Coenzyme Q10 Depletion: Etiopathogenic or Predisposing Factor in Statin Associated Myopathy?

The role of coenzyme Q10 (CoQ10) in the pathogenesis of statin-associated myopathy has been controversial. We read with great interest the study by Young et al., which demonstrated that oral CoQ10 supplementation does not prevent simvastatin-induced myopathy. Although conflicting with a previous investigation, this study suggests that CoQ10 is not immediately involved in statin-associated myopathy.

CoQ10 is a nonsterol isoprenoid co-metabolite in the endogenous biosynthetic pathway of cholesterol with an important biologic role, maintaining the mitochondrial respiratory chain, impairing the energy production in skeletal muscle cells, ultimately inducing myopathy. Although statins were found to reduce the serum CoQ10 levels, they showed no effect on CoQ10 levels within the skeletal muscle cells, with the exception of high-dose treatment with simvastatin, which was found to reduce intramuscular CoQ10. Furthermore, a direct association between reduced levels of intramuscular CoQ10 and mitochondrial myopathy has not been conclusively shown.

There is accumulating evidence that statin-associated myopathy is mediated through the reduction of the bioavailability of downstream intermediate isoprenoid comabolites (i.e., geranyl pyrophosphate and farnesyl pyrophosphate) and the resultant dysprenylation of proteins (e.g., small guanosine triphosphatases, lamin) and selenocysteine transfer ribonucleic acid. This effect results in impaired intracellular trafficking and signaling, induction of apoptosis, altered gene expression, and impaired protein synthesis.

Although CoQ10 depletion does not appear to play an etiopathogenic role in statin-induced myopathy, it is most likely that it is a critical predisposing factor, especially in subjects in whom other CoQ10-depleting conditions co-exist. Such conditions include old age, increased doses of statin treatment, increased statin bioavailability due to renal or hepatic dysfunction, hereditary metabolic syndromes, such as familial mitochondrial encephalomyopathy, and other co-morbidities, such as cancer, heart failure, diabetes, familial hypercholesterolemia, and hypothyroidism. Clinicians should be aware of the increased myopathic potential when prescribing statins in patients susceptible to myopathy. After eliminating and treating CoQ10-depleting conditions in such patients, it may be worth prescribing CoQ10 supplementation. However, on the basis of the current evidence, routine CoQ10 supplementation for all patients taking statins to prevent myotoxicity is not recommended.

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