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Statin-associated muscle symptoms: is Proprotein convertase subtilisin/kexin type 9 inhibitors a therapeutic option?

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The efficacy and safety of statin therapy are well established. However, despite their favourable profile, muscle symptoms reported with statin therapy limit their use negatively impacting adherence and cardiovascular benefits of this treatment. It is important that clinicians are cautious before attributing muscle symptoms to statin therapy, without further investigation of their cause. Moreover, this is complicated by the lack of internationally agreed clinical definitions of statin-induced myopathy and diagnostic tools.

Recently the European Atherosclerosis Society (EAS) Consensus Panel has circumvented the lack of consensus regarding the causality of statins with muscle symptoms by the use of the term statin-associated muscle symptoms,

Table 1 Definition of statin-associated muscle symptoms from reference[1]

Symptoms	Biomarker	Comment
Muscle symptoms	Normal CK	Often called 'myalgia'. May be related to statin therapy. Causality is uncertain in view of the lack of evidence of an excess of muscle symptoms in blinded randomized trials comparing statin with placebo.
Muscle symptoms	CK >ULN <4× ULN CK >4 <10× ULN	Minor elevations of CK in the context of muscle symptoms are commonly due to increased exercise or physical activity, but also may be statin-related; this may indicate an increased risk for more severe, underlying muscle problems.[19]
Muscle symptoms	CK >10× ULN	Often called myositis or 'myopathy' by regulatory agencies and other groups (even in the absence of a muscle biopsy or clinically demonstrated muscle weakness). Blinded trials of statin vs. placebo show an excess with usual statin doses of about 1 per 10 000 per year.[4] Pain is typically generalized and proximal and there may be muscle tenderness and weakness. May be associated with underlying muscle disease.
Muscle symptoms	CK >40× ULN	Also referred to as rhabdomyolysis when associated with renal impairment and/or myoglobinuria.
None	CK >ULN <4× ULN	Raised CK found incidentally, may be related to statin therapy. Consider checking thyroid function or may be exercise-related.
None	CK >4 × ULN	Small excess of asymptomatic rises in CK have been observed in randomized blinded trials in which CK has been measured regularly. Needs repeating but if persistent, then clinical significance is unclear.

CK, creatine kinase; ULN, upper limit of the normal range.

SAMS (*Table 1*), thus providing an accessible resource for the diagnosis, assessment, and management of SAMS, as well as an update on current thinking about the aetiology of statin myopathy.

Understanding and clearly defining is critical for optimal treatment. Therefore, the management of SAMS is a key in the effective treatment of patients with cardiovascular disease (CVD), through achievement of maximum-tolerated statin dosing and other practical aspects. Combination therapy with ezetimibe and the addition of Proprotein convertase subtilisin/kexin type 9 inhibitors in high-risk patients with elevated LDL-C is supported by a pharmacological and clinical evidence and is the logical approach to maintain patients on statin therapy with the final aim to optimize the cardiovascular benefits of this treatment.

Conflict of interest: none declared.

Reference

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