

# Treatment of hypertensive emergencies

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Hypertensive emergencies are diagnosed if there is a systolic blood pressure higher than 180 mmHg or a diastolic blood pressure higher than 120 mmHg with the presence of acute target organ damage (1-6). Hypertensive urgencies are diagnosed if there is a systolic blood pressure higher than 180 mmHg or a diastolic blood pressure higher than 120 mmHg in an otherwise stable person without clinical or laboratory evidence of acute target organ damage (1-6). These persons need intensification of their antihypertensive drug therapy.

Patients with hypertensive emergencies include those who have a dissecting aortic aneurysm, acute pulmonary edema, acute myocardial infarction, unstable angina pectoris, 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 (1-6). These patients need effective and rapid acting medications administered intravenously to lower the elevated blood pressure safely, protect target organ function, ameliorate symptoms, reduce complications, and improve clinical outcomes (1-6). 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 (7).

The drug of choice in treating acute aortic dissection is intravenous esmolol (1,5). The loading dose is 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 blood pressure within 5 to 10 min is needed for patients

with acute aortic dissection. The target blood pressure goal in these patients is a systolic blood pressure 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, clevidipine, or nitroprusside (1,2,5). Beta blockers are contraindicated in the treatment of acute pulmonary edema. Except for acute aortic dissection, the blood pressure 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 (1). 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. The initial infusion rate of intravenous clevidipine is 1–2 mg/h. The maximum infusion rate is 32 mg/h.

Patients with an acute myocardial infarction or unstable angina pectoris and severe hypertension should be treated with intravenous esmolol (8). Intravenous nitroglycerin may also be administered if needed (8). The target blood pressure is less than 140/90 mmHg in patients with acute myocardial infarction or unstable angina pectoris who are hemodynamically stable (8). A blood pressure of less than 130/80 mmHg at hospital discharge should be considered (8). Caution should be used in lowering the blood pressure in these patients to avoid lowering the diastolic blood pressure to less than 60 mmHg as this may decrease coronary perfusion and aggravate myocardial ischemia (8).

The drugs of choice in treating patients with a hypertensive emergency and acute renal failure are clevidipine, fenoldopam, and nicardipine (5). 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. In 104 patients with a hypertensive emergency with renal dysfunction treated in an emergency department with intravenous nicardipine or labetalol, within 30 min of administration, the target systolic blood pressure was reached in 92% of patients treated with intravenous nicardipine versus 78% of patients treated with intravenous labetalol (9).

The drugs of choice in treating patients with a hypertensive crisis and eclampsia or pre-eclampsia are hydralazine, labetalol, and nicardipine (5,6). 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 (10,11). A systematic review and meta-analysis reported that clevidipine was the drug of choice for treating acute postoperative hypertension (10).

Drugs of choice for treating a hypertensive emergency caused by a pheochromocytoma or by an hyperadrenergic state caused by use of cocaine, amphetamines, phencyclidine, or monoamine oxidase inhibitors or by abrupt cessation of clonidine or other sympatholytic drugs are intravenous clevidipine, nicardipine, or phentolamine (1). 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 (5,6,12). The initial dose of enalaprilat administered intravenously is 1.25 mg over 5 min. Additional doses of intravenous enalaprilat may be given up to 5 mg every 6 h as needed to reach the blood pressure

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) (13). This study showed that the target blood pressure 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 (13).

A study randomized 226 patients in an emergency department with a hypertensive emergency to treatment with intravenous nicardipine versus intravenous labetalol (14). Within 30 min, the target blood pressure level was reached in 91.7% of patients treated with intravenous nicardipine versus 82.5% of patients treated with intravenous labetalol (14). A subgroup of this study included 141 patients with signs and/or symptoms of target organ damage (15). Within 30 min, 91.4% of these patients randomized to intravenous nicardipine reached their target blood pressure level versus 76.1% of these patients randomized to intravenous labetalol (15).

A Cochrane systematic review of pharmacological interventions for hypertensive emergencies included 15 randomized controlled trials of 869 patients treated with seven drug classes (4). There were insufficient data to determine which antihypertensive drug is most effective in decreasing mortality and morbidity (4). 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 blood pressure level of less than 140 mmHg within 1 h or to less than 180 mmHg within 1 h using intravenous antihypertensive drugs chosen by the different physicians (16). The reduction of the systolic blood pressure 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 systolic blood pressure to less than 180 mmHg within 1 h (16). 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 (17). Intensive blood pressure lowering in acute cerebral hemorrhage also seems to reduce hematoma growth (18).

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 (3).

The 2013 American Heart Association/American Stroke Association acute ischemic stroke guidelines state that it is unknown what the blood pressure target level should be for patients with acute ischemic stroke or which antihypertensive drug should be recommended (19). These guidelines currently recommend not reducing the blood pressure during the initial 24 h of acute ischemic stroke unless the blood pressure is above 220/120 mmHg or there is a specific medical disorder that would benefit from blood pressure reduction. In patients with acute ischemic stroke eligible for acute reperfusion therapy, these guidelines recommend lowering the blood pressure to below 180/110 mmHg before administering fibrinolytic therapy with intravenous labetalol or with intravenous nicardipine with consideration of other intravenous antihypertensive drugs when appropriate (19).

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## Footnote

*Conflicts of Interest:* The author has no conflicts of interest to declare.

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