Lipid-modifying therapy in diabetes: New evidence and guidance

The incidence of cardiovascular disease (CVD) is declining in the UK, but it remains an important cause of mortality, particularly in the subgroup of the population with diabetes, where it is not reducing at the same rate (Ford, 2011). The recent publication of an updated NICE guideline on the modification of blood lipids for the primary and secondary prevention of CVD has reinforced the primacy of statin therapy in managing people with diabetes (NICE, 2014).

In an article in this edition of the Journal, starting on page 248, Mike Kirby examines the implications of this guideline for people with diabetes, outlining the need for a cardiovascular risk assessment and specific treatment with statin therapy. In a previous article published in the Journal (Kirby and Betteridge, 2012), he and his co-author had outlined the scientific case for statin therapy in diabetes, and this is reinforced by the new NICE publication. The guideline also underlines the need for a robust cardiovascular risk assessment in all people with diabetes aged over 40 years, which should include lipid analysis, as well as assessment and informed discussion of the risk of CVD, leading on to treatment and referral where necessary.

NICE clinical guideline 181

This new NICE guideline updates and replaces the previous one on lipid modification and statin use (clinical guideline 67 [NICE, 2008]). The publication takes account of emerging evidence on statin and non-statin lipid-modification therapy, the novel QRISK®2 risk assessment tool (Hippisley-Cox et al, 2008), and the evolving cost-effectiveness of statins, as more of these agents become available as generics. The guideline also suggests that the risk assessment tools should not be used to assess CVD risk in people with type 1 diabetes or those known to be at high risk of CVD for other reasons, such as: pre-existing CVD; inherited disorders of lipid metabolism; or an estimated glomerular filtration rate of less than 60 mL/min/1.73 m^2, albuminuria or both.

The guideline goes on to recommend that people with diabetes should be engaged in a discussion about their CVD risk, as well as being encouraged to adopt a diet with a reduced saturated-fat content and to participate in moderate physical activity.

The threshold for primary prevention has been halved in the updated guideline: atorvastatin 20 mg is recommended in people with a 10-year risk of CVD of at least 10%, including those with type 2 diabetes. It is also now advised that statin treatment be considered for primary prevention in all adults with type 1 diabetes and that treatment with atorvastatin 20 mg be offered to those who are above 40 years of age, have had the condition for over 10 years, have established nephropathy, or have other risk factors for CVD.

NICE recommends that ezetimibe be considered for people with primary hypercholesterolaemia. However, other lipid-modifying therapies – fibrates, nicotinic acid, bile acid sequestrants and omega-3 fatty acid compounds – are not recommended for the prevention of CVD in people with type 1 or type 2 diabetes.

A 10-year risk of at least 10%

The recommendation to offer statin therapy to anyone with a 10-year risk of a cardiovascular event of at least 10%, aside from the clear value of its application to people with diabetes, has not been without controversy. The risk filter is estimated to include 25% of the population aged 30–85 years (NICE, 2014). While risk-assessment tools are now embedded in GP clinic systems, making this numerical assessment relatively straightforward, the provision of a truly informed choice to an individual who is at a 10% risk can be much more problematic and the discussion is potentially complex. One significant consideration is that the background incidence of CVD is falling, yet the trials on which we must base our practice are, in some instances, up to 20 years old.

In parallel to the emergence of the updated NICE guideline, there has also been the publication

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of new Joint British Societies recommendations on the prevention of CVD (JBS3 Board, 2014). These suggest aiming for a non-HDL-cholesterol below 2.5 mmol/L, which approximately equates to an LDL-cholesterol of 1.8 mmol/L. Healthcare professionals working in primary care will have to decide if they want to pursue these targets or follow the more pragmatic advice suggested by NICE (2014) of a 40% reduction in non-HDL-cholesterol.

Statin adherence and tolerability

Healthcare professionals working in primary care will be aware of the difficulties of ensuring adherence to lipid-modifying regimens. But what predicts poor adherence? A recent study has analysed this, finding that people with cardiovascular comorbidities who had risky drinking behaviours or a cluster of lifestyle risks were at increased risk of non-adherence (Halava et al, 2014). However those who were overweight, obese or former smokers had better adherence.

A recent study has found little harm to the liver from statin therapy (Russo et al, 2014). Conversely, we now know that statins may increase the risk of diabetes, although the prevailing view remains that people in whom statins raise the risk for diabetes are typically already at a high risk of developing the condition, and thus may have gone on to do so regardless of statin use (e.g. Nichols et al, 2007). Interestingly, another study has found that caloric and fat intake have increased over time among people taking statins, but that this was not the case for a comparison group not receiving the agents (Sugiyama et al, 2014). It may thus be important to discuss dietary composition in statin users.

Healthcare professionals will also be very aware that they frequently have consultations relating to statin therapy and apparent side effects. A recent analysis has focused on this aspect of the agents (Desai et al, 2014). It appears that statins cause a modest increase in the incidence of severe myopathy but are not associated with a significantly increased risk of myalgias. Muscle toxicity often occurs in the setting of a very high statin dose that is no longer recommended (simvastatin 80 mg) or in the presence of drugs that are known to interact with statins – for example, fibrates such as gemfibrozil. The latest Medicines and Healthcare products Regulatory Agency (2014) advice on statin safety is quite clear, stating that the benefits of statins outweigh the risks.

On balance then it is important to have a detailed, informed, and documented discussion about risks and benefits with people with diabetes unhappy about their statin therapy. Whilst the statin atorvastatin has emerged as the statin of first choice, others are available and doses and types of statins may be changed or altered. It is reassuring there is no real evidence of significant harm, although symptoms of myalgia are certainly a nuisance to many patients.

Known knowns

Writing in this Journal in 2007, I observed that while "we know what we know about treating lipid abnormalities in those with type 2 diabetes, there is still a lot that we know we don't know, about the optimum dose and type of statin" (Kenny, 2007). We still do not have clarity on the apparent pleiotropic effects of statins. However, looking back on this editorial, things that have certainly changed are that we are now clear on which statin to use first, how to assess risk, what to do about type 1 diabetes, and which targets to pursue. We also know that the updated NICE guideline will place a considerable burden on primary care, comprising robust discussions with patients about their risk, the documentation of this and then ensuring long-term adherence to a therapy that can have certain "nuisance" side effects. ■

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