Hypertension in diabetes

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SYNOPSIS

Good management of blood pressure is at least as important as good control of blood glucose and the reduction of cholesterol in preventing the complications of diabetes. The degree to which blood pressure is lowered and the choice of drugs must be influenced by the doctor's awareness of the patient's other health problems and the potential adverse effects. Age alone should not be a factor in determining the target blood pressure. Controlling the blood pressure often requires more than one antihypertensive drug. Tight control of the patient's blood pressure reduces macrovascular complications, but may not significantly reduce all-cause mortality. Treatment therefore includes the management of the patient's other risk factors.

Index words: cardiovascular, complications, ACE inhibitors, calcium antagonists.

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Introduction

About half the diabetic population are hypertensive and, depending on the ethnic group, between 5% and 25% of people with hypertension have diabetes. Hypertension and diabetes are a critical combination for the development of both micro- and macrovascular disease. The major cause of excess mortality in diabetes is cardiovascular disease. Nephropathy is also a major consequence of diabetes and hypertension; diabetic nephropathy is a major contributor to the growing need for renal transplants. The addition of diabetes to even mild grade hypertension (WHO-ISH guidelines 140/90 to 159/99 mmHg) immediately places the patient in a high-risk category. Such patients require a comprehensive assessment of their vascular risk factors including history of previous cardiovascular events.

South Asians who have migrated to countries such as Australia and the UK have an especially high mortality from coronary heart disease. The low proportion of deaths from coronary heart disease in Japanese people with diabetes, despite high rates of smoking and hypertension, suggests that the more favourable lipid profiles of the Japanese are protective. This emphasises the importance of managing lipids in hypertensive patients with diabetes.

The Diabetes Control and Complications Trial and the UK Prospective Diabetes Study (UKPDS) showed the importance of good blood glucose control in the prevention of microvascular complications. Neither study was able to show that tight blood glucose control reduced heart attacks and strokes. The role of hypertension, smoking and hyperlipidaemia as precipitants of macrovascular disease in people without diabetes is well established. Logically, all these factors must be attacked to prevent complications of diabetes due to large vessel disease. This involves lifestyle changes (see box) as well as drugs.

Does a policy of tight blood pressure control reduce the risk of complications?

The impact of a tight blood pressure control policy was investigated in a UKPDS sub-study.[1] This randomly allocated nearly 1200 patients to tight control (target blood pressure less than 150/85 mmHg) or less rigorous control (less than 180/105 mmHg). Reductions in risk in the group assigned to tight control, compared with the group assigned to less tight control, were 44% (95% confidence interval 11–65%, number needed to treat (NNT) 22) for strokes and 32% (6–51%, NNT 18) in deaths related to diabetes. However, the reductions in deaths due to myocardial infarction and all-cause mortality were not statistically significant. Although the risk of amputations was reduced by 49% this was not a statistically significant effect. When all macrovascular events (myocardial infarction, sudden death, stroke and peripheral vascular disease) were combined, the group assigned to tight blood pressure control had a statistically significant 34% risk reduction (NNT 18). These results are comparable with the outcomes of:

- a meta-analysis of clinical trials of improved blood pressure control in the general population
- patients with diabetes in the Hypertension Optimal Treatment (HOT) study[2]
- the sub-group of patients with type 2 diabetes in the Systolic Hypertension in the Elderly Program (SHEP).

Is such a policy cost-effective?

These studies of hypertension and diabetes all confirm the importance of good blood pressure control as well as good blood glucose control. A cost-effectiveness analysis of the

Lifestyle strategies to reduce cardiovascular risk

Stop smoking
Lose weight
Reduce sodium intake (less than 2 g or 88 mmol per day)
Moderate alcohol intake (no more than 2 drinks per day)
Regular exercise
Relax and manage/relieve stress *
Use less saturated fat, more fish oils *
Maintain adequate potassium, calcium and magnesium intake *

* Objective evidence equivocal

UKPDS data concluded that tight control of blood pressure in hypertensive patients with type 2 diabetes substantially reduced the cost of complications, and increased the interval without complications. The cost-effectiveness ratio compared favourably with accepted healthcare programs to reduce cardiovascular risk such as cholesterol lowering and advice on lifestyle. The costs ranged between £390 and £1049 per extra year free from diabetic end-points and between £261 and £720 per life gained.[3]

How tight is tight control?

The prospective observational part of the UKPDS[4] hypertension sub-study showed a clear reduction in end-points associated with diabetes if the systolic blood pressure was reduced by 10 mmHg. Practitioners have three sets of guidelines to assist them (see Table 1) but must ultimately be guided by common sense and their knowledge of the patient when setting individual targets. Factors such as renal disease, previous treatment, risk of falling and compliance with medication have to be balanced against the significant benefits to be gained by rigorous blood pressure control. Home blood pressure monitoring may help to guide the effectiveness of therapy.

Elderly diabetic patients with the highest systolic and pulse pressure have the highest absolute risk of adverse cardiovascular outcomes. They therefore have the most to gain from tight blood pressure control and should not be undertreated simply because of their age.

Are all drugs equal or are some more equal than others?

There is now agreement that thiazide diuretics[5] and beta blockers are effective in reducing morbidity and mortality in patients with diabetes and hypertension.[6,7] These drugs should be first-line therapy in spite of the fact that the patient has diabetes. The two areas of uncertainty are whether there are particular risks in using calcium antagonists, or particular benefits in using ACE inhibitors. This choice is controversial in the treatment of hypertension even in patients without diabetes. Two recent meta-analyses[6,7] using the same trials, but different selection criteria, reached conflicting conclusions. Both studies are consistent with the recommendations of the sixth report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure, that diuretics or beta blockers are first-line therapy for the treatment of uncomplicated hypertension. The studies support the option of ACE inhibitors as first-line treatment, and suggest that they may have particular benefits in patients (such as those with diabetes) who are at high risk of heart failure.

The evidence about calcium antagonists in hypertension is much less clear. One review[8] suggested that calcium antagonists reduce the risk of both major cardiovascular events and cardiovascular death by 28% compared to placebo. However, a more recent study, comparing calcium antagonists with other antihypertensive drugs, found that they had similar rates of cardiovascular mortality, but a significantly increased risk of myocardial infarction (26%), congestive heart failure (25%) and major cardiovascular disease (combined 10%).[9]

Table 1

Recommended blood pressure targets in the treatment of hypertension

WHO-ISH*	JNC VI †	NHF ‡
<130/85 mmHg (young, middle-aged, diabetic)	<140/90 mmHg (lower if tolerated)	<130/85 mmHg (under 65 years, diabetes, renal disease)
<140/90 mmHg (elderly)		<140/90 mmHg (over 65)

* World Health Organization-International Society of Hypertension

† Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure

‡ National Heart Foundation

Not surprisingly, systematic reviews of studies that have reported outcomes in patients with diabetes and hypertension are equally confusing. All agree in concluding that intensive control of blood pressure reduces cardiovascular morbidity and mortality. They also agree that combination therapy is frequently required and may be more beneficial than monotherapy, but like the studies of hypertension overall, they disagree on the role of calcium antagonists. Perhaps the safest advice in these circumstances is to be cautious about using calcium antagonists as first-line drug therapy in patients, such as those with diabetes, who are at high risk of coronary heart disease and heart failure. This does not preclude the use of calcium antagonists when combination therapy is required to achieve optimal blood pressure control. To achieve a target of less than 130/85 mmHg will require combination therapy in more than 60% of patients.

The MICRO-HOPE sub-study[10] of the heart outcomes prevention evaluation study included 3577 people with diabetes. They had at least one other risk factor or a previous cardiovascular event, but had no clinical proteinuria, heart failure or low ejection fraction. The study had a combined primary outcome of myocardial infarction, stroke or cardiovascular death. After adjustment for the changes in systolic blood pressure (2.4 mmHg) and diastolic blood pressure (1.0 mmHg) an ACE inhibitor lowered the risk of the combined primary outcome by 25% (12–36%). As the study was not designed to be a trial of the effect of lowering blood pressure, and medication was not titrated to achieve prespecified target blood pressure levels, only general comparisons can be made with other studies. It suggests that the benefits of treatment may result from mechanisms other than the lowering of blood pressure. Whether these mechanisms are unique to ACE inhibitors is unclear.

While AT_1 receptor antagonists (commonly referred to as angiotensin II antagonists) may have the same benefits as ACE inhibitors, this has yet to be shown in clinical trials. The new combinations of an ACE inhibitor or an AT_1 receptor

antagonist with a thiazide may be of value when there is the need to add a thiazide to improve blood pressure control after titration of the other drug to the maximum tolerated dose.

Conclusion

While current evidence may be difficult to interpret in some areas of the treatment of hypertension in diabetes, there is no conflict in recommending tight blood pressure control and the use of combination therapy if necessary to achieve this result. The final choice of drugs and optimal blood pressure control for each patient must be influenced by knowledge of the potential harms and benefits to each individual. It is no different in this respect from the control of blood glucose. Blood pressure and glucose both need to be individually tailored as part of a comprehensive cardiovascular risk management strategy. This includes a discussion of the aims and potential problems of treatment with the patient.

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FURTHER READING

See resources on the following web site:

'Diabetes on the Internet 2001' www.diabetes.org.au/ct_2001.htm

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Self-test questions

The following statements are either true or false (answers on page 23)

3. Tight control of blood pressure may not significantly reduce fatal myocardial infarctions in patients with diabetes.
4. To achieve a target blood pressure of 130/85 mmHg most patients with hypertension and diabetes will require only one antihypertensive drug.

Patient support organisations

Diabetes Australia

Diabetes Australia consists of twelve organisations:

- the eight State and Territory Associations of Diabetes Australia
- Australian Diabetes Society
- Australian Diabetes Educators Association
- Kellion Diabetes Foundation
- Diabetes Research Foundation – Western Australia.

All funds raised by or on behalf of Diabetes Australia are re-invested into research, health services, provision of self-management products and services, and public awareness.

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