Management of hypertension in diabetes: blood pressure goals and choice of agents

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Introduction
Diabetes and hypertension are common diseases and are closely interrelated and often coexist. About 151 million people are estimated to have diabetes worldwide and it is predicted that the global prevalence will double by 2030.1 The coexistence of hypertension and diabetes is particularly pernicious with increased risk of cardiovascular disease and nephropathic complications (see Table 1).2 Hypertension is twice as common in diabetic patients compared with the non-diabetic population.1 In patients with type 1 diabetes, the prevalence of hypertension rises from 5% at 10 years, to 33% at 20 years, and 70% at 40 years disease duration. As many as two-thirds of patients with type 2 diabetes have hypertension. However, the prevalence of hypertension in diabetes varies worldwide. In Africa, prevalence rates between 30% and 45% have been reported among diabetic clinic patients.3-7 Blacks are twice more likely to have both diseases than Whites and about 90% of patients with this dual diagnosis have type 2 diabetes.2

Pathogenesis
There are many factors that contribute to hypertension in diabetes. In addition to the development of diabetic nephropathy, other factors are hyperinsulinaemia, obesity, extracellular fluid (ECF) volume expansion, increased arterial stiffness, hyperlipidaemia and coagulation abnormalities.2,8,9 Hyperinsulinaemia, due to insulin resistance or to insulin administration, may increase systemic blood pressure. Insulin promotes renal sodium retention and also increases sympathetic activity. It modifies ion transport across cell membranes producing increased cytosolic calcium levels in insulin-sensitive vascular and renal tissues. Thus, there is increased vascular reactivity to vasoconstrictors and increased total exchangeable body sodium.10-12 Hyperinsulinaemia may be a link to explain the association between obesity and hypertension both in non-diabetic patients and those with type 2 diabetes.

Table 1 Complications of hypertension in diabetes

<table>
<thead>
<tr>
<th>Microvascular complications</th>
<th>Macrovacular complications</th>
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</thead>
<tbody>
<tr>
<td>Retinopathy</td>
<td>Coronary artery disease</td>
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<tr>
<td>Nephropathy</td>
<td>Cerebrovascular disease</td>
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<tr>
<td>Autonomic neuropathy</td>
<td>Peripheral vascular disease</td>
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Treatment: blood pressure goals and choice of agents
The goals of management are to reduce blood pressure to currently recommended target levels and thus to reduce the risk of cardiovascular and renal complications with little or no metabolic adverse effect. Previous blood pressure goals of <130/85 mmHg promoted by recommendations13 have been replaced by the American Diabetes Association (ADA) guidelines14 that support reduction to <130/80 mmHg, with an optimal target of <120/80 mmHg, particularly in patients with proteinuria or renal insufficiency. This goal is also endorsed by the Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 6) guidelines,15 two other American professional societies,16,17 the European Society of Hypertension (ESH), the European Society of Cardiology (ESC),18, 19 and by the International Society of Hypertension (ISH). The achievement of this blood pressure control target is essential if the excess risk of target organ complications in hypertension and diabetes is to be reduced.

To achieve this goal, early and rigorous control of blood pressure with lifestyle modifications and anti-hypertensive drugs is paramount and should be introduced early.

Lifestyle modifications
The Dietary Approaches to Stop Hypertension trial has shown that lifestyle changes such as aerobic exercise and diets low in sodium and high in potassium can decrease blood pressure.20 There is also associated improvement in insulin resistance, which may enhance glycaemic control, reduce cardiovascular risk and slow down albumin excretion rate, thus improving renal function.21 Low salt intake is particularly important in these patients, because excess sodium intake blunts the effects of anti-
hypertensive drugs.  

Although lifestyle modifications are beneficial, consistency is often difficult and only a few patients are able to achieve blood pressure control with these interventions.

**Antihypertensive medications**

Currently, the available body of evidence is in support of the use of combinations of drugs to achieve target blood pressure goals.  The process of treatment decision making should be individualised with the combination of drugs tailored to the severity of hypertension and presence of associated risk factors and co-morbidities.

**Thiazide diuretics**

Thiazide diuretics have been shown to improve morbidity and mortality in patients with hypertension.  The use of low-dose thiazide diuretics (e.g. hydrochlorothiazide <25 mg per day) in these patients is well documented and widely recommended. In the prespecified diabetic subgroup of ALLHAT, treatment that began with chlorthalidone reduced the primary endpoint of fatal coronary heart disease and myocardial infarction to the same degree as treatment based on lisinopril and amlo-dipine.  The potential ability of thiazide diuretics to worsen glycaemic control seems to be small and does not produce more cardiovascular events than other classes of antihypertensive drugs.  Also, all long-term studies with low-dose diuretics have not been shown to have a negative impact on serum lipid parameters.

**Angiotensin-converting enzyme inhibitors**

Angiotensin-converting enzyme inhibitors (ACEI’s) are often the preferred agents in the treatment of HBP in diabetic hypertension, though their particular role is for those with nephropathy or microalbuminuria. Many clinical trials worldwide have shown that ACEIs have renoprotective and probable cardiovascular benefits.  They have also been shown to reduce fibrinolysis, endothelial dysfunction, and to increase insulin sensitivity.  These drugs may be used alone, but are much more effective when combined with a thiazide diuretic or other antihypertensive drugs. ACEIs are metabolically neutral; their main side-effects are dry cough and angio-oedema, but they may give rise to mild hyperkalaemia, especially in some elderly patients with type 2 diabetes.

**Angiotensin receptor blockers**

Angiotensin receptor blockers (ARBs) are especially recommended for use in type 2 diabetes with nephropathy or microalbuminuria. The result of the Candesartan and Lisinopril Microalbuminuria (CALM) study showed that candesartan was as effective as lisinopril in blood pressure reduction and reduction of microalbuminuria. ARBs have an antiproteinuric effect that is independent of blood pressure lowering. ARBs should also be considered when ACEs are contraindicated, or are causing serious adverse reactions.

**Calcium channel blockers**

Although controversy exists on the use of calcium channel blockers (CCBs), particularly dihydropyridines, in patients with hypertension and diabetes, these agents may still be useful as part of combination treatment. Several clinical outcome trials have shown that CCBs reduced cardiovascular disease events in diabetics compared to placebo.  CCBs in combination with ACEI’s further reduce blood pressure and albuminuria. They have no adverse effect on carbohydrate and lipid metabolism.

**Beta blockers**

Beta blockers (BBs) are beneficial in patients with hypertension and diabetes because they reduce cardiovascular events and delay renal disease progression. They are particularly useful in the setting of coronary artery disease. These agents have adverse metabolic effects and may also blunt adrenaline-mediated hypoglycaemic awareness. However, these potential problems are usually less with cardioselective agents and are not absolute contraindications. Carvediol, has been shown to cause fewer alterations in lipid and glucose levels compared with traditional beta blockers.

**Moxonidine**

This drug reduces central sympathetic drive, plasma catecholamine concentrations and peripheral vascular resistance. It has been shown to have neutral or beneficial effects on lipid and glucose metabolism. The weight of available evidence appears to favour moxonidine as part of combination treatment for resistant hypertension in diabetes.

**Conclusion**

Hypertension in patients with diabetes is a common coexistence with substantial morbidity and mortality. Prompt and aggressive control of blood pressure in patients with diabetes has dramatic and significant benefits and should be accorded the greatest priority in diabetes management. The blood pressure reduction goal should be <130/80 mmHg. Lifestyle modifications should be emphasised and continuously reinforced. Although the choice of antihypertensive drugs is best patient-individualised and achievement of blood pressure goals often requires combination treatment, thiazide diuretics, ACEIs or ARBs may be the first-line drugs.

**References**

5. Osuntokun BO. Hypertension in Nigerian diabetics: a study of
Review Article


27. Veterans Administration Cooperative Study Group on Antihypertensive Agents. Effect of treatment on morbidity in hypertension II. Results in patients with diastolic blood pressure averaging 90 through 114mmHg. JAMA 1971; 215: 43–52.


