Clinical Review

Accelerated Hypertension – management in the acute setting

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Abstract

Accelerated hypertension is a rare but life threatening disease. The commonest cause is poorly controlled essential hypertension but other causes exist. Diagnosis is made by the finding of severe hypertension with associated end organ disease affecting brain, eyes, heart or kidney. Treatment should be tailored to the individual patient and usually should be given orally. There is no clear evidence that one class of antihypertensives is more effective than another and the main aim of therapy should be a controlled fall in blood pressure.

Keywords

Hypertension, Accelerated, Emergency management.

Key Points:

1. The commonest cause of accelerated hypertension is poorly controlled essential hypertension.
2. Early diagnosis and institution of anti-hypertensive medication are key to successful treatment.
3. Hypertensive encephalopathy, aortic dissection and seizures require rapid reduction in blood pressure, using intravenous agents with careful monitoring in a high-dependency unit.
4. Gradual reduction in blood pressure using oral medication, is the safest approach in the absence of these complications.

Introduction

Accelerated hypertension is a rare, but potentially life-threatening medical emergency. The mortality associated with hypertensive encephalopathy has fallen from 90% to 10-15% with the advent of more effective treatments, and recognition of its importance.[1,2] The condition is more common in Afro-Caribbean populations, with current incidence in a European population around 1-2/100,000 per year.[3]

Hypertensive urgency vs. emergency

The severity of the accelerated hypertension is determined more by the presence of end-organ damage than by the absolute level of blood pressure (BP). The term '***hypertensive urgency***', is defined as a BP of greater than 110mmHg diastolic, without evidence of end organ damage.[4] This can normally be treated in the outpatient setting, with the aim of reducing BP over a period of a few days.

In contrast, a '***hypertensive emergency***' occurs when elevated blood pressure is associated with evidence of acute end organ damage involving the eyes, brain, heart or kidneys. Such patients require hospital admission to for rapid control of BP. When the brain is involved, as in hypertensive encephalopathy, the patient may suffer decreased conscious level, seizures, coma and death.

It is important to recognise that the absolute level of BP may not be as important as the rate of increase. Patients with longstanding hypertension may tolerate systolic BP of 200 mm Hg or diastolic BP of up to 150 mm Hg without developing hypertensive encephalopathy, while children or pregnant women may develop encephalopathy with diastolic BP 100 mm Hg. Apart from these groups, however, it is unlikely that a hypertensive emergency will develop in a patient with a diastolic BP of less than 110mmHg.[5]

The majority of cases of accelerated hypertension occur in patients with essential hypertension but other, rarer causes should also be considered (see Table 1).

1.	**Poorly controlled essential hypertension**
2.	**Renal Disease-**
	Acute Nephritis
	Vasculitis
	Haemolytic uraemic syndrome/ Thrombotic Thrombocytopaenic Purpura
3.	**Vascular disease-**
	Renovascular disease
4.	**Eclampsia**
5.	**Drugs-**
	Erythropoietin
	Cyclosporine
	Recreational Drugs-Cocaine, LSD, Amphetamines
6.	**Neurological**
	Cerebral Haemorrhage
	Subarachnoid Haemorrhage
	Cerebral Infarction
	Head Injury
	Autonomic Hyper reactivity (Guillain Barre syndrome)
7.	**Endocrine**
	Conns syndrome
	Cushings disease
	Phaeochromocytoma

Table 1. Causes of Accelerated Hypertension.

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Pathophysiology

The pathophysiology of accelerated hypertension is not fully understood. The major systems involved are the Renin Angiotensin system and the endothelium.

The first step appears to be an increase in systemic vascular resistance. Adaptive mechanisms occur within the endothelium (secretion of Nitric Oxide) which initially controls the increase in vascular resistance. Eventually these mechanisms are unable to cope with the increase in vascular resistance, leading to endothelial damage. Fibrinoid necrosis of the arterioles associated with deposition of fibrin and platelets ensues. The resulting ischaemia prompts further release of vasoactive substances, which drives the cycle of destruction.

Hypertensive encephalopathy results from failure of auto-regulation of cerebral blood flow. As systemic blood pressure rises there is a compensatory constriction of cerebral vessels to prevent hyperperfusion. Once a BP of 180-190mmHg systolic is reached in previously normotensive individuals cerebral auto-regulation becomes impaired leading to disruption of endothelial function. The end result of this is micro-haemorrhage and cerebral oedema.

Clinical Assessment

A thorough history and examination should be carried out to identify any precipitating cause, and to assess the presence of end-organ damage.

1. History

The symptoms of accelerated hypertension relate to end organ damage. The patients may also complain of more vague symptoms such as weight loss and non-specific abdominal pain.

Neurological Symptoms

Around 70% of patients will have symptoms of headache prior to the diagnosis being made.[1] The headache may precede severe hypertension by weeks or months.

Other symptoms are of focal neurological deficit relating to cerebral ischaemia, focal intra-cerebral haemorrhage or sub-arachnoid haemorrhage.[1]

Patients with hypertensive encephalopathy may complain of headache, drowsiness, confusion and seizures.

Vision

Up to 70% of patients will note deterioration in their vision prior to presentation.[1]

Cardiovascular Symptoms

Patients may present with increased breathlessness associated with acute left ventricular failure. This occurs as a consequence of pressure overload on the left ventricle. If fibrinoid necrosis develops in the coronary arteries patients may suffer myocardial ischaemia and infarction.

Renal symptoms

Patients may notice oliguria and oedema due to associated acute renal failure. They may have had symptoms relating to pre-existing renal disease or vasculitis.

In addition to enquiry about the above symptoms the history should highlight the following:

Prior history and treatment of hypertension.

Systematic enquiry looking for other causes of hypertension (see Table 1)

Smoking Status

Prior history of renal disease

2. Examination

Examination should include:

Lying and standing BP (to look for concomitant volume depletion)

Palpation of all pulses in extremities

BP in both arms (aortic dissection)

Gallop rhythm (fluid overload)

Bibasal crepitations (fluid overload)

Abdominal examination (renal artery bruits, aortic aneurysm and enlarged kidneys)

Neurological examination looking for focal neurological deficit and to assess conscious level

Fundoscopy (Grade III and IV retinopathy)

(Note that fundoscopic changes are not always found in patients with hypertensive encephalopathy but if present the prognosis is similar for patient with either grade III or grade IV changes)

Purpura and jaundice (secondary to microangiopathic haemolytic anaemia-MAHA)

3. Investigations

Initial investigations need to be carried out to determine the presence and severity of end organ damage (Table 2).

Investigation	Reason
Electrocardiograph	Left ventricular hypertrophy and myocardial ischemia
Chest Radiograph	Cardiomegaly and pulmonary oedema
Urinalysis	Renal parenchymal disease
Urea and Electrolytes	Renal Impairment, hypokalaemia
FBC	Anaemia and thrombocytopenia- Suggestive of MAHA
Echocardiogram	Left ventricular hypertrophy and function
Renal Ultrasound	Renal size and morphology and evidence of underlying parenchymal disease

Table 2. Initial Investigation of Suspected Accelerated Hypertension.

Further investigations should then be undertaken to look for specific causes of hypertension, depending on the clinical presentation.

Treatment

General Principles

Ideal treatment requires the patient to be managed in a high dependency unit for monitoring. This is mandatory if using intravenous (IV) therapy in which case an arterial line should be placed for continuous blood pressure monitoring. The patient should have IV access and if renal

impairment is present a central venous cannula should be inserted. This is useful for identifying concomitant intravascular volume depletion, which is often present due to a pressure induce diuresis. Hydration state should be optimised as hypertension may be exacerbated by volume depletion. If continual BP monitoring is not employed the BP should be estimated every 15 minutes to ensure that the blood pressure is responding to treatment. The patient should also be rested and encouraged not to indulge in stressful activity!

Treatment should also be tailored to the presentation and there is no one correct form of treatment for a hypertensive crisis. There is a lack of randomised evidence to support one treatment regime over another. In an observational study of accelerated hypertension, patients typically received atenolol, followed by bendrofluazide, then hydralazine or nifedipine. Patients with left ventricular failure, advanced renal failure or other contraindications received methyldopa and frusemide.[6] In this study 50% of deaths were from acute myocardial infarction and 13% from stroke. Increasing age and elevated creatinine were associated with a higher mortality.

Initial drug treatment

Oral vs. IV therapy

Intravenous therapy is only indicated when very rapid reduction in BP is required. In practice this means patients with hypertensive encephalopathy, any patient who is having seizures secondary to hypertension and patients with acute aortic dissection. For all other cases, precipitous lowering of blood pressure may be extremely hazardous, resulting in watershed cerebral infarction. Gradual reduction in BP over a period of a few hours using oral therapy is adequate for the vast majority of cases.

Beta Blockers

Oral beta-blockers (e.g. atenolol 50-100mg) are effective therapy for the reduction in blood pressure in hypertensive emergencies.[7] They need to be used with caution in patients with evidence of pulmonary oedema or left ventricular dysfunction, as they may cause worsening of symptoms.

Intravenously, labetalol and esmolol are both useful. Labetalol is a blocker of the alpha and beta-adrenergic receptors. Labetalol produces a prompt and controlled reduction in BP in patients with hypertensive crises. It is commonly used for eclampsia, often in combination with hydralazine. One of the advantages of this drug is that it is also effective as an oral anti-hypertensive agent and once the initial parenteral treatment has been established, it can be followed with oral administration.

Esmolol is a beta-adrenergic blocking agent that has an extremely brief elimination half-life (<10 minutes). This agent is available for intravenous use both as a bolus and as an infusion. The use of both of these drugs should be avoided in acute heart failure as it may lead to a further deterioration. They are also useful in aortic dissection in combination with a vasodilator.

Calcium Channel blockers

Nifedipine (10-20mg) orally has been shown to be effective at reducing blood pressure.[7,8] Nifedipine causes direct vasodilatation of arterioles reducing peripheral vascular resistance promptly. The onset of action begins within 15 minutes of oral administration and peaks at 30 minutes. The duration of action may be four to six hours. It will usually give a gradual decrease in BP. It has also been shown to improve cerebral haemodynamics but the clinical significance of this is uncertain.[8] It should not been given sublingually as this may lead to a precipitous fall in BP with resultant cerebral hypoperfusion. Nifedipine also produces reflex tachycardia, which in turn, in patients with pre-existing coronary artery disease may induce myocardial ischaemia.

Intravenously, nicardipine and nifedipine can be used to treat hypertensive emergencies.[9]

Nitrates

Glyceryl trinitrate and isosorbide dinitrate given either sublingually or by buccal administration are effective at reducing BP. Furthermore, nitrates used as an IV infusion are useful anti-hypertensives especially if the patient has myocardial ischaemia or pulmonary oedema.

Angiotensin converting enzyme inhibitors (ACEI)

ACEI have also been shown to be safe and effective in the treatment of accelerated hypertension although their use is not widespread due to concerns of worsening renal function.[10] In sclerodermic renal crisis (where a predominant feature is hypertension) early administration of ACEI (e.g. enalapril 10mg) has been demonstrated to improve both renal and overall survival. If the patient can not take oral therapy they should be treated with IV enalapril (1.25-5mg).[11]

Care should be taken in patients with underlying vascular disease, or where there is a clinical suspicion of renal artery stenosis, in which case they are contraindicated.

Hydralazine

Hydralazine is a potassium channel opener which may be effective both orally and intravenously. It is the treatment of choice in combination with Labetalol for controlling BP in pre-eclampsia. Administration in combination with a beta-blocker may reduce the tendency for this drug to cause a reflex tachycardia.

Sodium Nitroprusside

Sodium nitroprusside is a combined arterial and venous vasodilator, which decreases both the afterload and preload. It is effective only when used IV, but extremely potent. The onset of action of this drug is within seconds, with duration of action of one-to-two minutes and a plasma half-life of three to four minutes. Care has to be taken to avoid a precipitous drop in BP. The dose range is 0.25-10microgrammes/kg/min. Continuous BP measurement is recommended. If the infusion is stopped, the BP begins to rise immediately and returns to the pre-treatment level within one to ten minutes.

Nitroprusside is degraded by light and therefore the infusion has to be shielded. It should not be given for greater than 48 hours due to the potential for thiocyanate poisoning.

Further treatment

If initial treatment with intravenous therapy or short-acting oral therapy has been required, conversion to maintenance oral therapy should occur as soon as BP has been stabilised. As there appears to be little difference in efficacy and outcomes between different anti-hypertensive groups the decision on which to use will depend on the patient characteristics.

Prognosis

After initial treatment and stabilisation of BP the long-term prognosis is dependent on end organ damage, especially of the kidneys and heart. Renal function will usually recover, unless there is underlying glomerulonephritis.[12] Long term follow up is required to ensure BP remains well controlled, to limit ongoing end-organ damage.

Conclusions

At present no treatment is proven to be superior for hypertensive emergencies. The treatment used is dependent on experience and the particular clinical setting. Whatever what drug is used the main treatment goal is to reduce the BP, and the risk of end-organ damage.

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