Hypertension Curriculum Review

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Hypertensive Crises: Emergencies and Urgencies

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Recent national surveys show that 50–55 million adult Americans have arterial hypertension. Unfortunately, hypertension control rates are disappointing, with approximately 35% of patients treated and controlled to the most liberal blood pressure (BP) goal of ≤140/90 mm Hg. In patients with untreated or poorly controlled hypertension, BPs tend to progress to higher levels with the associated risks of target organ damage (TOD).

Hypertensive crises encompass a spectrum of clinical situations that have in common BP that is not controlled together with progressive or impending TOD. Most hypertensive emergencies and urgencies are preventable and are the result of untreated or inadequately treated mild-to-moderate hypertension, or nonadherence to antihypertensive therapy. Patients with hypertensive crises may present with a range of BP, varied clinical symptoms, and the presence or absence of target organ involvement.

The following case is an example of the dilemma often faced by the emergency department (ED) physician or occasionally by the office practitioner.

CASE

A 53-year-old male with a long history of hypertension has been treated with multiple medications. The patient also gives a history of poor adherence with medications. Currently he is reportedly taking Maxzide-25 mg (triamterene 37.5 mg and hydrochlorothiazide 25 mg/d); Bertek Pharmaceuticals, Research Triangle Park, NY, and atenolol 50 mg b.i.d., with BPs that have ranged 160–175/90–100 mm Hg. An angiotensin-converting enzyme inhibitor was recently prescribed, but that prescription was not filled.

At a recent office visit, an electrocardiogram revealed evidence of left ventricular hypertrophy, and a metabolic panel revealed normal electrolytes with a serum creatinine of 1.3 mg/dL.

In the past 3 weeks the patient has noted progressive dyspnea upon exertion and moderate pedal edema; he finally presented to a local ED in pulmonary edema.

Question: Does this patient have a hypertensive urgency or emergency?

DEFINITIONS

Hypertensive emergencies represent severe elevations in BP that are complicated by evidence of progressive target organ dysfunction and require immediate BP reduction (not necessarily to normal levels) to prevent or limit TOD. Examples include hypertensive encephalopathy, intracerebral hemorrhage or infarction, unstable angina pectoris or acute myocardial infarction, acute left ventricular failure with pulmonary edema, dissecting aortic aneurysm, or eclampsia of pregnancy. Hypertensive urgencies represent severe elevations of BP, often with evident target organ damage, but without evidence of progressive target organ dysfunction. Examples include upper levels of stage 2 hypertension, severe headache, shortness of breath, epistaxis, or severe anxiety. However, the majority of patients present as noncompliant or inadequately treated hypertensives with little to no evidence of TOD. These patients do not require hospital admission or acute lowering of BP and can be effectively managed in the ED with oral agents and appropriate follow-up within 24 hours to several days, depending upon individual patient characteristics.

PREVALENCE

Hypertensive crises affect upwards of 500,000 Americans each year, or approximately 1% of hypertensive adults. While this incidence appears to be low, remember that more than 50 million Americans suffer from hypertension. Based on definitions from the Seventh Report of

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the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, one recent study noted that hypertensive crises account for more than 25% of all patient visits to the medical section of an ED. Hypertensive emergencies accounted for one third of these cases. Although BP level is not considered a criterion for the diagnosis of a hypertensive emergency, all patients in that study had diastolic BPs exceeding 120 mm Hg. The most prevalent associated complications included cerebral infarction (24.5%), encephalopathy (16.3%), and intracerebral or subarachnoid hemorrhage (4.5%). Acute congestive heart failure (CHF) and pulmonary edema were seen in 36.8%, acute myocardial infarction or unstable angina in 12%, acute aortic dissection in 2%, and eclampsia in 4.5%.

On the basis of the above definitions, our patient should be considered to have a hypertensive emergency, even though BPs were not markedly elevated. The recognition of a hypertensive urgency or emergency depends more on the clinical state of the patient, not on the absolute level of BP. This patient suffers from significant deterioration in left ventricular function and clinically apparent CHF.

INITIAL ASSESSMENT

Early triage is imperative to ensure the most timely and appropriate therapeutic strategy for each patient and to limit morbidity and mortality. Each patient presenting to an ED with severely elevated BP deserves early assessment in an effort to identify the true hypertension emergency for early admission to an intensive care unit (ICU) for appropriate parenteral therapy.

HISTORY

A brief, but thorough, history should address the duration as well as the severity of hypertension, all current medications, including prescription and nonprescription drugs, and of particular importance, the use of recreational drugs. A history of other comorbid conditions and prior cardiovascular or renal disease is essential to the evaluation. Direct questioning regarding dosages and the level of compliance with current antihypertensive medications may establish inadequacy of treatment or frank nonadherence.

Look for historical information suggestive of neurologic, cardiovascular, and/or renal symptoms. Check for specific manifestations such as headache, seizures, chest pain, dyspnea, and edema. The common clinical characteristics of the hypertensive emergency are listed in Table I.

PHYSICAL EXAMINATION

The physical examination should begin with an assessment of BP, with an appropriate size cuff in both upper extremities and in a lower extremity if peripheral pulses are markedly reduced. This brief assessment should aid in establishing the degree of involvement of affected target organs and may provide clues to the possible existence of a secondary form of hypertension, such as renovascular hypertension, should a continuous bruit be observed upon abdominal examination. Careful palpation of the abdomen will help rule out any significant organomegaly, including the presence of polycystic kidneys. A careful funduscopic examination should be performed to detect the presence of hemorrhages, exudates, and/or papilledema.

INITIAL LABORATORY STUDIES

Initial laboratory studies should be limited and rapidly expedited. A urinalysis with microscopic examination of the urinary sediment, a chemistry panel, and an electrocardiogram should immediately be obtained. The urinalysis may reveal significant proteinuria, red blood cells, and/or cellular casts. Cellular casts are suggestive of renal parenchymal disease. Electrolyte abnormalities, particularly hypokalemia or hypomagnesemia, increase the risk of cardiac arrhythmias, and the chemistry panel will also identify evidence of renal and/or hepatic dysfunction. The electrocardiogram should provide evidence of coronary ischemia and/or left ventricular hypertrophy, and the finding of pulse deficits may raise the question of aortic dissection. When the clinical examination suggests cerebrovascular ischemia or hemorrhage, or in a comatose patient, a computed tomographic scan or magnetic resonance study of the head should be immediately obtained.

Initial therapy will be determined on a presumptive diagnosis based on the information available during the initial triage evaluation. Again, keep in mind that the level of BP alone does not determine a hypertensive emergency; rather, it is the degree of target organ involvement that will determine the rapidity with which BP should be reduced to a safer level to prevent or limit TOD.

The attached algorithm (Table II) can help the clinician identify those patients meeting the criteria of a hypertensive emergency and requiring immediate admission to an ICU for continuous monitoring of BP and initial administration of parenteral antihypertensive therapy. For these patients, BP reduction should not be delayed until the results of all diagnostic studies are available for review, but should be initiated as soon as the patient's clinical status is established.

INITIAL TREATMENT OF THE HYPERTENSIVE EMERGENCY

Parenteral therapy may be initiated in the ED if suitable supervision and monitoring of BP can be provided. More appropriately, the patient should be admitted to

an ICU where continuous monitoring of BP is available. The initial goal for BP reduction is not to treat to a normal BP, but rather to achieve a progressive, controlled reduction in BP to a safer level to minimize the risk of hypoperfusion in cerebral, coronary, and renovascular circulation. Under normal conditions, blood flow to these organs remains relatively constant despite wide fluctuations in BP. In the presence of severe hypertension, the autoregulatory range is shifted upwards so that higher levels of BP are tolerated but may place organ circulation at risk with sudden reductions in BP. As an example, studies on the autoregulation of cerebral blood flow suggest that the lower limit of autoregulation is about 20%–25% below the resting mean arterial pressure in normotensive subjects and in those with uncomplicated essential hypertension. These observations have lead to the suggestion that initial reduction in mean arterial pressure should not exceed 20%–25% below the pretreatment BP. As an alternative, mean arterial pressure can be reduced within the first 30–60 minutes to 110–115 mm Hg. If this level of BP is well tolerated and the patient is clinically stable, further gradual reductions toward a normal BP can be implemented over the next 24 hours. Excessively rapid reductions in BP have been associated with acute deterioration in renal function, ischemic cardiac or cerebral events, occasionally retinal arterial occlusion, and acute blindness.

A significant exception to the above recommendations should be recognized in patients with ischemic stroke. With the awareness that cerebral autoregulation is disrupted in ischemic tissue, there is no clear evidence from clinical trials to support the use of antihypertensive treatment during an acute stroke in the absence of other concurrent disorders such as aortic dissection or CHF. Antihypertensive treatment may adversely affect cerebral autoregulation in acute stroke. Hypertension associated with an acute ischemic stroke spontaneously decreases to prestroke levels within several days.

HOW URGENT IS "URGENT" HYPERTENSION?

Hypertensive urgencies have been defined as severe elevations in BP, often with evidence of chronic TOD, but without progressive target organ dysfunction. Unfortunately, the term "urgency" has led to overly aggressive management of many patients with severe, uncomplicated hypertension. Aggressive dosing with oral agents or even hospitalization for IV agents has often been recommended for patients seen in an ED with severe, but uncomplicated, hypertension. Aggressive dosing with oral agents, or even IV agents to rapidly lower BP is not without risk to the individual patient. Oral loading doses of antihypertensive agents can lead to cumulative effects with hypotension, sometimes following discharge from the ED.

This tendency to over-treat in the absence of any evidence of short-term benefits suggests that it is time to discard the term "hypertensive urgency" in favor of a less ominous term such as "uncontrolled blood pressure." Most of these patients are actually noncompliant or inadequately treated, and normalization of BP is not necessary before discharge from the ED (Table II). It is, however, critical that confirmed follow-up has been established with continued outpatient observation to ensure progressive, adequate BP control and to rule out secondary hypertension. It has been demonstrated that patients who are discharged from the ED without confirmed follow-up, as well as those who continue to be noncompliant, will return to the ED within weeks, and some will progress to hypertensive emergencies if not adequately managed.

Finally, there is little justification today to admit patients with uncontrolled BP (urgency) to a hospital for further evaluation and management when these issues can be efficiently and cost-effectively addressed in the outpatient setting.

PARENTERAL AGENTS FOR HYPERTENSIVE EMERGENCIES

A number of parenteral agents are effective in treating hypertensive emergencies. Dosing recommendations, onset and duration of effect, and selected precautions are outlined in Table III. There are few comparative studies or randomized clinical trials to provide definitive conclusions and/or recommendations regarding the efficacy and safety of comparative agents. Clinical outcomes and adverse effect results are primarily generated from observational studies and from clinical experience.

Sodium nitroprusside is a very predictable, potent vasodilator with an extremely rapid onset of action within seconds of initiating an infusion and a rapid offset of effect within 1 to 2 minutes, which necessitates constant monitoring and supervision of BP during administration. The drug's effectiveness in reducing preload and afterload in patients with impaired left ventricular function has enhanced its popularity with clinicians. Nitroprusside does not cause sedation or somnolence but is rapidly degraded by light, requiring periodic exchange of solution.

In patients with significant renal impairment, accumulation of a major metabolite, thiocyanate, may occur over several days with toxic effects. In the presence of poor tissue perfusion and depressed hepatic function, an intermediate metabolite, cyanide, can also accumulate and lead to cyanide poisoning.

Nicardipine is an IV form of the dihydropyridine calcium antagonist and has proven effective in a high percentage of emergencies, regardless of the etiology, and particularly at higher infusion rates. Ease of admin-

Table I. Clinical Characteristics of the Hypertensive Emergency	
Blood Pressure	Usually >220/140 mm Hg
Funduscopic findings	Hemorrhages, exudates, papilledema
Neurologic status	Headache, confusion, somnolence, stupor, visual loss, seizures, focal neurologic deficits, coma
Cardiac findings	Prominent apical pulsation, cardiac enlargement, congestive heart failure
Renal symptoms	Azotemia, proteinuria, oliguria
Gastrointestinal symptoms	Nausea, vomiting

Table II. Algorithm for Triage Evaluation

	Uncontrolled Blood Pressure (BP)		
	Most common	Less common	Hypertensive Emergency
BP	>180/110 mm Hg	>180/110 mm Hg	Usually >220/140 mm Hg
Symptoms	Headache, anxiety, often asymptomatic	Severe headache, shortness of breath, edema, epistaxis	Shortness of breath, chest pain, nocturia, dysarthria, weakness, altered consciousness
Exam	No target organ damage, no clinical cardiovascular disease	Target organ damage, clinical cardiovascular disease present/ stable	Encephalopathy, pulmonary edema, renal insufficiency, cerebrovascular accident, cardiac ischemia
Therapy	Observe 1–3 hours, initiate/ resume medication, increase dosage of inadequate agent	Observe 3–6 hours, lower BP with short-acting oral agent, adjust current therapy	Baseline labs, IV line, monitor BP, may initiate parenteral therapy in emergency room
Plan	Arrange follow-up <72 hours, if no prior evaluation, schedule appointment	Arrange follow-up evaluation <24 hours	Immediate admission to intensive care unit, treat to initial goal BP, additional diagnostic studies

istration is a particular advantage of this agent, which is administered as a continuous infusion starting at 5 mg/h. Infusion rate can be increased by 2.5 mg/h at intervals of 15–20 minutes until a desired reduction in BP has been achieved or until a maximal recommended infusion rate of 15 mg/h has been reached. The dosing of nicardipine is not dependent upon body weight and like other calcium antagonists, has been shown to reduce both cerebral and coronary ischemia. Tachycardia, headache, nausea, and vomiting may occasionally be observed.

Nitroglycerine is a preferred drug in coronary heart syndromes or myocardial ischemia. This agent dilates collateral coronary vessels and like nitroprusside, has both rapid onset and offset of effect. Its use also requires close nursing supervision. Unfortunately, at lower infusion rates nitroglycerine has its primary effect on capacitance vessels while much higher infusion rates are required to affect arteriolar vasodilation.

Nitroglycerine may be of particular use in patients with severe coronary ischemia and modest elevations in BP. It is also frequently used in acute hypertension following open heart surgery. Tolerance may be observed within 24–48 hours of instituting an infusion.

Fenoldopam is a selective, peripheral dopamine 1 receptor agonist that induces systemic vasodilation, especially in the renal circulation. This agent also has effects on renal proximal and distal tubules. It does not bind to dopamine 2 receptors or β-adrenergic receptors and has no α-adrenergic agonist effects, but it is an α-1 antagonist.

Fenoldopam's unique effects on the kidney provide increased urine flow, together with natriuresis and diuresis, and improve creatinine clearance, making this agent especially attractive in hypertensive emergencies associated with renal insufficiency. Fenoldopam improves cardiac hemodynamics with efficacy similar to that observed with sodium nitroprusside. The onset of clinical effects is rapid (within 5 minutes), and effects dissipate within 30 minutes of discontinuation. While the most common adverse effects reported include headache, flushing, tachycardia, and dizziness, a dose-related increase in intraocular pressure has been observed in both normotensive and hypertensive patients. No dosage adjustments are required for patients with renal or hepatic impairment.

Enalaprilat, the active form of enalapril, is administered IV in a dose of 1.25 mg at 6-hour intervals. Onset of action is seen within the first 30 minutes. This agent may be particularly useful in hypertensive emergencies associated with CHF or high plasma angiotensin II concentrations. The response to enalaprilat in hypertensive emergencies can be unpredictable, in part due to variable degrees of plasma volume expansion.

Diazoxide is rarely used any longer in the treatment of hypertensive emergencies. Its potent

Table III. Parenteral Agents for Hypertensive Emergencies

Agent	Dose	Onset/Duration of Action (After Discontinuation)	Precautions
Parenteral Vasodilators			
Sodium nitroprusside	0.25–10 μg/kg/min as IV infusion	Immediate/2–3 min after infusion	Nausea, vomiting; with prolonged use may cause thiocyanate intoxication, methemoglobinemia acidosis, cyanide poisoning; bags, bottles, and delivery sets must be light resistant
Glyceryl trinitrate	5–100 μg/min as IV infusion	2–5 min/5–10 min	Headache, tachycardia, vomiting, flushing, methemoglobinemia; requires special delivery system due to drug binding to PVC tubing
Nicardipine	5–15 mg/h IV infusion	1–5 min/15–30 min, but may exceed 12 h after prolonged infusion	Tachycardia, nausea, vomiting, headache, increased intracranial pressure; hypotension may be protracted after prolonged infusions
Diazoxide	50–150 mg as IV bolus, repeated or 15–30 mg/min by IV infusion	2–5 min/3–12 h	Hypotension, tachycardia, aggravation of angina pectoris, nausea and vomiting, hyperglycemia with repeated injections
Fenoldopam mesylate	0.1–0.3 μg/kg/min IV infusion	<5 min/30 min	Headache, tachycardia, flushing, local phlebitis
Hydralazine	5–10 mg as IV bolus or 10–40 mg IM, repeat every 4–6 h	10 min IV/>1 h (IV), 20–30 min IM/4–6 h (IM)	Tachycardia, headache, vomiting, aggravation of angina pectoris
Enalaprilat	0.625–1.25 mg every 6 h IV	15–60 min/6 h	Renal failure in patients with bilateral renal artery stenosis, hypotension
Parenteral Adrenergic Inhibitors			
Labetalol	20–80 mg as IV bolus every 10 min, up to 2 mg/min as IV infusion	5–10 min/2–6 h	Bronchoconstriction, heart block, orthostatic hypotension
Esmolol	500 μg/kg bolus injection IV or 25–100 μg/kg/min by infusion, may repeat bolus after 5 min or increase infusion rate to 300 μg/kg/min	1–5 min/15–30 min	First-degree heart block, congestive heart failure, asthma
Phentolamine	5–15 mg as IV bolus	1–2 min/10–30 min	Tachycardia, orthostatic hypotension

Table IV. Management of Uncontrolled Blood Pressure

Agent	Dose	Onset/Duration of Action (After Discontinuation)	Precautions
Captopril	25 mg p.o., repeat as needed SL, 25 mg	15–30 min/6–8 h SL, 15–30 min/2–6 h	Hypotension, renal failure in bilateral renal artery stenosis
Clonidine	0.1–0.2 mg p.o., repeat hourly as required to total dose of 0.6 mg	30–60 min/8–16 h	Hypotension, drowsiness, dry mouth
Labetalol	200–400 mg p.o., repeat every 2–3 h	30 min–2 h/2–12 h	Bronchoconstriction, heart block, orthostatic hypotension
Prazosin	1–2 mg p.o., repeat hourly as needed × 2	1–2 h/8–12 h	Syncope (first dose), palpitations, tachycardia, orthostatic hypotension

vasodilator effects in response to small miniboluses of 50 mg administered at 10- to 15-minute intervals were unfortunately associated with reflex tachycardia, hyperglycemia, hyperuricemia, and sodium and water retention. It offers no major advantages over several other agents that have comparable efficacy and more acceptable adverse event profiles.

Hydralazine has limited usage today in pregnant women with preeclampsia. Five to 20 mg are administered by IV bolus and may be repeated. The major

advantage in this agent in the preeclamsic patient is its ability to improve uterine blood flow. It is relatively contraindicated in patients with coronary atherosclerosis because administration is associated with reflex tachycardia, sodium and water retention, and intense flushing. Headache and increased intracranial pressure have also been observed.

ORAL AGENTS FOR UNCONTROLLED HIGH BLOOD PRESSURE

Several oral agents can be particularly useful as add-on drugs for the occasional patient with uncontrolled hypertension who may benefit from additional treatment and a period of observation before leaving the ED (Table IV). Captopril, a short-acting converting-enzyme inhibitor, is very well tolerated and can effectively reduce BP. Given by mouth, onset of effect is usually observed within 15–30 minutes, and dosing may be repeated in 1–2 hours, depending upon the response. The drug has been administered sublingually with onset of action observed within 10–20 minutes and maximum effect reached within 1 hour. Responsiveness to captopril can, of course, be enhanced by the co-administration of a short-acting loop diuretic such as furosemide. Administration may lead to acute renal failure in patients with unsuspected high-grade bilateral renal artery stenosis, and some reflex tachycardia is frequently observed.

Labetalol is a combined α- and β-adrenergic blocking agent which, when administered orally in a dose of 200–400 mg, can reduce BP within 2–3 hours. In some patients onset of effect may be observed within 1–2 hours. Like other β-blocking agents, labetalol has the potential to induce heart block and to worsen symptoms of bronchospasm in the asthmatic patient. Caution must be observed in patients with more than first degree heart block, symptomatic bradycardia, or CHF.

Clonidine is a centrally-acting α-adrenergic agonist with an onset of action of 30–60 minutes following oral administration. Maximal effects are usually seen within 2–4 hours. A single 0.2-mg dose appears to be as effective as the traditional loading regimen of 0.1 mg hourly for several hours. The most common adverse effect seen in the acute setting is drowsiness, affecting up to 45% of patients. Clonidine may be a poor choice when monitoring of mental status is important. The transdermal patches of clonidine are not effective in this situation since it may take 48–72 hours to build up a subcutaneous reservoir of active drug beneath the patch.

Prazosin is an α-adrenergic blocking agent that may have limited benefit in the early management of a patient with pheochromocytoma. Side effects include first-dose syncope, palpitations, tachycardia, and orthostatic hypotension.

SUMMARY

Patients presenting to an ED or a clinician's office with uncontrolled hypertension deserve prompt triage to establish the presence of a true hypertensive emergency. Those with hypertensive emergencies warrant prompt admission to an ICU for continuous monitoring of BP as well as prompt initiation of parenteral antihypertensive therapy. The term "hypertensive urgency" has lead to overly aggressive management of many patients in the ED setting, and not without some increased risk. I believe this term should be abandoned in favor of a less onerous term such as "uncontrolled blood pressure" which can be managed on an ambulatory basis following the initiation or adjustment of appropriate oral antihypertensive therapy. A key to the management of patients with severe hypertension is the assurance of appropriate follow-up care, and achievement of optimal hypertension control.

SUGGESTED READING

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