Brief Communication

Oral use of "Low and Slow" Rosuvastatin with Co-Enzyme Q_{10} in patients with Statin-Induced Myalgia: Retrospective case review

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ABSTRACT

Background: Statins have proven efficacy in reducing vascular disease, but statin-induced myalgia is relatively common in clinical practice, and can sometimes leave patients who are high risk for vascular disease unable to take these important preventative treatments. Low or intermittent dose rosuvastatin has been shown to be useful in lowering cholesterol with fewer side-effects. Supplementation with co-enzyme Q_{10} is suggested to reduce statin-induced myalgia. **Materials and Methods:** A retrospective review of patients attending a tertiary referral lipid clinic with statin-induced myalgia was carried out. Patients were counseled on commencing low-dose rosuvastatin, titrated at monthly intervals, and supplemented by co-enzyme Q_{10} 100 mg daily. **Results:** Forty Three patients were reviewed. Six were unable to tolerate the regime at all. The remaining 37 patients tolerated rosuvastatin between 5 mg weekly and 20 mg daily. Total and LDL-cholesterol levels fell by a mean of 29.1% and 27.5%, respectively. 62.2% of patients achieved total cholesterol under 5.0 mmol/L. **Conclusions:** In this retrospective review of clinical practice, "low and slow" rosuvastatin supplemented by co-enzyme Q_{10} led to clinically meaningful reductions in total and LDL-cholesterol in patients with statin-induced myalgia.

Key words: Low and slow Rosuvastatin, statin induced myopathy

Introduction

Statins are first-line agents in the management of hypercholesterolemia. Their principal effect is to reduce serum low-density lipoprotein-cholesterol (LDL-C) through inhibition of cholesterol synthesis and increased hepatic low-density lipoprotein receptor activity.

Adverse effects of statins are usually mild, but can be problematic in a small proportion of patients. Around 5-10% of patients report muscle symptoms whilst taking statins, although only around 1-3% of patients actually have muscle symptoms related to statins.[1] Several mechanisms for statin-associated muscle symptoms have been suggested, including mitochondrial dysfunction secondary to impaired endogenous synthesis of co-enzyme Q_{10} (also called ubiquinone).[2] Oral supplementation of co-enzyme Q_{10} has been shown to be a safe intervention and can reverse the decline in plasma levels of the co-enzyme Q_{10} seen with statin use.[3]

There is some suggestion that rosuvastatin may cause less myalgia compared to other statins by virtue of its hydrophilic nature. Use of low or infrequent dose rosuvastatin in patients with statin-induced myalgia has been shown to be effective in lowering LDL-C levels and in improving tolerability.[4]

The aim of this study was to retrospectively review the effect of slowly titrated low-dose rosuvastatin, in addition to co-enzyme Q_{10} supplementation, in patients with statin-

Access this article online	
Quick Response Code:	Website: www.ijem.in
	DOI: 10.4103/2230-8210.104144

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induced myalgia referred to a single center tertiary referral lipid clinic.

Materials and Methods

All patients referred to a lipid clinic with symptoms of statin-induced myalgia were included in the study. We defined statin-induced myalgia as per the National Institute of Health and Clinical Excellence (NICE) guidelines, as any patient in whom statin therapy was deemed appropriate, but who was unable to tolerate the statin due to myalgic symptoms.[5] Patients were only defined as statin-intolerant if they had tried at least three different statins and developed myalgic symptoms with each.

Patients were counseled to take rosuvastatin 5 mg once weekly for 4 weeks. If tolerated, the dose was increased to twice weekly, for 4 weeks, and then titrated incrementally until the patient was on the maximum tolerated dose, to a maximum of 5 mg daily initially. If side-effects developed, patients were advised to go back one step. If completely intolerant to rosuvastatin, they were advised to stop the therapy. In addition, patients were asked to take co-enzyme Q_{10} supplements at a dose of 100 mg daily starting at least 1 week before the first rosuvastatin tablet. Patients were seen at 12 weekly intervals for at least a year, with fasting lipid profiles, creatine kinase, and liver biochemistry checked prior to each visit, and rosuvastatin dose was titrated according to total cholesterol target (5.0 mmol/L or 193 mg/dl in most, 4.0 mmol/L or 155 mg/dl in patients with diabetes or known ischemic heart disease).

Data was analyzed for adverse effects, discontinuation rates, and changes in lipid profiles.

Results

Forty three patients were followed up for a mean of 16.2 months. Six discontinued therapy, all within the first 12 weeks of commencement of therapy, 5 due to recurrence of severe myalgic symptoms and 1 because of an increase in liver transaminases. No significant rises in creatine kinase levels (above 1000 iu/L) were seen in any patients on this regime, including the patients with the severe myalgic symptoms.

Of the remaining 37 patients, the maximum tolerated rosuvastatin dose ranged from 5 mg every week to 20 mg daily. The mean reduction in total cholesterol was 29.1%, and in LDL-C was 27.5%. Of these 37 patients, all achieved a total cholesterol of 7.0 mmol/L (271 mg/dl) or less, 23 (62.2%) achieved a total cholesterol of 5.0 mmol/L (193 mg/dl) or less, and 16 (43.2%) achieved a total cholesterol of 4.0 mmol/L (155 mg/dl) or less. Eight patients discontinued the co-enzyme Q_{10} therapy, but continued rosuvastatin, without side-effects.

Discussion

We describe a small, single-center retrospective case series of patients with statin-induced myalgia treated with a low-dose, slowly titrated regime of rosuvastatin supplemented by co-enzyme Q_{10}. Within the limitations of the study, it is reasonable to suggest that this method of dealing with statin-induced myalgia may be clinically effective and worth a trial in patients who are genuinely statin-intolerant.

Some patients may develop mild myalgia with statin therapy, but are willing to continue therapy due to significant cardiovascular benefits. Many patients, however, have to stop therapy due to adverse effects, and management can prove a significant therapeutic challenge.

Co-enzyme Q_{10} has been suggested as having a possible role in the development of statin-induced myalgia. Inhibition of HMG-CoA reductase results in reduced synthesis of cholesterol and other products downstream of mevalonate. Mevalonate itself is a precursor for co-enzyme Q_{10}, and one postulated mechanism for statin-induced myalgia is through mitochondrial dysfunction, secondary to the depletion of co-enzyme Q_{10}.

Low-dose potent statin therapy has been suggested as a useful method of obviating statin-induced myalgia. Use of rosuvastatin 2.5 to 20 mg once a week has been shown to decrease LDL cholesterol by 25% and be tolerated by up to 70% of statin-intolerant patients. Twice-weekly or alternate-day regimens of rosuvastatin or atorvastatin alone or in combination with ezetimibe have also been well tolerated in patients with statin-induced myalgia. One randomized trial has shown that use of extended release fluvastatin 80 mg daily in patients with statin intolerance may be effective in reducing myalgic symptoms.

On the basis of our retrospective data of real clinical practice, and in the absence of hard outcomes data from randomized trials, we propose that a strategy of "low and slow" rosuvastatin combined with co-enzyme Q_{10} can lead to clinically meaningful reductions in serum cholesterol in patients previously affected by statin-induced myalgia. A randomized controlled trial of this regime is required to be undertaken to determine whether these results can be confirmed in the context of a clinical trial.

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Cite this article as: Vidyarthi M, Jacob P, Chowdhury TA. Oral use of "Low and Slow" Rosuvastatin with Co-Enzyme Q 10 in patients with Statin-Induced Myalgia: Retrospective case review. Indian J Endocr Metab 2012;16:S498-500.

Source(s) of Support: None, **Presentation at a meeting:** None