10 September 2001

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Dr Sam Sample
4 Sample Street
Sampletown NSW 2000

No. 13 Management of Hypertension - an update

Dear Dr Sample,

Hypertension is one of the most common conditions seen by general practitioners, accounting for 6% of all presenting problems. The Heart Foundation emphasises the importance of a therapeutic plan aimed at reducing blood pressure and overall cardiovascular risk when managing patients with hypertension.

In this issue of the *Prescribing Practice Review (PPR)* we have provided an overview of the current management guidelines as well as an update on new issues.

Please note that for uncomplicated hypertension, low dose thiazides and/or beta-blockers remain the recommended first-line agents.

The key messages that come through clearly in new evidence are:

Combination antihypertensive agents should not be used for initiation

Fixed-dose combination products are not recommended for initiation of treatment. Appropriate monotherapy should always be used first-line. Titration to the required dose is difficult with the fixed dosage of the combined drug components.

Alpha-blockers no longer recommended as an initial treatment option for hypertension

An alpha-blocker (doxazosin), used as an antihypertensive, has been linked with a higher incidence of congestive cardiac failure than a thiazide diuretic based regimen. An increased risk of stroke and combined coronary heart disease, particularly angina and coronary revascularisation, was also shown.

The Heart Foundation has changed its recommendations to advise that alpha-blockers should not be considered as initial treatment for hypertension. Prazosin and terazosin are the only alpha-blockers approved for use in Australia for the treatment of hypertension.

Calcium channel blockers - the debate continues

Calcium channel blockers have been associated with a significantly higher risk of myocardial infarction, congestive cardiac failure and combined major cardiovascular events when used in the treatment of hypertension compared to other antihypertensive agents but with possibly a better outcome for stroke.

You may like to take the opportunity to participate in the NPS Clinical Audit: Pharmacotherapeutic management of hypertension. See the back page of the *Prescribing Practice Review (PPR)* for details on how to register. For further information please contact the NPS on 02 9699 4499 or visit our website at www.nps.org.au

Yours sincerely

Dr Stephen Phillips
Chair, NPS Board

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September 2001

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PPR thirteen

Prescribing Practice Review—*PPR* For General Practice

Management of hypertension – an update

The management of patients with hypertension requires a therapeutic plan aimed at reducing blood pressure and overall cardiovascular risk.

In this issue we have provided an overview of the current management guidelines as well as an update on new issues.

Current recommendations for target blood pressure

- below 130/85 mmHg: for young and middle-aged people (<65 years), those with diabetes and renal insufficiency
- below 140/90 mmHg: for older people (>65 years)[1,2]

Lifestyle interventions are for life, even when the patient is prescribed an antihypertensive agent

Follow-up patients to ensure that they maintain a regular exercise program and healthy diet, limit their salt and alcohol intake, lose weight and quit smoking, if applicable.

Use thiazides and/or beta-blockers as first-line therapy except in those patients where there are compelling indications to use other drug classes

Although treatment options have expanded in recent years, low dose thiazide diuretics and beta-blockers have consistently reduced morbidity and mortality in the main randomised controlled hypertension trials.[3-6] Morbidity and mortality studies are being conducted internationally to establish the relative benefits of other classes of antihypertensive agents.

Low dose thiazides are safe and effective

There is a flat dose-response relationship for the antihypertensive effect of thiazides with little benefit gained from doses above those equivalent to between 12.5 mg (very low dose) and 25 mg (low dose) of hydrochlorothiazide. This dose range has been shown to cause fewer major metabolic side-effects than higher dose therapy.[2,3]

Generic drug name	Product name	Low dose equivalent	Very low dose equivalent
Thiazide diuretics			
bendrofluazide 5 mg	Aprinox®	2.5 mg (1/2 a tab)	Not practical
hydrochlorothiazide 25 mg	Dichlotride®	25 mg (1 tab)	12.5 mg (1/2 a tab)
hydrochlorothiazide 50 mg	Dichlotride®	25 mg (1/2 a tab)	Not practical
Thiazide-like diuretics			
indapamide 2.5 mg	Dapa-Tabs®, Indahexal®, Insig®, Napamide®, Natrilix®	Not practical	Not practical
indapamide 1.5 mg	Natrilix SR® (not available on PBS)	1.5 mg (1 tab)	Not possible
chlorthalidone 25 mg	Hygroton®	25 mg (1 tab)	12.5 mg (1/2 a tab)

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Limit use of indapamide to patients in whom an advantage can be anticipated

Indapamide has a similar effect to low dose thiazide diuretics on total cholesterol and a lesser effect on triglycerides.[7] There is no evidence that it is superior to low dose thiazide diuretics but it is considerably more expensive.

Select drugs based on compelling indications/contraindications

The WHO-ISH Guidelines detail the compelling and possible indications and contraindications of drug classes for patients with co-existing conditions.[2] For example, there are compelling indications to use an ACE inhibitor in patients with diabetic nephropathy or heart failure unless contraindicated because of bilateral renal artery stenosis, and there are compelling indications to use beta-blockers in patients post myocardial infarction or with angina unless contraindicated because of co-existing asthma.

Reserve angiotensin II (AT II) receptor antagonists for those patients in whom there is a clear indication for an ACE inhibitor but are intolerant because of an ACE inhibitor induced cough

There are no results yet of randomised controlled trials with AT II receptor antagonists measuring long-term health outcomes in hypertensive patients. In trials to date, adverse event rates were low and similar to placebo. The incidence of cough was 1% for AT II receptor antagonists and 5.5% for ACE inhibitors.[8]

New Issues

Combination antihypertensive agents should not be used for initiation

When drug treatment is needed, patients should start with one drug only.[2] The Drug Utilisation Sub-committee of the Pharmaceutical Benefits Advisory Committee tracked new prescriptions for products containing irbesartan or fosinopril in combination with hydrochlorothiazide. The data showed that 17% and 16% of patients respectively had not previously been dispensed an ACE inhibitor, AT II receptor antagonist or a thiazide diuretic in the four month period prior to starting the combination product.[9]

Where two drugs are required to control blood pressure, consider that the fixed doses in combination products make it difficult to titrate the dose to achieve optimal control of blood pressure. However, combination products may offer the right drug and dose combination once the patient is stabilised. The use of a fixed dose combination product in this situation may benefit some patients in terms of compliance.

Alpha-blockers no longer recommended as an initial treatment option for hypertension

An alpha-blocker, doxazosin (not available in Australia) has been linked with an overall increase in major cardiovascular events compared to a thiazide diuretic based regimen in the ALLHAT study.[10] Most significantly, an increase in the 4-year cumulative congestive cardiac failure incidence from 4.5% with a thiazide diuretic based regimen to 8.1% with an alpha-blocker based regimen was shown. An increased risk of stroke and combined coronary heart disease, particularly angina and coronary revascularisation, was also shown with an alpha-blocker based regimen compared to a thiazide diuretic based regimen.

The Heart Foundation has changed its recommendations from those previously outlined in the 1999 *Guide to Management of Hypertension for Doctors*[1] to advise that alpha-blockers should not be considered as initial treatment for hypertension. Prazosin and terazosin are the only alpha-blockers approved in Australia for the treatment of hypertension. For patients without congestive cardiac failure, alpha-blockers are still recommended to relieve symptoms of benign prostatic hypertrophy, or in combination with thiazide diuretics or beta-blockers when monotherapy has failed to achieve good blood pressure control.

Calcium channel blockers – the debate continues

The debate continues as to the potential beneficial and detrimental effects of calcium channel blockers (CCBs) used as antihypertensive agents. A meta-analysis of nine trials (27,743 patients) showed that CCB use was associated with a significantly higher risk of myocardial infarction, congestive cardiac failure and combined major cardiovascular events compared to other antihypertensive agents. However, there was no significant difference found for outcomes of stroke and all-cause mortality.[11]

Another meta-analysis of six of the same nine trials (26,129 patients) showed a reduced risk of stroke and an increased risk of coronary heart disease among patients receiving CCBs compared with diuretic or beta-blocker based regimens. Since these trends were similar in trials of dihydropyridine CCBs (e.g. amlodipine, felodipine and nifedipine) and non-dihydropyridine CCBs (e.g. verapamil and diltiazem), they do not support a difference in effect of these agents on coronary risk. Diltiazem and verapamil were not shown to have a reduced effect on the avoidance of stroke.[12]

Information available on drug therapy for hypertension

- *1999 Guide to Management of Hypertension for Doctors*. Available on the web site http://www.heartfoundation.com.au.
- *Therapeutic Guidelines: Cardiovascular 3rd Edition* provides comprehensive information on managing cardiovascular disease, including hypertension.
- *Australian Medicines Handbook 2000.*

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