Day to day clinical practice and current management of emergency hypertension in various clinical conditions.

KEYWORDS
Hypertensive emergencies, pathophysiology, pharmacology.

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ABSTRACT
Severe elevation of blood pressure >180/120 mmHg in presence of acute organ damage leads to hypertensive emergency and patients should have their BP lowered immediately but not to normal level. The most common clinical presentations of hypertensive emergencies are cerebral infarction, pulmonary edema, hypertensive encephalopathy and congestive heart failure. Other clinical presentations associated with hypertensive emergencies include intracranial hemorrhage, aortic dissection, and eclampsia, as well as acute myocardial infarction. Early screening, evaluation and proper management of hypertensive emergencies can prevent morbidity and mortality at the mass level.

1. Introduction-
Around 1 billion people are suffering from systemic high blood pressure (BP) across the worldwide where as emergency hypertension is found in upto 2.5 to 3.5% of patients with systemic hypertension. Globally cardiovascular disease accounts for approximately 17 million deaths annually, nearly one third of the total. Of these, complications of hypertension account for 9.4 million deaths worldwide every year. Hypertension is responsible for at least 45% of deaths due to heart disease and 51% of deaths due to stroke. Asymptomatic nature, previously undiagnosed, irregular or irresponsible treatment or rural unethical practice in developing countries results in hypertensive emergencies and increased morbidity and mortality. Early screening, evaluation and proper management of hypertensive emergencies can prevent morbidity and mortality at the mass level. Severe elevation of BP >180/120 mmHg in presence of acute organ damage leads to hypertensive emergency and patients should have their BP lowered immediately but not to normal level.

2. Pathogenesis and management approach.
The pathogenesis of hypertension is multifactorial; increase in mechanical stress and vascular wall damage could increase vascular permeability along with pressure. There is cell proliferation and activation of the coagulation cascade. The endothelial cell surface lining of the vascular compartment is damaged leading to endothelial cell dysfunction, which further promotes vasoconstriction and platelet aggregation. Activation of the renin-angiotensin-aldosterone system is responsible for raised blood pressure. Angiotensin II is a very potent vasoconstricting substance but in addition it also increases the elaboration of cytokines such as interleukin-6 and NF-kappaB, which is a pro-inflammatory factor. There is white blood cell adhesion, as well as proliferation of vascular smooth muscle cells. NADPH, which generates reactive oxygen species, is also increased. There is a reduction of nitric oxide, which is a protective substance, that leads to vasodilation and inhibition of platelet aggregation, and again, this leads to this inflammatory factor. So this is not a simple situation. There is not a single drug that attacks all of these potential targets within the cascade of hypertensive emergency. Oxidative stress then leads to a reduction in nitric oxide, which is a protective substance, and an increase in reactive oxygen species. Endothelial dysfunction is thought to be the final common pathway. There is a reduction in vasodilation and an increase in vascular adhesion molecules, the activation of coagulation, and platelet aggregation.

The history and the physical examination determine the nature, severity, and management of the hypertensive event. The history should focus on the presence of end-organ dysfunction, the circumstances surrounding the hypertension, and any identifiable etiology. The most common clinical presentations of hypertensive emergencies are cerebral infarction (24.5%), pulmonary edema (22.5%), hypertensive encephalopathy (16.3%), and congestive heart failure (12%). Other include intracranial hemorrhage, aortic dissection, eclampsia and acute myocardial infarction. In pregnant patients, acute hypertensive crisis usually results from severe preeclampsia and can lead to maternal stroke, cardiopulmonary decompensation, fetal decompensation caused by reduced uterine perfusion, abruption, and stillbirth.

The duration and severity of the patient’s preexisting hypertension should be evaluated along with the patient’s medication history. Details of antihypertensive drug therapy and compliance, intake of over-the-counter preparations such as sympathomimetic agents, and use of illicit drugs...
such as cocaine are important elements of the medication history. In addition, it is important to elicit information about the presence of previous end-organ dysfunction, particularly renal and cerebrovascular disease, and any others (eg, thyroid disease, Cushing disease, systemic lupus).

Patients may complain of specific symptoms that suggest end-organ dysfunction may be present. Chest pain may indicate myocardial ischemia or infarction, back pain may denote aortic dissection and dyspnea may suggest pulmonary edema or congestive heart failure. The presence of neurologic symptoms may include seizures, visual disturbances, and altered level of consciousness and may be indicative of hypertensive encephalopathy.

The physical examination should assess whether end-organ dysfunction is present. BP should not only be measured in both the supine position and the standing position (a significant difference may suggest aortic dissection). The presence of new retinal hemorrhages, exudates, or papilledema suggests a hypertensive emergency. Evaluation for heart failure may be indicated by raised jugular venous pressure, crackles on auscultation, and peripheral edema. Central nervous system findings may include changes in the patient’s level of consciousness and may be indicative of hypertensive encephalopathy.

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<p>| Table-1 Pharmacological Management of Emergency Hypertension |</p>
<table>
<thead>
<tr>
<th>Drug</th>
<th>Onset of action</th>
<th>Dose</th>
<th>Mechanism</th>
<th>Indication</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>Enalapril</td>
<td>15 min</td>
<td>0.625–2.5 mg every 6 hr IV</td>
<td>Angiotensin converting enzyme</td>
<td>Acute left ventricular failure</td>
</tr>
<tr>
<td>b</td>
<td>Esmolol</td>
<td>1-2 min</td>
<td>500 µg/kg bolus IV or 50–100 µg/kg/min by infusion</td>
<td>Short acting beta-1 selective blocker</td>
<td>Acute aortic dissection</td>
</tr>
<tr>
<td>c</td>
<td>Clonidine</td>
<td>15 min</td>
<td>0.1 mg oral</td>
<td>Centrally acting alpha adrenergic agonist</td>
<td>Hypertensive crises, particularly in hypertensive urgencies. Renal impairment may benefit from a lower initial dose. Patients should be carefully monitored</td>
</tr>
<tr>
<td>d</td>
<td>Furosemide</td>
<td>15 min</td>
<td>0.5-1 mg/kg (or 40 mg) IV over 1-2 minutes; may be increased to 80 mg if there is no adequate response within 1 hour not to exceed 160-200 mg/dose</td>
<td>Loop diuretic</td>
<td>Acute pulmonary edema, raised intracranial pressure</td>
</tr>
<tr>
<td>e</td>
<td>Hydralazine</td>
<td>5-20 min</td>
<td>5–20 mg IV bolus or 10–40 mg IM; repeat every 4-6 hr</td>
<td>Direct relaxation of vascular smooth muscle cells</td>
<td>Eclampsia</td>
</tr>
<tr>
<td>f</td>
<td>Labetalol</td>
<td>2-5 min</td>
<td>20–80 mg IV bolus every 10 min; 0.5–2.0 mg/min IV infusion</td>
<td>Competitive blocker of alpha-1 and beta adrenergic receptors</td>
<td>Most hypertensive emergencies, except acute left ventricular failure</td>
</tr>
<tr>
<td>g</td>
<td>Nicardipine</td>
<td>1-2 min</td>
<td>5–15 mg/hr IV infusion</td>
<td>Calcium channel blocker</td>
<td>Most hypertensive emergencies except acute heart failure</td>
</tr>
</tbody>
</table>

 Investigations: Obtain electrolyte levels, as well as measurements of blood urea nitrogen and creatinine levels to evaluate for renal impairment. Hematuria or proteinuria and microscopical urinalysis to detect red blood cells or RBC casts should also be performed. A complete blood cell and peripheral blood smear should be obtained to exclude microangiopathic anemia, and a toxicity screen, pregnancy test, and endocrine testing may be obtained, as needed. If there is clinical evidence of pulmonary edema or the patient has chest pain, ECG, chest radiography and 2D Echocardiography are indicated. Patients with neurologic signs should be evaluated with a head CT scan and/or MRI Imaging.

Treatment approach must be aggressive in the emergency department in presence of emergency medical officer and/or cardiac physician. After quick evaluation of severe hypertension with organ damage, we should start medicine either sublingually or intravenously. The indication of different pharmacological agents are depend on target organ damage with concerned pathophysiology of various clinical conditions. Parenteral intravenous drugs are ideally used in emergency hypertension which are capable to achieve target BP, not to normal level. Current pharmacological approach is beneficial to physicians for their daily routine practice, we can see table-1.
3. Current management of emergency hypertension in various clinical conditions.

3.1 Acute pulmonary edema
The treatment strategy in hypertensive emergency with acute pulmonary edema is to decrease preload and afterload and to lower the blood pressure thereby “unloading” the failing heart. Immediately treatment should start with sublingual nitroglycerin, intravenous (iv) loop diuretic; furosemide and iv morphine with sitting posture. This is accomplished by using vasodilators eg nitroprusside or nitroglycerin. Concomitant use of loop diuretic may be indicated for optimal results in cases of volume overload in the setting of acute left ventricular failure. Intravenous nitroglycerin is preferred in the case of heart disease or when arterial pressure (AP) is not too high (arbitrarily a systolic pressure of less than 180 mmHg may serve as criterion). Use of noninvasive mechanical ventilation has proven to be useful in cases of type A dissection.

3.2 Acute aortic dissection
Aortic dissection occurs when a false lumen is created in the wall of the aorta. Ascending aortic dissections require immediate evaluation by a cardiothoracic surgeon for an emergency surgical procedure. Type B dissections are usually managed medically in collaboration with a surgeon. The goal of therapy is to prevent progression of the dissection. The arterial pressure should be maintained as low as possible without compromising end-organ perfusion. This is typically done with a combination of iv sodium nitroprusside and a β-blocker, eg, esmolol; however, labetalol can also be used as a single agent. Beta-blockers are used to blunt the reflex tachycardia associated with the treatment of aortic dissection with sodium nitroprusside. Beta-blockers also limit the force and velocity of contraction, which, if left unchecked, can lead to propagation of the dissection. Calcium channel blockers are considered second-line interventions. The theory behind this management strategy is that reducing the force of left ventricular contractions, thus dilating the vessels, will enhance laminar flow and lessen stress on the aortic wall. Turbulent flow is increased by using a vasodilator alone. The target pressure should be lower and tolerated by the patient. Systolic levels of 100 to 120 mm Hg are ideal.

3.3 Acute coronary syndrome (ACS)
Initial pressure control is done with sublingual nitrate followed by iv morphine if pain does not abate. Then nitroglycerin is given continuously at a titration speed to reduce AP by 30%. A very abrupt reduction must be avoided as it may reduce coronary perfusion. The goal of antihypertensive therapy in acute Myocardial Infarction is to decrease cardiac work by decreasing afterload and increasing coronary perfusion pressures. After bedside 2D Echo assessment with fair LV function, a β-blocker must be administered until the heart rate is reduced. The current AHA/ACC guidelines suggest that oral β-blockers can be given any time within the first 24 hours of presentation. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers may be used for patients with hypertension and left ventricular dysfunction or pulmonary congestion within 24 hours.

3.4 Hypertensive encephalopathy
Hypertensive encephalopathy occurs mainly in patients with chronic uncontrolled or malignant hypertension. With sudden elevation of AP, the upper threshold of the self-regulatory capacity of the cerebral blood flow may be surpassed with consequent hyper cerebral perfusion leading to an endothelial dysfunction, rupture of the hematoencephalic barrier, cerebral edema and micro hemorrhages. Hypertensive encephalopathy is clinically characterized by acute or subacute symptoms such as headache, lethargy, confusion, vision disorders, vomiting and seizures. A CT scan of the brain will always be required to exclude other neurological affections, mainly stroke. The goal of therapy is to initially decrease the BP by not more than 20-25% of the mean arterial pressure. The basis of this goal is that hypoperfusion occurs at the lower end of the cerebral perfusion autoregulation curve, which approximates about 25% of the baseline mean arterial pressure. On the other hand, hyperperfusion occurs at the upper limit of the autoregulatory curve, which is the basis for cerebral dam-
3.5 Malignant hypertension
Malignant hypertension represent as an neuroretinopathy and acute or subacute renal failure. Clinical features like asthenia, malaise, weight loss and cardiovascular or neurological symptoms are usually found. If not properly managed, one year mortality is of approximately 80-90% reported. Previously inexisten proteinuria to overt acute renal failure and retinopathy manifests itself by papilledema at the eye. Treatment is with iv sodium nitroprusside until a 20% decrease of systemic blood pressure in 2 hours, followed by gradual pressure control in 2 or 3 days with oral medication.

3.6 Acute Stroke
Based on the guideline from the Stroke Council for the American Heart Association for acute ischemic strokes, if the patient is not eligible for thrombolysis, treatment starts only with blood pressures > 220/120 mmHg. With patients who are eligible for thrombolysis then treatment is initiated when the BP is > 185/110. Treatment is with nica-rdipine, sodium nitroprusside, or labetalol may be used to reduce AP by 10% to 20% in 24 hours. Arterial pressure, usually, drops spontaneously to the levels prior to ischemic stroke in 4 days, without any antihypertensive treatment. In subarachnoid hemorrhage, the same procedures suggested for hemorrhagic stroke are pertinent, however nimodipine must be the first choice of treatment, as it reduces risk of cerebral infarction associated to vasospasm. For any stroke condition, the neurological worsening associated to a decrease of BP must be treated by reducing or even interrupting nitroprusside administration.

3.7 Preeclampsia/Eclampsia
Preeclampsia is the combination of hypertension and proteinuria in a pregnant woman after the 20th weeks’ gestation. Preeclampsia becomes eclampsia when the patient has a seizure. Hypertension management is unique in pregnancy, in that many common drugs are contraindicated because of the potential toxic effects on the fetus. The elevated BP seen in eclampsia/preeclampsia can be quickly and safely lowered to “normal levels” at no increased risk for inducing cerebral or cardiac ischemia. Control of the BP is important to help prevent cerebral vascular complications; however, evidence for the prevention of the progression of preeclampsia into eclampsia is not clear. The classic agent used is hydralazine, although labetalol has recently gained favor. Labetalol had similar efficacy and fewer side effects. Magnesium sulfate is added to the regimen for seizure prophylaxis and has been shown to lower the progression of preeclampsia to eclampsia in randomized trials.

3.8 Hypertensive emergencies caused by excess of catecholamines
The goal of therapy is BP control without exacerbation of the condition. Several agents are recommended, including phenolamine, nitroprusside, and labetalol. Pure β-blockers are contraindicated, since they may exacerbate the condition due to unopposed alpha activity. True hypertensive emergencies caused by excess of catecholamines are rare.

The main causes are pheochromocytoma, users of MAO inhibitors that ingest food containing tyramine, cocaine or amphetamine users or sudden interruption of antihypertensives such as clonidine and beta-blockers (easily manipulated by restarting treatment). Occasionally pheochromocytomas present with the typical triad of headache, sudoresis (Profuse sweating) and severe hypertension.

In the setting of cocaine-induced catecholamine excess, benzodiazepines have been shown to decrease the centrally mediated and peripheral sympathomimetic outflow that contribute to the symptoms of cocaine, such as elevated BP, chest pain, and agitation. Benzodiazepines help to lower the systolic arterial pressure, lower the heart rate, and decrease psychomotor hyperactivity. Benzodiazepines treat both the central and peripheral manifestations of cocaine intoxication, with few side effects.

3.9 Perioperative hypertension
Nitroprusside, nitroglycerin, 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.

In the way of summary of current management of emergency hypertension in various clinical conditions with line of treatment, we can approach immediately in the emergency department with the help of the table-2 and also we can paste it on the wall of emergency room which may helpful for emergency medical offices in daily practice.

<table>
<thead>
<tr>
<th>Clinical conditions</th>
<th>Drug of choice</th>
<th>Other treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute pulmonary edema</td>
<td>Nitroglycerine iv</td>
<td>Frusemide iv, Enalaprilat iv</td>
</tr>
<tr>
<td>Acute stroke</td>
<td>Nimodipine s/l, Labetalol iv</td>
<td>Nicardipine s/l, Sodium nitroprusside iv</td>
</tr>
<tr>
<td>Hypertensive encephalopathy</td>
<td>Sodium nitroprusside iv, Labetalol iv</td>
<td>Nicardipine s/l, Enalaprilat iv</td>
</tr>
<tr>
<td>Malignant hypertension</td>
<td>Clonidine oral, Labetalol iv</td>
<td>Prazopress, Nicardipine sl</td>
</tr>
<tr>
<td>Preeclampsia (pregnancy)</td>
<td>Labetalol iv</td>
<td>Hydralazine iv, Nicardipine sl</td>
</tr>
<tr>
<td>Eclampsia (pregnancy)</td>
<td>Magnesium sulphate iv</td>
<td>Labetalol iv</td>
</tr>
<tr>
<td>Pheochromocytoma crisis</td>
<td>Phentolamine iv</td>
<td>Labetalol iv</td>
</tr>
<tr>
<td>Sympathetic excess syndrome</td>
<td>Clonidine oral</td>
<td>Labetalol iv</td>
</tr>
<tr>
<td>Sympathetic excess with cocaine</td>
<td>Benzendiazepine iv, Phentolamine iv</td>
<td>Clonidine , Avoid beta blocker</td>
</tr>
<tr>
<td>Acute aortic dissection</td>
<td>Labetalol iv, Nitroprusside iv</td>
<td>Avoid direct vasodilators</td>
</tr>
<tr>
<td>Acute coronary syndrome</td>
<td>Nitroglycerine iv</td>
<td>Esmolol iv but avoid in heart failure</td>
</tr>
<tr>
<td>Perioperative hypertension</td>
<td>Esmolol iv</td>
<td>Nitroglycerine iv</td>
</tr>
</tbody>
</table>
4. Conclusion

Hypertensive emergency consists of a syndrome where significant elevation of the systemic arterial pressure leads to acute target-organ damage, threatening life. It requires immediate treatment and assessment whether or not target-organ dysfunction is present; if it is, this differentiates emergency from urgency. Symptoms reflect target-organ damage, including primarily the brain, the heart, the eyes, and the kidneys, as well as the rest of the vasculature. Energetic measures must be taken for immediate treatment, initially with intravenous administration of drugs to reduce arterial pressure in emergency and orally in Urgency. And lastly, ischemic stroke is a special situation where BP should not be rapidly reduced nor should it be lowered too far.

REFERENCE