A patient with heart disease having myalgia with statin therapy: a challenging case history

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Patients who experience myalgia secondary to high-dose statin therapy may tolerate and benefit from low doses of other statins.

Case scenario

Mrs SA is 59 years old and suffered a myocardial infarction two years ago. She required a coronary stent to the culprit lesion and has progressed well since that time. Her background risk factors were hypertension, elevated LDL and low HDL cholesterol levels, plus a history of coronary disease in her father at 56 years.

Mrs SA's blood pressure and lipid levels have improved well, and her body weight and glucose levels are satisfactory. She is treated with a standard array of cardiac drugs: aspirin, clopidogrel, a ß-blocker, an ACE inhibitor and atorvastatin 80 mg daily (a typical dose in this context).

She attends her GP for a scheduled review. For the first time she is complaining of generalised myalgia. It is not very severe but has been present for a few months. History and examination are completed and she is sent for blood tests, the results of which are shown in the second row of the Table.

Key points

- **Statin drugs, in addition to other medications, form an essential part of therapy after a patient has had a myocardial infarction.**
- **Statins occasionally induce myalgia of varying severity in the short or longer term. Changes in the concentration of the muscle enzyme creatine kinase may not be diagnostic.**
- **Provided that other causes of myalgia have been excluded, patients may be tried on other statin drugs.**
- **One approach in such cases is for patients to take a very small dose of rosuvastatin, initially 2.5 or 5 mg on two days per week, which may avoid the return of myalgia yet still offer potential benefit.**
- **Unfortunately, some patients may experience a return of muscle symptoms with other statins and future lipid therapy may be very challenging.**

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Table. Patient's blood test results at baseline, at two-yearly review and during low-dose statin trial

Results	Total cholesterol (mmol/L)	LDL cholesterol (mmol/L)	HDL cholesterol (mmol/L)	Triglycerides (mmol/L)	Creatinine (µmol/L)	Glucose (mmol/L)	CK (IU/L)	ALT (IU/L)	AST (IU/L)	GGT (IU/L)
Before statin therapy	5.4	3.8	0.9	1.6	87	5.1	210	32	20	46
Two years on statin	3.5	1.8	1.0	1.5	81	5.2	265	35	21	40
Six weeks on rosuvastatin 5mg Mon and Thur	4.4	2.3	1.0	1.9	ND	ND	228	30	24	43
Six weeks on rosuvastatin 5mg daily	3.8	2.1	0.9	1.8	85	5.0	240	ND	ND	ND

Selected reference values: creatinine <110 µmol/L; glucose <5.5 mmol/L; CK <230 IU/L; transaminases (ALT and AST) <45 IU/L; GGT <55 IU/L.
ABBREVIATIONS: ALT = alanine transaminase; AST = aspartate transaminase; CK = creatine kinase; GGT = gamma glutamyl transpeptidase; HDL = high density lipoprotein; LDL = low density lipoprotein; ND = not done.

How should we interpret the history and findings?

At face value this patient seems to have developed a muscle problem secondary to her high-dose statin therapy. Although her creatine kinase (CK) level is higher than it was previously, a reading of 265 IU/L is not in itself diagnostic. In fact, some patients in this situation have no significant rise in CK.

The onset of muscle symptoms after two years of statin therapy is not so common, but it is well documented. Other causes for myalgia are possible (e.g. drug–drug interaction between statin and gemfibrozil or other drugs, vitamin D deficiency, viral illness or fibromyalgia). In this case a statin-induced cause remains the most likely diagnosis. Also, her GP has previously excluded hypothyroidism or vitamin D deficiency.

The rest of Mrs SA's blood tests appear to be very satisfactory. In particular, she has now achieved a highly favourable lipid profile with LDL and HDL cholesterol at goal levels for a patient with prior coronary artery disease.

How should her GP manage this situation?

Although there is ample clinical trial evidence that this patient should continue on statin therapy, it would not seem prudent for her to continue taking atorvastatin in the high dose of 80 mg/day. To do so may lead to further worsening of her symptoms and potentially the development of more serious muscle problems.

Case scenario continued

Mrs SA's GP provisionally diagnosed a statin-induced muscle problem and discussed further management with this consultant by phone. A potential role for coenzyme Q_{10} therapy or supplementary vitamin D was queried, but evidence of benefit in such situations is weak (except in cases of vitamin D deficiency). It was suggested that Mrs SA suspend all statin therapy for four to six weeks and await developments; her other treatments were to remain unchanged. Given the ongoing need for statin therapy, it was also decided that within six weeks (or sooner if she had recovered) she should return to a revised statin therapy regimen. (Other therapeutic possibilities such as ezetimibe or fenofibrate were discussed but were not felt to be early options.)

A revised statin therapy approach

Mrs SA could eventually be offered a reduced dose of atorvastatin, but her confidence with this therapy may already be 'shaken' and LDL cholesterol control may be compromised. In earlier years we might have preferred a switch to pravastatin or fluvastatin in this situation, but with the likelihood of inferior cholesterol control. An alternative approach would be to offer rosuvastatin in a very low dose (e.g. 2.5 or 5 mg twice weekly in the first instance), as this is a very potent statin drug, mg for mg. It is acknowledged that any statin therapy in this patient may see a return of muscle symptoms and she should be counselled accordingly.

Case scenario continued

Within two weeks, Mrs SA's muscle pains had fully resolved and she was started on low-dose rosuvastatin at 5 mg on Monday and Thursday mornings. Six weeks later she was still free of any side effects but her LDL cholesterol level was higher than desirable at 2.3 mmol/L. Rosuvastatin was cautiously increased to 5 mg daily. Six weeks later she was still well. Her blood tests were repeated; the results are shown in the Table.

Implications for further patient management

Mrs SA's LDL and HDL cholesterol levels are not ideal at this time, although her LDL cholesterol is reasonably well improved compared with her baseline level. This may be the best that can be achieved without the return of myalgia. Only 12 weeks have passed on this approach and it would be prudent to leave the dose unchanged for a further six to 12 months, still emphasising the importance of a healthy diet and weight maintenance.

The use of rosuvastatin in this way is not evidence-based. On the other hand, the view is still widely held that all statins probably have similar beneficial effects in this context. Also, statins have beneficial effects beyond reduction in LDL cholesterol. The outcome here represents a useful compromise. Should there be a return of myalgia with rosuvastatin (still a possibility) her further management would be even more challenging. **CT**

COMPETING INTERESTS: None. The views expressed are purely those of the author.