[14:40 - 15:10]

Overview about the Safety and Function of CoQ_{10}

Se-Young Choung

Department of Hygienic Chemistry, College of Pharmacy, Kyung Hee University, Seoul, Korea

Coenzyme Q_{10} (CoQ_{10}) was first isolated in 1957 in the mitochondria of beef heart and was found in highest concentrations in tissues with high energy turnover such as the heart, brain, liver, and kidney. Coenzyme Q_{10} is an essential cofactor in the mitochondria electron transport chain as a series of oxidation-reduction reactions involved in cellular respiration and the synthesis adenosine triphosphate (ATP), and is found in all cell membranes. Additionally, CoQ_{10} has demonstrated activity in preventing lipid peroxidation as an antioxidant scavenger and an indirect stabilizer of calcium channels to decrease calcium overload.

Coenzyme Q_{10} can be synthesized *in vivo*, but situations may arise when the need for it surpasses the body's ability to synthesize it. Coenzyme Q_{10} is well-absorbed by oral supplementation as evidenced by significant increases in serum CoQ_{10} levels after supplementation[1]. There is some evidence that CoQ_{10} in oil suspension has the highest bioavailability[2].

Coenzyme Q_{10}'s wide-ranging cellular properties implicate it for the potential treatment of numerous conditions that may improve with mitochondrial and antioxidant support. Coenzyme Q_{10} enhances phagocytic activity of macrophages and increases granulocyte proliferation, and it inhibits release of histamine in antigen-challenged animals. These facts are the first on the stimulation of the reticuloendothelial system by the CoQ_{10}. Its antioxidant activity helps prevent AIDS-related diseases and the damage of lymphocyte DNA caused by oxidative stress with orally intake of 100 or 300

mg/day for two weeks. Blood levels of CoQ_{10} are lower in AIDS patients and 200 mg/day increased T-helper/suppresser rations. Metastasis is prevented and remission is enhanced in breast cancer. The tumors in mice induced by 3, 4, 9, 10-dibenzpyrene, treatment by CoQ_{10} reduce tumor size, and increase survivors, and these therapeutic effects are dose-dependent. Also, it is expected that many cancer patients will have abnormally low levels of CoQ_{10} in blood, tissues and organs. Mechanisms in cancer include immune system enhancement and antioxidant activity. Gingival biopsies yield subnormal tissue level of CoQ_{10} in patients with periodontal disease. The supplementation of CoQ_{10} speeds healing after the periodontal surgery. The protection of the gastric mucosa is due to its antioxidant effects. Production of protective mucus and rapid cell turnover of gastric mucosa are highly energy-dependent processes. Individuals with a family history of obesity have a 50% reduction in thermogenic response to a meal and are often found to have low CoQ_{10} levels. Coenzyme Q_{10}, being essential for energy production, can be of benefit, and the supplementation may enhance aerobic capacity and muscle performance, especially in sedentary individuals. The 45mg BID of CoQ_{10} administrations increase blood level of it and decrease the ammonia, uric acid, triglycerides, FFA and total cholesterol in athletes. The ammonia-lactic acid ratio is indicated an index for energetic muscular system stress (metabolic waste production). When CoQ_{10} is deficient, muscular dystrophy is found in cardiac and skeletal muscle in animals and humans with hereditary muscular dystrophy. Coenzyme Q_{10} is especially indicated for the enhancement of myocardial function by enhancing energy production, improving contractility of the cardiac muscle, and providing potent antioxidant activity, in particular prevention of LDL oxidation. Specific cardiac problems which may benefit from CoQ_{10} include cardiomyopathy, congestive heart failure, angina, prevention of adriamycin toxicity, protection during cardiac surgery, mitral valve prolapse and hypertension. Pediatric cardiomyopathy represents a group of rare and heterogeneous disorders that often results in death.

About 40 % of children who present with symptomatic cardiomyopathy are reported to receive a heart transplant or die within the first two years of life. Based upon the biochemical rationale and a large body of data on patients with adult cardiomyopathy, heart failure, and mitochondrial diseases with heart involvement, a role for CoQ_{10} therapy in the patients is indicated, and preliminary results are promising. Additionally, the potential usefulness of CoQ_{10} supplementation as an adjunct to conventional therapy in pediatric cardiomyopathy, particularly in children with dilated cardiomyopathy, are warranted with orally intake of 10 mg/kg/day for two months. Heart failure is any structural or functional cardiac disorder that impairs the ability of the heart to maintain normal cardiac output, often by altering ventricular filling or pumping capabilities. This leads to several physical symptoms including fatigue, shortness of breath, an inability to exercise, and edema. Heart failure is characterized by generalized and cardiac-specific oxidative stress, and chronic oxidant injury contributes to impairment of myocardial function and ultimately heart failure clinical progression. The increase in oxidative stress in heart failure has led to investigations exploring the use of CoQ_{10} in inhibiting the progression of heart failure. The role that CoQ_{10} plays in the progression of heart failure has led to the development of an oxidative stress for the disease with 100 mg/day for 3 months, 50 mg TID for 4 weeks, 150 mg/day for 30-45 days, 100 mg BID for 12 weeks, and 33 mg TID for 3 months. Trials using CoQ_{10} at various doses for essential hypertension, typically as adjuvant therapy, found a mean decrease in systolic and diastolic blood pressure of 16 and 10 mm Hg with 120 mg/day for 8 weeks, respectively. Coenzyme Q_{10} with 200 mg/day for 12 weeks has been considered for improving glycemic control through various mechanisms, including a decrease in oxidative stress. Increased oxidative stress in diabetes mellitus may underlie the development of endothelial cell dysfunction by decreasing the availability of nitric oxide as well as by activating pro-inflammatory pathways. Coenzyme Q_{10}, a potent antioxidant and a critical intermediate of the electron transport chain, may improve endothelial

dysfunction by coupling endothelial nitric oxide synthase and mitochondrial oxidative phosphorylation. Degenerative brain disorders such as Alzheimer's and other dementias, Down syndrome, stroke, Parkinson's disease, multiple sclerosis, amyotrophic lateral sclerosis, Huntington's disease, Friedreich's ataxia, aging, and constitutive disorders demonstrate impairments of the mitochondrial citric acid cycle and oxidative phosphorylation enzymes. Coenzyme Q_{10} involved in mitochondrial metabolism provides clinical benefit. Coenzyme Q_7 (CoQ_{10} analog) at 10mg/day resulted in significant increases in sperm count and motility.

The deficiency may result from the impaired synthesis due to nutritional deficiencies, genetic or acquired defect in synthesis or utilization, the increased tissue needs resulting from illness. Coenzyme Q_{10} levels decline with advancing age. Cholesterol-lowering drugs such as lovastatin and pravastatin inhibit the enzyme 3-hydroxy-3-methyl glutaryl (HMG)-CoA reductase, required for synthesis of cholesterol as well as CoQ_{10}. Therefore, these drugs may compromise CoQ_{10}. Propranolol and metaprolol inhibit CoQ_{10}-dependent enzymes. Phenothiazines and tri-cyclic antidepressants have also been shown to inhibit CoQ_{10} –dependent enzymes. The beneficial outcome of CoQ_{10} supplementation comes continues to grow at a rapid pace. The pace is being matched by the increasing availability and appearance of this ingredient in dietary supplement products. Typical dose for most conditions is 30-60 mg BID. The available published human clinical data involving CoQ_{10} supports a high level of confidence in this ingredient with respect to its safe use in dietary supplements. The only adverse effect reported nausea with 600 mg/day and lower intakes of CoQ_{10} is not consistent and has no apparent dose-response relationship, indicating that it is not causally related. The absence of adverse effects in 900 mg/day intake of CoQ_{10} is completely consistent with and supports the observed safe level of 1200 mg/day identified. The level of 1200 mg/day intake has been studied in early Parkinson's disease patients in a strongly designed clinical of 16 months duration that found no

adverse effects. The 2400 mg/day intake of CoQ_{10} was administered to 16 Parkinson's disease patients for 8 weeks without any adverse effect[14]. The short duration and small cohort increase the uncertainty in the application of these data to healthy adults, although the data are consistent with this level being an observed safe level. The 3000 mg/day intake of CoQ_{10} was evaluated in 31 amyotrophic lateral sclerosis patients that were assessed with an extensive series of clinical and laboratory indices that might have shown any adverse effects[15]. However, the lack of control groups and the small number of subjects precludes use of these data to identify. The absence of a well-defined critical effect precludes the selection of a NOAEL, and therefore required use of the observed safe level or highest observed intake approach established by FAO/WHO to conduct the risk assessment. Though no toxicological basis was found, evidence from well-designed randomized, controlled human clinical trials indicates that the upper level for supplements for CoQ_{10} is 1200 mg/day[9].

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