

Letter to the Editors

Statins, lack of energy and ubiquinone

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The painful or tender myopathy with elevated CPK due to statin drugs is well described and uncommon [1, 2]. Statin myopathy can also occur without elevated CPK or pain [3, 4]. More common is a feeling of lack of energy in people taking these drugs. Since statins block mevalonate synthesis [5], they lower levels of ubiquinone, an essential compound for mitochondrial energy production, as well as lowering cholesterol. Thus, these people may truly lack energy.

A few people who described lack of energy or having aged rapidly while on statins were advised to take ubiquinone (co-enzyme Q₁₀, Co-Q₁₀) while continuing the statin. Their energy level improved and they felt better. A randomized double-blind trial comparing 35 mg Co-Q₁₀ bid with placebo bid was initiated after approval by the Weill Cornell IRB for patients on statins who felt lack of pep or energy since starting the statins and who did not have muscle pain, tenderness, or elevated CPK.

By the time this trial started, most patients in my geographical area with these symptoms either stopped the statin or started Co-Q₁₀ on their own, thus only three subjects were accrued in 1.5 years and the trial was stopped. The subjects' ages were 68, 69, and 75. Plasma Co-Q₁₀ levels were measured by sample pretreatment with 1,4-benzoquinone to change the reduced form of Co-Q₁₀ to the oxidized form, precipitation with 1-propanol, and assayed on an HPLC with red-ox electrical chemical detection in the laboratory of Dr M.F. Beal [6, 7]. The Co-Q₁₀ levels prior to study drug were 0.40, 0.35, and 0.36 $\mu\text{g ml}^{-1}$ (normal values are 0.69 ± 0.04 [5] and 1.06 ± 0.33 [8]). Assessment of symptoms of fatigue at end of day, ability to climb stairs, and strength, as well as vital signs, heart rate after 3 min step test, serum lactate and cholesterol were measured before and after 2 weeks of study drug. Two subjects received placebo and one received Co-Q₁₀. The results of these

assessments were not different between the Co-Q₁₀-treated and placebo-treated patients. At the 2-week visit, subjects were also asked how they felt. Both subjects taking placebo felt unchanged during the treatment period. The patient receiving Co-Q₁₀ stated that several days after starting study drug, she felt more energetic and could now walk 20 (short New York City) blocks instead of the two blocks that tired her before. One of the placebo patients was given open Co-Q₁₀, 35 mg bid, for an additional 2-week period. After 2 weeks, he claimed that he had more energy climbing stairs and was less tired than before. Statins lower levels of Co-Q₁₀ [5, 8], and our subjects had levels below published normal values. Statins also increase the lactate–pyruvate ratio suggesting decrease in mitochondrial oxidation [5]. Preliminary data suggest that Co-Q₁₀ also acts on skeletal muscle to modify gene expression and change the composition of muscle fibres of vastus lateralis muscle from older people toward that of young people reversing the age-related change in skeletal muscle fibre composition [9]. Whether the level of fatigue and feeling of lack of energy in some people taking statins is related to skeletal muscle effects of these drugs is unknown. The results of this abbreviated randomized double-blind trial suggest it may be due to decreased ubiquinone levels due to effective statin inhibition of mevalonate synthesis. This would be an unintended adverse effect of the intended pharmacological action of the statin. People taking statins who describe lack of pep or energy may really lack energy because of a deficiency of ubiquinone. A definitive study of the value of ubiquinone replacement therapy for this subset of patients without pain but with fatigue and low Co-Q₁₀ levels is highly desirable.

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