Therapies:

Statins, Muscle Damage, and Coenzyme Q10

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With some 36 million people considered as candidates for cholesterol-lowering statin drugs, nutrition professionals are likely to have a number of clients taking one or another of these drugs. Clients may ask about a potential side effect of statins that has been in the popular press recently—muscle pain, or a much more serious condition, rhabdomyolysis, which involves muscle tissue breakdown and can be fatal. Anyone who does an Internet search on the topic will find commercial websites recommending that statin users take an over-the-counter nutritional supplement, Coenzyme Q10 (CoQ10), to reduce the risk of muscle damage. While the argument for this use of CoQ10 is intriguing, the consensus among traditional health care professionals seems to be that it is premature to support the widespread use of CoQ10 at this time.

Complementary care practitioners, on the other hand, are likely to recommend it as safe and effective, if costly. This summary will help nutrition professionals to have an informed discussion with statin-taking clients regarding the use of CoQ10.

The connection between statin drugs and CoQ10

Statin drugs inhibit 3-hydroxy-3-methylglutaryl coenzyme A reductase, an enzyme in the mevalonate metabolic pathway. This pathway is common to both cholesterol biosynthesis and the synthesis of Coenzyme Q10 (also called ubiquinone). It is in this metabolic pathway that an important regulatory step in CoQ10 synthesis occurs—the formation of the isoprenoid side-chain from acetyl-CoA. It is well documented that statin drugs can lower serum CoQ10 levels. However, it is less clear that lower serum levels correspond to lower CoQ10 levels within muscle cells. Statin-induced myopathy may have several causes, with CoQ10 deficiency being just one of those causes.

CoQ10 acts as an electron carrier in the mitochondrial respiratory chain, where it serves to transport electrons from complex I (NADH-quinone oxidoreductase) and complex II (succinate-ubiquinone oxidoreductase) to complex III (ubiquinol-cytochrome c oxidoreductase). CoQ10 also serves to transfer electrons liberated from the beta-oxidation of fatty acids to complex III in the mitochondrial respiratory chain. This transfer of electrons produces energy-generating...
ATP via oxidative phosphorylation. Even a small decrease in CoQ10 concentration may depress ATP production and cause organ dysfunction. Another major role of CoQ10 is its antioxidant function in protecting the cell from free-radical induced oxidation. Inside cells, CoQ10 can prevent damage to intracellular membranes of mitochondria and other organelles. CoQ10 also helps to reduce the oxidation of LDL, which has been implicated as an important event in progression of atherosclerosis. And CoQ10 regenerates vitamin E, an important lipid-soluble antioxidant.

How does depletion of CoQ10 contribute to muscle pain?

Little is known regarding how statins produce muscle injury, but one theory posits that a reduction in CoQ10 synthesis leads to a shift toward anaerobic metabolism (with elevated lactate to pyruvate ratio) and mitochondrial dysfunction that can cause muscle weakness and pain, and ultimately, lead to muscle cell breakdown. In animals, statin-induced ubiquinone depletion has been found to cause decreased ATP production, increased injury after ischemia/reperfusion, increased mortality in cardiomyopathy, and skeletal muscle injury and dysfunction.

Mitochondrial dysfunction has recently been demonstrated by muscle biopsy in statin users with muscle complaints. These individuals did not have an elevation in serum levels of creatine kinase (CK), the traditional measure for muscle tissue breakdown, leading researchers to suggest that this test is not adequate for diagnosing statin-related myopathy. CoQ10 supplementation helps to reduce this pain, it is thought, because it improves mitochondrial efficiency by restoring normal transport of electrons in the respiratory chain. This leads to more end product, ATP, and also provides cellular protection against oxidative stress by reducing the number of free radicals generated during the energy-producing process.

Incidence of statin-related muscle complaints

There is a wide range of symptoms associated with statin use, from fatigue, pain, and muscle weakness to severe, life-threatening rhabdomyolysis. Predisposing factors for severe myopathy include higher dosage, concurrent use of a fibrate drug or high-dose niacin, hypothyroidism, carnitine deficiency, advanced age, relatively low body weight, female sex, use of multiple medications (clarithromycin, erythromycin, cyclosporine, protease inhibitors, ketoconazole, and others) multi-system disease, acute illness or major surgery. The combination of strenuous exercise and statin use has also been associated with an increased risk of skeletal muscle injury.

Evidence to support the use of CoQ10 for statin-induced muscle damage

A recent study presented at the American College of Cardiology 54th Annual Scientific Session in March,
2005, by the study’s investigator, Patricia Kelly, D.O. reported that 18 of 21 patients with significant myopathy who were taking statin therapy had a significant decrease in myopathic pain after 30 days supplementation with 100 mg/day of CoQ10 (p<0.001) compared to a group of patients taking vitamin E. The CoQ10 had no effect on creatine kinase levels. It also had no effect on blood lipid levels, and was well tolerated. 

Another recent study, by Australian researchers, found that patients who received 300 mg/day CoQ10 for an average of two weeks before cardiac surgery had improved mitochondrial function (p= .012) and in vitro contractility of myocardial tissue (p=0.001) compared to those who did not receive CoQ10.

A literature search of MEDLINE found two clinical trials and three published case reports in which CoQ10 was used to prevent or treat statin-associated myopathy. In one of these studies, 56 cancer patients treated with at least 30 mg/kg a day of lovastatin also received 240 mg of oral CoQ10 in four daily divided doses. The investigators reported that CoQ10 did not decrease the frequency of musculoskeletal toxicity but did significantly reduce its severity. In the other study, 16 cancer patients were administered 35 mg/kg of lovastatin daily, along with 240 mg of oral CoQ10, for seven consecutive days. Treatment was repeated every four weeks. The authors found elevated serum CK levels in two patients with mild myalgia. They reported that this toxicity was almost completely reversed with CoQ10 supplementation. However, it was not reported if additional CoQ10 was given to these two patients or if the original protocol achieved that result.

In one case study, a woman with rhabdomyolysis and liver toxicity recovered after discontinuation of three drugs, itraconazole, lovastatin, and niacin, and the addition of 210 mg of CoQ10 daily. In another case study, a man developed myopathy shortly after starting 20 mg daily of lovastatin. The drug was discontinued but muscle soreness and elevated CK levels persisted for six months. CoQ10 was then started at 30 mg daily, and a few days later the man was able to resume regular exercise without muscle cramps and fatigue. In a third case, a woman with rhabdomyolysis, ophthalmoplegia (paralysis of the eye muscles), mitochondrial encephalomyopathy with lactic acidosis (MELAS), and stroke-like episodes recovered after withdrawal of simvastatin and three months treatment with 250 mg of CoQ10 daily.

What dosages/forms are recommended?

Generally, health care providers who support the use of CoQ10 recommend a dose of 50 to 200 mg/day. Some practitioners contend that a blood level of 2.5 mcg/ml or higher is needed for optimal effect, but this level apparently is difficult to reach (normal blood levels of CoQ10 are about 1.0 micrograms/ml with deficiency in the range of 0.6 micrograms/ml). Langsjoen reported that long term observations on 424 cardiac patients, treated with 75 to 600 mg of CoQ10 per day for up to eight years found no adverse effects or drug interactions. Finnish researchers found that a single dose of 30 mg of CoQ10 had only a marginal elevating effect on plasma levels in non-coQ10-deficient individuals, while a daily dose of 200 mg resulted in a 6.1-fold increase in plasma levels. In 2002, a citizen petition to the Food and Drug Administration requested that labels on statin drugs include a black-box warning stating that all statin users should be advised to take 100-200 mg per day of supplemental CoQ10 to reduce the risk of myocardial and liver dysfunction and myopathies. In March 2005 the FDA issued a decision stating that the warning was not warranted based on current scientific evidence.

Some practitioners recommend an initial loading dose of 300 mg, with a meal that contains at least one tablespoon of fat such as peanut butter or olive oil, followed by 200 mg/day in divided doses for one week, then 100 mg/day thereafter. Individuals who take CoQ10 because of myopathy should also be urged to discuss their symptoms with their physician, as there are clinical guidelines for reducing the risk of serious complications.

CoQ10 is normally fat-soluble, and some but not all research suggests that a fat-soluble form of CoQ10 is absorbed better than CoQ10 in granular or powder form. Fat-soluble forms generally come in soft-gel caps, which are most often recommended.
products also contain vitamin E. To increase absorption, the supplement should be taken with a meal that contains fat, and if taking more than 100 mg/day, in divided doses that contain no more than 100 mg per dose. A specific CoQ10 formulation, UbiQ Gel (Tishcon Corporation, Westbury, NY), has received orphan drug status from the FDA for the treatment of mitochondrial cytopathies.

Safety issues?

Langsjoen reported that CoQ10 has no adverse impact on the cholesterol-lowering or anti-inflammatory properties of statin drugs. The National Cancer Institute (NCI) has stated that no serious toxicity associated with the use of CoQ10 has been reported. The NCI reports that liver enzyme (transaminase) elevation has been detected in patients taking doses of 300 mg/day for extended periods of time, but no liver toxicity has been reported. Researchers in one cardiovascular study reported a small number of cases of rash, nausea, and upper abdominal pain. Other reported effects have included dizziness, insomnia, sensitivity to light, irritability, headache, heartburn, and fatigue. CoQ10 can increase the contractility of the heart in patients with high blood pressure. It can reduce the body’s response to the anticoagulant drug warfarin, and it can decrease insulin requirements in people with diabetes.

Take Home Message

Given CoQ10’s good safety profile and possible benefits, it seems appropriate and safe to recommend this supplement to statin-users. Persons taking warfarin should inform their physician and have prothrombin times checked regularly. CoQ10 is available in tablet or capsule form. Based on bioavailability studies, the best preparations appear to be soft-gelatin capsules that contain CoQ10 in an oil base, emulsified or soluble form and stick with a reputable product line. Recommended dosing appears to be a minimum of 100 mg/day or 200 mg/day in split doses with meals.

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