

## ACCELERATED (MALIGNANT) HYPERTENSION

### Supporting information

This guideline has been prepared with reference to the following:

NICE. Hypertension in adults: diagnosis and management. 2023. London. NICE

<https://www.nice.org.uk/guidance/ng136>

### Recognition and assessment

**Risk of organ damage (eyes, strokes, encephalopathy, left ventricular seizure, renal failure) is high and immediate?**

A 2020 systematic review of eight observational studies found that the risk of acute pulmonary oedema/heart failure was 32%, ischaemic stroke 29%, acute coronary syndrome 18%, haemorrhagic stroke 11%, acute aortic syndrome 2%, and hypertensive encephalopathy 2% (Astarita, 2020).

Astarita A, Covella M, Vallelonga F et al. Hypertensive Emergencies and Urgencies in Emergency Departments: A Systematic Review and Meta-Analysis. *J Hypertens* 2020;38:1203-10

**Evidence Level: II**

### Immediate treatment

**Sustained high blood pressure alters cerebral auto-regulation?**

Hypertension has the effect of resetting the range of cerebral auto-regulation upwards, so that a decrease in cerebral blood flow occurs at a higher blood pressure than in normotensive patients (Gifford, 1991). A study of auto-regulation (Strandgaard, 1976) found that the lower limit occurred at an average mean arterial pressure of 113 mm Hg in 13 untreated hypertensive patients compared with 73 mm Hg in 10 normotensive patients.

Gifford RW. Management of hypertensive crises. *JAMA* 1991;266:829-35

Strandgaard S. Autoregulation of cerebral blood flow in hypertensive patients: the modifying influence of prolonged antihypertensive treatment on the tolerance to acute, drug-induced hypotension. *Circulation* 1976; 53: 70-7

<http://circ.ahajournals.org/content/53/4/720.long>

**Evidence Level: V**

**Sudden reduction of blood pressure will reduce cerebral perfusion and can be dangerous?**

In both normotensive and hypertensive individuals, the lower limit of cerebral auto-regulation is roughly 25% below the resting mean arterial pressure (MAP) (Gifford, 1991). Accordingly, the aim of treatment is to reduce MAP by 20-25% over a period of minutes to hours, depending on the nature of the emergency. Case reports (Ledingham, 1979; Graham, 1975) have demonstrated that patients with severe hypertension develop cerebral ischaemia or infarction when their blood pressure is suddenly lowered to normotensive levels, or by  $\geq 40\%$  (Dinsdale, 1983), due to inability of the "reset" auto-regulation mechanism to adjust quickly enough.

Dinsdale HB. Hypertensive encephalopathy. *Neurol Clin* 1983;1:3-16

Gifford RW. Management of hypertensive crises. *JAMA* 1991;266:829-35

Graham DI. Ischaemic brain damage of cerebral perfusion failure type after treatment of severe hypertension. *BMJ* 1975;4:739

<http://europepmc.org/backend/ptpmcrender.fcgi?accid=PMC1675562&blobtype=pdf>

Ledingham JG, Rajagopalan B. Cerebral complications in the treatment of accelerated hypertension. *Q J Med* 1979;48:25-41

<http://qjmed.oxfordjournals.org/content/48/1/25.full-text.pdf>

**Evidence Level: V**

**Parenteral therapy is indicated if the patient has hypertensive encephalopathy?**

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The risk of over-rapid reduction of blood pressure with parenteral therapy has to be balanced against that of irreversible target organ damage if treatment is not given. Hypertensive encephalopathy causes neurological damage of this degree of severity if untreated (Isles, 1994; Gifford, 1991).

Anderson RJ, Reed WG. Current concepts in treatment of hypertensive urgencies. *Am Heart J* 1986;111:211-9

Gifford RW. Management of hypertensive crises. *JAMA* 1991;266:829-35

Isles CG. Malignant hypertension and hypertensive encephalopathy. In: Swales JD (ed). *Textbook of hypertension*. Oxford: Blackwell Scientific, 1994. p1242

#### **Evidence Level: V**

#### **Patients without hypertensive encephalopathy, aortic dissection, intracranial haemorrhage, phaeochromocytoma crisis, acute pulmonary oedema, acute renal insufficiency or unstable may be treated with oral hypotensive drugs?**

In general, hypertensive emergencies (i.e. those threatening imminent target organ damage) are treated with parenteral drugs, and hypertensive urgencies (i.e. with no immediate threat of target organ damage) with slower-acting oral drugs to avoid the dangers of over-rapid reduction in blood pressure. Patients who are not emergencies but who are comatose or otherwise unable to take oral medication (e.g. in the immediate postoperative period) may, however, be treated with parenteral drugs (Gifford, 1991). Oral drugs are indicated in uncomplicated malignant hypertension, so long as blood pressure can be reduced within 24 hours (Gifford, 1991; Calhoun, 1990; Anderson, 1986).

Calhoun DA, Oparil S. Treatment of hypertensive crisis. *N Engl J Med* 1990;323:1177-83

Gifford RW. Management of hypertensive crises. *JAMA* 1991;266:829-35

#### **Evidence Level: V**

#### **Sublingual nifedipine can be dangerous when used for lowering blood pressure?**

Although administration of nifedipine capsules has been reported to be expedient and safe, it has not been approved by the FDA for labeling for treatment of hypertensive emergencies or of any other form of hypertension because of lack of outcome data. A review of the literature revealed reports of serious adverse effects such as cerebrovascular ischemia, stroke, numerous instances of severe hypotension, acute myocardial infarction, conduction disturbances, fetal distress, and death. Sublingual absorption of nifedipine has been found to be poor; most of the drug is absorbed by the intestinal mucosa. Given the seriousness of the reported adverse events and the lack of any clinical documentation attesting to a benefit, the use of nifedipine capsules for hypertensive emergencies and pseudoemergencies should be abandoned (Grossman et al, 1996).

Grossman E, Messerli FH, Grodzicki T et al. Should a moratorium be placed on sublingual nifedipine capsules given for hypertensive emergencies and pseudoemergencies? *JAMA*. 1996;276:1328-31

#### **Evidence Level: IV**

#### **Lowering diastolic blood pressure below 110-115 mm Hg in the first few days of controlling malignant hypertension is dangerous?**

The sudden reduction of blood pressure in malignant hypertension to "normal" levels reduces cerebral perfusion and disposes to end-organ ischaemia or infarction (Reed, 1986). Lowering the diastolic pressure to 110 mm Hg over several minutes to several hours, depending on the clinical situation, is regarded as a "reasonable goal" in order to relieve the emergency whilst avoiding this problem (Calhoun, 1990). This should be maintained "for several days" and then reduced to normotensive levels over the ensuing weeks, thus allowing the autoregulation mechanism time to adjust to the new levels (Calhoun, 1990).

Calhoun DA, Oparil S. Treatment of hypertensive crisis. *N Engl J Med* 1990;323:1177-83

Reed WG, Anderson RJ. Effects of rapid blood pressure reduction on cerebral blood flow. *Am Heart J* 1986;111:226-32

#### **Evidence Level: V**

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### **Sodium nitroprusside or labetalol by IV infusion is the most effective treatment if the situation demands that blood pressure be reduced rapidly?**

IV sodium nitroprusside has a rapid onset of action (1-2 min) and a short duration of action (1-5 min) which makes it particularly suited for emergency use (Isles, 1994). It remains the drug of choice in hypertensive emergencies and is almost universally efficacious (Friederich, 1995). A randomised, prospective clinical study (Hirschl, 1997) compared sodium nitroprusside with urapidil in 81 patients with blood pressure > 200/110 mm Hg. Efficacy was defined as blood pressure reduction below 180/95 mm Hg within 90 mins. This was achieved in 75 (93%) patients (nitroprusside: n=34 [97%]; urapidil: n=41 [89%]).

Labetalol is a combined alpha and beta-blocker also suitable for emergency reduction of blood pressure (Ram, 1991). In a study of 14 patients with severe hypertension, (Van den Bogaard 2013) 8 patients were treated with sodium nitroprusside and 6 patients were treated with intravenous labetalol before and after treatment for malignant hypertension. They found no difference in central systolic blood pressure (SBP) or diastolic blood pressure (PP) in subjects treated with SNP and labetalol, but labetalol produced a greater reduction in peripheral SBP and peripheral PP in the immediate treatment of malignant hypertension.

Friederich JA, Butterworth JF. Sodium nitroprusside: twenty years and counting. *Anesth Analg* 1995;81:152-62

Hirschl MM, Binder M, Bur A, et al. Safety and efficacy of urapidil and sodium nitroprusside in the treatment of hypertensive emergencies. *Intensive Care Med* 1997;23:885-8

Isles CG. Malignant hypertension and hypertensive encephalopathy. In: Swales JD (ed). *Textbook of hypertension*. Oxford: Blackwell Scientific, 1994. p1242

Ram, CV. Management of hypertensive emergencies: changing therapeutic options. *Am Heart J* 1991;122:356-63

Van den Bogaard B, Immink RV, Westerhof BE et al. Central versus peripheral blood pressure in malignant hypertension; effects of antihypertensive treatment. *Am J Hypertens* 2013; 26: 574-9.

#### **Evidence Level: IV**

### **Volume repletion is useful in the treatment of hyponatraemic hypertensive syndrome?**

Polyuria and consequent dehydration are key features of this syndrome and can result in high blood pressure becoming even higher (Brown, 1965), or in profound hypotension in response to small doses of converting enzyme inhibitors (Anon, 1986). Volume repletion restores the balance (Thomas, 1976).

Anon. Hyponatraemic hypertensive syndrome. *Lancet* 1986;i:718-9

Brown JJ, Davies DL, Lever AF, et al. Plasma renin concentration in human hypertension. 1: Relationship between renin, sodium, and potassium. *BMJ* 1965;ii:144-8

<http://europepmc.org/backend/ptpmcrender.fcgi?accid=PMC1845718&blobtype=pdf>

Thomas RD, Lee MR. Sodium repletion and beta-adrenergic blockade in treatment of salt depletion with accelerated hypertension. *BMJ* 1976;ii:1425-6

<http://europepmc.org/backend/ptpmcrender.fcgi?accid=PMC1690352&blobtype=pdf>

#### **Evidence Level: V**

## **Subsequent management**

### **Subsequent management after initial control of malignant hypertension is best maintained by atenolol, labetalol, or nifedipine?**

Patients may generally be sent home on the same type of medication that was administered in the accident and emergency department (Calhoun, 1990). Compliance may be better with atenolol than with nifedipine due to reduced side effects (Fletcher, 1992).

Calhoun DA, Oparil S. Treatment of hypertensive crisis. *N Engl J Med* 1990;323:1177-83

Fletcher AE, Bulpitt CJ, Chase DM, et al. Quality of life with three antihypertensive treatments: cilazapril, atenolol, nifedipine. *Hypertension* 1992;19:499-507

[http://hyper.ahajournals.org/content/19/6\\_Pt\\_1/499.long](http://hyper.ahajournals.org/content/19/6_Pt_1/499.long)

#### **Evidence Level: V**

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