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Cardiovascular protection in type 2 diabetes mellitus

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The cardiovascular (CV) event rate in patients with type 2 diabetes mellitus (DM) is 2 - 4 times higher than the population average, making macrovascular atherosclerotic disease the commonest cause of death in patients with type 2 DM. CV events are not only more frequent in patients with type 2 DM, but are also associated with higher morbidity and mortality.[1] Coronary artery disease, for example, tends to be more extensive and diffuse in diabetic patients and outcomes are worse after myocardial infarction or revascularisation. Type 2 DM is therefore best regarded as a cardiometabolic disorder (high CV risk state with elevated blood glucose) rather than a pure metabolic disorder in which the elevated blood glucose is the primary abnormality and focus of therapy. Type 2 DM keeps 'bad company': hypertension and dyslipidaemia are highly prevalent and combine with dysglycaemia to damage the vascular system. Single risk factor control is therefore inadequate for CV event prevention – removing only one gang member from the street does not solve the crime problem. Trials that simultaneously address multiple risk factors have reduced the CV event rate most, but even in these trials the residual (unprevented) risk remains unacceptably high.[2] Finding new strategies and treatments to reduce residual risk is high on the research agenda.

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CV protection in type 2 DM therefore requires multifactorial intervention. Lifestyle advice remains central to CV risk reduction. Smoking cessation must be pursued aggressively, regular exercise (within the patient's limitations) should be encouraged and dietary advice may help with lipid, glycaemic and blood pressure (BP) control. BP and lipid control are the 'low hanging fruit' of CV protection – they are often easier to achieve than tight glycaemic control and the numbers needed to treat (NNT) are lower.[3]

NNT for antihypertensive therapy (10/5 mmHg BP reduction over 10 years) to prevent a cardiac event is 26 and 49 for stroke, basing calculations on the event rates found in the United Kingdom Prospective Diabetes Study (UKPDS) control group.[3] The target BP is 130/80 mmHg. The antihypertensive regimen should be based on either an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin-receptor blocker (ARB). Diuretics, calcium-channel blockers and other agents may be added to achieve BP control. Most patients require at least two drugs for BP control.

Reducing cholesterol by 1 mmol/l for 10 years will prevent one cardiac event for every 25 patients treated and one stroke for every 118 patients treated.[3] The primary lipid target is low-density lipoprotein cholesterol (LDLC). The LDLC target for patients clinically free of CV disease is <2.5 mmol/l, while a target of <1.8 mmol/l is desirable for those with CV disease if health care resources are adequate. All patients with CV disease should receive a statin, irrespective of baseline lipid levels. Patients older than 40 years with one other CV risk factor or younger patients with multiple risk factors also need treatment. In clinical practice almost all patients with type 2 DM require a statin. The question is not which patients to treat but whether not treating a particular patient can be justified. Moderate hypertriglyceridaemia and low high-density lipoprotein cholesterol (HDLC) are common in diabetes and treatment of these abnormalities is a promising avenue to reduce residual risk. In a recent study the routine addition of a fibrate to statin therapy did not lower risk, except in the subgroup with the lowest HDLC and highest triglycerides.[4] Combination lipid-lowering therapy is therefore not routinely indicated and should only be initiated at specialist level.

In epidemiological studies there is a clear and consistent link between glycaemia and CV outcomes. In practice it has been difficult to prove that tight glycaemic control reduces not only microvascular complications (which has been conclusively proven) but also macrovascular events. The extensive and often controversial literature on the subject may perhaps be summarised as follows: Tight glycaemic control early in the disease course lowers CV events but the benefits are only seen after many years of follow-up. In older patients with established CV disease and other co-morbidities tight glycaemic control (HbA_{1C} <7.0%) often requires multiple drugs and complex insulin regimens and may be associated with harm.[1,3] The NNT for glycaemic control (HbA_{1C} reduced by 1%) is also higher than that for lipid or BP control, and is estimated to be 41 for coronary heart disease and 400 for stroke.[3] It is therefore important to aim for tight glucose control early in the disease course when patients are still free of co-morbidities and glycaemic control usually requires less complex therapy.

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These patients are likely to benefit from their 'banked good glycaemic control years' when they are older. Aiming for very tight glucose control in older and sicker patients is likely to cause more harm than benefit.

Unless contraindicated, all patients with clinically overt CV disease should take aspirin or clopidogrel (if allergic to aspirin). For the benefits of aspirin to outweigh its risks, prescription for primary prevention should be limited to those with an estimated 10-year risk of >10%. This risk level is generally found in men over 50 years and women over 60 years with at least one other major CV risk factor.[5]

References available at www.cmej.org.za