6.3 Antihypertensives

Hypertension

See also the Heart Foundation's Hypertension clinical information and the Australian guideline for assessing and managing cardiovascular disease risk

Observational studies show that the risk of cardiovascular (CV) morbidity and mortality rises as BP increases from 115/75 mm Hg; age, sex (male) and other CV risk factors contribute to this risk.

The distinction between normotension and hypertension is arbitrary: generally normotension is considered as clinic BP of 120 mm Hg systolic (SBP)/80 mm Hg diastolic (DBP) and below, and hypertension as >140/90 mm Hg.

The decision to start treatment should incorporate thorough assessment of BP, overall CV risk and end-organ damage.

Rationale for drug use

Reduce premature CV morbidity and mortality and microvascular disease affecting the brain, kidneys and retinas.

Reduce maternal and fetal morbidity and mortality in hypertensive disorders of pregnancy, see Hypertension in pregnancy p 251.

BP measurement

Confirm level of BP with multiple readings on different occasions; ensure correct cuff size; consider possibility of white coat effect on BP.

Measurement method affects the results: ambulatory and home BP are generally lower than clinic BP and are stronger predictor of outcomes.

Automated office BP measurement, which may be taken unobserved by staff, provides substantially lower SBP (by about 10–20 mm Hg) than conventional clinic readings. This method was used in the SPRINT study but is currently not often practised in Australia.

Before starting drug treatment

Look for secondary causes of hypertension (including drugs, eg NSAIDs, corticosteroids) and evidence of end-organ damage.

Identify and treat other modifiable CV risk factors, such as obesity and dyslipidaemia; encourage smoking cessation.

Encourage a healthy lifestyle for all patients (eg weight loss, increased physical activity, healthy diet). Such interventions can reduce BP (potentially avoiding or delaying the need for antihypertensives). Regular aerobic exercise can reduce daytime SBP by up to 3.2 mm Hg, and a weight loss of 10 kg in an overweight person may reduce SBP by 6–10 mm Hg.

Assess cardiovascular risk

CV risk assessment is unnecessary in people who are clinically determined to be at high risk: those with existing/established CV disease (eg MI, stroke, vascular disease), familial hypercholesterolaemia or moderate-to-severe chronic kidney disease.

Assess CV risk in all adults without known CV disease aged 45–79 years (from 35 years in people with diabetes or 30 years in Aboriginal and Torres Strait Islander people). A guideline and calculator for estimating the risk of a CV event within 5 years are available from *cvdcheck.org.au*.

Management with consideration of cardiovascular risk

In adults without known CV disease, consider drug treatment according to estimated risk, rather than targeting BP alone (although treat those with SBP >160 mm Hg or DBP >100 mm Hg).

High risk (10% or more) or clinically determined high risk: start drug treatment with antihypertensive and lipid-lowering therapy, unless clinically inappropriate.

Intermediate risk (5% to <10%): consider drug treatment.

Low risk (<5%): drug treatment is not routinely recommended.

BP targets

Australian guidelines recommend treating patients with uncomplicated hypertension to a target of <140/90 mm Hg or lower if tolerated.

In practice, BP can be lowered as far as it is tolerable; even if targets are not reached, any reduction in BP reduces risk of CV morbidity and mortality.

A lower target of SBP <120 mm Hg can be considered in selected CV populations at high risk, provided there is close monitoring for adverse effects (eg hypotension, electrolyte abnormalities). In the SPRINT study, patients at high CV risk showed fewer CV events and reduced mortality (but more treatment-related adverse events) when the target SBP was <120 mm Hg compared with <140 mm Hg. However, its generalisability and application to practice may be limited by its use of automated office BP measurement (see BP measurement p 248) and exclusion criteria (eg age <50 years, diabetes, heart failure, history of stroke).

Drug treatment

Generally start treatment with a single drug at the lowest recommended dose (this will satisfactorily reduce BP in about 25–50% of people).

The presence of coexisting conditions may affect the choice of antihypertensive (Table 6–3 p 249).

For uncomplicated hypertension, unless there is a contraindication or a specific indication for another drug, first consider:

- an ACE inhibitor (or sartan) or
- a dihydropyridine calcium channel blocker or
- if 65 or older, a thiazide diuretic (low dosage).

Choose an agent given once daily.

Generally allow 4–6 weeks to assess response to treatment. For those with marked hypertension or high CV risk, consider a shorter review period.

Not all patients respond to all drugs; monitor response carefully; if initial drug not tolerated or has no effect, change to a drug from a different class.

Table 6–3 Comorbidities affecting antihypertensive choice

Comorbidity	Drugs with favourable effect
diabetes with proteinuria or microalbuminuria, chronic kidney disease	ACE inhibitors (or sartans)
heart failure with reduced ejection fraction	ACE inhibitors (or sartans), beta-blockers (carvedilol, controlled release metoprolol, bisoprolol, nebivolol)
post MI	beta-blockers, ACE inhibitors (or sartans)
angina	beta-blockers, calcium channel blockers, ACE inhibitors
AF	ACE inhibitors or sartans (verapamil, diltiazem, beta-blockers may help rate control)
Comorbidity	**Drugs with unfavourable effect**
asthma, COPD	beta-blockers[1]
bradycardia, second- or third-degree atrioventricular block	beta-blockers, diltiazem, verapamil
heart failure with reduced ejection fraction	calcium channel blockers (especially verapamil, diltiazem)
gout	thiazide diuretics

[1] cardioselective beta-blockers (eg metoprolol) may be used cautiously in COPD or well-controlled asthma, see Respiratory p 271 in Beta-blockers

Inadequate effect

Add a second antihypertensive rather than increasing the dose of the first (which may cause adverse effects without improving BP control).

The preferred combinations are:

- ACE inhibitor (or sartan) with a calcium channel blocker or a thiazide diuretic
- calcium channel blocker with a thiazide diuretic.

Other effective combinations include a beta-blocker with an ACE inhibitor (or sartan) or a dihydropyridine calcium channel blocker. Use of beta-blockers with thiazide diuretics is also effective (but increases risk of diabetes compared with other combinations). Combination products may be convenient and less expensive, see Table 6–4 Antihypertensive combination products p 250.

Unless there are specific benefits, avoid:

- diltiazem or verapamil with beta-blocker (risk of severe bradycardia and heart block)
- ACE inhibitor (or sartan) with potassium-sparing diuretic (risk of hyperkalaemia)
- ACE inhibitor with sartan (benefit over ACE inhibitor alone is questionable, may increase renal complications; specialist use only, see Practice points p 261 in Sartans).

BP target still not reached

If both drugs are well tolerated, increase dose of one agent (non-thiazide) towards the maximum recommended; if this is still inadequate, increase the dose of the other antihypertensive.

If BP remains above the target despite maximum doses of at least 2 appropriate agents, consider other factors, eg poor compliance, high salt intake, secondary hypertension (including drug-induced), volume overload, sleep apnoea (can cause treatment resistance).

Three or more antihypertensives from different classes may be needed.

Resistant hypertension, which is uncontrolled BP despite 3 or more optimally tolerated antihypertensives (including a diuretic), occurs in >10% of patients. Consider primary aldosteronism especially if hypokalaemia is present. Seek specialist advice after ruling out compliance issues and other secondary causes.

Spironolactone (p 234) is an effective add-on drug for resistant hypertension uncontrolled by a combination of first-line agents (note: risk of hyperkalaemia is increased when combined with ACE inhibitors or sartans particularly in the presence of kidney disease).

Drug choice

See also Table 6–3 Comorbidities affecting antihypertensive choice p 249

It is the reduction in BP that is most important for reducing CV events, rather than the antihypertensives chosen. ACE inhibitors, calcium channel blockers, sartans and thiazide diuretics are usually used.

ACE inhibitors

First-line treatment, especially in patients with chronic kidney disease, diabetes with micro- or macroalbuminuria, heart failure or with left ventricular dysfunction, in particular following MI.

Sartans

May be used as an alternative first-line treatment especially in patients who are intolerant of ACE inhibitors.

Calcium channel blockers

The dihydropyridines (amlodipine, felodipine, lercanidipine, nifedipine) are suitable as first-line treatment.

In meta-analyses, they reduced the frequency of stroke but increased rates of heart failure compared with other antihypertensive classes, while the incidence of CV events and mortality were similar.

Verapamil and diltiazem are contraindicated for those who also have heart failure, while dihydropyridines may be used cautiously.

Thiazide diuretics

Are generally well tolerated and are a first-line treatment for hypertension in those aged >65 years. Due to their association with new-onset diabetes, they are no longer recommended as first-line monotherapy in younger patients.

Table 6–4 Antihypertensive combination products

Brand®[1]	ACE inhibitor	Calcium channel blocker[2]	Sartan	Thiazide or related diuretic	Potassium-sparing diuretic	Statin
Abisart HCT			irbesartan	hydrochlorothiazide		
Accuretic	quinapril			hydrochlorothiazide		
Adesan HCT			candesartan	hydrochlorothiazide		
Atacand Plus			candesartan	hydrochlorothiazide		
Avapro HCT			irbesartan	hydrochlorothiazide		
Avsartan HCT			irbesartan	hydrochlorothiazide		
Cadivast		amlodipine				atorvastatin
Caduet		amlodipine				atorvastatin
Candesan Combi			candesartan	hydrochlorothiazide		
Co-Diovan			valsartan	hydrochlorothiazide		
Coveram	perindopril arginine	amlodipine				
Coversyl Plus	perindopril arginine			indapamide		
Dilart HCT			valsartan	hydrochlorothiazide		
Exforge		amlodipine	valsartan			
Exforge HCT		amlodipine	valsartan	hydrochlorothiazide		
Fosetic	fosinopril			hydrochlorothiazide		
Idaprex Combi	perindopril erbumine			indapamide		
Indosyl Combi	perindopril erbumine			indapamide		
Karvezide			irbesartan	hydrochlorothiazide		
Micardis Plus			telmisartan	hydrochlorothiazide		
Mizart HCT			telmisartan	hydrochlorothiazide		
Moduretic				hydrochlorothiazide	amiloride	
Olamlo HCT		amlodipine	olmesartan	hydrochlorothiazide		
Olmekar		amlodipine	olmesartan			
Olmekar HCT		amlodipine	olmesartan	hydrochlorothiazide		
Olmertan Combi			olmesartan	hydrochlorothiazide		
Olmetec Plus			olmesartan	hydrochlorothiazide		
Perisyl Combi	perindopril erbumine			indapamide		
Prexum Combi	perindopril arginine			indapamide		
Pritor/Amlodipine		amlodipine	telmisartan			
Reaptan	perindopril arginine	amlodipine				
Renitec Plus	enalapril			hydrochlorothiazide		
Sevikar		amlodipine	olmesartan			
Sevikar HCT		amlodipine	olmesartan	hydrochlorothiazide		
Tarka	trandolapril	verapamil				
Teltartan HCT			telmisartan	hydrochlorothiazide		
Teveten Plus			eprosartan	hydrochlorothiazide		
Triasyn	ramipril	felodipine				
Twynsta		amlodipine	telmisartan			
Zan-Extra	enalapril	lercanidipine				

[1] generic brands that name the drugs in the brand name may also be available
[2] all, except verapamil, are dihydropyridines

Beta-blockers

Compared with other antihypertensive classes, they have less effect in reducing the incidence of stroke and are associated with an increased risk of diabetes.

They are recommended for hypertension when compelling indications, such as angina, are present, see Table 6–3 Comorbidities affecting antihypertensive choice p 249.

Other drugs

A number of other drugs, such as the selective alpha-blockers, are still used but there is no reliable evidence from randomised trials about their effects on CV morbidity or mortality.

Special cases

Elderly

Start treatment with the lowest dose and titrate slowly.

In a subgroup of SPRINT participants, ie selected ambulatory patients aged >75 with hypertension (excluding comorbidities, eg diabetes, heart failure, history of stroke), lowering SBP to <120 mm Hg significantly reduced the risk of CV and all-cause mortality. Note that this study used automated office BP (where a lower SBP target of <120 mm Hg is comparable to clinic SBP <130–140 mm Hg), see BP measurement p 248.

Aim for the lower BP targets only when treatment is well tolerated and with close monitoring (eg for orthostatic hypotension, electrolyte abnormalities, acute kidney injury).

Coronary artery disease

Monitor BP closely when using antihypertensives. Both high (SBP >140 mm Hg or DBP >80 mm Hg) and low (SBP <120 mm Hg or DBP <70 mm Hg) BP were associated with increased risk of CV morbidity and mortality in hypertensive patients with stable coronary artery disease in an international cohort study.

Diabetes

BP target <140/90 mm Hg is recommended. If preventing stroke is a priority, consider lowering to a SBP <120 mm Hg, provided the patient can be closely monitored for adverse effects, eg hypotension, acute kidney injury.

Controlling BP improves CV morbidity and mortality and reduces the progression of diabetic nephropathy in people with both hypertension and diabetes.

ACE inhibitors or sartans are preferred in diabetes as they delay progression of renal disease in patients with micro- or macroalbuminuria.

Calcium channel blockers, thiazide diuretics and beta-blockers may also be used, however, although thiazide diuretics and beta-blockers have beneficial effects on CV outcomes in diabetics, they tend to worsen glycaemic control compared with other classes.

Hypertensive crisis

Avoid precipitous BP reduction (>25% over 2 hours) to prevent serious events, eg MI, stroke. Monitor BP continuously.

Seek specialist advice. Aim is to limit acute end organ damage.

Rapid BP reduction is rarely required except in certain circumstances (eg aortic dissection, severe pre-eclampsia, intracerebral haemorrhage). Where there is no end organ damage, gradual BP reduction over several days is sufficient and safer.

To reduce BP over 2–6 hours, consider agents such as IV labetalol, sodium nitroprusside, glyceryl trinitrate, hydralazine and clevidipine. Beta-blockers may be needed to control reflex tachycardia. In most cases, aim towards 160/100 mm Hg rather than normal BP levels; then wait 24 hours before lowering further.

For less urgent BP reduction, use oral antihypertensive drugs and follow up within 24–72 hours.

Hypertension in pregnancy

For further information see *www.somanz.org/hypertension-in-pregnancy-guideline-2023*.

Stable hypertension (chronic, gestational, or non-severe pre-eclampsia): a target BP of <135/85 mm Hg is recommended. First-line oral drugs include methyldopa, labetalol and nifedipine; oral hydralazine can also be considered.

Avoid ACE inhibitors and sartans during pregnancy.

Severe hypertension (SBP >160 mm Hg or DBP >110 mm Hg): see local protocols and also Pre-eclampsia and eclampsia p 869. Oral nifedipine (conventional tablet, available through the SAS) and parenteral drugs, eg labetalol and hydralazine, are used for urgent BP reduction.