

Pharmacological management of hypertension

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ABSTRACT – Hypertension is a major risk factor for cardiovascular disease, and is both common and amenable to treatment. Several major new studies have appeared recently and in response the National Institute for Health and Clinical Excellence and the British Hypertension Society have collaborated to update their respective guidelines on primary hypertension, and to agree joint recommendations. The update focuses only on pharmacological aspects of treatment. Wherever possible, the recommendations are based on the clinical outcomes of mortality, stroke, myocardial infarction, heart failure, and new onset diabetes mellitus, rather than on blood pressure lowering. A brief treatment algorithm is included. In summary, either calcium channel inhibitors or thiazide-type diuretics should be the preferred initial agent for use in primary hypertension in most patients, although angiotensin converting enzyme (ACE) inhibitors (including angiotensin-II receptor inhibitors if ACE-intolerant) are preferred in patients younger than 55.

KEY WORDS: angiotensin converting enzyme inhibitors, angiotensin receptor blockers, beta-blockers, calcium channel inhibitors, primary hypertension, thiazide-type diuretics

Introduction

Hypertension is one of the major risk factors for stroke, coronary heart disease, heart failure and other cardiovascular diseases. It is both common and amenable to treatment, and as such it is a prime candidate for the application of national guidelines. In recent years, influential guidelines for use in the management of hypertension in the UK have been produced by both the National Institute for Health and Clinical Excellence (NICE) and the British Hypertension Society (BHS).^{1,2} While these were in agreement on many points there were some important differences, particularly in the suggested sequencing of pharmacological therapy.

Several major new studies have appeared since the most recent versions of both the NICE and BHS

guidelines. This new evidence suggested that both current guidelines could usefully be updated, and there were obvious potential advantages for consistency of patient care if the two organisations could jointly agree their recommendations. This guideline presents a concise version of the outcome of the resulting initiative,^{3,4} which aimed to update NICE guidance in collaboration with the BHS.

Limitations of the update

The guideline update is highly focused. It addresses only the pharmacological management of primary hypertension. It does not cover:

- hypertension during pregnancy or diabetes
- the specialist management of secondary hypertension (where the high blood pressure is happening because of another medical problem).

The full versions of NICE¹ and/or BHS guidelines² contain advice on measurement of blood pressure, routine screening tests, lifestyle interventions, estimations of 10-year cardiovascular disease risk and clinical features which might suggest secondary hypertension. These were therefore not reconsidered during this guideline update.

Clinical evidence

The analysis concentrated on important clinical outcomes, namely:

- mortality
- stroke
- myocardial infarction
- hospitalised unstable angina or heart failure
- new onset diabetes mellitus.

Evidence specific to younger patients was extremely sparse.

To formulate recommendations here it was necessary to consider papers in which blood-pressure lowering was the main outcome measure and to include papers pre-dating July 2004 in the search.

A detailed summary of the evidence is given in the updated full guideline.³ It is a challenge to summarise this evidence adequately for the purposes of a concise version and to do so it is necessary to make

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assumptions about the homogeneity of effectiveness of the various drugs that comprise each of the groups A–D shown in Table 1. These summary findings reflect the predominant populations of the major studies, composed mainly of older patients from white ethnic groups (Table 2).

Cost effectiveness

Overall, group B drugs were the least cost-effective option and the initial choices indicated in the recommended treatment algorithm were the most cost effective.

Conclusions from this evidence

The Guideline Development Group concluded that:

- Either group C or group D agents should be the preferred initial agent for use in primary hypertension in these patients.
- Group B drugs appeared the least appropriate choice in primary hypertension (although the full guideline lists patients who may still be treated with beta-blockers, for example those with co-existing ischaemic heart disease).

Subgroup analysis

Black populations

- A reasonably large sub-group analysis suggested that group B, and particularly group A, drugs were less effective at lowering blood pressure when compared with group C or group D drugs in black populations, regardless of age.
- Therefore, group C and D drugs are also the most appropriate initial therapy choice in uncomplicated hypertension in these patients.

Younger patients

Clinical outcome data were sparse for younger white patients, but the available evidence suggested that:

- Group A and B drugs are more effective initial therapy choices for younger patients (those under 55).

Table 1. The groups of antihypertensive agents tested.

Group A	Angiotensin-converting (ACE) inhibitors (including angiotensin-II receptor antagonists if ACE-inhibitor intolerant)
Group B	Beta-blockers
Group C	Calcium-channel inhibitors
Group D	Thiazide-type diuretics

Table 2. Summary of head-to-head comparisons of drug groups.

Comparison	Findings	
A versus B	A	B
	Lower incidence of <ul style="list-style-type: none"> • stroke • new onset diabetes Fewer study withdrawals	
A versus C	A	C
	Lower incidence of <ul style="list-style-type: none"> • heart failure • new onset diabetes 	Lower incidence of <ul style="list-style-type: none"> • stroke Fewer study withdrawals
A versus D	A	D
	Lower incidence of <ul style="list-style-type: none"> • new onset diabetes 	Lower incidence of <ul style="list-style-type: none"> • stroke
B versus C	B	C
		Lower incidence of <ul style="list-style-type: none"> • stroke • new onset diabetes
C versus D	C	D
	Lower incidence of <ul style="list-style-type: none"> • new onset diabetes 	Lower incidence of <ul style="list-style-type: none"> • heart failure

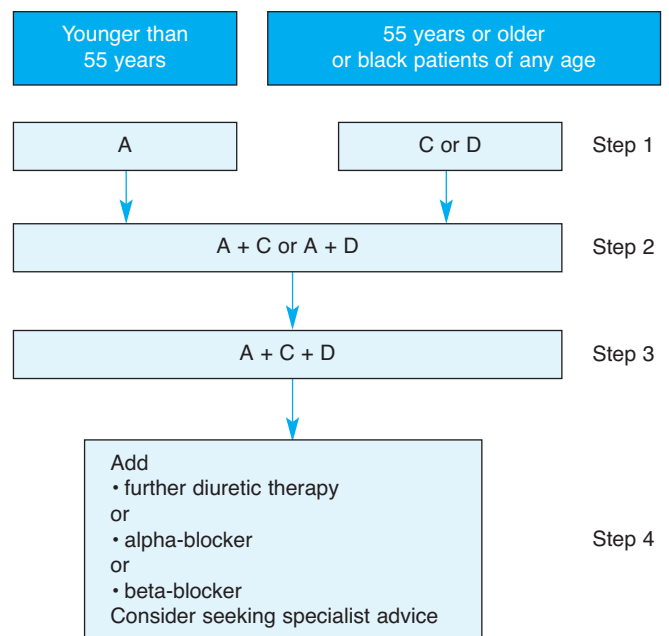


Fig 1. Choosing drugs for patients newly diagnosed with hypertension. Black patients are those of African or Caribbean descent, and not mixed-race, Asian or Chinese patients. Beta-blockers are not a preferred initial therapy for hypertension but an alternative to A in patients younger than 55 years in whom A is not tolerated or is contraindicated (including women of childbearing potential). A = angiotensin-converting (ACE) inhibitor (consider angiotensin-II receptor antagonist if ACE-inhibitor intolerant); C = calcium-channel blocker; D = thiazide-type diuretics. See summary of the guidelines, 6.2.

Summary of the guidelines

Treatment overview

This update was concerned only with pharmacological therapy for primary hypertension. Other aspects of the management of hypertension should be considered as detailed in National Institute for Health and Clinical Excellence clinical guideline 34.^{3,4}

General recommendations

- Lifestyle interventions such as a healthy, low-calorie diet, aerobic exercise and a reduction in excess alcohol consumption can produce worthwhile reduction in blood pressure and should be discussed with the patient.
- A formal assessment of cardiovascular disease (CVD) risk should be considered.

Benefits versus risks of drug treatments

Appropriate guidance and materials about the benefits of drugs and the unwanted side effects sometimes experienced should be provided in order to help patients make informed choices.

Recommendations for pharmacological treatment ^a	Grade
<p>1 Drug therapy reduces the risk of cardiovascular disease and death</p> <p>Drug therapy should be offered to:</p> <ul style="list-style-type: none"> • patients with persistent high blood pressure (BP) of 160/100 mmHg or more • patients at raised CVD risk (10-year risk of CVD \geq20% or existing CVD or target organ damage) with persistent BP of more than 140/90 mmHg. 	A
<p>2 Target blood pressure</p> <p>Antihypertensive drugs should be offered, adding different drugs if necessary, to achieve a target of 140/90 mmHg, or until further treatment is inappropriate or declined.</p>	A
<p>3 Titration of dose</p> <p>Drug doses should be titrated as described in the British National Formulary noting any cautions and contraindications.</p>	A
<p>4 Treatment steps</p> <p>4.1 <i>First choice therapy</i></p> <ul style="list-style-type: none"> • In hypertensive patients aged 55 and over, or black^b patients of any age, the first choice for initial therapy should be either a calcium-channel blocker or a thiazide-type diuretic. A • In hypertensive patients younger than 55, the first choice for initial therapy should be an angiotensin-converting (ACE) inhibitor.^c C <p>4.2 <i>Second-line agents</i></p> <ul style="list-style-type: none"> • If initial therapy was with a calcium-channel blocker or a thiazide-type diuretic and a second drug is required, add an ACE inhibitor.^c B • If initial therapy was with an ACE inhibitor,^c add a calcium-channel blocker or a thiazide-type diuretic. B <p>4.3 <i>Third-line agents</i></p> <p>If treatment with three drugs is required, the combination of ACE inhibitor,^c calcium-channel blocker and thiazide-type diuretic should be used. B</p> <p>4.4 <i>Fourth-line agents</i></p> <p>If BP remains uncontrolled on adequate doses of three drugs, consider adding a fourth and/or seeking expert advice. C</p> <p>If a fourth drug is required, one of the following should be considered:</p> <ul style="list-style-type: none"> • a higher dose of a thiazide-type diuretic or the addition of another diuretic (careful monitoring is recommended) C • beta-blockers • selective alpha-blockers. 	

Summary of the guidelines

Recommendations for pharmacological treatment^a Grade

5 Uncontrolled blood pressure

If BP remains uncontrolled on adequate doses of four drugs and expert advice has not yet been obtained, this should now be sought. C

6 The role of beta-blockers

Beta-blockers are **not** a preferred initial therapy for hypertension. B

However, beta-blockers may be considered in younger people, particularly:

- those with an intolerance or contraindication to ACE inhibitors and angiotensin-II receptor antagonists
- women of child-bearing potential
- patients with evidence of increased sympathetic drive.

6.1 Second-line agents to beta-blockers

In these circumstances, if therapy is initiated with a beta-blocker and a second drug is required, add a calcium-channel blocker rather than a thiazide-type diuretic to reduce the patient's risk of developing diabetes. C

6.2 Failure to control blood pressure

In patients whose BP is not controlled (ie over 140/90 mmHg) despite a treatment regimen including a beta-blocker, treatment should be revised according to the treatment algorithm (Fig 1). C

6.3 Patients with well-controlled blood pressure on beta-blockers

In patients whose BP is well controlled (ie 140/90 mmHg or lower) with a regimen which includes a beta-blocker, long-term management should be considered as part of their routine review. In these patients, there is no absolute need to replace the beta-blocker with an alternative agent. C

7 Other issues

7.1 Isolated systolic hypertension

Offer patients with isolated systolic hypertension (systolic BP >160 mmHg) the same treatment as patients with both raised systolic and diastolic blood pressure. A

7.2 Older patients: over 80 years

Offer patients over 80 years old the same treatment as other patients over 55, taking account of any comorbidity and their existing burden of drug use. A

7.3 Drug regimen

Where possible, recommend treatment with drugs taken only once a day. A

7.4 Cost

Prescribe non-proprietary drugs where these are appropriate and minimise cost. B

a See treatment algorithm (Fig 1) for patients newly diagnosed with hypertension.

b Including both Black African and Black Caribbean patients and not Asian, Chinese, mixed-race, or other ethnic groups.

c Use an angiotensin-II receptor antagonist if an ACE inhibitor is not tolerated.

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