European Society of Hypertension Scientific Newsletter:
Update on Hypertension Management
2006; 7: No. 28

TREATMENT OF HYPERTENSIVE URGENCIES AND EMERGENCIES

Enrico Agabiti Rosei, Massimo Salvetti, Department of Internal Medicine, University of Brescia, Italy and Csaba Farsang, 1st Department of Internal Medicine, St. Emeric Hospital, Budapest, Hungary

Hypertensive emergencies can be defined as severe elevations of blood pressure (BP) in the presence of acute target organ damage. Acute coronary syndromes, dissecting aortic aneurisms, acute pulmonary edema, hypertensive encephalopathy, acute cerebral infarction, intracerebral haemorrhage or acute arterial bleeding or eclampsia represent clinical conditions in which an immediate blood pressure reduction is needed to prevent the progression of target-organ damage (TOD) (Table 1). *Hypertensive urgencies* are characterised by severe elevations in BP (> 180/120 mm Hg) without evidence of acute TOD. In hypertensive urgencies BP can usually be reduced in the emergency department (ED) by orally administered drugs without hospital admission and with ambulatory follow-up [1].

Initial evaluation

Appropriate triage of patients is a crucial part of the initial evaluation. After a complete history (with particular attention to pre-existing hypertension and TOD) and an accurate physical examination (including fundoscopic examination), selected laboratory studies such as urinanalysis, creatinine, urea, electrolytes and a full blood count should be performed. When a secondary form of hypertension is suspected a sample for plasma renin activity, aldosterone and catecholamines should also be drawn. It is advisable to obtain in each patient an electrocardiogram and a chest radiogram (Table 2).
Blood pressure should be measured according to current Guidelines, both in sitting and standing positions [2]. A significant difference in BP between the two arms should raise the suspicion of aortic dissection. In the ED blood pressure should then be strictly monitored.

Treatment of hypertensive emergencies

Patients should be admitted to an intensive care unit for clinical surveillance and continuous BP monitoring. Aggressive treatment with parenteral drugs will be the preferred approach; in the majority of cases, however, the initial goal should be a partial reduction (and not normalisation) of BP, with a reduction in BP of no more than 20–25% within the first minutes up to one or two hours, with possible cautious further decreases in subsequent hours [3, 4]. In most hypertensive emergencies a rapid lowering of BP is beneficial, with the exception of cerebrovascular accidents, in which it is advisable to take a more cautious approach [5–7]. An excessive reduction of BP values is potentially dangerous, possibly leading to ischaemic complications such as acute myocardial infarction and stroke.

Several parenteral agents are available for the treatment of hypertensive emergencies (Table 3); the choice of first-line antihypertensive agents should be tailored to the patient's clinical status.

Table 1. Hypertensive emergencies

Hypertensive encephalopathy
Severe hypertension associated to acute target organ damage: — acute coronary syndromes — pulmonary edema — acute aortic dissection — intracerebral haemorrage, subarachnoid haemorrage — acute brain infarction — acute or rapidly progressing renal failure
Severe hypertension after thrombolysis for ischemic stroke
Pheochromocytoma crisis
Guillain-Barré syndrome
Spinal cord injury
Drugs related hypertension (sympathomymetics, cocaine, phencyclidine, phenylproponolamine, lysergic acid diethylamide, cyclosporin, antihypertensive treatment withdrawal, interaction with MAO inhibitors)
Eclampsia
Postoperative bleeding
Post coronary artery bypass hypertension

Table 2. Diagnostic workup

Repeated blood pressure measurements (first measurements at both arms)
Clinical history and physical examination: — cardiovascular — CNS — fundus oculi
Selected laboratory studies: — urinanalysis, creatinine, urea, electrolytes and a full blood count — when a secondary form of hypertension is suspected a sample for plasma renin activity, aldosterone and eventually catecholamines should also be drawn
Electrocardiography
Chest X rays
Further investigations (according to the clinical presentation): — echocardiography (TT, TE) — brain CT scan or MRI — abdominal ultrasonography — thoraco-abdominal CT scan or MRI — vascular ultrasound

Table 3. Drugs for hypertensive emergencies

Drug	Dose	Onset	Duration	Adverse effects
Sodium nitroprussiate	0.25–10 μg/kg/min	Immediate	1–2 min	Hypotension, vomiting, cyanate toxicity
Labetalol	20–80 mg bolus 1–2 mg/min infusion	5–10 min	2–6 h	Nausea, vomiting, heart block, bronchospasm
Glyceryl trinitrate	5–100 μg/min	1–3 min	5–15 min	Headache, vomiting
Enalaprilat	1.25–5.00 mg bolus	15 min	4–6 h	Hypotension, renal failure, angioedema
Furosemide	40–60 mg	5 min	2 h	Hypotension
Fenoldopam	0.1–0.6 μg/kg/min	5–10 min	10–15 min	Hypotension, headache
Nicardipine	2–10 mg/h	5–10 min	2–4 h	Reflex tachycardia, flushing
Hydralazine	10–20 mg bolus	10 min	2–6 h	Reflex tachycardia
Phentolamine	5–10 mg/min	1–2 min	3–5 min	Reflex tachycardia
Urapidil	25–50 mg bolus	3–4 min	8–12 h	Sedation

Nitroprusside is a highly effective short acting arteriolar and venous dilator, which can be used in most hypertensive emergencies. In patients with primary intracerebral haemorrhage caution is needed because of a potential antiplatelet effect and intracranial pressure increase. The risk of cyanate toxicity is greater when the drug is used for long periods (days) or in patients with hepatic or renal dysfunction. With nitroprusside BP should be continuously monitored intra-arterially; hypotension can, however, be managed in most cases by discontinuing the infusion. *Nitroglycerin* is a venous and, to a lesser degree, arteriolar dilator, particularly indicated in acute coronary syndromes and pulmonary edema. *Labetalol* is an alpha- and beta-adrenergic blocker, which can be given as an intravenous bolus or infusion; it is highly effective and is indicated in most hypertensive emergencies, in particular in aortic dissection and in acute coronary syndromes. It may be given also after cocaine or amphetamine use, that may induce transient but significant hypertension leading to stroke and/or serious cardiac damage. *Urapidil,* an alpha-blocker with additional actions in the central nervous system (it activates 5-HT_{1A} receptors) has also been found effective, since it induces vasodilatation without tachycardia. Finally it must be remembered that *furosemide* can be particularly indicated when volume overload is present, as in left ventricular failure. In the presence of volume depletion, in contrast, diuretics could cause additional reflex vasoconstriction and should therefore be avoided.

Specific hypertensive emergencies

In patients with *acute coronary syndromes* a severe elevation of BP values is not uncommon; on the other hand, myocardial ischaemia may also be induced by acute elevations in BP in patients without haemodynamically relevant coronary artery disease through an increase in left ventricular wall stress and myocardial oxygen consumption. In this setting intravenous vasodilators, such as nitroglycerin and nitroprusside, should be the initial drugs, in combination with a beta-blocker (labetalol, metoprolol, esmolol or atenolol), which may further decrease BP and reduce heart rate and, consequently, myocardial oxygen consumption. In the presence of *acute left ventricular failure* BP should be rapidly controlled. The preferred drugs are intravenous nitroglycerin or nitroprusside in combination with loops diuretics for volume overload control. In patients with *aortic dissection* and hypertension BP control is crucial. The treatment should be started immediately and systolic BP rapidly reduced to less than 100 mm Hg; the ideal drug should not only allow the reduction of BP but also reduce heart rate and cardiac contractility with the aim of reducing stress on the aortic wall. This can be achieved with a combination of a beta-blocker and a vasodilator, such as nitroprusside or nitroglycerin, administered intravenously. *Pheochromocytoma crises* can be managed with an intravenous alpha-blocker such as phentolamine, followed by the concomitant infusion of a beta-blocker; nitroprusside may also be added. Beta-blockers should always be associated with alpha-blockers in patients with pheochromocytoma, since inhibition of beta-receptor induced vasodilation may lead to a further increase in BP values in the presence of alpha-adrenergic vasoconstriction. Simultaneous alpha- and beta-blockade may be also achieved with monotherapy with labetalol. In patients with *acute stroke* the use of antihypertensive therapy is still controversial. Autoregulation of blood flow is impaired in ischaemic areas of the brain, and BP reduction may further reduce flow in the ischaemic penumbra and further expand the size of the infarction. It seems reasonable to recommend the institution of antihypertensive treatment only in the presence of BP values above 220/120 mm Hg (or mean BP > 140 mm Hg) in ischaemic stroke and to obtain an initial reduction of BP values of about 10–15%. Treatment may be initiated with intravenous labetalol, and, if needed, with nitroprusside or nitroglycerin. In patients with acute stroke treated with thrombolysis BP should be kept below 185/110 mm Hg. In primary *intracerebral haemorrhage* treatment should be started if BP values are greater than 180/105 mm Hg. *Acute postoperative hypertension* is not uncommon, particularly after cardiothoracic, vascular, head and neck and neurosurgical procedures. For most non-cardiac types of surgery there is no agreement on BP thresholds for treatment, and the patient's baseline BP, type of surgical procedure and associated clinical conditions should be taken into account in patient management. It seems reasonable to maintain blood pressure within 20% of preoperative arterial pressure. For cardiothoracic surgery there is more evidence of an increased risk associated with a postoperative increase in BP values, which should be kept below 140/90 mm Hg [8, 9]. Labetalol (and other beta-blockers), nitroprusside, nitroglycerin, or fenoldopam should be the preferred intravenous drugs for BP control.

Treatment of hypertensive urgencies

In the majority of patients with severe hypertension no signs of acute TOD are usually observed. In these patients BP should be lowered gradually over a period of 24–48 hours; this can often be achieved by orally administered drugs without hospital admission and with close ambulatory follow-up. Clinical surveillance is advisable during the first few hours after drug administration. Blood pressure lowering should be gradual: there is no proven benefit from a rapid reduction in BP in asymptomatic patients who have no evidence of acute TOD, and the precipitous fall in BP could do more harm than good. In Table 4 recommended oral agents for hypertensive urgencies are reported. An initial approach with a combination of antihypertensive drugs will increase the likelihood of effective BP reduction. The degree of BP reduction induced by sublingual nifedipine can neither be predicted nor controlled and this preparation is not recommended [10].

Conclusions

In the presence of severe elevations of BP a prompt and accurate initial work-up is crucial for the identification of acute TOD. Treatment should be started promptly in the ED with parenteral or oral drugs according to the findings of the initial evaluation. Blood pressure should be rapidly reduced but a precipitous fall in BP should be avoided and, in the majority of cases, reduction rather than normalisation of blood pressure should be the initial goal of treatment.

Table 4. Drugs for hypertensive urgencies

Drug	Dose	Time to peak	Half life	Side effects
Captopril	12.5–25 mg p.o.	15–60 min	1.9 h	Renal failure in patients with renal artery stenosis
Labetalol	200–400 mg p.o.	20–120 min	2.5–8 h	Bronchospasm, depression of myocardial contractility, A-V block, nausea, elevation of liver enzymes
Furosemide	25–50 mg p.o.	1–2 h	0.5–1.1 h	Volume depletion
Amlodipine	5–10 mg p.o.	1–6 h	30–50 h	Headache, tachycardia, flushing, peripheral edema
Felodipine	5–10 mg p.o.	2–5 h	11–16 h	Headache, tachycardia, flushing, peripheral edema
Isradipine	5–10 mg p.o.	1–1.5 h	8–16 h	Headache, tachycardia, flushing, peripheral edema
Prazosin	1–2 mg p.o.	1–2 h	2–4 h	Syncope (first dose), palpitations, tachycardia, orthostatic hypotension

References

1. Vaughan CJ, Delanty N. Hypertensive emergencies. Lancet 2000; 356: 411–417.
2. Guidelines Committee. 2003 European Society of Hypertension — European Society of Cardiology guidelines for the management of arterial hypertension. Journal of Hypertension 2003; 21: 1011–1053.
3. Varon J, Marik PE. Clinical review: The management of hypertensive crises. Critical Care 2003; 7: 374–384.
4. Elliott WJ. Management of Hypertension Emergencies. Current Hypertension Reports 2003; 5: 486–492.
5. International Society of Hypertension Writing Group. International Society of Hypertension (ISH) Writing Group: statement on the management of blood pressure in acute stroke. Journal of Hypertension 2003; 21: 665–672.
6. Brott T, Bogousslavsky J. Drug therapy: treatment of acute ischemic stroke. N Engl J Med 2000; 343: 710–722.
7. Goldstein LB. Blood pressure management in patients with acute ischemic stroke. Hypertension 2004; 43: 137–141.
8. Howell SJ, Sear JW, Foex P. Hypertension, hypertensive heart disease and perioperative cardiac risk. Br J Anaesth 2004; 61: 1661–1675.
9. Haas CE, Leblanc JM. Acute postoperative hypertension: a review of therapeutic options. Am J Health Syst Pharm 2004; 61: 1661–1675.
10. Grossman E, Messerli FH, Grodzicki T, Kowey P. Should a moratorium be placed on sublingual nifedipine capsules given for hypertensive emergencies and pseudoemergencies? JAMA 1996; 276: 1328–1331.