HYPERTENSION EMERGENCIES

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Hypertensive emergencies

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Hypertension urgencies

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- Hypertensive urgencies are diagnosed if there is a SBP higher than 180 mmHg or a DBP higher than 120 mmHg in an otherwise stable person without clinical or laboratory evidence of acute target organ damage .

- These persons need intensification of their antihypertensive drug therapy.

- Patients with hypertensive emergencies :
- dissection of Aorta
- acute pulmonary edema
- acute MI, unstable angina
- acute renal failure,
- acute intracranial hemorrhage,
- acute ischemic stroke,
- hypertensive encephalopathy,
- eclampsia or pre-eclampsia,
- peri-operative hypertension,
- a pheochromocytoma crisis,
- and a sympathomimetic hypertensive crisis caused by use of cocaine, amphetamines, phencyclidine, or monoamine oxidase inhibitors or by abrupt cessation of clonidine or other sympatholytic drugs

- These patients need effective and rapid acting medications administered intravenously to lower the elevated BP safely, protect target organ function, ameliorate symptoms, reduce complications, and improve clinical outcomes .
- The 1-year mortality incidence of hypertensive emergencies is more than 79%, and the median survival is 10.4 months if these persons are not treated with antihypertensive drug therapy

- The drug of choice in treating acute aortic dissection is IV ESMOLOL.
- The loading dose 500–1,000 mcg/kg/min administered over 1 min followed by a 50 mcg/kg/min infusion rate.
- The maximum infusion rate is 200 mcg.
- Rapid and immediate reduction of BP within 5 to 10 min is needed for patients with acute aortic dissection.
- The target blood pressure goal in these patients is a SBP below 120 mmHg.
- If the blood pressure remains elevated after beta blockade, a vasodilator such as intravenous nitroglycerin or nitroprusside may be administered.

- The drugs of choice in treating a hypertensive emergency with acute pulmonary edema are intravenous nitroglycerin, or nitroprusside .
- Beta blockers are contraindicated in the treatment of acute pulmonary edema.
- Except for acute aortic dissection, the BP in patients with hypertensive emergencies should be lowered within minutes to 1 h about 20% to 25% and then gradually to 160/100 mmHg within the next 2 to 6 h, and then cautiously to normal over the next 24 to 48 h .
  The initial infusion rate of intravenous nitroglycerin is 5 mcg/min.
- The maximum infusion rate is 20 mcg/min.
  The initial infusion rate of intravenous sodium nitroprusside is 0.3 to 0.5 mcg/kg/min.
- The maximum infusion rate is 10 mcg/kg/min.

- Patients with an acute MI or unstable angina and severe hypertension should be treated with intravenous esmolol . Intravenous nitroglycerin may also be administered if needed .
- The target BP is less than 140/90 mmHg in patients with acute MI or unstable angina who are hemodynamically stable .
- A blood pressure of less than 130/80 mmHg at hospital discharge should be considered .
- Caution should be used in lowering the BP in these patients to avoid lowering the DBP to less than 60 mmHg as this may decrease coronary perfusion and aggravate myocardial ischemia .

- The drugs of choice in treating patients with a hypertensive emergency and acute renal failure are clevidipine, fenoldopam, and nicardipine .
- The initial infusion rate of intravenous fenoldopam is 0.1 to 0.3 mcg/kg/min.
- The maximum infusion rate is 1.6 mcg/kg/min.
- The initial infusion rate of intravenous nicardipine is 5 mg/h.
- The maximum infusion rate is 30 mg/h.

- The drugs of choice in treating patients with a hypertensive crisis and eclampsia or pre-eclampsia are hydralazine, labetalol, and nicardipine .
- Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, direct renin inhibitors, and sodium nitroprusside are contraindicated in treating these patients.
- The maximum initial dose of intravenous hydralazine administered by slow intravenous infusion is 20 mg. This dose may be repeated every 4–6 h if needed.

- The initial dose of intravenous labetalol is 0.3 to 1.0 mg/kg with a maximum initial dose of 20 mg followed by an intravenous infusion of 0.4 to 1.0 mg/kg/h up to 3 mg/kg/h.
- The total cumulative dose is 300 mg.
- This dose can be repeated every 4 to 6 h if needed

- Drugs of choice used for treating postoperative surgical hypertension include administration of intravenous clevidipine, esmolol, nitroglycerin, and nicardipine .
- A systematic review and meta-analysis reported that clevidipine was the drug of choice for treating acute postoperative hypertension

- Drugs of choice for treating a hypertensive emergency caused by a pheochromocytoma or by an hyperadrenergic state caused by use of cocaine, amphetamines, phencyclidine, cessation of clonidine or other sympatholytic drugs are or monoamine oxidase inhibitors or by abrupt intravenous clevidipine, nicardipine, or phentolamine .
  The initial dose of phentolamine is an intravenous bolus dose of 5 mg.
- Additional bolus doses of 5 mg should be administered intravenously every 10 min as needed to reduce the blood pressure to the target level

- Intravenous enalaprilat may be administered to patients with a hypertensive emergency associated with a high plasma renin state .
- The initial dose of enaliprilat administered intravenously is 1.25 mg over 5 min. Additional doses of intravenous enaliprilat may be given up to 5 mg every 6 h as needed to reach the BP Target level.

- A study randomized 104 patients with acute heart failure with hypertension to receive intravenous clevidipine versus standard of care intravenous antihypertensive drugs (87% intravenous nitroglycerin or nicardipine) .
- This study showed that the target BP level was reached in 71% of patients treated with clevidipine versus 37% of those receiving standard of care intravenous antihypertensive drugs.
- Clevidipine was also more effective than standard of care drugs in improving dyspnea at 45 min

- There were insufficient data to determine which antihypertensive drug is most effective in decreasing mortality and morbidity .
- Randomized clinical trials are needed to investigate initial and long-term mortality outcomes in patients with hypertensive emergencies treated with different antihypertensive drugs. Randomized clinical trial data are also needed to determine how fast or how much the blood pressure should be lowered in a hypertensive emergency.

- A study randomized 2,794 patients with a hypertensive emergency and acute intracerebral hemorrhage to a target BP level of less than 140 mmHg within 1 h or to less than 180 mmHg within1 h using intravenous antihypertensive drugs chosen by the different physicians .
- The reduction of SBP to less than 140 mmHg was associated with a 13% borderline reduction in the primary outcome of death or major disability but with improved functional outcomes compared with reduction of the SBP to less than 180 mmHg within 1 h .
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- A meta-analysis of four randomized clinical trials including 3,315 patients with a hypertensive emergency and acute intracerebral hemorrhage demonstrated that intensive blood pressure lowering in these
- patients to less than 140 mmHg was associated with a 13% borderline reduction in 3-month death or dependency . Intensive blood pressure lowering in acute cerebral hemorrhage also seems to reduce hematoma growth

- The antihypertensive drug of choice for treating acute cerebral hemorrhage needs to be investigated by randomized clinical trials.
- Rapid acting, easily titratable drugs administered intravenously such as clevidipine, nicardipine, labetalol, and urapidil are reasonable first-line drugs for treating these patients

- **Malignant hypertension:** Severe BP elevation (commonly >200/120 mm Hg) associated with advanced bilateral retinopathy (hemorrhages, cotton wool spots, papilledema).
- **Hypertensive encephalopathy:** Severe BP elevation associated with lethargy, seizures, cortical blindness and coma in the absence of other explanations.
- **Hypertensive thrombotic microangiopathy:** Severe BP elevation associated with hemolysis and thrombocytopenia in the absence of other causes and improvement with BP-lowering therapy.
- Other presentations of hypertensive emergencies include severe BP elevation associated with cerebral hemorrhage, acute stroke, acute coronary syndrome, cardiogenic pulmonary edema, aortic aneurysm/dissection, and severe preeclampsia and eclampsia.

- The clinical presentation of a hypertensive emergency can vary and is mainly determined by the organ(s) acutely affected. There is no specific BP threshold to define a hypertensive emergency.
- Symptoms include headaches, visual disturbances, chest pain, dyspnea, neurologic symptoms, dizziness, and more unspecific presentations.
- Medical history: preexisting hypertension, onset and duration of symptoms, potential causes (nonadherence with prescribed antihypertensive drugs, lifestyle changes, concomitant use of BP elevating drugs [NSAIDS, steroids, immune-suppressants, sympathomimetics, cocaine, antiangiogenic therapy]).

- **Thorough physical examination:** Cardiovascular and neurologic assessment. Laboratory analysis: hemoglobin, platelets, creatinine, sodium, potassium, lactate dehydrogenase (LDH), haptoglobin, urinalysis for protein, urine sediment. **Examinations:** Fundoscopy, ECG.
- Additional investigations may be required and indicated depending on presentation and clinical findings and may be essential in the context: troponins (chest pain), chest x-ray (congestion/fluid overload), transthoracic echocardiogram (cardiac structure and function), CT/MRI brain (cerebral hemorrhage/stroke), CT-angiography thorax/abdomen (acute aortic disease). Secondary causes can be found in 20%–40% of patients presenting with malignant hypertension[118] and appropriate diagnostic workup to confirm or exclude secondary forms is indicated.

- **Diagnostic Tests and Acute Therapeutic Management**
- The overall therapeutic goal in patients presenting with hypertensive emergencies is a controlled BP reduction to safer levels to prevent or limit further hypertensive damage while avoiding hypotension and related complications. There is a lack of randomized controlled trial data to provide clear cut guidance on BP targets and times within which these should be achieved. Most recommendations are based on expert consensus. The type of acute HMOD is the main determinant of the preferred treatment choice. The timeline and magnitude of BP reduction is strongly dependent on the clinical context. For example, acute pulmonary edema and aortic dissection require rapid BP reduction, whereas BP levels not exceeding 220/120 mm Hg are generally tolerated in acute ischemic stroke for certain periods. Table 12 provides a general overview of timelines and BP targets as well as preferred antihypertensive drug choices with most common clinical presentations. Availability of drugs and local experience with individual drugs are likely to influence the choice of drugs. Labetalol and nicardipine are generally safe to use in all hypertensive emergencies and should be available wherever hypertensive emergencies are being managed. Nitroglycerin and nitroprusside are specifically useful in hypertensive emergencies including the heart and the aorta.

- **Specific Situations**
- **Sympathetic hyperreactivity:** If intoxication with amphetamines, sympathomimetics or cocain is suspected as cause of presentation with a hypertensive emergency use of benzodiazepines should be considered prior to specific antihypertensive treatment. Phentolamine, a competitive alpha-receptor blocking agent and clonidine, a centrally sympatholytic agent with additional sedative properties are useful if additional BP-lowering therapy is required. Nicardipine and nitroprusside are suitable alternatives.
- **Pheochromocytoma:** The adrenergic drive associated with pheochromocytoma responds well to phentolamine. Beta-blockers should only be used once alpha-blockers have been introduced to avoid acceleration of hypertension. Urapidil and nitroprusside are additional suitable options.

- **Follow-Up**
- Patients who experienced a hypertensive emergency are at increased risk of cardiovascular and renal disease.[129,130] Thorough investigation of potential underlying causes and assessment of HMOD is mandatory to avoid recurrent presentations with hypertensive emergencies. Similarly, adjustment and simplification of antihypertensive therapy paired with advice for lifestyle modification will assist to improve adherence and long-term BP control. Regular and frequent follow-up (monthly) is recommended until target BP and ideally regression of HMOD has been achieved.