MINIMIZING THE RISK of Cholesterol-Lowering Therapy

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Medications prescribed to prevent heart problems may also create new risks for the patient. Hepatic hydroxymethyl glutaryl coenzyme A (HMG CoA) reductase inhibitors (statins), which have been available since 1987, have been used as prophylaxis against cardiac problems. In 1990, Folkers et al.[1] disclosed a side effect of the statin lovastatin (Mevacor) that was potentially harmful to the heart and had not been previously disclosed in the package literature. Although the article by those authors was written about lovastatin in particular, statins in general work by blocking the production of cholesterol at the mevalonate pathway. Blocking this pathway also decreases the production of coenzyme Q_{10}. The symptoms of coenzyme Q_{10} deficiency include cardiac disorders such as arrhythmias, angina, congestive heart failure, and fatigue; hypertension; and depression of the immune system.

Statin Use and Heart Disease

In 1990, Folkers and Langsjoen were issued US Patent 5,082,650 for a formulation of coenzyme Q_{10} designed to prevent the deleterious effects of Mevacor. In the portion of the patent titled "Summary of the Invention," it was stated that "the present invention comprises the heretofore overlooked and very serious side effect of Mevacor (any statin) to depress body levels of Coenzyme Q_{10} and to depress correspondingly cardiac function of the pumping of blood by the heart throughout the body, and the circumvention of this death-threatening side effect by the clinical administration of a formulation of Coenzyme Q_{10}."[2]

In another study[3] of cardiomyopathy, 137 patients who received coenzyme Q_{10} were compared with 182 patients who received conventional therapy without coenzyme Q_{10}. In the group who received coenzyme Q_{10}, the survival rate was approximately 75% at 46 months after the initiation of treatment. In those treated with conventional therapy without coenzyme Q_{10}, the survival rate was about 25% at 36 months. The mean serum coenzyme Q_{10} level increased from 0.85 ± 0.26 µg/mL to a value ranging from 1.7 to 2.3 µg/mL in the group treated with coenzyme Q_{10}. In the study cited, the improved cardiac function and prolonged survival rate in the group treated with coenzyme Q_{10} indicate that the correction of coenzyme Q_{10} deficiency is essential in patients with cardiomyopathy who undergo treatment with statins.

Data[1] suggest that this finding can be extrapolated to the use of drugs that inhibit HMG-CoA reductase in the treatment of patients with hypercholesterolemia. Those with an elevated tissue level of coenzyme Q_{10} and strong cardiac function may be able to withstand a reduced coenzyme Q_{10} level without exhibiting overt adverse effects, but those with a low tissue level of coenzyme Q_{10} and modest or poor cardiac function who are treated with a statin may experience adverse or life-threatening effects. Understanding the role of coenzyme Q_{10} in bioenergetics is the basis for protecting all patients with hypercholesterolemia.

Young people (as well as the elderly) can exhibit a low tissue level of coenzyme Q_{10} and compromised cardiac function, and the depletion of coenzyme Q_{10} can also cause hepatic disease. In a study by Langsjoen et al.,[4] 100 mg of coenzyme Q_{10} was given orally to 143 patients with chronic cardiomyopathy in addition to conventional therapy for 6 years. The mean ejection fraction of 44% increased to 60% within 6 months after the initiation of treatment with coenzyme Q_{10} and stabilized at that level for the duration of the study; 85% of the patients studied who were treated with coenzyme Q_{10} exhibited a significant improvement in their level of classification according to the New York Heart Association (NYHA) classification of functional capacity. Survival figures were encouraging among patients studied. There was no evidence of toxicity or intolerance to coenzyme Q_{10} 100-mg oral supplements. Results of that study indicated that coenzyme Q_{10} is a safe and effective long-term therapy in the treatment of chronic cardiomyopathy.

Coenzyme Q_{10} was administered at a dosage of 75 mg to 600 mg in an 8-year study[5] of 424 patients with various forms of cardiovascular disease. Results of the study indicated that coenzyme Q_{10} is a safe and effective adjunctive treatment for many types of cardiovascular disease. The clinical responses were gratifying, and the medical and financial burden of multidrug therapy was eased as a result of that treatment. Coenzyme Q_{10} is a critical adjuvant therapy in patients with congestive heart failure (CHF), even when traditional therapy is successful. Its use may minimize the need for other medications, improve the patient's quality of life by improving his or her cardiac function, and decrease the incidence of cardiac complications caused by CHF.[6] Since statins were approved for medical use, the number of hospitalizations to treat patients with CHF has tripled, and CHF was listed as a primary or secondary diagnosis in more than 2.6 million patients in the United States who were discharged form the hospital or died.[7]

Additional Benefits of Coenzyme Q_{10} Therapy

Because coenzyme Q_{10} benefits patients with CHF, its use in combination with statins should be of value in patients who have a high cholesterol level.[2] A US patent[2] was issued to Merck & Co, Inc (Rahway, New Jersey), for the following therapy: "A method of counteracting HMG-CoA reductase inhibitor-associated skeletal muscle myopathy in a subject in need of such

treatment which comprises the adjunct administration of a therapeutically effective amount of HMG-CoA reductase inhibitor and an effective amount of Coenzyme Q_{10} to counteract said myopathy." Merck is also the assignee for US Patent 4,929,437, which applies to a pharmaceutical composition and method of counteracting elevated transaminase levels associated with HMG-CoA reductase inhibitor. The method described comprises the adjunct administration of an effective amount of a statin inhibitor and an effective amount of coenzyme Q_{10}. Merck was impressed enough with the potential effect produced by coenzyme Q_{10} in conjunction with the use of statins to apply for and receive patents for that combination of therapies. It does not seem prudent to wait for Merck or any other drug company to apply for an Investigational New Drug application and to conduct trials specified by the Food and Drug Administration to prove that the combination of a statin and coenzyme Q_{10} is safe and effective. Coenzyme Q_{10} seems to produce important life-changing benefits such as increasing the pumping ability of the heart and improving the quality of life according to the NYHA classification scale. I would recommend this supplement for any patient or anyone taking a cholesterol-lowering medication; it produces little (if any) risk to patients. It is sold as a nonprescription drug, and if it is recommended by pharmacists, coenzyme Q_{10} could improve the quality of life for those who use statins or have heart disease. Its use may even save the lives of those with coenzyme Q_{10} deficiency.

Case Reports

Case Study 1[1]

The patient, a 55-year-old white man with ischemic cardiomyopathy, was designated as having class III disease according to the NYHA classification of functional capacity. In May after his diagnosis, treatment was initiated with orally administered coenzyme Q_{10} 100 mg, which was given once daily.

When therapy was initiated, the patient's baseline blood level of coenzyme Q_{10} was 0.67 µg/mL, and his baseline ejection fraction was 60%. One month later, his blood level of coenzyme Q_{10} had increased to 1.73 µg/mL, and his ejection fraction had increased to 74%. Data on the patient's blood levels of coenzyme Q_{10} and ejection fractions during a 3-year period indicate that daily therapy with orally administered coenzyme Q_{10} maintained a therapeutic level of coenzyme Q_{10} of 1.73 to 2.78 µg/mL and ejection fractions of 64% to 70%. During 3 years of therapy with coenzyme Q_{10}, the patient's classification of ischemic cardiomyopathy had improved from class III to class II status, and his quality of life had significantly improved.

After 3 years of that therapy, 40 mg of Mevacor daily was added to the patient's treatment regimen. Six months later, the patient's NYHA classification status had

steadily deteriorated from class II to almost class IV, which is life-threatening. During this decline, the patient exhibited clinical decompensation and chest pain and required surgical revision of one graft.

According to a review of the documentation of this patient's clinical deterioration, his coenzyme Q_{10} blood level was 2.52 µg/mL when treatment with Mevacor was initiated. Approximately 6 months later, his blood coenzyme Q_{10} level had diminished to 1.15 µg/mL and further decreased to the very low level of 0.64 µg/mL after 5 subsequent months, at which time the ejection fraction had diminished to 54%. During the patient's surgical revision and recovery, the oral administration coenzyme Q_{10} was not feasible for 3 weeks, but after that 3-week period, administration of coenzyme Q_{10} was resumed at 166 mg per day. One month after the reinitiation of therapy with coenzyme Q_{10}, the patient's blood level of coenzyme Q_{10} had increased to 1.39 µg/mL and stabilized at 1.55 µg/mL 2 months later (at which time the administration of Mevacor was reduced from 40 mg/day to 20 mg/day) and then to 1.66 µg/mL after 5 subsequent months. The reduction of the dosage of Mevacor from 40 mg to 20 mg daily and an increase in the dosage of coenzyme Q_{10} resulted in the cardiac stabilization of this patient with acceptable blood levels of coenzyme Q_{10} and ejection fractions. Clearly, the administration of MEVACOR over time significantly reduced the blood level of coenzyme Q_{10} and reduced the pumping of blood by the heart as monitored by the ejection fraction.

Case Study 2[1]

A 46-year-old white man with dilated cardiomyopathy was classified as class III according to the New York Heart Association classification of functional capacity. His baseline blood level of coenzyme Q_{10} was 0.78 µg/mL and his control ejection fraction was 62% at the time of assessment. The patient's medical record indicated that his blood level of coenzyme Q_{10} increased to the range of 1.79 to 2.31 µg/mL after treatment with 100 mg of coenzyme Q_{10}, and his ejection fraction increased to the range of 68% to 71%. During that period of 2 years and 4 months, his cardiac function and his quality of life had improved from the NYHA class III to class I status, and his cardiac function stabilized at a clinically reasonable level.

Six months after that time, treatment with 20 mg daily of Mevacor was initiated, and during the subsequent 18 months, the patient's coenzyme Q_{10} blood level had steadily declined (2.29 µg/mL, 1.82 µg/mL, 1.50 µg/mL, 1.12 µg/mL). At that time, therapy with Mevacor was terminated, and 5 months later, the patient's coenzyme Q_{10} blood level had increased to 1.87 µg/mL. These data indicate that treatment with Mevacor reduced the blood level of coenzyme Q_{10} over time and that the effect reversed when therapy with Mevacor was terminated.

References

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