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Hypertensive emergency: diagnostic and therapeutic strategies

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ABSTRACT

Hypertensive emergencies are life-threatening conditions with end-organ damage caused by sudden increases in blood pressure that exceed 180/110-120 mmHg. Clinical conditions affecting the brain, arteries, retina, kidney and heart are encountered. The brain and cardiovascular system are most commonly affected. Ischemic stroke and acute pulmonary edema are the most common conditions. Some patients may experience end-organ damage independent of blood pressure values. This condition develops due to microangiopathy and deterioration of autoregulation that provides organ blood flow by damaging the vascular endothelium due to increased blood pressure. High blood pressure also increases end-organ damage in a vicious cycle by activating the renin-angiotensin-aldosterone system. This pathophysiology is important in treatment. As a general approach, rapid blood pressure reduction is not desired. Perfusion in end-organs that cannot adapt to autoregulation is impaired, and organ dysfunction deepens with ischemia and necrosis. In the general approach, a 10-20% decrease is targeted in the first hour, while a 5-15% decrease in blood pressure in the remaining 23 hours is sufficient. However, in ischemic stroke, blood pressure control is reduced according to both the treatment and the degree of pressure. If thrombolytic therapy is not to be given, if the blood pressure is not above 220/120 mmHg, no intervention is made. In aortic dissection, the aim is to reduce systolic blood pressure to 100-120 mmHg in a period of 20 minutes. In short, according to the target organ damage, short-acting intravenous antihypertensive drugs that can be treated stepwise and are selected according to the selected target values. In the selection of these drugs, options that may cause secondary damage to organ damage are avoided. Nitroprusside and nitroglycerin, which can increase central pressure, are not preferred primarily in ischemic stroke. Or, in adrenergic crisis, beta blockers can worsen blood pressure without sufficient alpha blockade. It should also be well known that such drugs have important side effects such as severe hypotension and cardiogenic shock.

Keywords: End organ damage, hypertensive emergency, treatment

INTRODUCTION

Hypertension (HT) is the most important risk factor that can be controlled to reduce adverse outcomes related to cardiovascular disease.[1] In addition, hypertensive emergency (HE) causes end-organ damage (EOD) within hours, causing serious morbidity and mortality. The brain, arteries, retina, kidney and heart (BARKH) are the end organs damaged by high blood pressure. The critical threshold value is systolic blood pressure (SBP) above 180 mmHg and diastolic blood pressure above 110-120 mmHg. HE may develop after pre-existing HT or may result from a newly developing clinical condition. There is no critical threshold value in a young person who develops acute kidney injury such as eclampsia or glomerulonephritis, where the life-threatening blood pressure level suddenly increases rapidly. In this case, the acceleration of the increase rather than the patient's blood pressure value brings about EOD. In short, HE can develop even at lower blood pressure (BP) values.[1-3] It has been determined that the rate of patients presenting to the emergency department with an SBP value over 180 mmHg is 13.8%, and that one in 200 patients presents with HE. The rate of HE among patients presenting to the emergency department due to hypertension worldwide varies between 1-3%. More than 95% of patients presenting to the emergency department with HE have cerebral and cardiac EOD. The most common conditions are hypertensive pulmonary edema and heart failure. This is followed by myocardial infarction, ischemic and hemorrhagic stroke. Other end-organ damages are encountered less frequently. The in-hospital mortality rate of these patients is around 2.5-4%.[4-7]

PATHOPHYSIOLOGY

The factors that trigger HE are generally the hypertensive patient's skipping medication doses or suddenly stopping taking them, difficulties in reaching a health institution, increased salt consumption, increased use of non-steroidal anti-inflammatory drugs, glucocorticoid consumption, pseudoephedrine, cocaine and amphetamine-like stimulants.[8-9]

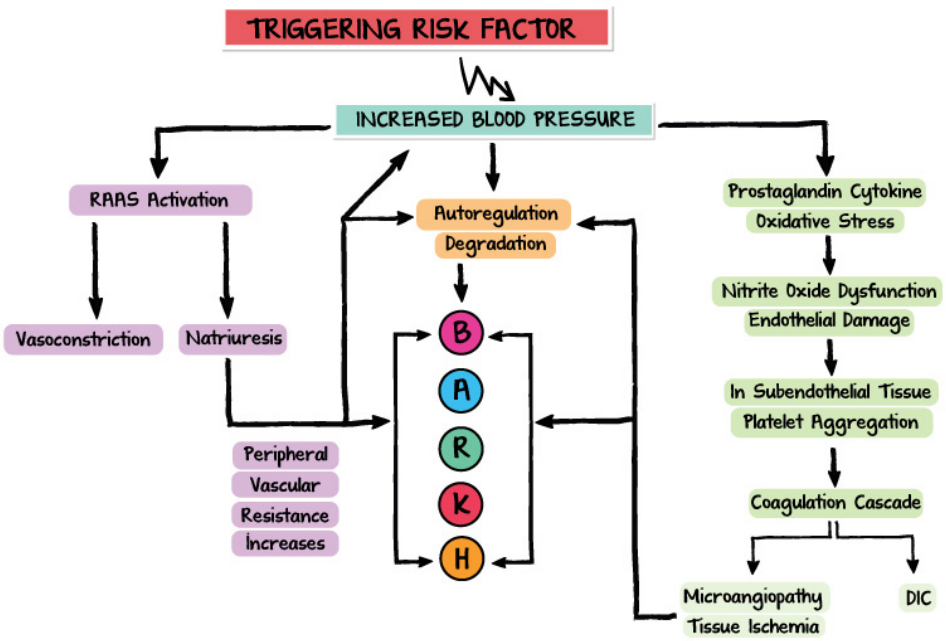

Figure 1. Hypertensive emergency pathophysiology
RAAS: Renin Angiotensin-Aldosterone System, BARKH: Brain, Arteries, Retina, Kidney, Heart
DIC: Disseminated Intravascular Coagulation

There is an autoregulation mechanism that provides perfusion of organs. This balance correlates with systemic blood pressure. While the mean arterial pressure for cerebral perfusion is 70-90 mmHg in individuals with normal blood pressure values, this value increases to 110-150 mmHg in individuals who have been hypertensive for a long time. Autoregulation, especially in brain tissue, may not respond sufficiently to sudden and rapidly increasing blood pressure. Vasogenic edema develops in the brain, leading to increased intracranial pressure (ICP). Clinical symptoms such as headache, nausea and vomiting occur. In addition, hypertensive damage develops in other tissues containing BARKH. In sudden decreases, it leads to ischemia, namely optic nerve ischemia, coronary ischemia or necrosis of penumbra tissue, together with hypoperfusion. This situation constitutes the basic strategy of emergency treatment of HE. The organs of patients who have been hypertensive for a long time establish a balance to continue blood circulation. This process increases permeability in the capillary area and leads to hyperperfusion. Increased systemic blood pressure activates the renin angiotensin-aldosterone system (RAAS). RAAS increases vasoconstriction, and fluid loss develops with pressure natriuresis. This increases peripheral resistance in organs containing BARKH. Autoregulation is disrupted and a vicious circle is entered. Thus, systemic blood pressure continues to increase. Increased pressure leads to the release of prostaglandins, cytokines and oxidative stress factors. Nitric oxide loses its function and the vascular endothelium is damaged. Subendothelial tissue is exposed and the coagulation cascade begins with platelet aggregation. Thus, microangiopathy and tissue ischemia or necrosis occur in the arterioles. We encounter hematuria, bleeding and exudate in the fundus. If the pressure continues, disseminated intravascular coagulation may develop (Figure 1).[6,10-12]

DIAGNOSTIC APPROACH TO HYPERTENSIVE EMERGENCY

HE includes many clinical conditions that develop as a result of BARKH injury, along with increased systolic and diastolic blood pressure values, along with history and physical examination. The most common symptoms are angina, visual disturbances, dyspnea and headache. Physical examination of patients, including all systems, is very important in early diagnosis and treatment. When HE develops in patients with brain damage, ischemic or hemorrhagic stroke, transischemic attack, increased intracranial pressure syndrome (ICP), posterior reversible encephalopathy syndrome (PRES), hypertensive encephalopathy and intracranial hemorrhage due to head trauma are seen. Patients develop symptoms such as sudden changes in consciousness, agitation, nausea, vomiting, seizures, delirium, visual disturbances and loss of strength in the extremities. Chest pain, back pain and dyspnea suggest acute coronary syndrome or aortic dissection and aneurysm. Sudden onset of dyspnea and pretibial edema suggest pulmonary edema and heart failure, while hematuria, pretibial and periorbital edema suggest acute kidney injury. Retinal hemorrhage, exudate and papilledema on fundoscopic examination are important in terms of retinopathy and ICP. Hypertension developing after the 20th week of pregnancy or an increase in preexisting blood pressure suggests preeclampsia and eclampsia. High liver enzymes and thrombocytopenia indicate HELLP syndrome in pregnant women. Sudden discontinuation of antihypertensive agents such as clonidine may lead to HE. Increased consumption of cocaine, amphetamine, monoamine oxidase inhibitors and tyramine-containing foods and pheochromocytoma may cause HE by causing adrenergic crisis. Postoperative bleeding from vascular anastomosis sites or patients scheduled for emergency surgery may enter the HE state. Blood tests and radiological imaging to be performed on patients are decided according to the patient's clinical picture (Table 1).[9,13,14]

MANAGEMENT OF HYPERTENSIVE EMERGENCY TREATMENT

The most important goal of treatment is not to reduce the numbers but to prevent hypoperfusion and reduce the damage

Table 1. Tests requested for specific conditions in hypertensive emergencies

Causes of hypertensive emergencies	Recommended tests
Acute coronary syndrome	ECG, high sensitive troponin I/T, echocardiography
Acute pulmonary edema	ECG, Chest X-ray, echocardiography,
Heart failure (Decompensated)	Blood urea nitrogen /creatinine, electrolyte (Na, K, Cl, Ca) Arterial blood gas, high sensitive troponin I/T B-type natriuretic peptide
Aortic dissection	D-dimer, ECG Chest CT angiography, Transthoracic echocardiography
Acute kidney injury	Creatinine, blood urea nitrogen electrolytes Arterial blood gas Urinalysis (proteinuria, hematuria) Renal ultrasound
Stroke	ECG (for arrhythmia, atrial fibrillation) INR, aPTT (coagulation tests) Brain CT (to differentiate between hemorrhagic and ischemic stroke) Diffusion MRI
Preeclampsia/ eclampsia	Complete blood count Creatinine, liver function tests (AST, ALT) 24-hour urine analysis or spot urine test for proteinuria Obstetric ultrasound (to assess pregnancy status)
Hypertensive encephalopathy	Complete blood count Blood urea nitrogen /creatinine, electrolyte ECG Fundoscopy (to assess for papilledema) Brain CT or MRI
Pheochromocytoma crisis	Serum and urine electrolytes Abdominal CT or MRI Plasma free metanephrines 24-hour urinary catecholamines

ECG: Electrocardiogram. CT: Computed Tomography; MRI: Magnetic Resonance Imaging; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase

that may occur in EOD. While doing this, aggressive approaches may lead to secondary damage. Intravenous antihypertensive drugs are used first. Their short duration of action and gradual treatment features help to control HE.[15] The most important part to be careful about is that if the arterial blood pressure value is reduced, the hypotension that may develop due to these drugs may lead to cardiogenic shock and even death. In addition, organ autoregulation cannot adapt to the rapid blood pressure decrease and may lead to worsening ischemia in the end organ.[2] For this, close arterial blood pressure monitoring is required. While extremity measurements can be made at the beginning of treatment, intraarterial blood pressure monitoring is important in the ongoing process. It is also important to make measurements from both arms and even the lower extremity. A difference of 10-20 mmHg between the arms is within acceptable limits, while more than this suggests aortic coarctation or another vascular anomaly going to the lower extremity. If there is HE here, treatment is planned according to the extremity where the high blood pressure measurement is made.[3,4,15]

In the general treatment approach, the aim is to reduce the initial measurement by 10-20% within the first hour. The target value here is calculated to be below 180/120 mmHg. A 5-15% decrease is achieved within the next 23 hours. This means reaching values below 160/110 mmHg on average. It is planned to bring the blood pressure to normal limits in the following 24-48 hours. In rare cases such as aortic dissection, preeclampsia and pheochromocytoma, the target value is below 130 mmHg for systolic pressure and below 80 mmHg for diastolic pressure. However, this general approach includes differences according to the affected organ as a result of EOD. Again, the antihypertensive drug selected varies accordingly (Table 2).[2,16,17]

ACUTE ISCHEMIC STROKE

In ischemic stroke, vasodilation and a decrease in perfusion pressure occur distal to the occluded vessel. The blood circulation of this distal tissue depends on systemic tension. In fact, increased blood pressure is thought to be a kind of protective mechanism. The brain's autoregulation cannot respond to sudden drops in blood pressure and may cause necrosis of the healthy penumbra tissue. Therefore, blood pressure regulation is provided according to the treatment to be applied to the patient in ischemic stroke.18 If thrombolysis or thrombectomy is not to be applied, no intervention is made unless the blood pressure rises above 220/120 mmHg. A 15% decrease is targeted after 24 hours from the moment the stroke begins.[18-19]

If thrombolysis or thrombectomy is to be performed, the blood pressure is reduced below 185/110 mmHg before the procedure. This value is kept below 180/105 mmHg during the procedure and for the following 24 hours. Antihypertensive treatment is started in stable patients who have been above 140/90 mmHg for more than 3 days. 18-19 Blood pressure is measured every 15 minutes for the first 2 hours. Measurements are made every 30 minutes for the next 6 hours. Blood pressure is monitored every hour for the remaining 16 hours.[18]

Labetolol, nicardipine and clevidipine are the primary agents in treatment. Nitroprusside is a secondary agent that can be preferred because it increases ICP and impairs platelet functions. It is an alternative to other agents in uncontrolled HE. Drugs that can reduce blood pressure suddenly and have long-term effects, such as nifedipine, should be avoided.[18]

ACUTE HEMORRHAGIC STROKE

Lowering blood pressure by more than 70 mmHg from the initial value increases the likelihood of renal function and neurological deterioration. Studies have shown that rapid reduction of blood pressure reduces the growth of bleeding.[19] If the patient's SBP value at the time of admission is above 220 mmHg, this value is reduced to below 220 mmHg within the first hour. It is aimed to keep it between 140-160 mmHg within the next few hours. If the patient's clinical condition is unstable, the dose of the antihypertensive drug is reduced. If the patient's SBP value at the time of admission is between 150-220 mmHg, it is reduced to below 140 mmHg within 1 hour. Nicardipine and labetolol are the drugs of choice for this. Nicardipine is more preferred above the initial SBP value of 160 mmHg. If it is below, labetolol is more preferred. Nitroprusside and nitroglycerin are not preferred due to their potential to increase intracranial pressure.[20]

HYPERTENSIVE ENCEPHALOPATHY

Arterioles respond to increased systemic blood pressure with vasoconstriction to maintain central perfusion at a constant flow. This is autoregulation of the brain. However, in sudden and rapid increases, this response cannot occur

Table 2. Characteristics of drugs used in hypertensive emergencies

Drugs	Minimum dose	Maximum dose	Indication	Side effects	Warning
Nitroglycerin	5 mcg/minute	100 mcg/minute	ACS Pulmonary edema	Headache, tachycardia, methemoglobinemia	Hypotension, Bradycardia, Azotemia, Tolerance with long-term use, Right-sided AMI, Caution in those using phosphodiesterase inhibitors.
Nicardipine	5 mg/hour (Increase by 2.5 mg/hour every 15 minutes)	15 mg/hour	Stroke	Headache, hypotension, tachycardia, angina	Half-life of 3-6 hours Do not use in ACS and severe aortic stenosis.
Esmolol	Loading dose: 500-1000 mcg/kg over per minute. Maintenance dose: 50 mcg/kg /minutes infusion	200 mcg/kg/minute	Aortic Dissection, stroke, Intraoperative postoperative	Excessive sweating, Shock, Altered consciousness, Dizziness	Do not use in pulmonary edema. Avoid in asthma, adrenergic crisis, heart block, heart rate <50 bpm, if Verapamil was used, metabolic acidosis, pulmonary hypertension.
Nitroprusside	0.25-0.5 mcg/kg/minute	8-10 mcg/kg/minute	Aortic dissection	Cyanide intoxication (starts at doses >2 mcg/kg/min) |	Do not administer the maximum dose for more than 10 minutes, Avoid use in subarachnoid hemorrhage, azotemia and optic atrophy. Discontinue the drug if lactic acidosis or bicarbonate depletion occurs.
Labetalol	Starting dose: 20 mg, 20-80 mg administered every 10 minutes. Infusion dose: 0.5-2 mg/minute	200 mg	Preeclampsia, Eclampsia (Max dose: 160 mg), ACS: (Max dose 120 mg)	Rash Elevated liver enzymes, Thrombocytopenia, Hyperkalemia, Worsening of Raynaud's syndrome	Do not use in pulmonary edema. Avoid use in asthma, COPD, heart failure, 1st-degree heart block, bradycardia, and hyperadrenergic conditions.
Hydralazine	10 mg	20 mg	Preeclampsi Eclampsia	Increases cardiac workload, may reduce placental blood flow	Avoid in pulmonary edema.
Urapidil	Starting dose: 10-50 mg Initial infusion dose: 2 mg/minute Maintenance dose: 9 mg/hour		Severe hypertensive heart disease uncontrolled by other agents. Intraoperative Postoperative	Dizziness, headache, angina, priapism, tachycardia, bradycardia.	Contraindicated in aortic coarctation and active arteriovenous shunt disease. Avoid in patients on phosphodiesterase inhibitors. Reduce dose in hepatic or renal impairment, and in elderly patients.

ACS: Acute coronary syndrome

and hyperperfusion occurs. As a result, vasogenic edema and increased ICP develop.[21] Headache, drowsiness, seizures, changes in consciousness and visual disturbances occur. Hypertensive retinopathy and microangiopathic hemolytic anemia may often accompany. With the regulation of blood pressure, the patient's symptoms begin to improve. However, rapid pressure reduction can lead to organ hypoperfusion. For this, blood pressure is reduced by 10-20% in the first hour. This decrease should be maintained for 2-6 hours. A decrease of more than 25% is not desired within 24 hours. When the initial blood pressure decrease is tolerated by the patient, it is appropriate to reduce it gradually to 160/110 mmHg over 48 hours.2,21 Nicardipine and labetalol are primarily preferred. Nitroglycerin is not used due to its venodilator effect and potential to increase ICP.[2,22]

SUBARACHNOID HEMORRHAGE

The target value for uncontrolled aneurysm hemorrhage is below 160 mmHg. However, in patients with a good level of consciousness, below 140 mmHg may be beneficial. When blood pressure control is required, intravenous labetalol, nicardipine or clevidipine are preferred. The use of vasodilators such as nitroprusside or nitroglycerin should be avoided because of their tendency to increase cerebral blood volume and ICP.[23]

ACUTE HEAD TRAUMA

To control increased ICP due to trauma, intervention is performed when systemic blood pressure increases when cerebral perfusion pressure exceeds 120 mmHg and ICP exceeds 20 mmHg. Rapid blood pressure regulation has been associated with poor outcomes. It is beneficial for patients to have their heads 30 degrees above heart level. Valsalva maneuvers that increase ICP should be avoided.[2]

PREECLAMPSIA-ECLAMPSIA

The main treatment for this condition, which occurs after the 20th week of pregnancy, is delivery. However, in patients who develop HE, the goal is to reduce blood pressure control to below 160/105 mmHg within 150-180 minutes. Labetalol and nicardipine may be preferred in treatment. If eclampsia or proteinuria, severe hypertension (blood pressure above 160/110 mmHg) and preeclampsia accompanied by neurological findings are treated with magnesium sulfate. 4 g magnesium is given intravenously as a 5-minute infusion. Then, treatment is continued by infusing 1 g per hour. If magnesium is given with nifedipine, there is a risk of hypotension. Emergency delivery is considered in patients whose blood pressure cannot be controlled within 6 hours. Diuretic treatment is avoided.[19]

ACUTE PERIOPERATIVE HYPERTENSION AND POSTOPERATIVE SURGICAL HYPERTENSION

HE may progress with fear, pain, adrenargic stimulation and intravascular volume variability. Blood pressure above 180/100 mmHg increases the risk of bleeding. Surgery may need to be postponed or blood pressure may need to be regulated. Nicardipine, nitroglycerin, and esmolol are drugs that have been successfully used. Esmolol has an important role in cardiac surgery because it reduces the potential for supraventricular or ventricular tachycardia. Routine perioperative use of beta blockers is not recommended in non-cardiac surgeries. Preoperative use of angiotensin converting enzyme inhibitors carries the risk of perioperative hypotension, and discontinuation may lead to postoperative hypertension. Calcium channel blockers may be preferred in the preoperative period. There is no harm in routine loop diuretic use in patients with heart failure.[19,22]

ACUTE SYMPATHETIC CRISIS

Pheochromocytoma, paraganglioma, sudden discontinuation of clonidine or short-acting beta blocker antihypertensive drugs, cocaine, amphetamine, LSD, etc. use, consumption of monoamine oxidase inhibitors and tyramine-containing foods (cheese, vinegar, alcohol, etc.) and autonomic dysfunction (Gullian Barre, acute spinal cord injury) may cause sympathetic overactivity and cause HE. Changes in consciousness, palpitations, angina, seizures and agitation may be observed.[2,16]

Phentolamine and doxazosin are used to reduce the increased blood pressure in pheochromocytoma. Nicardipine is preferred as an alternative treatment. In patients without sufficient alpha receptor blockade, the use of beta blockers leads to an increase in blood pressure.[16]

When antihypertensive drugs, especially clonidine, are administered to a person using the drug, the blood pressure is brought under control in a short time, while this period may be longer with other drugs.[2]

In autonomic dysfunction, phentolamine, nitroprusside or labetolol may be preferred.[2]

Benzodiazepine is initially used to control hypertension due to narcotic consumption. Nitroglycerin or nicardipine may be preferred as additional agents for blood pressure regulation. The use of beta blockers in the control of high blood pressure caused by these sympathomimetic drugs carries the concern of myocardial ischemia.[2,16]

CARDIAC EMERGENCIES

Acute coronary syndrome (ACS) and acute pulmonary edema are important end-organ damages for HE. The main purpose in ACS is to reduce afterload without reducing left ventricular diastolic filling and to reduce myocardial oxygen consumption. Because in HE, the deteriorated endothelium and underlying atherosclerosis trigger type 1 myocardial infarction (MI). Or, it disrupts the oxygen supply-demand balance and leads to type 2 MI. In the presence of HE with ACS, it is recommended to reduce SBP below 140 mmHg within 1 hour. Nitroglycerin is primarily recommended here. It can reduce ischemia by increasing coronary blood flow. Use with beta blockers such as labetalol reduces reflex tachycardia and indirectly myocardial workload. However, when using it, it should be determined that patients have right MI, use of phosphodiesterase (in the last 24-48 hours), pulse is not below 50 and above 100 per minute and SBP is not below 90 mmHg. Patients can quickly go into prolonged hypotension and cardiogenic shock. Agents that can lead to poor outcomes such as nifedipine should be avoided. It can cause uncontrolled hypotension and impair organ perfusion.[24-25]

Acute hypertensive pulmonary edema is the most common cardiac complication of HE. These patients often have known HT, as well as left ventricular hypertrophy and diastolic dysfunction. Increased systemic pressure increases left ventricular filling pressure, paving the way for pulmonary congestion. Patients may present with cough, pink frothy sputum, dyspnea, inability to lie on their backs, fear of death and palpitations. Congestion, cardiomegaly or mediastinal expansion may be seen in the form of cotton wool on lung imaging. Nitroprusside and nitroglycerin are effective in treatment by reducing preload and afterload. The first step is to reduce blood pressure by 15-25% and basically to gradually reduce SBP below 140 mmHg. Unless contraindicated, beta blockers reduce reflex tachycardia. Loop diuretics are important in reducing symptoms by adding them to the treatment. However, excessive diuresis is not a desired condition. In both pulmonary congestion and ACS, urapidil reduces peripheral vascular resistance and provides an alternative treatment.[25-26]

AORTIC SYNDROMES

Although it can be seen most frequently as aortic dissection, aortic aneurysm rupture, intramural hematoma and aortic ulcer constitute this syndrome. It is the least common cardiac complication of HE. Although aortic dissection is the most common symptom of tearing pain in the chest and back, it can also present with syncope, abdominal pain, flank pain or stroke findings. As the vascular tissue is dissected, the clinical condition of the patients becomes more severe. Progressive clinical conditions such as pericardial tamponade, MI and acute kidney injury may be added. For this reason, SBP should be reduced to 100-120 mmHg and pulse rate should be reduced to less than 60 beats per minute within the first 20 minutes of treatment. Nitroprusside and nitroglycerin are primarily preferred for blood pressure control. Nicardipine is used as an alternative. In addition, beta blockers (esmolol, labetolol) are preferred to control the pulse.[25,27]

RENAL EMERGENCIES

Patients present with newly developed, mostly microscopic hematuria and increased creatinine values. It is recommended that patients' blood pressures be reduced by 20-25% within 3-24 hours. Nicardipine and labetolol are among the drugs that can be preferred.[22,28]

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