Management of hypertensive emergencies

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Most hypertensive crises represent failure of medical management and are preventable by appropriate early identification and therapy. Controlled therapeutic trials in patients with severe hypertension have clearly demonstrated that control of blood pressure can prevent accelerated hypertension and aortic dissection. The number of other complications such as congestive heart failure, progressive azotemia, stroke, and hypertensive neuroretinopathy is also considerably reduced by aggressive antihypertensive therapy.

Although hypertensive emergencies are not common, they still represent a major management problem for emergency room and primary care physicians. Severe and sudden elevation in blood pressure, regardless of cause, is a direct threat to life. In such situations, rapid reduction of blood pressure by parenteral administration of antihypertensive drugs is urgently indicated if the integrity of the cardiovascular system is to be maintained. Prompt reduction of blood pressure will reduce both the morbidity and mortality from hypertensive crises.

Hypertensive crises

1. Hypertensive encephalopathy (from any cause)
   a. Essential hypertension
   b. Acute or chronic glomerulonephritis

c. Pre-eclampsia and eclampsia
d. Renal vascular hypertension
2. Head injuries
3. Severe burns
4. Pheochromocytoma
5. Sudden release of increased tissue stores of catecholamines when certain drugs or foods are ingested by patients receiving monoamine oxidase inhibitors
6. Clonidine withdrawal
7. Some cases of acute coronary insufficiency
8. Some cases of malignant hypertension

Severe or moderate hypertension complicated by

1. Acute left ventricular failure
2. Intracranial hemorrhage
3. Acute dissecting aneurysm of the aorta
4. Leaking abdominal aortic aneurysm
5. Postoperative bleeding at vascular suture lines
6. Severe epistaxis

Miscellaneous conditions (when hypotensive drugs cannot be given orally)

1. Postoperative hypertension
2. Acute intestinal obstruction
3. Loss of consciousness

Although not true hypertensive emergencies, these miscellaneous conditions represent clinical situations in which antihypertensive agents must be administered parenterally and are therefore included for completeness.

Hypertensive encephalopathy

Hypertensive crises are often accompanied by the symptoms of acute hypertensive encephalopathy. The symptoms are confusion, severe headache, blurred vision, somnolence, nausea, vomiting, transient focal neurologic signs, and sometimes coma and convulsions.

Initial management of hypertensive crises

1. Hospitalization in intensive care if available
2. Brief evaluation
   a. Brief history and physical examination
   b. Plasma catecholamines or urine for metanephrine levels, VMA
   c. Blood urea nitrogen, creatinine, electrolytes
   d. Urinalysis
   e. Complete blood count
   f. Chest roentgenogram
   g. Electrocardiogram
3. 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.
4. Further diagnostic studies
   Additional studies are undertaken only after blood pressure has been controlled or reduced to a level determined to represent adequate control for the individual patient.

Treatment should be delayed for only a brief history and physical evaluation aimed at excluding a catecholamine-related form of hypertension and assessing the cerebrovascular, coronary vascular, and cardiovascular status of the patient. These few studies will enable the physician to assess the target organ status of the patient before instituting therapy with parenteral antihypertensive agents.

Method of administration of antihypertensive drugs

In the management of hypertensive emergencies, blood pressure must be reduced without delay and hypotensive agents should, therefore, be administered parenterally. The simplest method is to inject intramuscularly the chosen

agent (reserpine, hydralazine) in adequate doses as often as necessary to keep the blood pressure within the desired range. When blood pressure must be reduced more promptly, intravenous injections may be given and repeated intermittently by slowly injecting the drug (hydralazine, pentolinium) directly from a syringe at intervals, or by bolus injection of an agent such as diazoxide; or a continuous infusion (sodium nitroprusside, trimethaphan) may be administered under constant supervision.

Drugs available for treatment of hypertensive emergencies (*Tables 1 and 2*)

To combat hypertensive crises, the drugs available for parenteral administration can be classified according to their mechanisms of action into those that directly dilate the resistance vessels and, therefore, reduce peripheral resistance and those that act to interfere with sympathetic innervation of the cardiovascular system.

Direct vasodilators

Diazoxide

Our experience has demonstrated that in approximately 85% of administered doses, diazoxide is effective when given rapidly by intravenous push (15 to 20 seconds) from a syringe without diluting the commercial preparation. The usual bolus dose is 300 mg (5 mg/kg of body weight).

In patients with recognized or suspected cerebrovascular or coronary vascular insufficiency, an intermittent pulse administration may be preferred. Fifty to 100 mg of diazoxide is injected rapidly at 5- to 15-minute intervals, thus allowing a more gradual reduction in blood pressure in contrast to the precipitous reduction which occurs following an effective 300-mg bolus.

Advantages

1. Not primarily orthostatic
2. Blood pressure decreases precipi-

Table 1. Drugs available for the treatment of hypertensive emergencies

Preparation	Method of administration and dosage		
	IM, mg*	Intermittent IV, mg	Continuous IV, mg/liter
Direct vasodilators			
Hydralazine (Apresoline)	10–60	20–40/20 ml†	50–100
Diazoxide (Hyperstat)	. . .	300 (bolus) or 50–100 (minibolus); repeat q 5–15 min	. . .
Sodium nitroprusside (Nipride)	. . .	. . .	50–400
Sympathetic inhibitors			
Reserpine (Serpasil)	1–5	. . .	. . .
Ganglion-blocking agents			
Pentolinium (Ansolysen)	1–25	5/20 ml†	50–150
Trimethaphan (Arfonad)	. . .	. . .	1000
Methyldopate (Aldomet ester)	. . .	250–500/100 ml‡	. . .
Phentolamine§ (Regitine)	5–20	5–20 (rapidly)	100–500

* Start with smallest dose listed.

† Inject from syringe at rate of 1 ml/min until desired effect is obtained.

‡ Infuse over period of 30 to 60 minutes.

§ For pheochromocytoma; also for monamine oxidase crises and clonidine withdrawal.

Table 2. Drugs of choice for parenteral administration in the management of selected hypertensive crises

Hypertensive emergency	Preferred drugs	Drugs to avoid or use with extra caution
Hypertensive encephalopathy	Sodium nitroprusside Diazoxide Pentolinium Trimethaphan Hydralazine	Reserpine Methyldopate
Severe hypertension associated with acute or chronic glomerulonephritis	Diazoxide Hydralazine Methyldopate Sodium nitroprusside	
Eclampsia and pre-eclampsia	Diazoxide Hydralazine	Pentolinium Trimethaphan
Head injuries	Sodium nitroprusside Pentolinium Trimethaphan	Reserpine Methyldopate
Severe body burns	Diazoxide Sodium nitroprusside Reserpine Pentolinium Trimethaphan	
Pheochromocytoma, MAO inhibition, and clonidine withdrawal	Phentolamine Sodium nitroprusside	All others
Acute coronary insufficiency	Sodium nitroprusside Pentolinium Trimethaphan Reserpine Methyldopate	Hydralazine Diazoxide
Brain stem ischemia	Sodium nitroprusside Hydralazine Trimethaphan	Reserpine Diazoxide
Malignant hypertension	Diazoxide Reserpine Pentolinium Trimethaphan Sodium nitroprusside	
Acute left ventricular failure	Sodium nitroprusside Pentolinium Trimethaphan Diazoxide Hydralazine	

Table 2. *Continued*

Hypertensive emergency	Preferred drugs	Drugs to avoid or use with extra caution
Intracranial hemorrhage	Sodium nitroprusside Pentolinium Trimethaphan	Reserpine Methyldopate
Dissecting or leaking aneurysm of aorta	Reserpine Trimethaphan Pentolinium	Hydralazine Diazoxide
Postoperative hypertension	Methyldopate Hydralazine Sodium nitroprusside Diazoxide Reserpine	Pentolinium Trimethaphan

tously within 5 minutes after an effective 300-mg bolus
3. Blood pressure can be reduced more gradually with pulse administration (50- to 100-mg boluses)
4. The effect may persist for 12 hours or longer
5. Hypotension is seldom induced
6. Does not cause sedation or somnolence

Disadvantages

1. Precipitous reduction in blood pressure may be hazardous in patients with cerebral or coronary insufficiency
2. Hyperglycemia in susceptible patients (measure blood glucose daily)

Hydralazine

Hydralazine has been effective in managing hypertensive encephalopathy complicating acute or chronic glomerulonephritis or eclampsia. The onset of hypertensive action is usually apparent within 30 minutes following an effective intramuscular dose and within 10 minutes when the drug is administered intravenously.

Advantages

1. Not primarily orthostatic
2. Prompt onset of action after intramuscular or intravenous administration
3. Hypotension is rarely induced
4. Does not cause sedation or somnolence

Disadvantages

1. Not consistently effective in the management of hypertensive encephalopathy complicating essential hypertension
2. Contraindicated in patients with acute coronary insufficiency since it tends to increase heart rate and cardiac work

Sodium nitroprusside

The hypotensive response occurs within seconds after the infusion is started and is dissipated almost as rapidly when the infusion is stopped. The nitroprusside ion is converted to thiocyanate and serum levels of thiocyanate should be determined daily if infusions are continued for longer than 72 hours. Thiocyanate intoxication may occur

after prolonged administration, especially when renal function is impaired. Infusion should be discontinued if the serum concentration of thiocyanate exceeds 12 mg/dl. Hemodialysis or peritoneal dialysis may be utilized to remove thiocyanate from the serum.

Advantages

1. The most predictably effective agent available for the treatment of hypertensive crisis, and usually effective when other hypotensive drugs have failed
2. Instantaneous onset of action
3. Blood pressure can be titrated to any level by carefully adjusting the rate of infusion
4. Preload and afterload are reduced; this is an advantage in acute heart failure
5. Does not cause sedation or somnolence

Disadvantages

The rapidity of 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

Sympathetic inhibitors

Reserpine

This agent is not used as frequently as it was before the advent of diazoxide and sodium nitroprusside.

Advantages

1. Intramuscular administration is convenient
2. Hypotension is rarely caused if doses are appropriately spaced
3. Blood pressure is reduced gradually
4. Not primarily orthostatic in action

Disadvantages

1. Delay of 2 to 3 hours between injection and maximal effect is not desirable in acute emergencies
2. In effective doses, reserpine often produces profound somnolence which may obscure neurologic evaluation
3. The cumulative effect can lead to severe hypotension

Ganglion blocking agents

Pentolinium and trimethaphan block both the sympathetic and parasympathetic systems. Since their effect is primarily orthostatic, large doses are required to reduce blood pressure in supine patients. Following an effective dose of pentolinium intramuscularly, the blood pressure begins to fall within 30 minutes and the maximal effect is usually realized within 1 hour. A significant hypotensive effect is usually apparent within 5 to 10 minutes after either of these drugs is injected intravenously.

Advantages

1. Intramuscular administration is convenient (pentolinium only)
2. Maximal hypotensive effect in 30 to 60 minutes (after intramuscular injection)
3. Initial dose may be given intravenously by titration from a syringe for prompt hypotensive effect (pentolinium)
4. Continuous intravenous infusion may be used for smooth and precise control of blood pressure
5. These agents reduce preload and afterload—an advantage in congestive heart failure

Disadvantages

1. Frequent monitoring of blood pressure is mandatory during intravenous administration
2. Effect is primarily orthostatic; there-

fore, larger doses are required for bedfast patients
3. Repeated administration leads to parasympatholytic side effects (i.e., urinary retention, paralytic ileus)

Methyldopate ester

Methyldopa is less effective than reserpine but has the same disadvantages and must be given intravenously.

Advantages

1. Not primarily orthostatic
2. Intravenous administration is a substitute for reserpine; sedation is not so profound
3. Useful in the postoperative patient
4. Blood pressure is reduced gradually

Disadvantages

1. Delayed onset of action similar to reserpine
2. Consistently less effective than reserpine
3. Sedation

Phentolamine

The alpha receptor blocker, phentolamine, is specifically indicated for managing hypertensive crises associated with increased circulating catecholamines, whether from pheochromocytoma, sudden release of tissue catecholamine stores by certain drugs or foods containing tyramine in patients receiving monoamine oxidase inhibitors, or occasionally from abrupt withdrawal of clonidine. The effect of phentolamine is short-lived, usually lasting less than 5 minutes. It may be desirable to administer phentolamine by constant intravenous infusion after the blood pressure has been controlled initially by rapid intravenous injection of 5 to 15 mg from a syringe.