Hypertension

Definitions (WHO).

- Mild HT/Grade I: 140/90 – 159/99
- Moderate HT/Grade II: 160/100 – 179/109
- Severe HT/Grade III: ≥180/110

Epidemiology

- ↑Risk of CVS disease
- >90% of >80yo affected. Elderly females more likely to be refractory to Rx
- Most primary HT, consider secondary causes esp if a crisis.

Management:

- Rapid reduction of BP in asymptomatic may be detrimental.
- Incidental HT in ED – common, refer to LMO unless a crisis when urgent Rx is needed
- **Hypertensive crisis** = Hypertensive Emergency or Hypertensive Urgency

Hypertensive Emergency

Acute hypertension >180/120 (diastolic usually >130) assoc with end organ dysfunction.
Clinical syndromes:

- Hypertensive encephalopathy. Abrupt MAP>160mmHg exceeds autoregulation → vasospasm → ischaemia → cerebral oedema/bleeds. Triad HT+ALOC+retinopathy. Symptoms of ↑ICP. Inv end organ damage: CT, ECG, CXR, Cr/Ur, urinalysis, ophthal. Rx: ABC, IV **SNP** or **labetalol** to reduce MAP by 20-25% in ~2-4hrs (min BPdia of 110mmHg) Mx: usually combination Rx: e.g. **SNP** + **β-blockers** or **nitrates**.
- Hypertensive retinopathy (see below) – Grade III – IV.
- APO – **nitrates**, (& NIV), avoid drugs which give reflex ↑HR
- Aortic dissection – IV **β-blockers** (to HR 60) + **SNP** or **nicardipine** →BPsys 110-120mmHg
- Acute renal insufficiency/RAS – **CCB** or **SNP**, **hydralazine**. ?Diuretics.
- Pre-eclampsia/HELLP – **$MgSO_4$ ± hydralazine** or **labetalol**. Delivery if antenatal.
- ICH/SAH – **nicardipine**: lower to MAP 110-130 (sysBP 180-160mmHg). Avoid **SNP** and **hydralazine**
- CVA – thrombolysis /neuroSx if eligible, **nicardipine** if BP>220/120 (or >185/105 if for thrombolysis). Aim to reduce BP by 10-15% over 24hrs.
- Ischaemic chest pain – **nitrates** etc
- Hyperadrenergic states e.g. stimulant toxicity, thyroid storm, phaeochromocytoma may resemble HT emergency but need to target adrenergic excess rather than HT per sae – often use **BDZ**, **phentolamine**, **nitrates**/ **SNP** **NOT β-blockers**

Common path in HT crisis = fibrinoid necrosis & endothelial damage/loss of autoreg.
Lifestyle: Wt reduction, exercise, salt restriction, high potassium diet
Pharmacological: See below. Note ACEI less effective in black-skinned patients.

Hypertensive Urgency

- Usually BP>180/120. No end organ dysfunction yet. Reduce BP over 24-48hrs.
- Can usually use an oral antihypertensive e.g. ACEI

Malignant Hypertension

- Progressive severe HT + hypertensive retinopathy +/- headache, but no encephalopathy

Types of Pharmacological Agents

- Some may be used together in combination formulations. ♥ = Drug used in HT Emergency:

Direct vasodilators

- ♥ ***sodium nitroprusside (SNP)*** – veins>arterioles. Activates guanyl cyclase via NO. Unstable in light. $T_{1/2}$ 1min. Met by RBC to CN and then by liver to thiocyanate ($T_{1/2}$ 3-7 days). SE: ↑ICP, HypoBP, thioCN & CN toxicity if prolonged use. Dose: 0.5-10mcg/kg/min.
- ♥ ***GTN*** – mild to mod antiHT effect (also used in ACS, APO, oesophageal spasm). Veins>arteriole. Infusion dose: 3-200mcg/min IV.
- ♥ ***hydralazine*** – Reduces BPdia>BPsys. $T_{1/2}$ 2-4hrs. SE: lupus-like syndrome, nausea, headache, reflex ↑HR. Dose: 5mg IV increments. 25-100mg PO.
- ***diazoxide*** – ?Antag. Ca^{2+}→peripheral arteriolar dilatation. SE: ↑BSL, may → angina as ↑HR & CO, interrupts labour, can't give IM/via CVC. Painful IV. Protein bound. $T_{1/2}$ 20hrs.
- ***minoxidil*** – Opens K+ channels in smooth muscle. SE: hair growth, periph. oedema.
- ***fenoldopam*** – Dop agonist^{+}→periph arteriolar dilatation. IV infusion: 0.1-1.6mcg/kg/min

Alpha1 blockers

- ***prazosin*** – specific α1blocker. Blocks NA, causes arteriolar & venous dilatation. Well abs from GIT. Hep. metab. excr. In bile/faeces. $T_{1/2}$ 3hrs. SE: 1st dose HypoBP, reflex ↑HR, urinary incontinence (so used in BPH). Dose 0.5-5mg bd
- ***doxazosin*** - $T_{1/2}$ 22hrs. Daily dosing of 1-4mg.
- ***phentolamine*** - α1 & α2 competitive antagonist. Direct arterial vasodilator. Used in adrenal crisis and stimulant overdose. Also may be used if intra-arterial injection of thiopentone or adrenaline.

Beta blockers (CI: stimulant use, asthma, CCF)

- ***atenolol*** – β1 selective. $T_{1/2}$ 7-9hrs. Effects on HR, contractility, ↓BP, ↓IOP, ↓renin. SE: Slows AV conduction, heart block, may precipitate LVF, bronchoconstriction, may mask hypoglycaemia, lethargy, depression. Acute dose: 1mg increments to 15mg.
- ♥ ***metoprolol*** – β1> β2 blocker. Rapid 1st pass metab. IV Dose 1mg increments to 5mg. In aortic dissection can give 3 x 5mg doses
- ***propranolol*** – Non-selective. Also blocks Na+ channels. High 1st pass metab.hep metab & renal excretion. $T_{1/2}$ 3-6hrs.
- ♥ ***esmolol*** – very short acting β1 selective. Load 500mcg/kg over 1 min, then slow 50mcg/kg/min for next 4 mins. Titrate then to infusion 50-200mcg/kg/min.

Combined α-blockers & β-blockers (CI: stimulant use, asthma, CCF)

- ♥ ***labetalol*** – Renal/liver excretion. $T_{1/2}$ 6-8hrs. 10-20mg IV q10min or 1-2mg/min IV
- ***carvidilol*** – racemic with enantiomers have different effects. Lipophilic. 1st pass metab. Highly protein bound. $T_{1/2}$ 6-10hrs. SE: dizziness, diarrhoea+usual.

Calcium Channel Blockers

- Block Ca^{2+} flow though voltage-gated L-type (slow inactivating) channels. Hepatic metab.
- ***verapamil*** – racemic mixture, non-selective CCB, relaxes arteriolar sm. SE: Depresses cardiac contractility(→HF). Slows SA & AV nodes (→block, may promote aberrant pathways). Slows gut motility (→constipation). 90% protein bound. $T_{1/2}$ 3-6hrs. Dose 1mg IV increments. PO 40-80mg, 160mg SR.
- ***diltiazem*** – Cardioselective CCB. SE: AV block, HF
- ***nicardipine*** – Dihydropyridine CCB. Doesn't ↓LV function or sig ↑ICP. Longer $T_{1/2}$, so cannot rapidly titrate. CI: heart block, recent AMI, RF. Dose 5-15mg/hr infusion. PO dose 20-40mg tds or 30-60mg bd or SR prep.

- ***nifedipine***, ***amlodipine*** – selective relaxation of arteriolar sm. No cardiac depression – more often reflex stim. (less with SR preps). Nifedipine: onset within 1hr – faster if capsule perforated. SE: Rapid BP drop (capsules), reflex ↑HR, angina, headache, periph. oedema, flushing, nausea, hypoK^+, teratogenic in early preg. Amlodipine – $T_{1/2}$ 35-45hrs.

ACE Inhibitors

- Block A(I) → A(II). Also block bradykinin metab → dry cough, angioedema. Particularly useful with diabetic nephropathy. SE: hyperK^+, proteinuria, worsening renal fn if RAS.
- ***captopril*** – 60% Metab Liver, rest excr unchanged by kidney. $T_{1/2}$ 2hrs.
- ***perindopril*** – A(II)CE inhibitor, renal excretion, $T_{1/2}$ >24hrs. od dosing.
- Others: ***enalapril*** - $T_{1/2}$ 11hrs. od/bd dosing; ***ramipril*** - $T_{1/2}$ 50hrs; ***lisnopril*** – 100% renally excreted unchanged.

Angiotensin II Receptor Blockers

- As effective as ACEI, β-blockers, CCB or diuretics. Don't affect bradykinin metab.
- ***losartan*** - AT(II)-1 receptor antagonist. Highly protein bound. Hep metab & Biliary excr→urine & faeces. $T_{1/2}$ 2hrs. V. active metab (EXP3174) with $T_{1/2}$ 6-9hrs.
- ***candesartan*** - AT(II)-1 receptor antagonist. Highly protein bound. Renal excr. $T_{1/2}$ 9hrs. SE: GIT effects, periph.oedema.
- ***irbesartan*** - AT(II)-1 receptor antag. Highly protein bound. Hep metab. $T_{1/2}$ 12-20hrs.

Diuretics

- Loop diuretics (***frusemide***) – Used often when renal impairment. Inhibit luminal $Na^+/K^+/2Cl^-$ transporter in thick ascending loop of Henle. Increase renal blood flow & PG synthesis. Loss of Na^+, Cl^-, K^+, Mg^{2+}, & Ca^{2+}. Highly protein bound, urinary excr. $T_{1/2}$ 1.5hrs. SE: salt loss, ↑uric acid, rashes, ototoxicity (esp. rapid IV admin). NSAIDs may ↓effect
- Thiazides (***bendrofluazide***, ***hydrochlorothiazide***) – Inhibit Na^+ & Cl^- resorption in proximal segment of distal tubule. Also vasodilatation via Ca^{2+}-dependent K^+ channels in blood vessels. Urinary excreted unchanged. SE: hypoNa^+, hypoK^+, ↑uric acid, ↓BSL, sulphur containing (allergic reactions)
- Potassium sparing (***spironolactone***, ***amiloride***) – Mild naturetic effect on collecting ducts. Used when mineralocorticoid excess. Spironolactone binds at aldosterone Na^+/K^+ exchange site in distal convoluted tubule. May cause gynaecomastia. Amiloride inhibits Na^+ flux through ion channels in distal convoluted tubule & collecting duct, and inhibits vascular smooth muscle contraction.
- ***indapamide*** – Naturetic effect in proximal distal tubule and may reduce response of vascular sm to pressor amines. Binds to RBC carbonic anhydrase. Hepatic metab. SE: electrolyte imbalance, hypoNa^+, hypoK^+.

Centrally acting

- ***α-methyldopa*** – metabolised to false sympathetic transmitter methylNA
- ***clonidine*** – α1 presynaptic > α2 postsynaptic agonist. Also used for opioid withdrawal & migraine prophylaxis. SE: dry mouth/eyes, drowsiness, can cause initial HT if given rapidly IV. Rebound possible on stopping. Dose 75-150mcg init.

Sympathetic ganglia & terminal blockers

- ***trimetaphan***, (ganglia)– poorly tol., fixed mydriasis. *Guanethidine*, *reserpine* (NA terminals) – depression

Hypertensive retinopathy

Retinal changes depend on factors such as the level of the blood pressure and the state of the arterioles. The primary response to hypertension is arteriolar spasm and narrowing. This can occur more readily in younger patients with no sclerotic protection of their arterioles.
Patients with essential hypertension and elderly normotensives develop compensatory arterial changes such as silver wiring and AV nipping. Retinal haemorrhages are unusual and suggest an associated retinal vascular accident.
Cotton wool spots, flame haemorrhages and disc swelling are more typical of malignant hypertension especially in young patients.

Classification

Modern practice classifies changes into two groups:

- compensated hypertensive retinopathy - grade 1 and 2 in older sources:
    - arteriolar changes - mild, generalised attenuation; increased tortuosity; increased opacity with resultant heightened light reflex - "copper" or "silver" wiring (Grade I)
    - plus constriction of veins at the arteriovenous crossings - "AV nipping" (Grade II)
- accelerated hypertensive retinopathy - grade 3 and 4 in older sources:
    - cotton wool spots (retinal infarcts due to pre - capillary closure), flame haemorrhages, and hard exudates - may surround the macula forming a partial or complete "star" (Grade III)
    - papilloedema and often, retinal oedema at the posterior pole of the eye. Visual impairment accompanies macula involvement. (Grade IV)

Complications

- Central and branch, retinal vein and artery, occlusion
- Ischaemic optic neuropathy
- Vitreous haemorrhage

Management

Successful hypotensive therapy will quickly resolve any haemorrhages and within a few weeks, any cotton wool spots. Hard exudates may take many months to clear. Papilloedema may resolve but potential optic atrophy is a serious sequelae.

Prognosis

The 5 year survival of patients with compensated hypertensive retinopathy is about 70%; that for accelerated hypertensive retinopathy, about 1%.