ABC of Blood Pressure Reduction

LIAM T BANNAN
D G BEEVERS
NOEL WRIGHT

DRUG TREATMENT

As with detection, the treatment of most hypertensive patients is the responsibility of general practitioners, and few cases need referral to hospital. About 80% of patients may be adequately treated with thiazides or β -adrenergic blockers, or both. These two groups are effective and have an acceptably low incidence of side effects. In adequately treated patients the major problem is persuading the patient to comply with long-term treatment. The primary physician has a major role, particularly in regularly following up his patient.

Thiazides first	Beta-blockers first
Older patients	Young patients
Black patients	Anxious patients
<i>Special problems</i>	
Heart failure (mild)	Angina/ Ischaemic heart disease
Asthma	Gout
Brittle diabetics on insulin	Mild maturity onset diabetics
Cheap	Expensive

Thiazide diuretics

Thiazide diuretics are the cheapest effective way of lowering blood pressure by 10-15 mm Hg. They do so by reducing blood volume and by a direct vasodilator effect. After increased excretion of sodium and water by the kidney, the main initial effect is a reduction of extracellular fluid volume leading to a fall in cardiac output. Subsequently peripheral resistance is diminished and cardiac output returns to near pretreatment levels. Thiazide diuretics are well absorbed from the gut and are mainly excreted through the kidney.

For practical purposes, a thiazide that is cheap and has a duration of action of at least 24 hours should be used—for example, bendrofluazide 5 mg or hydrochlorothiazide 50 mg once daily. Only when patients are taking digitalis or develop symptomatic hypokalaemia should either potassium supplements or potassium-sparing agents be given. When they are necessary they must be used in adequate doses, and the amount in the potassium-diuretic combination tablets is too small to be of any use. While they are more potent as diuretics, the loop diuretics such as frusemide are less potent as antihypertensive agents and should not be used unless there is concomitant renal or cardiac failure.

Side effects of thiazide diuretics

Thiazide diuretics may cause clinically unimportant increases in serum cholesterol concentration, excess renal loss of potassium, impaired glucose tolerance, and hyperuricaemia. If these side effects cause symptoms the diuretic should be withdrawn. Alternatively gout and diabetes should be treated with standard drugs. Rarer side effects include photosensitivity, raised serum calcium concentrations, and blood dyscrasias.

In theory the effects of thiazides on cholesterol and sugar metabolism might have an adverse effect on coronary risk score, although this would be greatly offset by the beneficial effect of lowering blood pressure.

Beta-blockers

Beta-blockers inhibit competitively the action of catecholamines on beta-adrenergic receptors. Some block both β_1 -receptors (heart rate and force of contraction) and β_2 -receptors (vascular and bronchial smooth muscle), whereas others block β_1 -receptors, and are relatively cardioselective. They lower blood pressure by reducing cardiac output and by a central effect on the vasomotor centre. They also lower peripheral resistance and block the release of renin from the renal juxtaglomerular apparatus. All beta-blockers are well absorbed from the gastrointestinal tract. They are eliminated by metabolism in the liver or excretion by the kidney, or both. If blood pressure is not reduced by one beta-blocker it is unlikely to be reduced by another. The individual beta-blocker is chosen because of its relative freedom from side effects, ease of dosage, and cost. There is little to choose between the many beta-blockers available, but we prefer those that are cardioselective—for example, atenolol or metoprolol. Many beta-blockers can be given once daily, and these are preferable in treating hypertension, as a single daily dose regimen increases tablet adherence.

Side effects of beta-blockers

Beta-blockers should not be given to patients with reversible obstructive airways disease. If they must be used in such patients those that are cardioselective have theoretical advantages but should be used in conjunction with bronchodilators. Beta-blockers should also not be used in patients with congestive cardiac failure except when the failure is causally related to hypertension. In general patients with heart block should not be given beta-blockers. Beta-blockers may interfere with the ability to recognise hypoglycaemia and should therefore be used with caution in brittle diabetics. Beta-blockers may aggravate peripheral vascular disease. They may also cause central nervous system side effects such as vivid dreams.

Third step

Either a thiazide diuretic or a beta-blocker may be used as the initial drug in the treatment of blood pressure. If one fails to reduce the blood pressure to a satisfactory level the other should be added. Hypokalaemia is less likely to occur with the combination of a thiazide and beta-blocker than with a thiazide alone. At present a multicentre international trial is in progress to investigate differences in prognosis between patients treated with thiazide diuretics and those treated with beta-blockers. If the combination of a beta-blocker and a thiazide diuretic fails to lower the blood pressure sufficiently and patient compliance is not in doubt a vasodilator should be added.

When thiazides are used in conjunction with beta-blockers the need for potassium supplements is further reduced. Combined beta-blocker and thiazide tablets are now available, and they have much to recommend them, as they simplify drug regimens.

Methyldopa

Methyldopa has largely been replaced by beta-blockers, but some patients cannot take beta-blockers. In these a centrally acting drug such as methyldopa remains the main choice either alone or with a thiazide, although prazosin (see later) may be effective.

Methyldopa's major site of action is the brain stem. It interferes with sympathetic outflow from the vasomotor centre and thereby reduces peripheral resistance. It also has a minimal direct effect on the postganglionic sympathetic nerve fibres. Absorption from the gut varies, but on average less than half is absorbed. Excretion is mainly by the kidney. Initially it should be given in a dose of 250 mg twice daily, increasing to a maximum of 2 g/day. Side effects are dose-related and can be prevented if doses are kept below 750 mg/day.

Side effects of methyldopa—Methyldopa may cause sleepiness, orthostatic hypotension, impotence, dry mouth, and nasal congestion. Twenty per cent of patients develop a direct positive Coombs test, but haemolytic anaemia is rare. Fluid retention occurs and combination with a diuretic enhances its antihypertensive effect. Drug fever and occasionally drug-induced hepatitis are other well-documented side effects.

Methyldopa, therefore, has advantages in patients with obstructive airways disease, diabetes, and gout, in whom either a beta-blocker or a thiazide is unsatisfactory. Methyldopa remains the main antihypertensive agent for use in pregnancy.

Dr Liam Bannan, BSC, MRCPI, is an honorary research fellow, University of Birmingham, Dr D G Beevers, MD, MRCP, a senior lecturer in medicine, University of Birmingham, and Dr Noel Wright, MB, FRCPD, a consultant physician, Dudley Road Hospital, Birmingham.