Prevention of cardiovascular disease in type 2 diabetes

June Van Valkenburg

Introduction

In recent years, the global incidence of type 2 diabetes has increased dramatically. Cardiovascular-related morbidity and mortality are major issues in people with type 2 diabetes. This article considers the evidence, much of it derived from large-scale studies, showing the benefits of primary prevention of cardiovascular disease in type 2 diabetes e.g. by treatment of risk factors such as hypertension and hyperlipidaemia. Aspirin and HRT may be useful. The current body of evidence can be incorporated into a management plan — the steps involved in the implementation of such a plan are given.

Type 2 diabetes affects about 3% of the UK population (Marshall, 1999). Cardiovascular disease (CVD) remains the cause of death in 60–70% of people with type 2 diabetes (Wingard and Barrett-Connor, 1995). Throughout the world, the prevalence of type 2 diabetes has been increasing dramatically in the last few years. This can be attributed to changes in food consumption and lifestyle resulting in decreasing levels of physical activity and increasing obesity (Nathan et al, 1997).

In the last decade, the CVD mortality rate has declined in people without diabetes (by 36% in men and 27% in women). In men with diabetes, there has been a decrease of 13%. However, the rate has increased by 23% in women with diabetes (Gu et al, 1999).

Haffner et al (1998) found that the risk of myocardial infarction (MI) in people with diabetes without previous MI was as high as people without diabetes with one previous MI. Therefore, their cardiovascular risk factors should be treated just as aggressively. The finding was based on a seven year analysis of 1373 people without diabetes and 1059 people with diabetes.

The Health Survey of England 1991–94 (involving 39629 adults) found a considerable unmet need for cardiovascular risk factor intervention, especially for hypertension and hyperlipidaemia (Colhoun et al, 1999). Of subjects with diabetes, 51% had hypertension. Two-thirds of patients with diabetes/hypertension received antihypertensive treatment, yet only half achieved blood pressure (BP) of under 160/90 mmHg.

Of subjects aged below 70 years, 29% required lipid-lowering therapy but 94% of them were not receiving it.

Primary prevention studies

Studies have looked at primary prevention of CVD in people with type 2 diabetes. Some of these are mentioned below.

Treating hypertension

In the hypertensive part of the UK Prospective Diabetes Study (UKPDS Group, 1998), people with type 2 diabetes (mean BP of 160/94 mmHg) were randomised to intensive or conventional antihypertensive treatment using either a β-blocker or angiotensin converting enzyme (ACE) inhibitor. The average BPs achieved were 144/82 mmHg in the intensive group and 154/87 mmHg in the conventional group. In the intensive group, treatment of hypertension was associated with reduction of risks for stroke (44%), deaths related to diabetes (32%) and microvascular disease (37%).

The Hypertension Optimal Treatment (HOT) study (Hansson et al, 1998) demonstrated the benefits of lowering BP to ±140/85 mmHg in people with hypertension. In people with diabetes, there was a 51% reduction in major cardiovascular events (non-fatal MI, non-fatal stroke, and

ARTICLE POINTS

1 People with diabetes are at high risk of cardiovascular disease (CVD).

2 Studies show that CVD can be reduced by treating hypertension, hyperlipidaemia and microalbuminuria.

3 There is evidence that aspirin or hormone replacement therapy may reduce CVD risk.

4 Readers may formulate a primary prevention plan using the evidence provided in the article.

5 A plan for the primary prevention of CVD is successful when it prevents the long-term development of CVD.

KEY WORDS

- Type 2 diabetes
- Cardiovascular disease
- Primary prevention
- Risk factor reduction

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PAGE POINTS

1 Tight control of hypertension reduces the risk of cardiovascular events.

2 Treatment of hyperlipidaemia reduces the risk of cardiovascular events.

3 People with impaired fasting glucose have a higher rate of recurrent cardiovascular events than people without diabetes.

4 Microalbuminuria is a risk factor for CVD in people with diabetes.

5 Aspirin treatment should be considered when appropriate to reduce CVD risk.

cardiovascular death) in the group with target diastolic BP <80 mmHg, as compared to the group with a target of <90 mmHg.

These studies provide evidence that the life-threatening complications of type 2 diabetes can be significantly reduced by tight control of hypertension.

Treating hyperlipidaemia

The Scandinavian Simvastatin Survival Study (Herman et al, 1999) showed the benefits of reducing LDL-cholesterol levels in people with diabetes. In this study, lipid-lowering therapy produced a greater reduction in the rate of coronary events in people with diabetes than in people without diabetes (55% versus 32%). Following simvastatin treatment, the number of hospitalisations related to CVD was reduced more in people with diabetes (40% versus 23% in people without diabetes). For people with diabetes, the average length of stay was reduced by 2.4 days and there was a net cost saving of $1801 per subject.

The Cholesterol and Recurrent Events Trial (Goldberg et al, 1998) was a five-year placebo controlled study that looked at the effect of pravastatin on coronary events (defined as CHD, death, nonfatal MI, coronary artery bypass graft and revascularisation). There were 4139 people in the study: 586 with diabetes and 3553 without diabetes, of whom 342 had impaired fasting glucose. Pravastatin was shown to reduce the absolute risk of coronary events by 8.1% for people with diabetes, compared with 5.2% for people without diabetes. Pravastatin treatment was associated with a lower recurrence rate for coronary events. Impairment of fasting glucose was associated with a higher recurrence rate.

The Long-Term Intervention with Pravastatin in Ischemic Disease (LIPID) study (1998) was a double-blind, randomised trial that compared the effects of pravastatin with placebo in 9014 patients over 6.1 years. All patients had a history of MI or unstable angina. Overall, pravastatin reduced the incidence of MI (by 29%), fatal CHD/nonfatal MI (24%), stroke (19%) and coronary revascularisation (20%). In the subgroup of 782 people with diabetes, the incidence of fatal CHD/nonfatal MI was reduced by 19%.

It is not known whether the reductions in morbidity and mortality following treatment for hyperlipidaemia would apply to people with diabetes without documented CVD. These studies, however, provide strong evidence for the aggressive treatment of hyperlipidaemia in people with diabetes.

Treating microalbuminuria

Microalbuminuria is another risk factor for CVD in people with diabetes. Marshall's (1999) analysis of five studies provided evidence that screening for microalbuminuria and early treatment with an ACE inhibitor may be useful as a means of primary prevention of CVD. In all studies, there was a positive correlation between mortality rate and albumin excretion in people with type 2 diabetes. Microalbuminuric patients with type 2 diabetes had a 4-fold higher risk of premature death from a cardiovascular event, as compared with normoalbuminuric patients. It was concluded that 'microalbuminuria may be viewed as one of a cluster of risk factors for both macrovascular and end-stage renal disease'.

Treatment with aspirin

Yudkin (1993) found that the effect of aspirin on cardiovascular deaths in people with diabetes was greater than in people without diabetes (reductions of 9.70 per 1000 and 2.64 per 1000, respectively.) He suggested that patients with microalbuminuria should be considered for aspirin therapy because of their increased cardiovascular mortality risk. Furthermore, he concluded that aspirin treatment in people with diabetes leads to an increased life expectancy of approximately one year (similar to the potential benefit of antihypertensive treatment).

The Antiplatelet Trialists' Collaboration (1994) showed that people with diabetes taking antiplatelet drugs experienced 17% fewer vascular events, compared with 22% fewer in people without diabetes. Wood et al (1999) surveyed 629 patients at a diabetes clinic of large teaching hospital. Only 62.9% of patients with macrovascular complications were receiving aspirin (a total of 86.2% of patients not receiving aspirin had no known contraindication).

The HOT Study showed that aspirin significantly reduced the frequency of

major cardiovascular events by 15% and all MI by 36%. The benefit of aspirin was the same in the groups of people with diabetes and ischaemic heart disease as in the whole HOT population (Hansson et al, 1998).

Clear evidence-based guidelines for aspirin treatment in people with diabetes are needed. Aspirin treatment should be considered in people with diabetes as a means of primary prevention of CVD.

Hormone replacement therapy

Hormone replacement therapy (HRT) is currently used in postmenopausal women to decrease the risk of MI and osteoporotic fractures. A case-controlled study by Lawrenson et al (1999) showed that women with diabetes who were prescribed HRT were 40% less likely to suffer from acute heart disease than women with diabetes who had never been prescribed HRT. It has been suggested that HRT should be prescribed as part of a primary preventive strategy. However, Lawrenson et al (1999) advised caution and said further studies were needed to determine whether HRT should be given routinely to postmenopausal women with diabetes.

Implementation of a primary prevention plan

The primary prevention of CVD should commence when type 2 diabetes is diagnosed. The diagnosis is often made in primary care, and this is where implementation of a primary prevention plan should begin.

Primary care providers should seek to give consistent high quality care to all people with type 2 diabetes. A primary prevention plan is not static — it will change over time to incorporate the latest evidence.

Table 1 lists the treatment targets recommended by different organisations for the primary prevention of CVD in type 2 diabetes.

In line with the finding of Lawrenson et al (1999), HRT could be considered in postmenopausal women with diabetes who have no contraindication. Lifestyle modifications that could be considered when formulating a plan are:

- Weight reduction when indicated
- Smoking cessation
- Regular physical exercise
- Healthy diet
- Limiting of alcohol intake.

PAGE POINTS

1 The diagnosis is often made in primary care, and this is where implementation of a primary prevention plan should begin.

2 A primary prevention plan is not static — it will change over time to incorporate the latest evidence.

Tight control of hypertension has been shown to reduce the incidence of complications in diabetes.

Table 1. Suggested treatment targets for the primary prevention of cardiovascular disease in type 2 diabetes

	Joint British Recommendations	British Diabetic Association	American Diabetes Association
Hypertension control (mmHg)	BP < 140/85	BP < 140/80	BP < 130/80
Lipid control:			
Total cholesterol (mmol/l):	< 5.0	< 5.2	
LDL (mmol/l):	< 3.0	—	< 2.6
HDL (mmol/l):	—	> 1.1	> 0.9 (men) > 1.5 (women)
Fasting triglycerides (mmol/l):	—	< 1.7	< 2.3
Microalbuminuria	—	—	Screen annually and institute ACE inhibitor if indicated
Aspirin	Aspirin 75 mg daily for those aged > 50 and with well controlled hypertension or men at high risk of CHD	—	—
Glycaemic control			
Fasting glucose: (mmol/l)	—	4.0–7.0	—
Preprandial: (mmol/l)	—	4.0–7.0	4.4–6.7
Bedtime: (mmol/l)	—	—	5.6–7.8
HbA_{1c}	—	< 7.0	< 7.0

Wood et al (1998), British Diabetic Association (1997), American Diabetes Association (1999)

STEP-BY-STEP GUIDE TO IMPLEMENTING A PRIMARY PREVENTION PLAN

- Formulation of the plan and specific target goals by the primary care team (GPs, practice nurses and nurse practitioners) for their own work location.
- Clinical audit of the current population of people with type 2 diabetes without clinically overt CVD or other major atherosclerotic disease. The parameters adopted for the primary prevention plan should be used in the audit. The audit should evaluate the percentage of patients having the cardiovascular risk factors addressed (e.g. percentage of patients screened for microalbuminuria annually) and also the percentage of patients meeting the cardiovascular risk factors targets (e.g. percentage of the population receiving antihypertensive treatment that meets the target goal).
- Provision of an educational programme about the plan to all primary care providers on site.
- Comparison of audit data with standards set by management plan.
- Incorporation of the primary prevention plan into diabetes care.
- Setting of a time frame for continued reassessment of the plan. At least one year would be needed to see each person with diabetes at least twice. People with newly diagnosed diabetes and those with uncontrolled diabetes whose medications are being altered would need to be seen more frequently.
- Reaudit after a specific time frame which should also include major cardiovascular events as end-points.
- Incorporation of reaudit results into the primary prevention plan if progress towards target goals is not being achieved.

A step-by-step guide to implementing a primary prevention plan, drawing on evidence outlined in this article, is shown above.

The goal of primary prevention of CVD is to prevent the long-term development of cardiovascular events. Therefore, the effectiveness of the primary prevention plan could only be determined by carrying out regular audits. In the short term, general practices could assess their achievements by monitoring their target goals. ■

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