NovaQ10

Coenzyme Q10

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Summary

Coenzyme Q10 is a fat-soluble compound primarily synthesized by the body and also consumed in the diet.
Coenzyme Q10 is required for mitochondrial ATP synthesis and functions as an antioxidant in cell membranes and lipoproteins.
Endogenous synthesis and dietary intake appear to provide sufficient coenzyme Q10 to prevent deficiency in healthy people, although tissue levels of coenzyme Q10 decline with age.
Oral supplementation of coenzyme Q10 increases plasma, lipoprotein, and blood vessel levels, but it is unclear whether tissue coenzyme Q10 levels are increased, especially in healthy individuals. Coenzyme Q10 supplementation has resulted in clinical and metabolic improvement in some patients with hereditary mitochondrial disorders.
Although coenzyme Q10 supplementation may be a useful adjunct to conventional medical therapy for congestive heart failure, additional research is needed.
Roles for coenzyme Q10 supplementation in cardiovascular diseases, neurodegenerative diseases, cancer, and diabetes require further research.
Coenzyme Q10 supplementation does not appear to improve athletic performance.
Although coenzyme Q10 supplements are relatively safe, they may decrease the anticoagulant efficacy of warfarin.
Although the use of cholesterol-lowering medications known as HMG-CoA reductase inhibitors (statins) decreases circulating levels of coenzyme Q10, it is unclear whether coenzyme Q10 supplementation provides any health benefit to patients taking these drugs.

Introduction

Coenzyme Q10 is a member of the ubiquinone family of compounds. All animals, including humans, can synthesize ubiquinones, hence, coenzyme Q10 cannot be considered a vitamin (1). The name ubiquinone refers to the ubiquitous presence of these compounds in living organisms and their chemical structure, which contains a functional group known as a benzoquinone. Ubiquinones are fat-soluble molecules with anywhere from one to 12 isoprene (5-carbon) units. The ubiquinone found in humans, ubidecaquinone or coenzyme Q10, has a "tail" of ten isoprene units (a total of 50 carbon atoms) attached to its benzoquinone "head" (diagram) (2).

Neurodegenerative diseases

Parkinson's disease

Parkinson's disease is a degenerative neurological disorder characterized by tremors, muscular rigidity, and slow movements. It is estimated to affect approximately 1% of Americans over the age of 65. Although the causes of Parkinson's disease are not all known, decreased activity of complex I of the mitochondrial electron transport chain and increased oxidative stress in a part of the brain called the substantia nigra are thought to play a role. Coenzyme Q10 is the electron acceptor for complex I as well as an antioxidant, and decreased ratios of reduced to oxidized coenzyme Q10 have been found in platelets of individuals with Parkinson's disease (57, 58). One study also found higher concentrations of oxidized coenzyme Q10 in the cerebrospinal fluid of patients with untreated Parkinson's disease compared to healthy controls (59). Additionally, a study of coenzyme Q10 levels in postmortem Parkinson's disease patients found lower levels of total coenzyme Q10 in the cortex region of the brain compared to age-matched controls, but no differences were seen in other brain areas, including the striatum, substantia nigra, and cerebellum (60). A 16-month randomized placebo-controlled trial evaluated the safety and efficacy of 300, 600, or 1,200 mg/day of coenzyme Q10 in 80 people with early Parkinson's disease (61). Coenzyme Q10 supplementation was well tolerated at all doses and was associated with slower deterioration of function in Parkinson's disease patients compared to placebo. However, the difference was statistically significant only in the group taking 1,200 mg/day. A smaller placebo-controlled trial showed that oral administration of 360 mg/day of coenzyme Q10 for four weeks moderately benefited Parkinson's disease patients (62). More recently, a randomized, double-blind, placebo-controlled trial in 106 patients with midstage Parkinson's disease reported that 300 mg/day of nanoparticular coenzyme Q10 for three months had no therapeutic benefit (63). Another trial found that 2,400 mg/day of coenzyme Q10 for 12 months was not effective in early Parkinson's disease (64). A phase III clinical trial of coenzyme Q10 (1,200-2,400 mg/day) and vitamin E (1,200 IU/day) supplementation in patients with Parkinson's disease was recently terminated because it was unlikely that such a treatment was effective in treating Parkinson's disease (65).

Huntington's disease

Huntington's disease is an inherited neurodegenerative disorder characterized by selective degeneration of nerve cells known as striatal spiny neurons. Symptoms, such as movement disorders and impaired cognitive function, typically develop in the fourth decade of life and progressively deteriorate over time. Animal models indicate that impaired mitochondrial function and glutamate-mediated neurotoxicity may play roles in the pathology of Huntington's disease. Coenzyme Q10 supplementation has been found to decrease brain lesion size in animal models of Huntington's disease and to decrease brain lactate levels in Huntington's disease patients (66, 67). Feeding a combination of coenzyme Q10 (0.2% of diet) and remacemide (0.007% of diet) to transgenic mice that express the Huntington's disease protein (HD-N171-82Q mice) resulted in improved motor performance and/or survival (68, 69). Remacemide is an antagonist of the neuronal receptor that is activated by glutamate.

It was recently shown that the R6/2 mouse model of Huntington's disease exhibits a progressive decline in behavioral and neurological symptoms similar to that of the human condition (70). Thus, R6/2 mice may be an ideal model to investigate potential therapies for Huntington's disease. Some, but not all, studies employing these mice have shown that dietary supplementation with coenzyme Q10 (0.2% of diet) improves motor performance and overall survival and helps to prevent body weight loss; coenzyme Q10 supplementation has also been associated with reductions in the various hallmarks of Huntington's disease, i.e., brain atrophy, ventricular enlargement, and striatal neuronal atrophy (68, 71). Interestingly, co-administration of coenzyme Q10 with remacemide, the antibiotic minocycline, or creatine has been shown to result in even greater improvements in most measured parameters (68, 71, 72).

To date, only one clinical trial has examined whether coenzyme Q10 might be efficacious in human patients with Huntington's disease. A 30-month, randomized, placebo-controlled trial of coenzyme Q10 (600 mg/day), remacemide, or both in 347 patients with early Huntington's disease found that neither coenzyme Q10 nor remacemide significantly altered the decline in total functional capacity, although coenzyme Q10 supplementation (with or without remacemide) resulted in a nonsignificant 13% decrease in the decline (73). A recent 20-week pilot trial examined the safety and tolerability of increasing dosages of coenzyme Q10 (1,200 mg/day, 2,400 mg/day, and

3,600 mg/day) in eight healthy subjects and in 20 patients with Huntington’s disease; 22 of the subjects completed the study (74). All dosages were generally well tolerated, with gastrointestinal symptoms being the most frequently reported adverse effect. Blood levels of coenzyme Q10 at the end of the study were not higher than the levels resulting from the intermediate dose, suggesting that the 2,400 mg/day effectively maximizes blood coenzyme Q10 levels and potentially avoid any side effects with higher dosages (74). A phase III clinical trial administering 2,400 mg/day of coenzyme Q10 or placebo for five years is currently recruiting participants with Huntington’s disease (75). At present, there is insufficient evidence to recommend coenzyme Q10 supplements to Huntington's disease patients.

Friedreich's ataxia

Friedreich's ataxia (FRDA) is an inherited, autosomal recessive neurodegenerative disease caused by mutations in the gene that encodes frataxin, a protein of unknown function that is primarily located in the mitochondria. Decreased expression of frataxin is associated with accumulation of iron within the mitochondria, thereby resulting in increased oxidative stress; imbalances in iron-sulfur containing proteins, including mitochondrial aconitase; and reduced activities of the mitochondrial respiratory chain (76). Clinically, FRDA is a progressive disease characterized by limb ataxia and CNS abnormalities that result from sensory nerve degeneration (77, 78). In addition, FRDA patients experience symptoms of hypertrophic cardiomyopathy and diabetes (79). A pilot study administering coenzyme Q10 (200 mg/day) and vitamin E (2,100 IU/day) to ten FDRA patients found that energy metabolism of cardiac and skeletal muscle was improved after only three months of therapy (80). Follow-up assessments at 47 months indicated that cardiac and skeletal muscle improvements were maintained and that FRDA patients showed significant increases in fractional shortening, a measure of cardiac function. Moreover, the therapy was effective at preventing the progressive decline of neurological function (81). A recent study reported that both coenzyme Q10 and vitamin E deficiencies are quite common among FRDA patients and that cosupplementation with both compounds, at doses as low as 30mg/day of coenzyme Q10 and 4 IU/day of vitamin E, may improve disease symptoms (82). Large-scale randomized clinical trials are necessary to determine whether coenzyme Q10, in conjunction with vitamin E, has therapeutic benefit in FRDA.