Coenzyme Q_{10} in the Treatment of Mitochondrial Disorders

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Mitochondria, specialized compartments present in every cell of the body (except red blood cells), produce 90% of the energy needed to support growth and sustain life. Mitochondrial disorders result from a decrease in the ability of the mitochondria to make energy in the form of adenosine 5'triphosphate (ATP). There are over 40 known types of mitochondrial disorders. These disorders often affect tissues that have a high-energy demand, such as the heart, brain, eyes, and skeletal muscles. The symptoms may range from isolated eye problems to severe developmental delay with muscle weakness. Because of the diverse symptoms, there is limited information on effective treatment therapies. The goal of cofactor treatment is to increase ATP production and to reduce the buildup of toxic metabolites. The use of supplemental vitamins and cofactors is largely unproven and their use in mitochondrial disorders remains controversial. Coenzyme Q_{10} is the most widely used supplement in the treatment of oxidative phosphorylation (OXPHOS) disorders.

What is CoQ_{10}?

CoQ_{10} , or ubiquinone, is a natural substance found in our body that helps transfer electrons in the respiratory chain. This process is part of ATP synthesis, or energy production. CoQ_{10} also acts as an antioxidant and helps protect cells against oxidative damage. CoQ levels in the body are maintained by the body's own production of CoQ and from dietary sources, mainly of animal origin.

Is it Effective?

CoQ_{10} has been reported to have a beneficial effect on clinical outcome and biochemical measures in a variety of mitochondrial disorders. The positive effects have included a reduction of serum lactate and pyruvate (Abe et al 1991b; Bresolin et al 1988c; Goda et al 1987b; Nishikawa et al 1989b; Ogasahara et al 1985b; Yamamoto et al 1987b) , improvement in cardiac conduction defects and eye movements (Ogasahara et al 1985a), reduced muscle weakness (Abe et al 1991a; Ihara et al 1989b; Yamamoto et al 1987a) and improved exercise tolerance (Bresolin et al 1988b; Goda et al 1987a), improved oxygen utilization during exercise (Abe et al 1999), decreased peripheral nerve damage (Ihara et al 1989a), improvement in neurological function (Bresolin et al 1988a), increased respiratory chain activity, and acceleration of post-exercise recovery (Bendahan et al 1992; Nishikawa et al 1989a). Most reports regarding treatment have been case studies or anecdotal reports with limited numbers of patients, various treatment periods, and CoQ_{10} dosages ranging from 30 to 300 mg/day.

Several short-term studies have shown variable results with CoQ_{10} treatment. Two trials in patients with muscular dystrophies and neurogenic atrophies showed an improvement in cardiac function and physical performance (Folkers & Simonsen 1995). In another short-term study in patients with mitochondrial encephalomyopathies, a trend of effectiveness of CoQ_{10} was noted by improved muscle endurance, decreased fatigability of daily activities, and decreased serum lactate and pyruvate levels, but statistical significance was only noted in global muscle strength (Chen et al 1997). In a study with CoQ_{10} supplementation in patients with mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS), there was an improvement in neuromuscular symptoms, but no difference in fasting glucose or glycemic control (Andersen et al 1997).

Longer-term studies of six months duration have evaluated the effectiveness of CoQ_{10} treatment. Phosphorous magnetic resonance spectroscopy (^{31}PMRS) was utilized to study the effect of CoQ_{10} treatment on brain and skeletal muscle mitochondrial function. Baseline brain and skeletal muscle metabolism was compared to 36 age-matched healthy controls. Mitochondrial function in both brain and muscle was reduced by 25% and 29%, respectively, compared to controls. Treatment with CoQ_{10} statistically improved phosphorylation potential and calculated ATP synthesis in both brain and skeletal muscle in all patients studied (Barbiroli et al 1997).

In a multi-center trial of CoQ_{10} in mitochondrial cytopathies, a 25% decrease in post-exercise lactate levels was observed in over one-third of the patients (Bresolin et al 1990). A bicycle ergometry study in patients with mitochondrial encephalomyopathies treated with CoQ_{10} showed no change in metabolic parameters after three months of treatment, but after six months of treatment, a decrease in lactate/pyruvate ratios at rest and in association with exercise was noted in approximately half of the patients (Chan et al 1998). It is unclear why some patients respond and others with the same clinical phenotype and biochemical defect do not show any beneficial effects.

The longest-term study examined supplementation of CoQ_{10} in patients with the 3243 MELAS mutation. The group of the MELAS patients with diabetes experienced an increased insulin secretory response and improved lactate response after exercise with the CoQ_{10} treatment. In addition, there was no progression of hearing loss (a common symptom in this disorder). The CoQ_{10} treatment did not affect the insulin secretory response of the patients with impaired or normal glucose tolerance (Suzuki et al 1998).

While most cases of decreased CoQ_{10} levels are secondary to other causes, primary muscle CoQ_{10} deficiency has been documented (Musumeci et al 2001b; Rotig et al 2000; Sobreira et al 1997). In patients with muscle CoQ_{10} deficiency, CoQ_{10} administration resulted in dramatic improvements in strength, seizure control, muscle weakness, and ability to walk (Musumeci et al 2001a).

Availability and Use of CoQ_{10}

Commercially prepared CoQ_{10} supplements are available as powder-filled, hard

shell capsules; oil-based suspensions in a soft gel capsule; emulsions in a soft gel capsule and liquid. There are limited reports on the bioavailability or absorption of CoQ in these preparations. CoQ can be purchased from a variety of sources, including the local drug store. Animal and human studies have demonstrated that approximately 2 to 10 % of the dose administered is taken up into the blood (Weber 2001; Zhang et al 1995). Dosages of 90 to 150 mg/day of CoQ_{10} have been shown to increase plasma concentrations by 180% (Kaikkonen et al 1997). The benefit of CoQ_{10} supplementation in mitochondrial disorders is unclear. Many patients report improvement in clinical symptoms, and side effects from large pharmaceutical dosages are extremely rare. It is hoped that CoQ_{10} may enhance enzyme function and result in an increase in energy production. CoQ's role as an antioxidant may help slow the progression of the disease. Dosage in the treatment of mitochondrial disorders varies but clinicians currently recommend 4 to 15 mg/kg/day to determine the effectiveness in an individual patient (Gold & Cohen 2001). **Remember, consult your physician before starting any treatment.**

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