Consistent with previous evidence from randomised controlled trials and observational studies, a Finnish observational study has found an increased risk of new onset diabetes among people who take statins. However, as the MHRA concluded in 2012, this risk is outweighed by the overall benefits of statins. Health professionals should continue to follow the MHRA advice about the risk of new onset diabetes, and use statins in accordance with NICE guidance.

Overview and current advice

NICE guidance on lipid modification is summarised in the Key therapeutic topic: lipid modifying drugs and the NICE pathway: cardiovascular disease (CVD) prevention. NICE recommends that, before offering statin treatment for primary prevention of CVD, the benefits of lifestyle modification should be discussed with the person and, if possible, the management of all other modifiable CVD risk factors should be optimised. If lifestyle modification is ineffective or inappropriate NICE recommends offering atorvastatin 20 mg daily for primary prevention to people who have a 10% or greater 10-year risk of developing CVD, including those with type 2 diabetes. NICE has produced a patient decision aid on taking a statin to reduce the risk of coronary heart disease and stroke to help a person making this decision weigh up the possible advantages and disadvantages of the different options.

Statins should also be offered for primary prevention to people with chronic kidney disease (CKD). For all adults with type 1 diabetes, primary prevention with atorvastatin 20 mg daily may be considered and it should be offered to adults who are older than 40 years, or who have had diabetes for more than 10 years, or who have established nephropathy, or who have other CVD risk factors. For people with established CVD (secondary prevention), treatment should usually start with atorvastatin 80 mg daily; although a lower initial dose of 20 mg daily is recommend for some people such as those with CKD or where there are potential drug interactions. In addition NICE recommends statins as the initial treatment for all adults with familial hypercholesterolaemia.

In January 2012, the MHRA advised health professionals that statin use may be associated with a level of hyperglycaemia in some people where formal diabetes care is appropriate. The risk appears to be mainly in people already at increased risk of developing diabetes. However, the MHRA concluded
that the overall benefits of statins strongly outweigh any risks, including in those at risk of developing diabetes or those with pre-existing diabetes.

New evidence

A Finish observational study has examined the association between use of statins and new-onset diabetes. Men aged between 45 to 73 years were randomly selected from the population register of an area of Eastern Finland. The study included 8749 men (mean age 57 years, mean body mass index [BMI] 26.8 kg/m²) with no history of diabetes, followed-up for 5.9 years. At the start of the study 2412 (24.5%) of the men were taking a statin; the majority of these were taking either simvastatin (65.9%) or atorvastatin (18.1%). The primary outcome measure was a diagnosis of type 2 diabetes, defined by the following criteria: an abnormal fasting plasma glucose or 2-hour plasma glucose result in an oral glucose tolerance test or HbA1c ≥ 6.5% (48 mmol/mol); initiation of glucose-lowering medication; or physician diagnosis.

During the 5.9 years of follow-up, 625 men were diagnosed with type 2 diabetes, with a higher incidence of new onset diabetes among participants taking a statin compared with those not taking a statin. After adjusting for a wide range of potential confounding factors including age, BMI, waist circumference, physical activity, smoking, alcohol intake, family history, beta-blocker and diuretic treatment, the fully adjusted hazard ratio (HR) for new onset diabetes for those treated with a statin was 1.28 (95% confidence interval [CI] 1.04 to 1.58, p<0.001). Participants who developed diabetes were reported to be older, more obese, less physically active and have lower levels of HDL-cholesterol and higher levels of fasting plasma glucose, 2-hour plasma glucose and HbA1c at baseline.

Commentary

A limitation of the evidence about the risk of new-onset diabetes with statins is that different studies used different criteria for diagnosing diabetes. Furthermore, observational studies such as the one discussed in this evidence summary are prone to confounding, which limits the conclusions that can be drawn. Nevertheless, this study is in keeping with the existing evidence base from RCTs. In 2010, a meta-analysis of 13 large RCTs of statins (n=91,140) found that their use was associated with an increased risk of new onset diabetes compared with placebo or standard care (odds ratio [OR] 1.09; 95% confidence interval [CI] 1.02 to 1.17). In absolute terms, this was equivalent to 1 additional case of diabetes per 255 (95% CI 150 to 852) people taking statins for 4 years.

That meta-analysis was considered in the full NICE lipid modification guideline. The guideline also considered evidence from a study that reported findings from 3 RCTs (average follow-up about 5 years) on the risk of new-onset diabetes in patients receiving statin therapy. In those 3 trials, a major cardiovascular event occurred in 17.5% of the patients with diabetes at baseline compared with 10.8% of those without diabetes at baseline. However, the event rate in patients with diabetes of new onset during those studies (11.3%) was much lower than that of patients with diabetes at baseline and was not appreciably higher than that of patients without new-onset diabetes (adjusted HR: 1.02, 95% CI: 0.77 to 1.35). The meta-analysis authors concluded that these results suggest that the cardiovascular risk accompanying statin-associated diabetes might not be equivalent to that usually associated with diabetes.

In its review of the evidence, the MHRA concluded that the increased risk of new-onset diabetes with statins appears to be mainly in patients already at increased risk of developing diabetes. Raised fasting blood glucose at baseline is a key factor in determining this increased risk and may be sufficient to identify those at risk. Other risk factors include:

- history of hypertension
- raised triglycerides
- raised body mass index at baseline
The overall benefits of statins strongly outweigh any risks, including in those at risk of diabetes and those with diabetes at baseline. The MHRA advises that steps should be taken to identify people who are at risk of new onset diabetes, to recognise it if it occurs, and to manage the condition appropriately. People at risk should be monitored both clinically and biochemically according to NICE guidance on type 2 diabetes (currently being updated, publication expected August 2015).

Study sponsorship

This cohort study was supported by the Academy of Finland, the Finnish Diabetes Research Foundation, the Finnish Cardiovascular Research Foundation the University of Eastern Finland and the Kuopio University Hospital.

References


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