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The Role of Coenzyme Q10 Supplementation with Statin Drug Use and Chronic Diseases

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Abstract

Patients with chronic diseases exhibit a deficiency of Coenzyme Q10 (Coq10). Also, there is no doubt lowering cholesterol medication, statin drugs will "reduce the natural levels of CoQ10 in the body" Known to have antioxidant effects, Coq10 is essential for the proper functioning of adenine triphosphate (ATP) energy production in the cells. There is medical literature with positive recommendations for Coq10 supplementation with statin drugs. Unfortunately, because of controversial studies cited in the literature, there exists misinformation about the benefits of Coq10 supplementation in patients taking statins. Thus, the objective this mini-review is to discuss the beneficial role Coq10 supplementation provided to individuals taking statins and to encouraging doctors and health professionals to prescribe Coq10. Some of the negative feedback stems from the low bioavailability of oral Coq10 supplements. However, newer sublingual Coq10 supplementation formulas are much more absorbable. Additionally, solubilized CoQ10 in oil formulations show enhanced bioavailability. Coq10 protects the mitochondria and low levels of Coq10 produce mitochondrial dysfunction, reducing adenine triphosphate production. Various chronic diseases respond positively to Coq10 supplementation. Systematic reviews and clinical trials show persons taking statin medication have deficient levels of Coq10 and Coq10 supplementation decreases the negative side effects of statins. Unfortunately, many clinicians do not understand that the statin drugs block the rate-controlling enzyme of the mevalonate pathway, 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase (HMG-CoA reductase) whose detrimental consequences are broader than muscle-related adverse events. Providing significant improvement in endothelial function, Coq10 supplementation has been shown, also, to be efficacious in persons with heart failure. We argue in our medical communities; a perceptual shift is urgently needed, providing a positive approach to Coq10 supplementation with statin drug users and chronic disease patients.

Keywords: Coenzyme Q10 deficiency; Statins; Chronic diseases; Q10 supplementation

Introduction

To generate energy through the Krebs cycle, cells utilize Coenzyme Q10 (Coq10). Also known as ubiquinone, ubidecarenone, coenzyme Q, and abbreviated at times to CoQ10, CoQ, or Q10 this coenzyme is abundant in the bodies of most healthy animals. Beyond, being a critical cofactor in the mitochondrial respiratory chain, Coq10 has a wide range of therapeutic effects. Coq10 is a powerful antioxidant, reducing free radicals that can damage DNA. Additionally, Coq10 helps regulate gene expression linked to overall tissue metabolism. Coq10 levels decrease with age and chronic diseases such as diabetes, cardiovascular diseases and Parkinson's disease. Although not known if disease causes the deficiency or if deficiency appears first causing cells to age faster. Telling, however, is the co-relationship in increasing risk of degenerative diseases in the aging population.

Not all mechanism(s) underlying the efficacy of Coq10 are yet fully understood. Mutations in enzymes involved in the Coq10 biosynthesis are linked to a primary deficiency of Coq10; while, hypercholesterolemic patients on statins therapy are classified as having secondary Coq10 deficiency. Statins block the 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, reduce the production of mevalonate, a key precursor in the metabolism of dolichol, cholesterol and Coq10 synthesis. So, the patients using statins suffer with side effects that include: muscle pain, nausea, diarrhea, liver and kidney damage, rhabdomyolysis and increased blood sugar levels, insulin resistance, in type 2 diabetes [1,2].

Although, various reports showed Coq10 supplementation is safety and efficacy used in chronic diseases, the routine co-prescription of Coq10 with statin drugs is not the norm. Thus, this mini-review's objective is to elucidate the efficacious role provided by Coq10 supplementation in individuals taking statins. Further, the aim of this paper is to provide relevant information to support a positive decision for doctors and health professionals to co-prescribe Coq10 with statin prescriptions. Our assumption is that Coq10 utilized will be a "natural" verses a "synthetic" supplement.

History and effects of Coq10 in the human body

Most aerobic, healthy organisms, mammals and bacteria contain Coq10. In humans, the Coq10 molecule has 10 (ten) isoprenoid units in its tail, it is a lipid-soluble molecule found mainly in the Golgi complex of all cellular membranes. It's was discovered in 1957 by Fred L. Crane and the chemical structure was reported a year after by Karl Folkers and colleagues [3,4].

The lipid-soluble properties of Coq10 exhibits a chemical structure similar the vitamin K. However, Coq10 is not classified as a vitamin

because Coq10 is not synthesized *de novo* in the body and endogenous levels of Coq10 in the body are determined by both production rate and consumption. Besides its antioxidant function, Coq10 is critical in the bioenergetic maintenance of skeletal and heart muscles and plays a central role in normal cell respiration. So, deficient levels of Coq10 has been linked to degenerative muscle disorders, cardiovascular disease and oncogenic response due to abnormal cell division patterns [5-7].

Pharmacokinetic Parameters of Coq10

As a lipophilic substance, Coq10 is better absorbed when taken with a healthy fat and follows the usual gastrointestinal lipid absorption process. Transported into systemic circulation, the uptake mechanism of Coq10, like vitamin E, circulates through the lymphatic system. Coq10 has few negative side effects and possesses a remarkable safety profile. Reported adverse gastrointestinal effects: nausea, upset stomach and vomiting, during clinical trials showed that, because no dose-response relationship was defined, the gastrointestinal effects are not related with the active ingredient [8,9].

1,200 mgCoq10 taken daily produces no adverse side effects and levels as high as 3,000 mg/day were tested without adverse effects; although at this level there is no adequate product safety information [9-11]. Taken orally, Coq10 in a crystalline form is poorly absorbed. Unfortunately, because of insolubility and high molecular weight of samples used, it is difficult to compare the bioavailability of supplements used in many studies. Variables that can affect the absorption of Coq10, include: formulation, dosing intervals, dose administered and intake of food or liquids [11]. Circumventing absorption deficits, Coq10 formulated as a sublingual, 30-50mg provides quick entry into the bloodstream.

Studies with the Coq10

Our main source of energy production is through the Krebs cycle found in the mitochondria. Dysfunctional mitochondria, mitochondriopathies, and the resulting deficiency of adenine triphosphate (ATP) are the basis of all chronic diseases; because it is in the mitochondria where free radicals are produced. Without adequate, available antioxidant, mitochondria are damaged. When levels of Coq10 are deficient, mitochondrial dysfunction develops [12,13]. Mitochondrial dysfunction mainly occurs in high energy demand organs and tissues, explaining why cardiovascular tissue and brain neurons are among the most susceptible [13]. Coq10, an essential nutrient for mitochondrial function, protects the mitochondria.

Various chronic diseases respond positively to Coq10 supplementation, but, unfortunately, some doctors and health professional still are not prescribing Coq10. Resistance to prescribe Coq10 can be understood as: a lack of knowledge about the physiological role of Coq10, especially the symptoms of Coq10 deficiency, and concern about the gastrointestinal side effects linked with Coq10. Finally, in many medical community doctors are not allowed to prescribe a non- patentable drug, and many doctors are prohibited from suggesting a natural alternative. Non-the-less, our aim is that the strong evidences provided below will encourage doctors and health professionals to rethink their position and begin co- prescribing Coq10, especially with statins drugs.

In the last years, various systematic reviews and clinical trials have been published showed that persons taking statins develop deficient levels of Coq10 and supplementation of Coq10 decreases the negative side effects of statins [14-16]. Correspondingly, it is crucial that clinicians understand that statins block the HMG-CoA reductase, thus reducing the levels of Coq10 producing consequences beyond muscle-related adverse events. A randomized trial of Coq10 in patients with statin myopathy demonstrated that Coq10 reduced the pain intensity in muscle pain, myalgia patients; showing Coq10 supplementation is a useful clinical practice strategy [17].

Six randomized controlled trials and nine observational studies reported that statins reduce plasma and serum Coq10 levels by 16-54% and Coq10 deficiency was identified as a strong mortality predictor in chronic heart failure [14-18]. Also, statins may unmask pre-symptomatic neuromuscular disorders, thus, elevated serum creatine kinase (CK) levels and adverse muscle events should be monitoring after discontinuation of statins [19]. A placebo-controlled trial in coronary artery disease (CAD) patients during statins therapy exhibited 300 md/dayCoq10 supplementation lowers inflammation and significantly enhances antioxidant enzymes activities [20]. Recently, a clinical trial showed that the deficient levels of Coq10 are present in hepatocellular carcinoma patients with higher post-surgery inflammation. Coq10may be considered as an antioxidant therapy in this hepatocellular carcinoma patients [21].

An article showed that in rats, Coq10 may protect hepatocytes and other types of cells, and reduce toxic effects of statins [22]. Ubiquinol is the reduced form of Coq10 and has a high oral bioavailability. In a 12-week baseline, double-blind, prospective, randomized-controlled trial, a comparison was made with microRNA (miRNA) profiles and liver enzymes compared to two group of simvastatin-treated patients; one group with and the other group without ubiquinol supplementation. Ubiquinol supplementation at the microRNA (miRNA) level may provide beneficial change to Coq10 liver deficiency [23].

Medical literature also shows Coq10 supplementation is efficacious in persons with heart failure. Coq10 supplementation significantly improved endothelial function, even though simvastatin has a significant depressive effect on mitochondrial respiration [24-26]. Although we present recent evidences on the physiological efficacy of Coq10, there remain controversial studies. We question these studies from the perspective of the ambiguity of follow-up time frame and dosages of Coq10 [27,28]

In clinical practice, patients taking statin drugs and persons with chronic diseases, pharmaceutical prescription of Coq10 would be efficacious. The current medical paradigm needs urgent attitude changes about prescribing Coq10. Additionally, a pharmacogenetic approach in identifying aberrant genes involved in CoQ10 biosynthesis may be a method to identify individual where statin therapy would be contraindicated [29-31].

Conclusion

Patients with chronic diseases, and, especially, patients taking statin drugs are shown to have deficient levels of Coq10. Both individuals suffering from chronic diseases and those taking statin drugs can benefit from Coq10 supplementation. Even though there is conflicting reporting about the use of Coq10, clinicians and health professionals should be aware of secondary Coq10 depletion that occurs in persons taking statins. Reduction of statin drug side effects offers an opportunity, through Coq10 supplementation to improve patient's life quality. Recommendations for future clinical trials with people taking statin drugs should include a pharmacogenetic analysis of new sublingual formulations of Coq10.

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