampsia
Collagen vascular diseases, characteristically scleroderma
Acute neurological insults such as ischemic stroke or intracranial hemorrhage
Acute and chronic renal parenchymal diseases
Drug-induced-abrupt drug withdrawal, drug interactions, idiosyncratic reactions
Withdrawal from antihypertensive agents such as beta-agonists
Sympathomimetic agents such as cocaine, amphetamines, phencyclidine
Coarctation of aorta
Autonomous hyperactivity such as from Guillain-Barré syndrome, spinal cord syndromes

The most common etiology of hypertensive crisis is a sudden increase in BP in patients with pre-existing chronic hypertension. Nonadherence to the antihypertensive treatment regimen is a frequent cause of such a sudden increase in BP [6,8-10].

Diagnostic Evaluation:

Table 2: Diagnostic evaluation in hypertensive crisis

Diagnostic evaluation in hypertensive crisis: [Ref: 3-5,7,8,10-13, 21-23, 32]
Complete blood count and peripheral blood smear: findings of anemia, schistocytes are suspicious for microangiopathic hemolytic anemia.
Chemistry panel: evaluate for electrolyte disturbances such as hypokalemia as a clue to secondary causes, and to assess renal function.
Urinalysis: hematuria, moderate-to-severe proteinuria are markers for glomerular damage.
Electrocardiogram: may show left ventricular hypertrophy suggesting chronic hypertension, assess for myocardial ischemia.
Fingerstick glucose test: to exclude hypoglycemia.
Chest x-ray: to evaluate for cardiac size and mediastinum.
Computed tomography or magnetic resonance imaging of the brain: indicated for evaluation of altered mental status or neurological deficits.
Urine toxicology screen: to evaluate for illicit drugs such as cocaine as a possible etiology of hypertensive crisis.

Plasma renin and aldosterone levels, serum and urine metanephrine levels obtained prior to initiating treatment may assist in evaluating for secondary causes of hypertension. Several antihypertensive agents interfere with the interpretation of these tests. However, a diagnostic evaluation should not delay the treatment [10-13].

Treatment of hypertensive crisis:

A hypertensive emergency requires treatment in a monitored setting in an intensive care unit, and an intra-arterial line may be required for accurate monitoring of the blood pressure [3,5,8,11]. It is recommended that BP should be reduced initially by not more than 25% of mean arterial pressure over minutes to hours. After the first 24 hours, further BP reduction should be achieved over days. However, a more aggressive reduction in BP is required in cases of aortic dissection, pulmonary edema, and postoperative bleeding to prevent life-threatening complications [12-14]. Parenteral antihypertensive agents are used to treat hypertensive emergencies. An ideal antihypertensive agent in such situations should have a rapid onset and offset of action with a predictable dose-response curve and minimal adverse reactions [12,15-17].

Table 3: Parenteral medications for hypertensive emergencies: [Ref: 3-5, 7, 10, 12, 14-20,22, 24-27, 32]

Drug	***Mechanism of action***	***Dosage***	***Onset of action***	***Duration of action***	***Indications***	***Adverse effects***	***Remarks***
Sodium nitroprusside	Direct arterial and venous vasodilator	0.25 – 10 µg/kg/min. Average effective dose 3 µg/kg/min.	1-2 min	3-4 min after the infusion is stopped	Most hypertensive emergencies	Nausea, vomiting, muscle twitching, diaphoresis, thiocyanate and cyanide intoxication especially with renal insufficiency and prolonged infusions for more than 48 hours	Caution with high intracranial pressure or azotemia, caution with the acute coronary syndrome as it can cause coronary steal, inactivated by light.
Nicardipine	Dihydropyridine calcium channel blocker. Vasodilator.	5mg/h, can increase by 2.5mg/h to max 15mg/h	Within 10 min	2-6h after stopping	Most emergencies; Postoperative crisis, especially post cardiothoracic surgery	Hypotension, dizziness, flushing, dysesthesias, headache, reflex tachycardia	Caution in liver cirrhosis. Avoid in heart failure. Caution with coronary ischemia.
Fenoldopam	Peripheral Dopamine-1 receptor agonist, leads to vasodilation in cardiac, renal	0.1µg/kg/min. to a max of 1.6 µg/kg/min. Titrate in 0.05 to 0.1	10 min. Max effect in 30	1h after stopping	For most hypertensive emergencies, especially with renal failure	Headache, dizziness, reflex tachycardia, atrial fibrillation, worsening angina, tachyphylaxis after	Contraindicated in glaucoma due to a dose-dependent increase in intraocular pressure.

	and splanchnic vascular beds	µg/kg/min increments.	min.			48h, nausea, flushing	Can be used without invasive BP monitoring. Increases renal blood flow with improved creatinine clearance in the setting of renal dysfunction.
Nitroglycerine	Direct venous vasodilator	5 µg/kg/min to max 200 µg/kg/min.	2-5 min	5-10 min	For hypertensive emergencies with the acute coronary syndrome and cardiogenic pulmonary edema	Hypotension, tachycardia, headache, nausea, vomiting, methemoglobinemia, tolerance with prolonged use	Dilates coronary vessels
Enalaprilat	Angiotensin-converting enzyme inhibitor	1.25 mg IV at 4-6 h intervals, max 5 mg in 6h.	15 min-4 h	12-24h	Acute left ventricular failure, Scleroderma crisis	Renal failure, hyperkalemia, BP response is variable and unpredictable, precipitous BP fall in high- renin states	Avoid in acute myocardial infarction. Contraindicated in pregnancy
Hydralazine	Direct arterial vasodilator	10-20 mg IV	10-20 min	1-4h	Used in Eclampsia/pre-eclampsia	Headache, nausea, flushing, reflex tachycardia, aggravation of angina.	Caution in coronary artery disease, chronic kidney disease. Contraindicated in myocardial ischemia, elevated intracranial pressure and in aortic dissection.
Labetalol	Alpha and nonselective beta-adrenergic blocker	Bolus:20mg/5 min until desired effect (max 80 mg) Infusion:1-2 mg/min infusion	5-10min	1-8h	Most emergencies except acute left ventricular failure	Orthostatic hypotension, heart block, dizziness, nausea, vomiting	
Esmolol	Adrenergic inhibitor	250-500 µg/kg/min for 1 min, then 50-100 µg/kg/min for 4 min, may repeat sequence	1-2 min	10-20 min	Aortic dissection, perioperative	Hypotension, nausea	
Phentolamine	Alpha-adrenergic inhibitor	5-15mg IV	1-2 min	3-10 min	Catecholamine excess	Tachycardia, headache, flushing, hypoglycemia	
Clevidipine	Ultra-short acting dihydropyridine calcium channel blocker. Vasodilator.	Bolus: 1-2mg/h with potential doubling every 90 sec for the desired effect. Maintenance: 4-6 mg/h and not to exceed 21mg/h.	1-5min	5-10 min after stopping	Most emergencies except left ventricular failure	Avoid in heart failure.	Metabolism is independent of renal and hepatic function. An arterial line is not required. It can be administered peripherally.

The choice of specific antihypertensive agent depends on the etiology and presentation of a hypertensive crisis. All the antihypertensive agents used in the hypertensive crisis require close monitoring of the BP [18-22].

The goal of therapy for hypertensive urgencies is to lower the BP over several hours to days to no more than 25% to 30% lower than the baseline. Rapid aggressive lowering of BP to a level below the body's ability for autoregulation may precipitate cerebral or myocardial ischemia [19, 20,23-27]. Oral antihypertensives such as clonidine or captopril are preferred for the treatment of hypertensive urgency. Clonidine 0.2 mg by mouth loading dose, then 0.1 mg every 20 minutes to a maximum of 0.8 mg until diastolic BP is reduced by 20 mmHg or more below 110 mmHg. Clonidine may lead to side effects such as dry mouth, sedation, and dizziness. Another option includes labetalol 200 to 300 mg single dose followed by 100 to 200 mg q8h. Labetalol may lead to bradycardia [10-13, 21-23,28].

Management of specific hypertensive emergencies:

1. Cardiovascular emergencies:

A. Acute cardiogenic pulmonary edema or flash pulmonary edema: Acute cardiogenic pulmonary edema from severe hypertension is treated with nitroprusside or nitroglycerine [29,30]. The use of intravenous loop diuretics may have adverse effects in such a scenario. Intravenous loop diuretics may lead to volume depletion and hemodynamic side effects [21-23,29,30]. If nitroglycerin or nitroprusside infusion is not available readily, then sublingual nitroglycerin tablets with repeated administration until desired BP is achieved can be used. Beta-blockers and calcium channel blockers should be avoided in acute decompensated flash pulmonary edema state because these agents will impair inotropy and chronotropy and further worsen the symptoms [12,22,29,31].

B. Aortic dissection: The BP in the setting of acute aortic dissection must be corrected immediately rather than normalizing slowly as is done with other presentations of hypertensive emergencies. Beta blockade prior to vasodilation for aggressive blood pressure reduction to decrease the shear force and afterload [30-31].

C. Myocardial ischemia: Nitroglycerine is the agent of choice to lower the BP. Nitroprusside is added if further lowering of the BP is required [30-31].

2. Neurological emergencies:

The neurological deficits from severe hypertension are expected to be reversed when BP is appropriately controlled. The primary neurological disorders not resulting from severe hypertension itself does not improve with the reduction of BP [22,23,32].

A. Hypertensive encephalopathy: It is characterized by altered mental status, irritability, headache due to cerebral edema from severe hypertension. Sodium nitroprusside or labetalol are the antihypertensives of choice. Antihypertensives such as nitroglycerin may increase intracranial pressure and hence should be avoided [13,21,32]. If there is no clinical improvement despite appropriate BP reduction, then a primary neurological deficit leading to secondary hypertension should be considered [23,32].

B. Intracranial hemorrhage: Neurologic consultation should be sought to guide BP management. Nimodipine prevents vasospasm in cases of subarachnoid hemorrhage [21-23,32].

C. Ischemic stroke: Generally, the elevated BP should not be treated unless BP is more than 220/120 mmHg or there is some evidence of acute end-organ damage elsewhere such as myocardial ischemia or aortic dissection. Additionally, patients who are eligible for thrombolytic therapy, the BP less than 185/110 mmHg is required. The goal of BP reduction is by 15% in the first 24 hours. Labetalol, calcium channel blockers may be used [1,2, 9-13, 21-23, 32].

Table 4: Antihypertensive agents of choice for specific hypertensive emergencies: [Ref: 2-5,7,10-13,14-20, 22, 24-27, 29-32]

Hypertensive emergency syndrome	***Suggested antihypertensives***
Aortic dissection	nitroprusside usually in combination with labetalol or esmolol, nicardipine with beta blocker, beta blocker alone
Acute coronary syndrome	beta blocker, nitroglycerin, clevidipine
Acute pulmonary edema	nitroglycerin preferred, fenoldopam, nicardipine, clevidipine
Hypertensive encephalopathy	clevidipine, labetalol, esmolol, nicardipine, fenoldopam, nitroprusside
Acute ischemic stroke or intracranial hemorrhage (when BP control is necessary)	Nicardipine, labetalol, clevidipine
Hypertensive emergency with acute or chronic renal failure	Labetalol, fenoldopam, nicardipine, clevidipine
Adrenergic crisis with hypertensive emergency	Nitroprusside, phentolamine, beta blocker
Eclampsia	Labetalol, nicardipine, hydralazine

CONCLUSION

The important aspect of treating hypertensive emergencies should include a plan for long-term therapy. Some antihypertensive agents may cause renal sodium and water retention and hence the administration of diuretics should accompany the use of such antihypertensives. It must be remembered that the initial goal of antihypertensive therapy is not to achieve a normal BP but to gradually lower the BP. With an exception in the treatment of aortic dissection, the initial goal of treatment in hypertensive emergencies is to reduce the mean arterial BP by 25% within two hours and minimum diastolic BP to 100 mmHg within 2 to 6 hours.

Conflict of interest

The authors declare no conflict of interest.

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