NLA CLINICAL PERSPECTIVE:

Assessment & Management of Statin-Associated Muscle Symptoms (SAMS)

NATIONAL LIPID ASSOCIATION

Listen to the Patient Experience

The patient experience of symptoms while taking statin therapy is real regardless of etiology and needs to be acknowledged and respected. The clinical approach should extend beyond tailoring patient expectations for adverse effects and informing them of the potential of nocebo effects, while emphasizing benefits and safety of statin therapy.

Facts about SAMS:

- Statins are **generally well tolerated**.
- Some degree of statin intolerance is reported in 5-30% of patients and contributes to reduced statin adherence and persistence, but many symptoms are unrelated to the statins.
- Statin-associated muscle symptoms (SAMS) are the most common form of statin intolerance.
- The **prevalence of SAMS is estimated to be about 10%** (range 5% to 25%), but more than 80% of cases are not caused by the statin.
- Approximately **60-80% of patients with SAMS are eventually able to tolerate some statin** regimen (one of the seven statins, often at low dose).
- Use of non-statin therapies can increase the likelihood of achieving LDL-C and non-HDL-C goals in patients with SAMS.

Shared Decision Making Helps Educate Patients and their Families to Improve Statin Tolerability

A framework of genuine shared decision-making includes addressing patient and family health literacy and creating a supportive clinical environment and trusting patient-clinician relationship in which patients can openly share concerns, ask questions, and express preferences, with the goals of improving clinical outcomes, limiting adverse effects, and optimizing patient experiences. Clinicians should:

- Provide clear information about the benefits and rationale for statin therapy for that individual patient
- Give clear written and/or online educational materials targeting an appropriate reading level (8th grade or less)
- Use the teach back technique by having the patient state back what are the benefits of statin therapy, what cholesterol goals are we trying to achieve, and what to do if they are having problems with their medication
- Include family members/caregivers in the discussion when appropriate
- Use motivational interviewing techniques
- Direct questioning about statin adherence
- Be respectful and provide non-judgmental discussion of potential symptoms, with reassurance, as appropriate
- If a patient is symptomatic, have them describe their symptoms more fully in terms of severity, impact, duration, aggravating and mitigating factors, and how it affects the quality of their life and physical function
- Reaffirm the benefits and goals of statin treatment and the consequences of discontinuation
- Use terms such as "reported" or "described" in lieu of "complained" when documenting SAMS
- Specifically document patient behaviors and reasoning while avoiding describing patients as "noncompliant" or "nonadherent"

Risk Factors for SAMS

It is important to first rule out potential risk factors that may cause or aggravate the patient's muscle symptoms and mitigate those that are modifiable.

Demographics	Genetics	Comorbid conditions	Social	Drugs*
Older age	Family history of SAMS	Hypothyroidism, including post-treatment of hyperthyroidism	New exercise routine	Fibrates (especially gemfibrozil)
Female sex	Known pathogenic variants in genes involved in statin metabolism *(testing not routinely recommended)*	Vitamin D deficiency	Strenuous exercise	Colchicine
Asian ethnicity**		Musculoskeletal disease	Alcohol use	Immunosuppressants
Low body weight		Immunologic disease	Cocaine and other stimulants	Antiarrhythmics
		Chronic Kidney Disease		Antivirals
		Organ or electrolyte dysfunction		Antibiotics
				Antifungals
				Antiseizures
				Other inhibitors of statin clearance

** Either through direct myotoxic effects or drug-drug interactions with statins*

*** Especially for high dose rosuvastatin*

Management Strategies to Address SAMS

Most patients can tolerate some degree of statin therapy. Management strategies for patients experiencing SAMS include:

- **Utilizing a lower dose of the same statin**
  - Even at a starting statin dose, many patients will achieve substantial LDL-C lowering while improving tolerability.
  - Intermittent statin dosing regimen (non-daily statin dosing) may be needed to facilitate patient tolerability in cases of persistent intolerance during low dose statin therapy.
- **Switching Statins**
  - Switching to a statin that is metabolized by a different enzyme system, avoids various transporters, or is less lipophilic may improve drug tolerability.
- **Evidence Based**
  - Some patients may be more accepting of statins that have been shown to have reduced rates of SAMS in clinical trials (e.g., fluvastatin-XL, or pravastatin instead of simvastatin).
- **Naturally Derived Statins**
  - Some patients may be more accepting of using a naturally derived statin medication (e.g., lovastatin).
- **Lowest Milligram Strength**
  - Some patients may be more accepting of using a drug with a lower milligram dosing (e.g., pitavastatin which is available as 1 mg, 2 mg, and 4 mg, as opposed to 10 mg to 80 mg for other statins).
- **Supplementation**
  - Well-designed randomized controlled trials are required before making recommendations on the impact of supplementation including vitamin D and CoQ10 in those with SAMS.
- **Nutraceuticals**
  - Nutraceuticals should not be promoted to replace pharmaceutical grade, evidenced-based, lipid-lowering therapies, however, they may have a niche role as complementary to statins and non-statins in some statin intolerant patients.

Statin Metabolism, Pharmacokinetics, and Drug-Drug Interactions

Clinicians need to consider how other medications might interact with the pharmacokinetics of a statin when selecting which statin to use.

Initiation of Non-Statin Therapy

Non-statin therapies need to be used when statin monotherapy is insufficient to achieve LDL-C and non-HDL-C goals, prioritizing therapies with proven cardiovascular benefit. Treatment of patients with SAMS is incomplete until LDL-C and non-HDL-C goals have been achieved.

Clinical Consequences of Statin Discontinuation

The relative mortality risk for statin nonadherence or withdrawal has been found to be even greater than the risk of increased cardiovascular events, approaching or exceeding a 2-fold increase in some settings, recognizing that some of the mortality risk could relate to conditions that led to statin nonadherence rather than nonadherence itself.

Read the National Lipid Association's Clinical Perspective in the *Journal of Clinical Lipidology*.

Authors: Bruce A. Warden, PharmD, John Guyton, MD, Adrienne Kovacs, PhD, Jessica Durham, NP, Laney K. Jones, PharmD, MPH, Terry A. Jacobson, MD, FNLA; Dave L. Dixon, PharmD, CLS, FNLA; P. Barton Duell, MD

Reference
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