Symptoms of small-fiber sensory neuropathy develop in a small number of patients, about 2-3 months after starting statin therapy. Neurologic examination reveals CTS, and for a thorough assessment of differential considerations.

Electrodiagnosis by EMG/NCV is critical for accurate diagnosis of Carpal Tunnel Syndrome. Figure 1: Fluorescence micrographs. Ultra-thin frozen sections labeled with a T-tubular marker (annexin A6, green) & a nuclear marker (Hoechst, blue) showing vacuolization (arrows) in a patient with statin-associated myopathy (A). The T-tubular system is undamaged in a control patient (B). Bar = 10 μm. CMAJ Mohaupt MG et al. July 7, 2009; 181 (1-2)

Figure 1: Fluorescence micrographs. Ultra-thin frozen sections labeled with a T-tubular marker (annexin A6, green) & a nuclear marker (Hoechst, blue) showing vacuolization (arrows) in a patient with statin-associated myopathy (A). The T-tubular system is undamaged in a control patient (B). Bar = 10 μm. CMAJ Mohaupt MG et al. July 7, 2009; 181 (1-2)

2) Myalgia with or without hyperCKaemia. Myalgia has been reported to occur in 9-25% of statin treated patients. Myalgia usually improves after discontinuation of the drug. If the muscle strength is normal and the myalgia is tolerable, literature suggests observing the patients for 2-3 months before performing a diagnostic work-up or changing the statin.

3) Muscle weakness with CK elevation. In some patients the myopathy is mild, subacute and temporally related to the initiation of statin therapy; in some others however, the myopathy is more chronic without a clear cause-and-effect relationship, raising the suspicion that the statin might not have been the culprit in inducing it, but rather in unraveling a pre-existing muscle condition. Muscle biopsies may show a few necrotic fibers without inflammation. At times, however, there may be findings suggestive of an immune-related inflammatory process similar to polymyositis. Such patients require immunotherapy. However, cases of statin-induced PM and DM have been reported by others. Whether statins can worsen a pre-existing myopathic condition and facilitate the unraveling of a full-blown immune-mediated or toxic myopathy remains an undocumented possibility. A large number of IBM or ALS patients take statins without overt signs of added muscle toxicity. In patients with pre-existing myopathy who have discontinued a statin fearing a worsening of their condition, some authors have recommended resumption of drug therapy if it is essential for their cardiovascular health.

4) Rhabdomyolysis. Is defined as an acute elevation of CK (>15 000 ULN) accompanied by myalgia, weakness & myoglobinuria. FDA estimates the incidence is similar for all statins (except for cervistatin) when used as monotherapy. The incidence is increased when statins are combined with other drugs. Most notable among them is Simvastatin when combined with amiodarone, gemfibrozil or cyclosporin. The risk is also dose-related occurring when simvastatin is given at doses greater than 20 mg/day. Rhabdomyolysis is a medical emergency that requires immediate discontinuation of drugs & admission for hydration & electrolyte control. Because these drugs need to be combined with others in several settings, we should be aware of the increased risks & monitor the patients very closely. Atorvastatin and pravastatin appear to be the most preferable statin in these circumstances because of the lower incidence of rhabdomyolysis.

Re-challenging the statin-intolerant patient

One recent study in 2010 looked at rosuvastatin at a mean dose of 5.6mg every other day. Out of 51 patients who previously experienced myalgias or elevated transaminase levels on a variety of different statins, 37 (72.5%) were able to tolerated every other day dosing, and 24 (46.9%) of these patients achieved their target LDL-cholesterol goals. Other statin drugs have not been studied as of yet.

Peripheral neuropathy

Symptoms of small-fiber sensory neuropathy develop in a small number of patients, about 2-3 months after starting statin therapy. Neuropathy is rare. Figures quote an incidence of 12/100,000 person-years & prevalence of 60/100,000. Patients are managed symptomatically & in some cases, another statin reintroduced with caution.

References: Dalakas MC. Toxic & Drug-induced Myopathies. J Neurol Neurosurg Psychiatry ‘09;80:832-838

Statin Toxicity - Myopathy & Myositis

by Mohammad A. Saeed, M. D., M. S., & Edgar S. Steinitz, M. D. Co-author & Editor

Statins are commonly prescribed medications that significantly reduce the risk of cardiovascular events. While generally well tolerated, rarely severe myotoxicity occurs. The spectrum of toxicity ranges from myalgias to life threatening rhabdomyolysis. There is a growing body of evidence suggesting that the risk of statin-induced myopathy is dose-dependent complicated by genetic predisposition. These fears and minor adverse effects such as muscle pain leads to noncompliance. Below are four types of statin related myopathic signs & symptoms, and how to approach this problem:

1) Hyper-CKaemia in asymptomatic patients. In lab testing in asymptomatic patients taking statins, there may be elevation of CK that does not exceed 5-6X ULN. These patients have normal strength & no complaints of fatigue or muscle pain. The CK usually fluctuates, reaching the highest levels after exercising. These patients need follow-up with clinical and lab examinations. Usually, CK stabilizes to a lower level, about 3X the ULN. Some estimates suggest up to 5% of all treated patients have hyper-CKaemia. The question whether to discontinue statins in this patient group remains a matter of debate. Studies have shown such elevations are inconsequential if the patients are asymptomatic and their CK elevation fluctuates from normal to less than 10X the ULN.

2) Myalgia with or without hyper-CKaemia. Myalgia has been reported to occur in 9-25% of statin treated patients. Myalgia usually improves after discontinuation of the drug. If the muscle strength is normal and the myalgia is tolerable, literature suggests observing the patients for 2-3 months before performing a diagnostic work-up or changing the statin.

3) Muscle weakness with CK elevation. In some patients the myopathy is mild, subacute and temporally related to the initiation of statin therapy; in some others however, the myopathy is more chronic without a clear cause-and-effect relationship, raising the suspicion that the statin might not have been the culprit in inducing it, but rather in unraveling a pre-existing muscle condition. Muscle biopsies may show a few necrotic fibers without inflammation. At times, however, there may be findings suggestive of an immune-related inflammatory process similar to polymyositis. Such patients require immunotherapy. However, cases of statin-induced PM and DM have been reported by others. Whether statins can worsen a pre-existing myopathic condition and facilitate the unraveling of a full-blown immune-mediated or toxic myopathy remains an undocumented possibility. A large number of IBM or ALS patients take statins without any overt signs of added muscle toxicity. In patients with pre-existing myopathy who have discontinued a statin fearing a worsening of their condition, some authors have recommended resumption of drug therapy if it is essential for their cardiovascular health.

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