

The National Lipid Association Addresses the Safety of Statins and Provides Recommendations to Clinicians and Patients

Expert Panel Proposes a Definition of 'Statin Intolerance'

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(JACKSONVILLE, FL)—With an estimated 15 million Americans taking a statin drug to reduce high cholesterol, patients and health care providers alike are seeking more information on the pros and cons of statin therapy. To that end the National Lipid Association (NLA) recently convened an Expert Panel on Statin Safety to examine various aspects of statin safety and statin tolerance. Results of the symposium findings are published this month in the *Journal of Clinical Lipidology*, addressing six specific statin related safety issues including the effects of statins on: cognition, diabetes risk, liver function, muscle symptoms, interactions with other drugs, and statin intolerance. The paper reflects an update of a consensus report that was published by the NLA in 2006 related to the muscle, liver, renal and neurologic effects of statins.

According to Dr. Terry A. Jacobson, Professor of Medicine at Emory University, who chaired the NLA Statin Safety Expert Panel, “With the number of new patients now eligible to receive statin drugs under the new 2013 ACC/AHA Cholesterol guidelines, this will provide welcome reassurance about the safety of these agents, particularly given recent negative media reports.” Dr. Jacobson pointed out that in starting any new drug the potential benefits must be weighed against the potential risks, and that “the initiation of statins was heavily weighted to overwhelming benefit those at increased cardiovascular risk.”

Highlights on findings from each of the Task Forces*:

- **The Statin Intolerance Task Force** presents a pragmatic definition of ‘statin intolerance’: **adverse symptoms, signs and/or laboratory abnormalities attributed by the patient and/or provider to a statin and perceived by the patient to interfere with daily life activities.** These include predominately muscle-related symptoms with muscle aches being the most common, but also may include other symptoms, liver enzyme increases, and isolated muscle enzyme (creatinine kinase) increases. These effects are generally temporally related to statin use, improve when the statin is stopped, and return when the statin is re-started. The Panel reaffirms that statins are safe, because mortality or permanent disability due to statin treatment is very rare. However, statin intolerance is not rare approaching 10-20% of patients. Because statins are safe, the Panel recommends that the clinician and patient should keep trying to adjust doses and type of statin in order to maintain statin therapy at some level when cardiovascular risk is high.

- **The Statin Cognition Safety Task Force** acknowledges that cognitive complaints have been reported in patients being treated with statins; however, it also notes that the incidence of cognitive impairment increases with age and a variety of other possible causes of cognitive complaints also need to be considered in statin users. The Task Force indicates that there is no definitive evidence that statins as a class have adverse effects on cognition and do not recommend baseline cognitive assessment prior to statin initiation, but do note that the possibility of a statin effect be considered.
- **The Statin Diabetes Safety Task Force** acknowledges that meta-analyses suggest a small increased risk (10-12%) for the development of diabetes with statins, and that the risk may be slightly higher with high-intensity statins compared to moderate-intensity statins. It is also possible that most of this risk is confined to patients who are already at high risk for the development of diabetes such as those with the risk factors of the metabolic syndrome. Clinical trial data strongly confirms the superior benefit of statins on CVD risk reduction in diabetes patients, and this effect outweighs the much smaller risk of new onset diabetes. The Panel recommends that statin treatment should continue in patients who develop diabetes on therapy, and that enhanced lifestyle/behavioral changes be instituted to control weight, increase physical activity, and improve diet quality.
- **The Statin Liver Safety Task Force** confirms the 2012 FDA labeling change for statins wherein post-statin treatment monitoring of liver enzymes is not routinely required. While statins may sometimes cause mild to modest increases in liver enzymes (transaminase levels), this is not typically reflective of liver damage or dysfunction. To assist clinicians in the management of patients with elevated liver enzymes either before statin therapy, or while on statin therapy, the Statin Liver Task Force provides clinicians a table describing potential non-statin causes of elevated liver enzymes. Also, the Statin Liver Task Force suggests a diagnostic and statin management algorithm, based upon the patient's clinical presentation, and liver enzyme and bilirubin levels.
- **The Statin Muscle Safety Task Force** defines "statin-associated muscle adverse events" to include myalgia (muscle aches, soreness, stiffness, and/or pain) and myopathy (muscle weakness). Myositis is a term used to describe muscle inflammation and includes pain and/or tenderness which may be accompanied by significant CK elevations. The Panel acknowledges that muscle symptoms can be exacerbated by acute and chronic physical activity, that the diagnosis of myopathy (weakness) is determined primarily by physical exam findings of proximal weakness in upper and lower extremities, and that many patients initially intolerant to one statin can tolerate a different statin, possibly with alternative dosing strategies.
- **The Clinician's Guide to Statin Drug-Drug Interactions** report includes a discussion of statin metabolism, with explanations of the transporters responsible for drug handling in the intestine, liver and kidney, and how they are important in determining the plasma

levels of statins. Most important, this report has tables for each of the 7 statins and the potential drug interactions, with the effects on plasma concentration AUC.

The NLA will host a special educational session on statin intolerance and the findings of this Panel on Saturday, May 3, 7:45 a.m. – 9:30 a.m. at the Annual Scientific Sessions meeting in Orlando, FL at the Hyatt Regency Grand Cypress Hotel.

To view the full document published by the Statin Safety Task Force go to www.lipidjournal.com

The National Lipid Association is a non-profit multidisciplinary health care community that focuses on the prevention of dyslipidemias and their associated cardiometabolic disorders and on enhancing the practice of lipid management in clinical medicine. The National Lipid Association received no funding or financial support in the development of this report. For more information go to www.lipid.org

Members of the Panel have disclosed their conflicts and can be found at www.lipidjournal.com