Statins: many people who stop treatment due to side effects may be able to restart treatment

A large US cohort study suggests that many people who have discontinued statins because of an adverse event, especially muscle pain, may be able to restart the same or a different statin. This would enable them to obtain the benefits of statin treatment. Decisions to restart statins should take account of patient preferences, and guidance on cautions and contraindications from the MHRA and as stated in manufacturers’ summaries of product characteristics.

Overview and current advice

A Statins are an essential therapeutic component of primary and secondary prevention of cardiovascular disease; they are recommended in NICE guidance on lipid management and care of people with type 1 and type 2 diabetes (all these guidelines are being updated and the update to the lipid guideline is expected in July 2014).

Nevertheless, statins are commonly discontinued by patients. A meta-analysis of 20 studies (n=376,162) found a summary adherence rate of 57% (95% confidence interval [CI] 51% to 64%) for statins in primary prevention and 76% (95% CI 70% to 82%) in secondary prevention, over a median of 24 months. If people stop lipid-modifying treatment they are at increased risk of cardiovascular events.

See the Clinical Knowledge Summaries information on lipid modification for a general overview of prescribing considerations. The NICE Evidence topic page on statins provides links to other evidence related to statins and their use.

New evidence

A US observational study evaluated the reasons for statin discontinuation among 107,835 patients (mean age 61 years, equal numbers of men and women) cared for in 2 academic medical centres and who received a statin prescription between 2000 and 2008 (inclusive). The study authors used natural language processing software to analyse electronic medical records.
The most commonly taken statins were atorvastatin (52% of patients) and simvastatin (33% of patients). More than half (53%) of all patients had their statin prescriptions discontinued at least once, but nearly a third of these (31%) had no reason recorded; they were simply noted to have had no statin prescription for 12 months.

Of all study patients, about 17 in every 100 (17.4%) had at least 1 statin-related event (a clinical event or symptoms documented by health professionals as having been caused by a statin). Myalgia or myopathy was the most common of these, affecting more than a quarter (27%) of those with a statin-related event, and about 5 in every 100 people in the study overall (4.7%). However, fewer than 1 in every 100 people in the study overall (0.92%) had an elevation of creatinine kinase (CK) to 3 to 10 times the upper limit of the normal range (ULN) – a marker of muscle damage – and only 0.006% of people in the whole study (7 out of 107,835 people) experienced rhabdomyolysis (CK at least 10 times ULN).

Statin prescriptions were discontinued in 59% of patients with a statin-related event, at least temporarily. A statin was restarted within the following 12 months in 59% of those in whom it had been previously discontinued, and most (92%) of these people were able to tolerate it (i.e. they were still being prescribed the statin 12 months after the original statin-related event).

More often than not, treatment was restarted with a different statin. However, 41% of people were restarted on the statin they were taking at the time of the statin-related event. Of these, nearly half (48%) were being prescribed that same statin 12 months later – and more than three quarters (77%) of these people were prescribed it at the same or higher dose than at the time of the statin-related event. Among those who restarted statin treatment with a different statin, a second statin-related event was documented in 13% of people.

A major limitation of the study is that it could take account only of what was prescribed, not what patients actually took (for example, about 40% of people with a recorded statin-related event continued to receive prescriptions, but it is not known whether they actually continued to take the statin). In addition, the authors recognise that the language processing software used to analyse the case records might not have correctly identified all the relevant information; and information about statin-related events, including laboratory data, was incomplete in many patients.

**Commentary**

**Commentary provided by the NICE Medicines and Prescribing Centre**

A common reason for people to discontinue statin therapy is the development of perceived adverse effects, especially muscular adverse effects. However, rates of statin-related myopathy reported in practice are often notably higher than might be expected from data reported in clinical trials, as discussed in a National Prescribing Centre Rapid Review. The reason for this anomaly is not clear. Clinical trials of statins have tended not to recruit older, sicker patients receiving multiple medications, although such patients are commonly seen in UK general practice. In addition, many large statin studies had an unblinded run-in phase and people who developed adverse reactions in these early stages may have been excluded from the studies or declined to continue.

However, statins are most frequently prescribed to middle and older-aged people, an age group in whom muscle and joint pain are far from uncommon. Many patients, and their health professionals, know that statins have been reported to cause muscle pain, and so it is natural to blame the statin if muscle pains arise. In addition, statins do not bring any directly-perceived benefits (unlike, say, pain relief with analgesics or symptom relief with inhaled corticosteroids in asthma), so there is no balancing benefit to offset the apparent harm, and this might lead patients to be more inclined to discontinue treatment.
Muscle-related adverse effects of statins seem to be related to dose. Myalgia is not necessarily an indicator of myopathy, but NICE lipid guidance advises that creatine kinase should be measured in people who develop muscle symptoms while taking statins. Statins currently in use can also increase liver enzymes (especially transaminases) but do not seem to be hepatotoxic. NICE lipid guidance advises that baseline liver enzymes should be measured before starting a statin. Transaminases should be measured within 3 months of starting treatment and at 12 months, but not again unless clinically indicated. People who have transaminases that are raised but are less than 3 times the ULN should not be routinely excluded from statin therapy.

Less well known side-effects of statins as a class include depression, sleep disturbances, memory loss, and sexual dysfunction. Statins may also very rarely be associated with interstitial lung disease⁴. Patients should be advised to seek help if they develop presenting features of interstitial lung disease such as dyspnoea, non-productive cough, and deterioration in general health⁴. NICE lipid guidance advises that if a person taking a statin develops an unexplained peripheral neuropathy, the statin should be discontinued and specialist advice should be sought.

There will clearly be situations in which rechallenge with statins is unwise or inappropriate. However, and despite its limitations, this study suggests that the same or a different statin may be cautiously restarted in selected patients, especially those with non-specific muscle pain. This approach may lead to them being able to recontinue statin treatment with the consequent reduction in risk of cardiovascular events. Decisions to restart statins should take account of patient preferences, and guidance on cautions and contraindications from the MHRA and as stated in manufacturers’ summaries of product characteristics.

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References