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Case Report

Hypertensive Crisis in the Setting of Non-Compliance

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Abstract

Hypertensive crisis is defined as severe hypertension with a blood pressure of greater than 180/120 mmHg, and may be further classified as urgency or emergency. Hypertensive urgency occurs over days to weeks, whereas hypertensive emergency occurs in hours to days and the patient presents with evidence of end organ damage. Patients of any age may present with hypertensive crisis, common etiologies include undiagnosed hypertension, noncompliance with therapy or inadequate therapy. Timely assessment of the patient is important and should include appropriate measurement of blood pressure, a thorough history and physical, and laboratory testing to evaluate for end organ damage. Antihypertensive agents utilized in the setting of hypertensive emergency should be short acting and easy titratable, with examples including labetalol, esmolol, nitroprusside, nitroglycerin, fenoldopam, and nicardipine. The patient may be switched to oral therapy once there is stable blood pressure control and there are no longer signs or symptoms of end organ damage. Selection of oral therapy and goal blood pressure is dependent upon patient characteristics such as age, race and co-morbidities.

INTRODUCTION

Hypertension is a common chronic condition that affects approximately 78,000,000 adults within the United States [1]. Hypertensive crisis is defined as severe hypertension with a blood pressure of greater than 180/120 mmHg, and may be further classified as urgency or emergency [2,3]. Hypertensive urgency occurs in the setting of days to weeks and patients present most commonly with a headache. Hypertensive emergency occurs in hours to days and the patient presents with evidence of end organ failure and severe headache. Signs and symptoms of end organ failure are listed in (Table 1). An estimated 7% of patients progress to hypertensive emergency prior to being prescribed antihypertensive therapy and 1 to 2% will progress while treated with anti-hypertensive therapy during their lifetime [2,4]. The mortality rate, if hypertensive emergency remains untreated, at 1 and 5 years is 70 to 90% and 100% respectively.

CASE PRESENTATION

A 44 year old white male with a medical history positive for hypertension presents to the emergency room with a chief complaint of headache that started about three days ago, somewhat lessened by aspirin. The onset is during light activity and has been intermittent; it is still present upon admission. The patient has a history of noncompliance, prescribed metoprolol tartrate 50mg twice daily, and in checking with his pharmacy it is found that he has not had his medication filled in over a month. The patient reports a weight gain of 20 pounds over the past few years and complains of excessive fatigue. Review of systems is unremarkable with the exception of complaints of headache. Physical exam reveals a blood pressure of 200/120 mmHg in the right arm, 198/122 mmHg in the left arm, and funduscopic exam reveals arteriovenous (A/V) nicking and papilledema. Laboratory values are within normal limits except for BUN 32 mg/dL and SrCr 2.4 g/dL.

Table 1: Potential findings of end-organ compromise [2,3].

System	Finding
Vital signs	Irregular pulse, blood pressure differential and/or asymmetrical pulses (aortic dissection)
Cardiovascular	S3 heart sound (heart failure), acute chest pain (myocardial infarction or aortic dissection)
Pulmonary	Jugular venous distension (heart failure), carotid pulses
Renal	Dypsnea, pulmonary edema (crackles, rhonchi, rales)
Neurologic	Oliguria or anuria, elevated serum creatinine and blood urea nitrogen
Ophthalmologic	Severe headache, dizziness, altered level of consciousness, lateral gaze
Extremities	Retinopathy, retinal hemorrhage, papilledema, visual changes
	Edema, diminished or delayed pulses

DISCUSSION

Patients at any age may present with hypertensive emergency, common etiologies include undiagnosed hypertension, noncompliance with therapy or inadequate therapy [5].Clinically, the patient would exhibit a blood pressure greater than 180/120 mmHg and target organ dysfunction. The patient in the case presents with a blood pressure of 200/120 mmHg and signs of end organ damage due to an elevated serum creatinine and an funduscopic exam revealing A/V nicking and papilledema.

Timely assessment of a patient with hypertensive crisis is important and should include appropriate measurement of blood pressure, a thorough history and physical and specific testing for end organ damage. The blood pressure should be checked in both arms utilizing an appropriate size cuff so as to not cause false elevations [6]. The cuff bladder must cover 80% of the arm circumference with the patient seated and the arm supported at heart level.

The history and physical examination are crucial to provide details regarding end organ damage. Patients with a history of hypertension should be assessed for duration of the disease, baseline blood pressure values and severity [2,5,7]. Additionally, a thorough medication history should be performed, including both over-the-counter and prescription medications, to evaluate for therapies that may precipitate a hypertensive crisis.

ANTI-HYPERTENSIVE AGENTS

The goal in hypertensive emergency is a reduction in MAP by no more than 25% within the first hour, then reduce to 160/110 to 100 mmHg within the next 2 to 6 hours [8].There are several classes of medications available for treatment of hypertensive emergency; choice of therapy should be based upon end organ damage as outlined in (Table 2) [2,3]. Patients with hypertensive emergency will be admitted to the hospital and treated with intravenous therapy as it is considered to be life-threatening. Preferred agents should be short acting and easily titratable; examples include esmolol, labetalol, nicardipine, fenoldopam, nitroglycerin and nitroprusside.

Esmolol and labetalol are both beta-adrenergic blocking agents utilized in the treatment of hypertensive emergency [2,3,7]. The antihypertensive effects of labetalol administered intravenously begin within 2 to 5 minutes, and peak at 5 to 15 minutes. Labetalol lowers blood pressure by reducing peripheral vascular resistance while maintaining cardiac output in contrast to esmolol which lowers blood pressure by reducing cardiac output. Esmolol has an onset of action within 60 seconds and duration of 10 to 20 minutes. It should be used with caution in patients with chronic obstructive lung disease and avoided in patients already on beta-blocker therapy; patients with bradycardia and those with decompensate heart failure [9].

Nicardipine is a second generation derivative calcium channel blocker with a high vascular selectivity. It has an onset of action between 5 to 15 minutes with duration of 4 to 6 hours and possesses coronary and cerebral vasodilatory properties [10]. Fenoldopam is a selective dopamine-1-receptor antagonist that reduces blood pressure by its vasodilatory action of peripheral dopamine-1 receptors resulting in systemic and renal vasodilation. The onset of action is within 5 minutes with a duration between 30 to 60 minutes [7,11]. Fenoldopam has efficacy in the setting of impaired renal function as clinical evidence has shown an improvement in creatinine clearance, renal blood flow and sodium excretion in hypertensive patients [12]. Its use should be avoided in patients with increased intraocular pressure and intracranial hypertension.

Sodium nitroprusside and nitroglycerin are effective in the treatment of hypertensive emergency in specific scenarios. Sodium nitroprusside is both an arterial and venous vasodilator with an immediate onset and short duration of action. It should be used with caution in patients with renal or liver dysfunction, cerebrovascular accident and coronary artery disease. Sodium nitroprusside contains 44% cyanide by weight that is released non-enzymatically and metabolized in the liver to thiocyanate which is eliminated renally [2,3,7]. Removal of the cyanide from the system is dependent upon the availability of thiosulfate, required for metabolism from cyanide to thiocyanate, renal function and liver function. Cyanide accumulation may result in coma, encephalopathy, convulsions, respiratory failure and irreversible neurological irregularities. Thiocyanate toxicity manifests as psychosis, delirium and possible hypothyroidism. Sodium nitroprusside should be reserved for patients not responding to other IV antihypertensive agents due to the potential toxicity. Nitroglycerin is a preload and after load, at higher doses, reducing agent with efficacy in patients with acute coronary syndrome or acute pulmonary edema presenting with hypertensive emergency.

Table 2: Targeted therapies[2,3,7].

Medication	Population	Dosing
Labetalol	Post-operative hypertension, Ischemic stroke, Hypertensive encephalopathy, Acute cardiac ischemia, Eclampsia	20 to 40mg IV q 30 min (max 300 mg/day) 2 mg/min continuous infusion (max 300 mg/day)
Esmolol	Post-operative hypertension	500 mcg/kg load over 1 minute, infuse at 25 to 50 mcg/kg/min, titrate by 25 mcg/kg/min q 10 to 20 min (max 300 mcg/kg/min)
Nicardipine	Post-operative hypertension, Ischemic stroke, Hypertensive encephalopathy, Acute renal failure, Eclampsia, Systolic heart failure	5 mg/hr, increase by 2.5 mg/hr q 5 to 15 min (max 15 mg/hr)
Fenoldopam	Ischemic stroke, Hypertensive encephalopathy, Acute renal failure, Systolic heart failure	0.1 to 0.3 mcg/kg/min, titrate by 0.1 mcg/kg/min q 15 min (max 1.6 mcg/kg/min)
Sodium Nitroprusside	Systolic heart failure	0.5 mcg/kg/min, titrate by 0.5 mcg/kg/min (max 2 mcg/kg/min)
Nitroglycerin	Acute cardiac ischemia with esmolol or labetalol	5 mcg/min, titrate by 5 mcg/min q 5 to 10 min (max 60 mcg/min)

MONITORING

Once therapy is initiated blood pressure should be measured every 15 to 30 minutes to evaluate response to therapy [13]. Ongoing physical assessment, laboratory and diagnostic testing should be performed during treatment to identify resolution of and new-onset end organ damage. The patient may be switched to oral therapy once the blood pressure is stable and there are no longer signs or symptoms of end organ damage. Selection of oral therapy and goal blood pressure is dependent upon patient characteristics such as age, race and co-morbidities [14].

OUTPATIENT THERAPY

Current guideline recommendations are to initiate therapy with a thiazide diuretic, dihydropyridine calcium channel blocker, angiotensin converting enzyme inhibitor (ACE inhibitor) or angiotensin receptor blocker (ARB) and titrate to a goal diastolic blood pressure of less than 90 mmHg [14]. The preferred agent in patients with diabetes mellitus and/or chronic kidney disease is either an ACE inhibitor or ARB, and in African American patients dihydropyridine calcium channel blocker or thiazide diuretic. Otherwise, selection of agent is dependent upon medication allergies, regimen, availability and cost. Patients should be monitored for attainment of blood pressure goal monthly, if not at goal current therapy dose should be increased or another antihypertensive agent from a different class added to therapy. Blood pressure should continue to be assessed until the patient reaches goal blood pressure. If the patient is unable to reach goal on a two drug therapy regimen at maximum therapeutic dose, a third antihypertensive medication should be added to the regimen. Current recommendations are to not prescribe the use of ACE inhibitors and ARBs simultaneously; other medication classes of antihypertensive medication may be prescribed to gain control of blood pressure if the patient requires greater than a three drug regimen [14]. These include potassium sparing diuretics, vasodilators and alpha agonists.

The goal blood pressure is dependent upon age. Patients less than 60 years of age should be titrated on medication to a goal blood pressure of less than 140/90 mmHg, if greater than or equal to 60 years of age the goal blood pressure is less than 150/90 mmHg [14]. Patients presenting with a blood pressure of greater than 160/100 mmHg should be initiated on therapy with two different antihypertensive therapies.

CASE CONCLUSION

The goal of the patient's therapy would be a reduction in MAP by no more than 25% within the first hour, then reduce to 160/100-110 mmHg within the next 2 to 6 hours using nicardipine 5mg/hr titrate by 2.5 mg/hr every 5 to 15 minutes to a maximum of 15 mg/hr, at goal reduce to 3 mg/hr. An alternative agent would be fenoldopam 0.1 to 0.3 mcg/kg/min titrate by 0.1 mcg/kg/min to a maximum of 1.6 mcg/kg/min. The patient present with A/V nicking and papilledema was indicating increased ocular pressure which is a contraindication to the use of fenoldopam. Nicardipine would be the preferred agent in this patient due to the presence of acute renal failure.

The goal blood pressure and oral antihypertensive therapy for this patient are based upon his age, race and past medical history [14]. The patient presented with an initial blood pressure of 200/120 mmHg in the right arm, 198/122 mmHg in the left arm and signs of acute kidney injury, but this is reversible with appropriate management of the hypertensive crisis. The patient was taking metoprolol tartrate at home, but current evidence no longer supports beta-blocker therapy as a first-line in the treatment of hypertension [14]. Appropriate therapy for this patient would be initiation of amlodipine 5 mg daily with chlorthalidone 25 mg daily. Acutely the patient was treated with the dihydropyridine calcium channel blocker nicardipine, once the blood pressure is controlled and there are no longer signs of end organ failure nicardipine may be titrated off upon initiation of amlodipine. Initiation of dual therapy is appropriate based upon the patient presenting with a blood pressure of greater than 160/100 mmHg to reach his goal of less than 140/90 mmHg [14].

Prior to discharge the patient should receive verbal and written counseling on amlodipine and chlorthalidone. Recommendations on purchase of home blood pressure monitoring devices should be provided, along with instructions on how to appropriately monitor at home [15] .These instructions should include selection of appropriate arm cuff size, when to monitor, how often to monitor, and what to do in situations of multiple elevated blood pressures. The patient should be told to take multiple readings (up to 3 at one minute intervals), monitor at the same time each day, and record and bring measurement log to follow-up appointments [15]. He should also receive counseling on noncompliance and the co-morbidities associated with non- and under- treatment of hypertension. A study by Saguner et al found that non adherence was the most important factor associated with hypertensive crisis [16]. The study concluded that improvement of medical adherence in antihypertensive therapy would assist in preventing admissions for hypertensive crisis.

The pharmacist's role initially begins with medication counseling in the inpatient setting.

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