Hypertension
treating to target

The choice of antihypertensive agent is determined by its effectiveness, and its indications and contraindications for the individual patient. Whichever agent is used, it is important to treat to goal.

FALINE S. HOWES
BMedSci, MB BS(Hons), MPubHlth, FRACGP

MARK R. NELSON
MB BS(Hons), MFM, FRACGP, FAFPHM, PhD

Dr Howes is a General Practitioner and Research Associate at the Menzies Research Institute, University of Tasmania, Hobart. Professor Nelson is Chair of General Practice and Senior Member at the Menzies Research Institute, University of Tasmania, Hobart, Tas.

Hypertension is the most frequently managed problem in Australian general practice.[1] The prevalence rate in the adult population is 29%.[2] The benefits of blood pressure lowering have been detailed in numerous randomised, placebo-controlled trials and meta-analyses.[3] However, hypertension is still described as the most important health problem that is suboptimally managed.

In the Australian Diabetes, Obesity and Lifestyle (AusDiab) study, treatment for hypertension was justified in 54% of patients not treated.[2] Of those taking antihypertensive medication, only 40% had reached target blood pressure readings (defined as <140/90 mmHg). Blood pressure control rates can therefore be substantially improved.

The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) and the Controlled Onset Verapamil Investigation of Cardiovascular Endpoints (CONVINCE) study achieved target blood pressure levels in 66% and 70% of patients, respectively.[4,5] Hence higher rates of blood pressure control are achievable.

Failure to reach blood pressure targets may be due to the patient, the GP or systems issues. This article discusses some of the reasons why

IN SUMMARY

- **The decision to treat elevated blood pressure with drugs should be determined by an individual's high absolute risk of having an adverse cardiovascular event.**
- **Not treating to target therefore means that such individuals are at high residual risk.**
- **Failure to reach blood pressure targets may be due to the patient, the GP or systems issues.**
- **The choice of antihypertensive agent is determined by its effectiveness, and its indications and contraindications for the individual patient.**
- **Most patients will require two or more drugs to reach their target blood pressure.**
- **Drug therapy should always be accompanied by appropriate advice on behavioural modifications.**

continued

Table 1. Blood pressure treatment targets in adults*

Patient group	Target (mmHg)
Patients with proteinuria >1 g/day (with or without diabetes)	<125/75
Patients with associated condition(s) or end organ damage:† • coronary heart disease • diabetes • chronic kidney disease • proteinuria (>300 mg/day) • stroke/transient ischaemic attack	<130/80
Patients with none of the above	<140/90 or lower if tolerated

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† Specific lower blood pressure targets have not been established for other high-risk groups (e.g. those with peripheral arterial disease, those with familial hypercholesterolaemia or those at high absolute risk of cardiovascular disease) due to the current lack of evidence from clinical trials. Targets will be set when evidence becomes available.

blood pressure targets set by the National Heart Foundation's guidelines are not reached, what the target blood pressure readings are and ways in which these targets may be achieved.[6]

Why are we not reaching blood pressure targets?

A qualitative study has investigated the barriers to initiating medication and treating elevated blood pressure to target levels in general practice.[7] In this study, the main barrier preventing or delaying diagnosis reported by GPs was a lack of confidence in the accuracy and representativeness of blood pressures recorded in their clinic. The other main barriers were the time-poor nature of general practice and perceived patient attitude. The fact that multiple readings are needed over several visits imposed some difficulties – for example, in patients who were infrequent attendees or were not interested in their blood pressure or saw a different doctor each time they attended. Initiation of treatment was often hampered by patient unwillingness to take medications.

The study also found that the decision to treat to target was clouded by doctors' fear of adverse events (particularly in the elderly) clinical inertia and perceived patient attitude. Adopting a patient-centred care approach and distrust of the evidence underlying the management of hypertension had a pervasive impact.

In this study, difficulties associated with initiating and treating to target were often discussed together, but overall treating to target was viewed as being more difficult. Looking at the study results from a treating to target perspective only, the barriers that prevented optimal management of hypertension were perceived patient attitude, GP attitude and systems issues.

Perceived patient attitude

GPs believe that patients often fail to take responsibility for their own health and resist making necessary lifestyle changes. Cost, access and adherence are also issues.

GP attitude

GPs undertook an informal risk–benefit analysis whereby they weighed up what they were trying to achieve against what the patient wanted. The witnessing of drug attributed side effects, particularly in the elderly, made GPs more risk averse.

Systems issues

GPs felt that there needed to be greater access to specialist care and home and ambulatory blood pressure monitoring, and improved Medicare support for the management of complex hypertension.

How can we reach blood pressure targets?

Patients with high absolute cardiovascular risk and elevated blood pressure need to be treated to recommended target blood pressures (Table 1), otherwise they will have a significant residual adverse risk.

Multiple large studies have shown that all antihypertensive medications have similar efficacy.[8] Therefore, medication choice after initiation is driven by the individual patient's response, comorbidity (Table 2) and the possible combinations of antihypertensive agents (Table 3).[9,10]

To facilitate a successful and sustainable treatment regimen, the lowest recommended dose of the selected drug should be started and then reviewed after six weeks. At this stage, if the patient is unable to tolerate the medication or if it is deemed to be ineffective, the patient should be switched to an antihypertensive drug from a different class. If there has been a partial response but target blood pressure has not been reached, rather than increasing the dose of the first agent, a second agent from a different pharmacological class should be added at a low dose. This approach minimises adverse events and maximises efficacy. The effective tolerated medications should be titrated up until target blood pressure is reached; however, additional medications may need to be added to achieve this.

Lifelong medication is usually required because age is the most important determinant of adverse risk. Once blood pressure has been stabilised, the interval between visits can be lengthened – for example, patients should be reviewed every three months for the next 12 months, and then six monthly thereafter while their blood pressure remains stable.

Behavioural modification is an important component of treatment and, if significant lifestyle changes are made and maintained, patients may be able to stop or reduce drug therapy.[11] Lifestyle interventions remain the cornerstone of hypertension management.

Combination therapy

About 60% of patients with elevated blood pressure will not achieve blood pressure targets with one medication alone.[6] Therefore, most patients will require a combination of two or more medications to achieve adequate blood pressure control.

Effective drug combinations for hypertension are shown in Table 3. The

Table 2. Choice of antihypertensive agent in patients with comorbid and associated conditions*

Condition	Potentially beneficial	Potentially harmful	
		Caution	Contraindicated
Angina	Beta blockers (except oxprenolol, pindolol), CCBs, ACE inhibitors		
Atrial fibrillation	Remodelling: ACE inhibitors, angiotensin II receptor antagonists† Rate control: verapamil, diltiazem, beta blockers		
Asthma/COPD		Cardioselective beta blockers (e.g. atenolol, metoprolol): use cautiously in mild/moderate asthma/COPD only	Beta blockers (except cardioselective agents)
Bradycardia, second- or third-degree atrioventricular block			Beta blockers, verapamil, diltiazem
Depression		Beta blockers, clonidine, methyldopa, moxonidine	
Gout	Losartan	Thiazide diuretics	
Heart failure	ACE inhibitors, angiotensin II receptor antagonists,† thiazide diuretics, beta blockers‡ (bisoprolol, carvedilol, metoprolol controlled release), spironolactone	CCBs (especially verapamil, diltiazem)	Alpha blockers in aortic stenosis Beta blockers in uncontrolled heart failure
Post myocardial infarction	Beta blockers (except oxprenolol, pindolol), ACE inhibitors, eplerenone		
Pregnancy	This section is currently under review§		
Chronic kidney disease	ACE inhibitors, angiotensin II receptor antagonists†		
Tight bilateral renal artery stenosis (unilateral in a patient with solitary kidney)		ACE inhibitors, angiotensin II receptor antagonists	
Post stroke	ACE inhibitors, angiotensin II receptor antagonists, low-dose thiazide-like diuretics		
Type 1 or type 2 diabetes with proteinuria or microalbuminuria	ACE inhibitor, angiotensin II receptor antagonists†	Beta blockers, thiazide diuretics¶	

ABBREVIATIONS: ACE = angiotensin-converting enzyme; CCB = calcium channel blocker.

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† Careful monitoring of kidney function is required if a combination of ACE inhibitors and angiotensin II receptor antagonists are used.

‡ Particular beta blockers are now indicated for the treatment of heart failure. See the Heart Foundation's *Guidelines for the prevention, detection and management of chronic heart failure in Australia, 2006* (available at www.heartfoundation.org.au).

§ This information is currently being reviewed by the Heart Foundation. Please visit www.heartfoundation.org.au/Professional_Information/Clinical_Practice/Hypertension for updated information.

¶ When used in combination with an ACE inhibitor, may be beneficial in type 2 diabetes.

Table 3. Recommended and discouraged combination therapy for the management of elevated blood pressure*[9,10]

First drug	Additional drug	Recommendation
The most effective combination (based on the best available evidence)		
ACE inhibitor or angiotensin II receptor antagonist†	CCB	Particular role in patients with diabetes or lipid abnormalities
Other effective combinations		
ACE inhibitor or angiotensin II receptor antagonist†	Thiazide diuretic	Particular role in patients with heart failure or post stroke
	Beta blocker	Recommended post myocardial infarction or in patients with heart failure
Beta blocker	Dihydropyridine CCB	Particular role in patients with coronary heart disease
Thiazide diuretic	CCB	
	Beta blocker	Not recommended in patients with glucose intolerance, metabolic syndrome or established diabetes
Combinations to avoid		
ACE inhibitor or angiotensin II receptor antagonist	Potassium-sparing diuretic	Avoid combination due to risk of hyperkalaemia
Verapamil	Beta blocker	Avoid combination due to risk of heart block
ACE inhibitor	Angiotensin II receptor antagonist	In a large trial,[9] combination therapy did not reduce cardiovascular death or morbidity in patients with vascular disease or diabetes, but increased the risk of hypotensive symptoms, syncope and renal dysfunction‡

ABBREVIATIONS: ACE = angiotensin-converting enzyme; CCB = calcium channel blocker.

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† ACE inhibitors and angiotensin II receptor antagonists have been shown to be equally efficacious in the prevention of combined end points of cardiovascular disease death, myocardial infarction, stroke and heart failure admissions in patients at high risk due to past cardiovascular events.

‡ Combination therapy reduces proteinuria. Trials to determine the effect of combination therapy on progression of renal disease in subjects with proteinuria are under way.[10]

angiotensin converting enzyme (ACE) inhibitor and calcium channel blocker combination has been given precedence due to the results of the Avoiding Cardiovascular Events Through Combination Therapy in Patients Living With Systolic Hypertension (ACCOMPLISH) trial.[12] If required, other useful agents include, for example, alpha blockers and centrally-acting agents. Each change in treatment needs to be trialled for at least six weeks.

Still not at target?

If target blood pressure is not reached despite maximal doses of at least two appropriate agents after a reasonable period, then the following factors outlined below should be considered.

Medication adherence

- Has the patient ceased medication due to side effects or cost?
- Could the patient change to a long-acting preparation with once-daily administration?
- Could the patient change to a combination preparation to enhance adherence?
- Would the patient benefit from the use of adherence aids (e.g. dosette boxes, Webster packs, written instructions or patient education materials)?

Other substances that may increase blood pressure

- Is the patient taking a prescribed medication (e.g. NSAIDs or prednisolone)?
- Is the patient taking an over the counter (e.g. NSAIDs) or a complementary medication (e.g. ginseng, St. John's Wort)?
- Is alcohol, recreational drugs or other drug use (including caffeine, licorice) an issue?
- Does the patient have a high salt intake (particularly in those taking ACE inhibitors or angiotensin II receptor antagonists)?

Adverse lifestyle factors

- Can the patient be motivated to take greater responsibility for his or her health and become a partner in management decisions?
- Can the patient increase physical activity or reduce kilojoule intake (if appropriate)?

Systems issues

- Are there any other social or economic barriers that are impacting negatively on the patient's health?
- Would the patient benefit from a Home Medicines Review?
- Is a practice recall or reminder system appropriate to assist in management?

Therapeutic inertia

- Do you need to increase a current agent or add another agent?

Measurement issues

- Could there be a white coat effect? Home blood pressure monitoring should be encouraged, if appropriate, or ambulatory blood pressure monitoring considered.
- Is there a blood pressure measurement artifact (e.g. inappropriate cuff size)?

continued

Secondary hypertension

- Does the patient have chronic kidney disease, primary aldosteronism, phaeochromocytoma or renovascular disease?
- Could the patient have obstructive sleep apnoea?
- Is the patient volume overloaded (in particular, chronic kidney disease should be ruled out)?
- Would the patient benefit from referral to a specialist?

Can we achieve blood pressure targets in the elderly?

It is recognised that achieving recommended blood pressure target levels in the very elderly may be difficult because of their altered physiological responses, comorbidity and polypharmacy, with the potential for side effects and medication interactions. The elderly are the most at risk of adverse cardiovascular events.

Randomised, controlled trials have demonstrated that drug therapy is just as effective in advanced age. The most recent study to show this was the Hypertension in the Very Elderly Trial (HYVET).[13] This placebo-controlled trial (mean age 83.6 years) showed a 39% reduction in the rate of death from a stroke, a 21% reduction in the rate of death from any cause, a 23% reduction in the rate of death from cardiovascular causes, and a 64% reduction in the rate of heart failure in patients taking active treatment versus placebo.

Most importantly, the HYVET study reported fewer serious adverse events in the active treatment group, and preliminary analyses revealed no increase in postural hypotension. If symptoms suggest postural hypotension, but it is not demonstrable in the clinic, it should be confirmed with ambulatory blood pressure monitoring. If confirmed, treatment should be based on the standing blood pressure. In the elderly, isolated elevated systolic blood pressure is more prevalent due to large vessel stiffness associated with ageing. In these circumstances, a calcium channel blocker or diuretic-based treatment regimen is recommended.

Conclusion

Drug therapy is warranted in patients with a high risk of adverse cardiovascular events together with appropriate behavioural modification. All groups of blood pressure lowering drugs have similar efficacy but specific agent recommendations are made based on the patient's characteristics. It is important to treat to goal whichever agent is used. Most often, this requires more than one drug to reduce fatal and nonfatal cardiovascular events. MT

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