NLA Scientific Statement on Statin Intolerance

A New Definition and Key Considerations for ASCVD Risk Reduction in the Statin Intolerant Patient

NATIONAL LIPID ASSOCIATION

Statin intolerance is defined as one or more adverse effects associated with statin therapy which resolve or improve with dose reduction or discontinuation and can be classified as a complete inability to tolerate any dose of a statin, or partial intolerance with inability to tolerate the dose necessary to achieve the patient-specific therapeutic objective.

Complete Intolerance:

Patient is unable to tolerate any statin dose or regimen.

Partial Intolerance:

Ability to tolerate a lower dose of statin than is required to achieve the desired therapeutic objective.

"Nocebo" Effect:

The expectations of harm result in perceived side effects that may be unrelated to the pharmacological effects of the drug.

Qualifying a Patient as Statin Intolerant

To classify a patient as having statin intolerance, a minimum of two statins should have been attempted, including at least one at the lowest approved daily dosage.

Facts about Statins & Statin Intolerance

- 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, as well as higher risk for adverse cardiovascular outcomes.
- Statin intolerance is a clinical syndrome that **can manifest on a continuum.** Some patients experience partial intolerance while others are completely intolerant.
- **Modifiable risk factors** may contribute to statin intolerance symptoms and addressing the risk factor may improve statin tolerance in some instances.
- **Most patients can tolerate some degree of statin therapy** (agent, dose and/or regimen) if they experience symptoms.

Therapeutic Objective:

A shared decision between provider and patient that should consider desired levels of atherogenic lipoproteins, individual ASCVD risk, the potential costs, risks, and benefits of proposed therapies, as well as patient preferences.

Keep Trying Statins

Once a patient starts one or more non-statin lipid lowering medications, the effort to identify a tolerable statin treatment regimen should not be abandoned as most patients with reported statin intolerance can tolerate some degree of statin therapy (agent, dose, and/or dosing regimen).

Identifying a Tolerable Statin Regimen

To identify a tolerable statin regimen, clinicians should consider using several different strategies. Finding an acceptable regimen may require modification of the statin, statin dose, and/or dosing regimen.

"Nocebo" Effect:

It is reasonable to attribute some proportion of statin-associated symptoms to the nocebo effect. For patients with statin intolerance, it is reasonable to consider the nocebo effect as a possible cause; however, this does not make such symptoms less clinically relevant and ASCVD risk related to elevated atherogenic lipoproteins should be addressed.

Reported Patient Complaints with Statin Therapy

Most Common: Myalgias (5-30% of patients)

- Skeletal muscle-related symptoms that can be characterized by soreness, aches, cramps, fatigue, and/or weakness without creatine kinase elevation

Less Common: Myopathy (~1 in 10,000 patients per year)

- Characterized by "Unexplained muscle pain or weakness, accompanied by creatine kinase concentration >10 times the upper limit of normal."

Rare: Rhabdomyolysis (~1 in 100,000 patients per year)

- Characterized by "creatine kinase concentration typically >40 times the upper limit of normal, which can cause myoglobinuria and acute renal failure."[1]

Other Signs or Symptoms

- Transaminase elevation, worsening glycemia, and, in rare cases, confusion and memory loss.

Initiation of Non-Statin Therapy

Non-statin therapy may be required for patients who cannot reach therapeutic objectives with lifestyle and maximal tolerated statin therapy.

High & Very High Risk Patients

In high- and very high-risk patients who are statin intolerant, clinicians should consider initiating non-statin therapy while additional attempts are made to identify a tolerable statin regimen in order to limit the time of exposure to elevated levels of atherogenic lipoproteins. It is equally important that they do not abandon attempts to identify a tolerable statin regimen after a non-statin therapy is initiated.

Read the National Lipid Association's complete Scientific Statement in the *Journal of Clinical Lipidology*

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References

1. Newman CB, Preiss D, Tobert JA, et al. Statin Safety and Associated Adverse Events: A Scientific Statement from the American Heart Association. Arteriosclerosis, thrombosis, and vascular biology. 2019;39:e38-e81.

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