

## MANAGING CARDIOVASCULAR RISK IN TYPE 2 DIABETES

People with Type 2 diabetes have significantly increased cardiovascular risk compared with the general population and reducing this risk is an integral part of diabetes management.

**Dr Stephen Lawrence**, Primary Care Medical Advisor for Diabetes UK, reviews the lifestyle advice and medication that healthcare professionals should offer to help patients reduce their risk of cardiovascular events

In Type 2 diabetes, as many as 70 per cent of deaths are due to cardiovascular (CV) disease and stroke, with 58 per cent of patients suffering a myocardial infarction (MI) and 12 per cent a stroke. It is therefore extremely important that we make every effort to reduce the CV risk for our patients since once they have had one MI, their risk of a subsequent attack is much greater. Such efforts are worthwhile, as has been shown by the landmark United Kingdom Prospective Diabetes Study which found that this increased risk may be attenuated by even a modest improvement in glycaemic control<sup>1</sup>. For example, a 1 per cent (11mmol/mol) reduction in HbA1c resulted in a 14 per cent fall in the risk of MI.

### Lifestyle Factors

First and foremost, it is important that our patients do understand the great contributions that can be made to reducing their CV risk by addressing key lifestyle factors. Smoking cessation can reduce this risk by up to 50 per cent and patients should be encouraged to engage with smoking cessation clinics. We should also encourage our patients to take aerobic exercise for at least 30 minutes five times a week. Advice on healthy eating (not a 'diabetic diet'), is also an important aspect of reducing CV risk through reducing the intake of saturated fats while maximising dietary intake of polyunsaturates and omega-3 oils. People with Type 2 should also be encouraged to restrict alcohol intake to within the recommended limits for men and women – namely 15 and 21 units weekly respectively – with at least two alcohol-free days per week. The monitoring and reinforcement of lifestyle advice should be a constant feature of the ongoing diabetes management in those with Type 2.

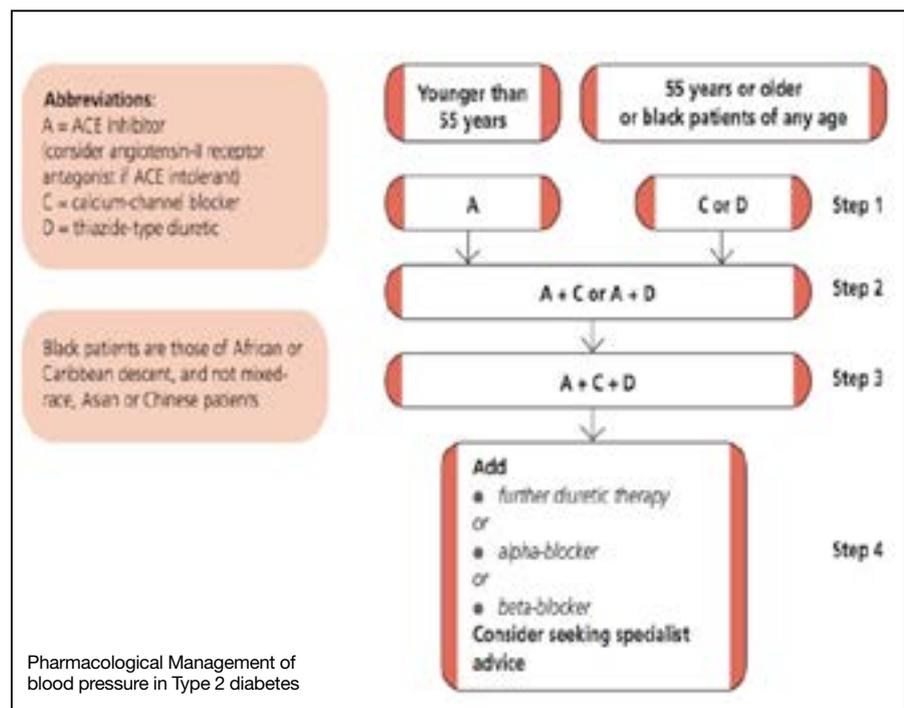
### Blood pressure control

When healthcare professionals consider a pharmacological approach to treating diabetes, they may tend to concentrate on glycaemic control. While this is

important in reducing CV risk, it is by no means the most significant contributor. Evidence suggests that control of blood pressure is of paramount importance with both lifestyle modification and medication playing a role.

Assuming that there are no pre-existing complications, such as chronic kidney disease (CKD), the target blood pressure for a person with Type 2 diabetes is 140/80mmHg or below. In the presence of CKD, the target ceiling falls to 130/70mmHg. The presence of CKD further increases the risk of CV disease in people with Type 2 diabetes.

It is important to consider the most appropriate pharmacological approach to addressing hypertension and diabetes. For Caucasian patients under the age of 55, an angiotensin-converting enzyme (ACE) inhibitor is the drug of choice, owing to the greater sensitivity of the renin/aldosterone system in this group. For patients aged over 55 years and Black (African, African-Caribbean) people with diabetes, the choice should be a calcium channel blocker or diuretic. Should you fail to reach the target level of blood pressure control, it is recommended that drugs be added in a stepwise fashion as in the algorithm below.



Prior to starting treatment with an ACE inhibitor, it is important to check urea and electrolytes and repeat this 10 days later. It is not unusual to see a temporary fall in the estimated glomerular filtration rate (eGFR) of less than 20 per cent. However, should the fall in eGFR be progressive or greater than 25 per cent, the ACE inhibitor should be stopped immediately and the patient referred to a renal physician in order to exclude renal artery stenosis. It is not unusual for patients to experience a cough with an ACE inhibitor, but this should settle within approximately 10 weeks of starting treatment. Should it continue, an alternative agent should be used, such as an angiotensin receptor blocker (ARB). The use of ACE inhibitors or ARBs in women of childbearing age should be avoided, unless the potential risks have been discussed with the woman and agreement has been reached.

### Lipid control

With regard to lipid control, it is important that patients recognise the contribution of lifestyle factors to this issue. Cardiovascular risk will be further reduced by starting the patient on statin therapy. The target total cholesterol value is 4mmol/l or less, while the low-density lipoprotein cholesterol value should be 2mmol/l or less. Counselling people with diabetes about the potential side effects of statin therapy, namely myalgia, increases the chances of treatment adherence. Liver function should be assessed via liver function tests prior to, and eight weeks after, initiating treatment. If the creatine kinase value rises to five times the upper limit of normal, then the statin treatment should be withdrawn. One should expect to see a reduction of total cholesterol of about 27 per cent, following the introduction of a statin at the recommended therapeutic dose. It is important to recognise, however, that subsequent doubling of the dose of the statin will only achieve a further 6 per cent reduction in lipid values.

The recommended statin therapy is simvastatin 40mg. Owing to the risk of potentially life-threatening myopathy, adverse drug reactions or intercurrent illness, the 80mg dose of simvastatin should be avoided, atorvastatin 40mg being preferred. The use of statins in women of childbearing age should be avoided, unless the potential risks have been discussed with the woman and agreement has been reached with her. One should consider adding a fibrate to statin therapy if triglyceride levels remain in the range 2.3–4.5mmol/l on a fasting sample, despite statin therapy. It is also important to consider any secondary causes of high serum triglyceride levels, including poor blood glucose control, alcohol intake, hypothyroidism, renal impairment and liver inflammation.

### The use of aspirin

Historically, prescribers have issued aspirin to people diagnosed with Type 2 diabetes from the outset, working on the assumption that diabetes confers a risk to the patient equivalent to that of a person without diabetes who has previously suffered a MI. However, recent studies have questioned the efficacy of aspirin for people with diabetes with regards to primary prevention. In 2009, the Medicines

and Healthcare products Regulatory Authority (MHRA) gave the following advice<sup>2</sup> on the use of aspirin for the primary prevention of vascular events:

‘Aspirin is not licensed for the primary prevention of vascular events. If aspirin is used in primary prevention, the balance of benefits and risks should be considered for each individual, particularly the presence of risk factors for vascular disease (including conditions such as diabetes) and the risk of gastrointestinal bleeding’.

In a recent study<sup>3</sup>, researchers analysed the outcomes of 18,646 men and women with Type 2 diabetes and no CV disease history, aged between 30 and 80 years, over an average of four years, beginning in 2006. Aspirin treatment was not associated with any benefit in terms of CV outcomes or mortality. In fact, patients who received aspirin had a significant 19 per cent increased risk of non-fatal or fatal CHD. There was also a borderline significant 41 per cent increase in risk of non-fatal or fatal haemorrhage with aspirin. Aspirin use was also associated with a significant 64 per cent increased risk of ventricular ulcer.

The results support current guidance from the MHRA, the European Society of Cardiology and the European Association for the Study of Diabetes, none of which recommend primary prevention with aspirin in patients with diabetes. However, the findings do conflict with the National Institute for Health and Care Excellence Type 2 diabetes guidelines<sup>4</sup> which recommend primary prevention with 75mg/day aspirin in patients aged 50 years or older, if their blood pressure is below 145/90mm/Hg and in patients younger than 50 who have another significant cardiovascular risk factor. The *BMJ* study<sup>3</sup> showed no association between aspirin use and beneficial effects on risks of CV disease or mortality in patients with diabetes and no previous CV disease. It supports the trend towards a more restrictive use of aspirin in these patients, which is also underlined by the increased risk of ventricular ulcer that is associated with the use of aspirin.

## References

- 1 UK Prospective Diabetes Study (UKPDS) Group (1998). Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* 352; 837–853
- 2 MHRA (2009). *Drug Safety Update*. Aspirin: not licensed for the primary prevention of thrombotic vascular disease. [www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON087716](http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON087716)
- 3 Ekström N, Cederholm J, Zethelius B et al (2013). Aspirin treatment and risk of first incident cardiovascular diseases in patients with type 2 diabetes: an observational study from the Swedish National Diabetes Register. *BMJ Open* 3; e002688 doi:10.1136/bmjopen-2013-002688
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