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Coenzyme Q-10 and Cardiovascular Health: To Take or Not to Take - That is the Question

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What is Coenzyme Q-10?

Coenzyme Q-10 (CoQ10), also known as 2,3-dimethoxy-5-methyl-1,6-decaprenyl-1,4-benzoquinone, is a well-known supplement in the cardiology world and has been used as an adjunctive therapy for various cardiovascular disorders for over 35 years (1). First discovered in 1957, CoQ10 (molecular formula: C₅₉H₉₀O₄) serves multiple functions in the human body. A coenzyme, by definition, is an organic, non-protein molecule that is necessary for the action of enzymes. Its primary action is as a key component of the electron transport chain, a medium for the transfer of electrons from NADH and succinate dehydrogenase to the cytochrome system, which is an essential process in the synthesis of ATP (2,3). CoQ10 also acts as a powerful antioxidant and free-radical scavenger that protects against DNA damage and oxidative stress (2). When metabolized to ubiquinol, it prolongs the antioxidant effect of vitamin E (2).

CoQ10 is synthesized endogenously in the body from phenylalanine and acetyl-CoA, and is found in the highest concentrations in organs with high rates of oxygen consumption, such as the heart and the brain (4). CoQ10 is acquired primarily from meat and poultry in the diet, and is manufactured as a dietary supplement by the fermentation of beets and sugarcane with yeast (2). Ingested CoQ10 is absorbed slowly from the gastrointestinal tract, distributes to the liver, and is incorporated into very low-density lipoproteins (2). Therefore, serum levels of CoQ10 may be depleted by cholesterol-lowering drugs, such as statins. Statins inhibit 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase and the formation of farnesyl pyrophosphate, which is essential for the synthesis of isoprenoid subunits of CoQ10 (5). Reduced levels of CoQ10 have also been found in the elderly and in a number of disease states (6). In cases of deficiency, dietary CoQ10 supplementation can replenish depleted stores and enhance the clinical benefit of anti-lipidemic agents.

In Vitro and In Vivo Studies on Animal Models

Numerous studies have been conducted on various animal models to assess the potential benefits of CoQ10 in cardiovascular disease. A study conducted by Hano et al. on rats showed that CoQ10 markedly improved the recovery of cardiac function during post-ischemic reperfusion by reducing Ca²⁺ overload and increasing high-energy phosphates (7). When Maulik et al. treated swine with dietary CoQ10 supplements (5 mg/kg/day) for 30 days and then subjected the animals to ischemia-reperfusion injury, they found that the treated group had better post-ischemic contractile function, smaller myocardial infarct size, and less creatine kinase release from coronary effluent compared with the control group (8). In contrast, a study on senescent rats by Lönnrot et al. found that CoQ10 supplementation (10 mg/kg/day) for 8 weeks did not have any significant effects on post-ischemic recovery (9). However, the lack of any benefit observed in the CoQ10-treated group in this study may have been affected by the age-related decrease in CoQ10 levels. Yokoyama et al. found that rats pre-treated with CoQ10 (20 mg/kg intramuscular and 10 mg/kg intraperitoneal) had better coronary endothelial function and lower free radical burst following ischemia and reperfusion than the untreated group (10). The authors of this study attributed the observed effects to the direct antioxidant function of CoQ10. In another study by Lee et al., researchers found that CoQ10 supplementation was associated with reduced oxidative stress and increased expression of genes involved in oxidative phosphorylation in the hearts of middle-aged mice (11). However, CoQ10 was not as effective as caloric restriction in inhibiting the aging process and the age-related alterations in gene expression.

Evidence from Clinical Trials

In general, studies on the benefits of CoQ10 in humans have been mostly favorable and very promising. Most reports lend evidence to the popular belief that the cardioprotective effects CoQ10 stem from the preservation of mitochondrial energy production and reduction of oxidative stress during reperfusion following myocardial ischemic injury (3). In a randomized study, Rosenfeldt et al. found that pre-treatment with CoQ10 (300 mg/day) for 7 days prior to cardiac surgery improved post-hypoxic myocardial contraction, reduced myocardial damage, and significantly shortened hospital stay by 2 days (4). These benefits may be especially important in patients over the age of 70, among whom the mortality and morbidity from cardiac surgery is much higher than in younger patients. However, not all clinical trials have reported beneficial results. In a double-blind, placebo-controlled, randomized trial, Taggart et al. found that short-term supplementation (600 mg in divided doses) 12 hours prior to coronary revascularization did not lead to improved myocardial protection in patients undergoing this interventional procedure (12). However, all of the patients in this study had well-preserved left ventricular function (ejection fraction > 0.50) and were undergoing the operation electively. In this case, the higher baseline health status of these patients may have obtunded the cardio-protective effects of CoQ10. In another randomized, double-blind, placebo-controlled trial conducted by Singh et al., patients with acute myocardial infarction (AMI) were treated with CoQ10 (120 mg/d) for 28 days (13). The treated group had a lower incidence of angina pectoris, arrhythmias, ventricular dysfunction, and cardiac events, including cardiac death and infarction. Indicators of oxidative stress (measured by levels of lipid peroxides, diene conjugates, and malondialdehyde) were also greatly reduced in the treatment group than in the placebo group. The authors of this study suggested that CoQ10 can provide rapid protective effects in AMI if administered within 3 days of the event.

Long-term studies seem to reinforce the beneficial effects observed with short-term CoQ10 supplementation. In a multicenter, randomized, controlled clinical trial, Morisco et al. found that patients with congestive heart failure who were treated with CoQ10 at a dosage of 2 mg/kg/day for one year had significantly reduced hospitalizations for worsening of congestive heart failure as well as fewer incidence of complications (14). There is some evidence that CoQ10 can also lower the risk factors for future cardiac events. In a randomized, double-blind, controlled trial, patients with prior history of AMI were treated orally with CoQ10 (120 mg/day) and were found to have a significant reduction in total and low-density lipoprotein cholesterol compared to baseline levels after 1 year (15). This study suggests CoQ10 treatment has the potential to slow down the progression of atherosclerosis, in conjunction with lipid lowering therapy. Another study examining the effects of CoQ10 on hypertension found a mean 18 mm Hg reduction in systolic blood pressure in the CoQ10-treated group, but no significant changes in diastolic blood pressure after 12 weeks of treatment with 60 mg of emulsified CoQ10 twice a day (1). Hypertension is the most prevalent cardiovascular disorder in the United States, affecting more than 50 million adults, and remains one of the most common risk factors for cardiovascular morbidity and mortality. Based on the results of this study, Burke et al. suggested CoQ10 may be offered to hypertensive patients as a safe, alternative treatment option.

Side Effects of CoQ10

In general, CoQ10 is a safe and well-tolerated supplement, with a high therapeutic index and low side effect profile. The long-term safety and tolerability of CoQ10 supplementation has been consistently confirmed in numerous clinical trials. The only potential drug interaction

recorded to date is antagonism of warfarin due to the vitamin K-like properties of CoQ10 (5). In a study by Rauscher et al., CoQ10 was found to exacerbate several diabetes-related effects in streptozotocin-induced diabetic rats, marked by increase in cardiac catalase activity, hepatic lipid peroxidation, and glutathione peroxidase activity in the heart and brain, with decrease in hepatic glutathione reductase activity (16).

Conclusion

Although evidence from both animal studies and clinical trials has shown that CoQ10 supplementation may provide protective effects in various cardiovascular diseases, literature is equally replete with findings that do not support this view. Currently, there are not enough clinical trials to have established unequivocal evidence in support of the benefit of CoQ10 antioxidant therapy for cardiovascular health. Although CoQ10 has the potential to mitigate disease process by reducing oxidative stress a priori, it has been found to have minimal beneficial effects on the quality of life, exercise capacity, and hemodynamic parameters of patients with heart failure and dilated cardiomyopathy. However, this may be due to the paucity of long-term studies assessing these criteria. Further investigation of the pharmacodynamics of CoQ10 is also warranted. While it is known that CoQ10 supplementation raises plasma concentrations, it remains unclear if exogenous CoQ10 enters cells and tissues. Likewise, the extent of distribution to various organs and the site of action remain largely unknown.

In summary, CoQ10 is a safe and well-tolerated nutritional supplement that seems to have favorable actions with regard to improving multiple facets of cardiovascular health. However, before an official recommendation can be made on whether or not to take CoQ10, more large multi-center, clinical trials are needed. In addition, issues such as optimum target dose, potential drug interaction, and monitoring parameters require further investigation. Until then, a judicious literature review by a panel of experts providing a balanced analysis of major studies would be helpful in sorting through the conflicting reports produced so far on the effects of CoQ10.

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