Clinical Pharmacology Update

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A compendium for the treatment of hypertensive emergencies[1]

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A decline in the prevalence of accelerated hypertension and hypertensive emergencies has been due, in part, to increased awareness, improved detection, and more aggressive therapy. Yet, such emergencies continue to present a challenge to the emergency-room and primary-care physician. This compendium reviews the agents currently available for parenteral administration to manage the hypertensive emergency. Those conditions most commonly associated with such emergencies and a plan for initial management are also presented. The indications, advantages, and disadvantages of each agent, as well as dosage recommendations and available preparations, are considered. The management of urgent hypertension with selected orally administered drugs is also discussed.

Index terms: Hypertension, drug therapy

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Death rates due to malignant hypertension and hypertensive emergencies have declined significantly during the past 25 years. Effective antihypertensive agents and more aggressive management, not only of patients with malignant hypertension but also of patients with mild to moderate hypertension, have reduced mortality. Control of blood pressure in patients with mild to moderate hypertension can prevent accelerated hypertension, hypertensive encephalopathy, and aortic dissection and greatly reduce the risks of stroke, congestive heart failure, and progressive renal failure. Most hypertensive emergencies represent a failure of medical management and are preventable by early identification and therapy. This compendium is designed as a treatment guide for the emergency-room and the primary-care physician to the management of hypertensive crises.

The hypertensive emergency

At times, high blood pressure poses an immediate threat to the integrity of the cardiovascular system. Recognition of these hypertensive emergencies and prompt institution of appropriate antihypertensive therapy may prevent serious cardiovascular morbidity and mortality. A hypertensive emergency depends more upon the patient's clinical state than on the absolute level of blood pressure. A patient with accelerated hypertension and a sustained blood pressure of 240/140mm Hg with no evidence of target-organ compromise does not necessarily require immediate reduction of blood pressure with parenteral agents; this can be called a *hypertensive urgency*, in which the immediate risk, though less, may lead to morbid complications if not treated aggressively. Prompt institution of oral antihypertensive therapy and close follow-up evaluations may suffice. In contrast, a patient with even modest hypertension complicated by acute aortic dissection or congestive heart failure represents a true

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hypertensive emergency. This patient requires hospitalization and immediate reduction of blood pressure in an intensive care unit. Thus, the degree of associated target-organ involvement and immediate risk to the integrity of the cardiovascular system determine a hypertensive emergency. The conditions of hypertensive emergencies and their inital management are delineated (*Tables 1* and *2*).

A brief, initial evaluation assesses target-organ involvement and rules out secondary causes of hypertension, such as a pheochromocytoma which should be identified early since it responds poorly to all but selected agents. A careful urinalysis will reveal renal involvement, and the kidney profile will help determine the degree of renal dysfunction. Moderate to severe renal impairment does not contraindicate aggressive, rapid reduction of blood pressure even though further transient impairment may follow. Dialysis can be initiated if renal failure complicates urgent blood-pressure therapy. A chest radiograph and an electrocardiogram help to assess cardiac involvement and rule out congestive heart failure, ischemia, or recent myocardial infarction. A complete blood count and blood smear should be obtained since microangiopathic hemolytic anemia may occur with accelerated or malignant hypertension or a hypertensive crisis.

Table 1. Hypertensive emergencies

Cerebrovascular emergencies
Hypertensive encephalopathy
Hypertensive intracerebral hemorrhage
Subarachnoid hemorrhage
Acute atherothrombotic brain infarction with severe hypertension
Malignant hypertension
Cardiac emergencies
Acute congestive heart failure
Acute coronary insufficiency
Postcoronary artery bypass hypertension
Acute aortic dissection
Other conditions
Pheochromocytoma
Rebound hypertension following sudden withdrawal of antihypertensive agents (clonidine, guanabenz in some cases)
Food or drug interactions with monoamine oxidase inhibitors
Severe pre-eclampsia and eclampsia
Acute glomerulonephritis
Postoperative hypertension (particularly vascular procedures)
Head injury
Severe body burns

Table 2. Initial management of the hypertensive emergency

Hospitalization in an intensive care unit
Brief, initial evaluation
History obtained and physical examination expeditiously performed
Plasma catecholamines or urine obtained for determination of metanephrine level, vanillylmandelic acid value, catecholamine value
Determination of creatinine clearance
Urinalysis with sediment examination
Complete blood count
Chest radiography
Electrocardiography
Initiation of drug therapy
Therapy should be initiated before the results of all initial laboratory studies are available in an attempt to reduce the blood pressure to a safer level
Further diagnostic studies
Additional studies are undertaken as indicated after blood pressure has been controlled or reduced to a level determined to represent adequate control for the individual patient

Drugs for treatment of hypertensive emergencies

Drugs administered parenterally are classified according to their mechanisms of action into those that directly dilate the resistance vessels, and therefore, reduce peripheral resistance, and those that interfere with sympathetic innervation of the cardiovascular system. *Tables 3* and *4* list these drugs, their method of administration, and their recommended dosage. *Table 5* lists commercial preparations for parenteral administration.

Direct vasodilators

Sodium nitroprusside (Nipride, Nitropress) is the most potent and predictable agent for managing hypertensive emergencies irrespective of etiology.[1] Skilled nursing care and careful titration with a continuous infusion device in an intensive care unit are required. The advantages, disadvantages, and adverse effects of sodium nitroprusside use are listed (*Table 6*).

Nitroglycerin (Nitroglycerin inj, Nitro-Bid IV, Nitrostat IV, Tridil), recently released for intravenous administration, has some of the same advantages as sodium nitroprusside. Nitroglycerin predominantly dilates the venous capacitance vessels, but arteriolar dilatation occurs at higher infusion rates. Preload reduction is the major hemodynamic effect of nitroglycerin. This

Table 3. Direct vasodilating drugs for the treatment of hypertensive emergencies

Preparation*	Method of Administration		
	IM	Intermittent IV	Continuous IV
Sodium nitroprusside			0.5–10 μg/kg/min
Nitroglycerin			5–100 μg/min
Diazoxide		50–100 mg bolus injection (within 30 sec) every 10–15 minutes	15–30 mg/min until the desired effect is achieved
Hydralazine hydrochloride	10–50 mg†	10–20 mg/20 ml‡	200 mg/L

* In most cases, a rapidly acting diuretic should be given intravenously at the beginning and at appropriate intervals throughout treatment.
† Start with smallest dose listed.
‡ Inject from syringe at rate of 1 ml/min until the desired effect is obtained.

agent's advantages, disadvantages, and adverse effects are listed (*Table 7*).

Diazoxide (Hyperstat) reduces arterial pressure by direct arteriolar vasodilatation without significant effect on capacitance vessels; thus reflexive increases in heart rate and cardiac output accompany reduced blood pressure. Although this nondiuretic benzothiadiazine derivative may be administered as a 300 mg bolus injection (5 mg/kg body weight), we recommend pulse administration of 50 to 100 mg injected rapidly at 10 to 15 minute intervals; this allows gradual reduction in blood pressure in contrast to the precipitous reduction following an effective 300 mg bolus.[5] Slow infusion of undiluted diazoxide (15 to 30 mg/min) also effectively reduces arterial pressure in most severely hypertensive patients. Slow infusion of diazoxide may require more than the standard 300-mg ceiling dose.[6] The advantages, disadvantages, and adverse effects of this drug are listed (*Table 8*).

Hydralazine hydrochloride (Apresoline) is less consistently effective for hypertensive emergencies than other vasodilator agents. For many obstetricians, however, hydralazine is still the drug of choice for severe pre-eclampsia or eclampsia. The advantages, disadvantages, and adverse effects of this vasodilator are listed (*Table 9*).

Sympathetic inhibiting drugs

Labetalol,* is the first of a new group of alpha- and beta-adrenergic receptor blocking agents that will soon become available for managing patients with severe hypertension and hyperten-

* Not yet approved by the Federal Drug Administration.

Table 4. Sympathetic inhibiting drugs for the treatment of hypertensive emergencies

Preparation*	Method of Administration		
	IM	Intermittent IV	Continuous IV
Labetalol†		20–80 mg by intermittent injection every 10–15 min	0.5–2.0 mg/kg/min
Trimethaphan camsylate			1,000 mg/L
Phentolamine	5–10 mg‡	5–10 mg bolus injection	200 mg/L
Reserpine	1–5 mg‡	1–5 mg from syringe over 3–5 min	
Methyldopate		250–500 mg in 100 ml over 30–60 min	

* In most cases, a rapidly acting diuretic should be given intravenously at the beginning and at appropriate intervals throughout treatment (see text).
† Not yet approved by FDA
‡ Start with smallest dose listed.

Table 5. Preparations for parenteral administration

Drug Generic (trade name)	Manufacturer	Preparation available
Hydralazine hydrochloride (Apresoline)	Ciba	Solution, 20 mg/ml in 1-ml container
Sodium nitroprusside		
(Nipride)	Roche	Powder (for solution), 50 mg in 5-ml container
(Nitropress)	Abbott	Powder (for solution), 50 mg in 5-ml container
Nitroglycerin		
(Nitroglycerin inj)	Abbott	Solution, 5 mg/ml in 5-ml container
(Nitro-Bid IV)	Marion	Solution, 5 mg/ml in 1-, 5-, 10-ml containers
(Nitrostat IV)	Parke-Davis	Solution, 0.8 mg/ml in 10-ml container
(Tridil)	American Critical Care	Solution, 5 mg/ml in 10-ml container
Diazoxide (Hyperstat)	Schering	Solution, 15 mg/ml in 20-ml container
Labetalol		
(Trandate)	Glaxo	Solution, 5 mg/ml in 20-ml container
(Normodyne)	Schering	Solution, 5 mg/ml in 20-ml container
Reserpine		
(Sandril)	Lilly	Solution, 2.5 mg/ml in 10-ml container
(Serpasil)	Ciba	Solution, 2.5 mg/ml in 2- and 10-ml containers
Methyldopate hydrochloride (Aldomet ester HCL)	Merck Sharp & Dohme	Solution, 250 mg/ml in 5-ml container
Trimethaphan camsylate (Arfonad)	Roche	Solution, 50 mg/ml in 10-ml container
Phentolamine mesylate (Regitine)	Ciba	Powder (lyophilized, for solution), 5 mg
Furosemide (Lasix)	Hoechst-Roussel	Solution, 10 mg/ml in 2-, 4-, and 10-ml containers
Bumetanide (Bumex)	Roche	Solution, 0.25 mg/ml
Ethacrynic acid (Edecrin)	Merck Sharp & Dohme	Powder (for solution), 50 mg

sive emergencies.[7,8] Following intravenous administration, inhibition of both alpha- and beta-adrenergic receptors promptly reduces systemic vascular resistance and arterial blood pressure without reflex tachycardia or significant changes in cardiac output. Labetalol is effective in 80% to 90% of patients with severe hypertension or hypertensive emergencies. Labetalol may be particularly advantageous for patients with coronary artery disease and has been administered safely to severely hypertensive patients with acute myocardial infarction when left ventricular performance is not impaired significantly. The advantages, disadvantages, and adverse effects of this drug are listed (*Table 10*).

Trimethaphan camsylate (Arfonad) interrupts adrenergic control of arterioles with resultant vasodilation, decreased venous compliance, improved peripheral blood flow to some vascular beds, and a decrease in blood pressure. This ganglion blocking agent is infrequently used today since more convenient and equally effective agents rapidly reduce arterial blood pressure. Some clinicians still consider trimethaphan camsylate to be the drug of choice for managing patients with acute aortic dissection because this agent reduces arterial blood pressure, cardiac output, and velocity of left ventricular ejection. Marked hypotension may limit its use intravenously. Infusion rates are best regulated by a constant infusion pump. The advantages, disadvantages, and adverse effects of trimethaphan camsylate are listed (*Table 11*).

Phentolamine mesylate (Regitine), a nonselective

Table 6. Use of sodium nitroprusside

Advantages
- The most predictably effective agent for the treatment of hypertensive crises; usually effective when other hypotensive drugs have failed
- Instantaneous onset of action
- Blood pressure can be titrated to any level by careful adjustment of infusion rates
- Preload and afterload are reduced—an advantage when acute congestive heart failure is present
- Does not cause sedation or somnolence

Disadvantages
- Rapid onset and evanescent effect necessitate constant observation by trained personnel in an intensive care setting if wide fluctuations in blood pressure are to be avoided
- Rapid degradation by light; this can be minimized by wrapping intravenous containers and tubing in aluminum foil

Adverse effects
- Side effects are infrequent with appropriate infusion rates. Nausea, retching, vomiting, and lightheadedness may accompany rapid blood pressure reduction
- Since nitroprusside is metabolized to thiocyanate and excreted by the kidneys, thiocyanate levels must be monitored, particularly in those patients with renal dysfunction. If the level exceeds 12 mg/dL, the drug should be discontinued to avoid thiocyanate psychosis, which may mimic hypertensive encephalopathy
- Cyanide intoxication, particularly with liver disease or poor tissue perfusion[2]

alpha-adrenergic blocking agent, is reserved for the treatment of hypertension associated with high circulating levels of catecholamines.[9] In addition to a pheochromocytoma, the drug is effective for management of a hypertensive crisis related to (*a*) drug and food interactions with monoamine oxidase inhibitors or (*b*) occasional rebound hypertension following sudden discontinuance of clonidine or guanabenz and inadvertent administration of an overdose of sympathomimetic amines. The resultant cardiac stimulation appears to be more than a reflex response to peripheral vasodilatation and may be associated with cardiac arrhythmias. The advantages, disadvantages, and adverse effects of phentolamine mesylate are listed (*Table 12*).

Reserpine (Sandril, Serpasil) is rarely used since the development of potent direct-acting vasodilating drugs. It depletes storage sites of catecholamines in the central nervous system, heart, and peripheral postganglionic sympathetic neurons and prevents norepinephrine release at sympathetic neuroreceptor sites. The major hypotensive action of the drug is peripheral postganglionic catecholamine depletion. The advantages,

Table 7. Use of nitroglycerin

Advantages
- Useful for management of hypertensive patients with coronary artery disease and unstable angina[5]
- Dilates collateral coronary blood vessels and perfuses ischemic myocardium. (This property is not shared by sodium nitroprusside)
- Particularly effective for management of hypertension occurring after a coronary bypass procedure[4]
- Useful for management of acute congestive heart failure whether the blood pressure before treatment is normal or elevated
- Blood pressure can be adjusted by careful titration of infusion rates

Disadvantages
- Rapid onset and brief duration of effect necessitate constant observation by trained personnel in an intensive care setting to avoid wide fluctuations in blood pressure
- Unpredictable absorption into plastic containers and tubing necessitates special intravenous equipment

Adverse effects*
- Headache, retching, nausea, and vomiting are likely to occur with rapid reduction in blood pressure

* No risk for cyanide and/or thiocyanate intoxication may allow higher maximal infusion rates of nitroglycerin than of sodium nitroprusside.

disadvantages, and adverse effects of reserpine are listed (*Table 13*).

Methyldopate ester (Aldomet ester) lowers blood pressure by reducing peripheral vascular resist-

Table 8. Use of diazoxide

Advantages
- Blood pressure can be reduced gradually with pulse administration (50- to 100-mg bolus)
- Slow intravenous infusion reduces blood pressure more gradually
- Effects may persist for 12 hours or longer
- Hypotension is seldom induced by appropriate dosages
- Does not cause sedation or somnolence

Disadvantages
- Precipitous reduction in blood pressure may be hazardous for patients with cerebral or coronary insufficiency; larger boluses (e.g., 300 mg) should be avoided when treating these high-risk patients

Adverse effects*
- Transient weakness, flushing, nausea, and vomiting may accompany rapid intravenous administration
- Hypotension is an unusual occurrence with appropriate dosages, *except* in patients receiving other antihypertensive agents, particularly other vasodilators
- Hyperglycemia occurs with repeated dosages. (Blood glucose must be measured daily)

* The development of hyperglycemia and hyperuricemia is rare since diazoxide therapy is short term in most instances.

Table 9. Use of hydralazine hydrochloride

Advantages
- Prompt onset of action after intramuscular or intravenous administration
- Hypotension is rarely induced
- Does not cause sedation or somnolence

Disadvantages
- Inconsistently effective for treating hypertensive encephalopathy
- Contraindicated for patients with acute coronary insufficiency since the drug tends to increase heart rate and cardiac work
- Venous capacitance vessels unaffected

Adverse effects
- Reflex tachycardia and palpitations
- Increased cardiac work may precipitate anginal symptoms in susceptible patients
- Rheumatoid arthritis*
- Systemic lupus erythematosus-like syndromes*
- Drug-induced fever, skin eruptions, gastrointestinal disturbances, and peripheral neuropathy, all resulting from slow acetylation of the drug*

* These adverse effects usually will not occur with short-term administration.

ance with little or no effect on cardiac output. This agent is less predictable than other parenteral drugs in hypertensive emergencies and, like reserpine, has a delayed onset of action and produces severe sedation. We reserve the use of methyldopate ester to control hypertension in the postoperative period. For several days postoperatively, the drug is administered intravenously until patients resume their usual antihypertensive medications. The advantages, disadvantages, and adverse effects of methyldopate ester are listed (*Table 14*).

Table 10. Use of labetalol

Advantages
- Can be administered by continuous intravenous infusion
- Blood pressure can be reduced more gradually with pulse administration (20- to 80-mg injections)
- The effect may persist for up to 24 hrs
- Reflexive tachycardia does not accompany blood-pressure reduction

Disadvantages
- Beta-blocking effects predominate
- Should be avoided for patients susceptible to beta-blocker side effects

Adverse effects
- Nausea, vomiting, flushing
- Tingling of the scalp and groin
- Should not be used for patients with a history of bronchial asthma, heart block greater than first degree, severe sinus bradycardia, and congestive heart failure
- Paradoxical hypertension may occur in patients with a pheochromocytoma

Table 11. Use of trimethaphan camsylate

Advantages
- Continuous intravenous infusion provides smooth, precise control of blood pressure
- Reduces preload and afterload, an advantage for patients with congestive heart failure
- Preferred drug for treating acute aortic dissection
- Does not significantly penetrate the blood-brain barrier

Disadvantages
- Frequent blood-pressure monitoring is mandatory during intravenous administration
- Effect is primarily othostatic; larger dosages are required for bedridden patients

Adverse effects
- Repeated administration leads to parasympatholytic side effects (e.g., urinary retention, paralytic ileus)
- Generalized ganglionic blockade produces parasympathetic effects (e.g., atony of the bladder and gastrointestinal tract with subsequent urinary retention or obstipation, cycloplegia, and mydriasis)
- Some bradycardia usually accompanies the hypotensive effect of the drug, although changes in heart rate depend upon existing vagal tone
- Cardiac output is reduced largely by increased venous capacitance and decreased venous return to the heart; the output of a failing left ventricle may be increased due to lessened peripheral resistance and decreased venous return to the heart

Table 15 lists the antihypertensive drugs of choice for parenteral administration in selected hypertensive emergencies. The order of preferred drugs varies slightly, depending upon the patient's clinical status and concurrent diseases.

Concomitant diuretic therapy

Rapid reduction of arterial pressure with parenteral antihypertensive agents leads to sodium

Table 12. Use of phentolamine mesylate

Advantages
- Specific for hypertension associated with a pheochromocytoma and other conditions with high circulating levels of catecholamines
- Effective when administration is by intermittent bolus injection or continuous intravenous infusion

Disadvantages
- Ineffective except when the catecholamine level is excessive
- Effects are transient

Adverse effects
- Cramping abdominal pain, nausea, vomiting, and diarrhea
- Stimulation of gastric secretion by repeated use may exacerbate peptic ulcer disease
- Significant tachycardia and cardiac arrhythmias may occur
- Anginal pain may be precipitated in patients with coronary insufficiency

and water retention, expansion of intravascular and extracellular fluid volumes, and subsequent "pseudotolerance" to the parenteral hypotensive agents. A rapidly acting loop diuretic (furosemide, 40 to 120 mg, or bumetanide, 1 to 5 mg) should be given intravenously at the onset of treatment and repeated as needed to prevent fluid retention. Larger doses may be required for patients with renal insufficiency. Care must be taken with a potent loop diuretic to avoid excessive diuresis with subsequent volume depletion or hyponatremia. The risk of hypokalemia must also be recognized, particularly in patients receiving digitalis glycosides. Transient tinnitus and ototoxicity have occurred after administration of high doses and after repeated administrations; the latter situation may be a lesser risk with bumetanide than with furosemide. The use of ethacrynic acid (50 to 150 mg) is an alternative in patients with known hypersensitivity to sulfonamide diuretics.

Other available or investigational agents

The use of several other agents currently available or undergoing clinical evaluation has been suggested for patients with hypertensive emergencies.

SQ 20881 (Teprotide), an investigational agent, lowers blood pressure in selected patients experiencing a hypertensive crisis, suggesting that converting enzyme inhibitors can be effective for hypertension of all severities.[10] The response to SQ 20881 appears positively correlated to the level of plasma renin activity. Yet, it is unlikely that SQ 20881 will be as effective as either diazoxide or sodium nitroprusside.

Saralasin (Sarenin), an angiotensin II competitive inhibitor, can be administered intravenously as a diagnostic aid to assess the angiotensin-dependent component of hypertension. Saralasin has the potential disadvantage of intrinsic agonistic activity in patients with severe or accelerated hypertension and low renin levels.

Prostaglandin A_1 (PGA_1), an experimental agent, lowers blood pressure promptly when infused intravenously.[11] The mechanism of action appears to relate to inhibition of adenyl cyclase, which regulates cellular function, vascular smooth muscle contractility, and sodium excretion. The initial infusion rate of PGA_1 should approximate 0.6 mcg/kg/min, with increments of 0.6 to 1.2 mcg/kg/min at five- to 10-minute intervals until a satisfactory response is achieved.

Calcium channel blockers have also been used.

Table 13. Use of reserpine

Advantages
• Intramuscular administration is convenient
• Blood pressure is reduced gradually after 2–3 hrs
Disadvantages
• Delay of 2–3 hrs between injection and maximal effect is undesirable in acute emergencies
• An effective dose produces somnolence, obfuscating neurologic evaluation
Adverse effects*
• The antihypertensive effect is usually associated with bradycardia
• Cumulative effects can lead to severe and prolonged hypotension

* Since reserpine reduces venous tone, postural hypotension and hemodynamic findings, similar to those related to trimethaphan camsylate usage, may be seen.

Verapamil has been administered intravenously during a hypertensive crisis, but little evidence supports its safety or efficacy in patients with hypertensive emergencies.[12,13] Effects are presumably due to direct vasodilation of arteriolar smooth muscle. Severe bradycardia is a potential hazard in patients concomitantly treated with beta-blockers or digitalis. Nifedipine, administered orally or sublingually, lowers blood pressure rapidly in patients with severe hypertension or experiencing a hypertensive crisis.[14,15]

Management of urgent hypertension

Several oral agents have proved useful for treatment of severe hypertension when immediate reduction of blood pressure with parenteral agents is not needed. Depending upon the initial dose and dosage frequency, blood pressure may be reduced in several to 24 hours.

Oral loading with clonidine (0.1–0.2 mg/hr) reduces blood pressure significantly within sev-

Table 14. Use of methyldopate ester

Advantages
• Useful in the postoperative patient
• Blood pressure is reduced gradually over several hours
Disadvantages
• Delayed onset of action similar to reserpine
• Consistently less effective than other parenteral agents
Adverse effects
• Sedation
• Drug-induced fever, hepatitis, or hemolytic anemia*

* Usually these complications only occur as a result of long-term oral administration and not short-term intravenous administration, except in the previously sensitized patient

Table 15. Antihypertensive drugs of choice for parenteral administration in selected hypertensive emergencies

Hypertensive emergencies	Preferred drugs	Drugs to avoid or use with caution
Hypertensive encephalopathy	Sodium nitroprusside Diazoxide Trimethaphan camsylate Labetalol	Reserpine Methyldopate ester
Acute intracranial hemorrhage	Sodium nitroprusside Trimethaphan camsylate Nitroglycerin	All others
Acute cerebral infarction	Sodium nitroprusside Trimethaphan camsylate Nitroglycerin	All others
Acute left ventricular failure	Sodium nitroprusside Nitroglycerin Trimethaphan camsylate Diazoxide* Hydralazine hydrochloride*	Labetalol
Acute coronary insufficiency	Nitroglycerin Sodium nitroprusside Labetalol Trimethaphan camsylate Reserpine Methyldopate ester	Hydralazine hydrochloride Diazoxide
Dissecting aneurysm	Reserpine + Trimethaphan camsylate + Guanethidine (po) + Beta-blocker (po) or Sodium nitroprusside + Beta-blocker (IV)	Diazoxide Hydralazine hydrochloride Nitroglycerin
Eclampsia	Hydralazine hydrochloride Methyldopate ester Diazoxide	Trimethaphan camsylate Reserpine Sodium nitroprusside
Catecholamine crisis Pheochromocytomas Monoamine oxidase inhibition Clonidine, guanabenz withdrawal	Phentolamine mesylate Sodium nitroprusside	All others
Head injury	Sodium nitroprusside Trimethaphan camsylate Hydralazine hydrochloride	Reserpine Methyldopate ester Diazoxide
Extensive body burns	Sodium nitroprusside Diazoxide Labetalol Hydralazine hydrochloride Reserpine Methyldopate ester	

Table 15—continued

Hypertensive emergencies	Preferred drugs	Drugs to avoid or use with caution
Malignant hypertension	Diazoxide Labetalol Sodium nitroprusside Hydralazine hydrochloride Reserpine	
Postoperative hypertension	Methyldopate ester Sodium nitroprusside Nitroglycerin Reserpine Hydralazine hydrochloride Labetalol Diazoxide	Trimethaphan camsylate

* Concomitant administration of venodilator (e.g., isosorbide dinitrate) to prevent reflexive tachycardia

eral hours.[16] Oral loading with guanabenz should have similar effects, and the potent vasodilator, minoxidil, has effectively lowered blood pressure in selected patients with urgent hypertension.

Captopril is effective for severe hypertension, particularly in patients with increased levels of angiotensin II. Nifedipine, administered orally or sublingually, may also rapidly and significantly reduce blood pressure. First-dose effects may be impressive, although repeated administration is best accompanied by an effective oral diuretic. Prazosin is effective in larger dosages in selected cases of severe hypertension,[17] particularly those associated with a pheochromocytoma.[18,19]

Patients with severe or malignant hypertension without impending complications may be treated with a three-drug regimen for rapid, initial control of blood pressure. A loop diuretic plus a beta-blocker and a direct vasodilating agent are effective for accelerated or resistant hypertension. Minoxidil, an extremely potent vasodilator, may be substituted for hydralazine hydrochloride if the initial response is suboptimal.[20,21] Additionally, nifedipine is effective for severe hypertension when added to a regimen containing a diuretic and a sympathetic inhibiting agent.

Regardless of the combination of medications administered to the patient with urgent hypertension, the goal should be to reduce diastolic blood pressure to <110 mm Hg within the first 24 hours and to <90 mm Hg within 48 to 72 hours.

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