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Coenzyme Q10 as a Treatment for Heart Disease

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What is Coenzyme Q10 (CoQ10)?

CoQ10 is a benzoquinone containing 10 isoprene units, which allows it to diffuse rapidly through the inner mitochondrial membrane. In this setting, the molecule works as a lipophilic electron carrier for the respiratory chain, transferring electrons from NADH, succinate and fatty acid oxidation intermediates to cytochromes. In other words, CoQ10 functions as an intermediary between two-electron carriers and the one-electron cytochromes (1). CoQ10 may also act as an antioxidant (2), protecting cell structures (3), and other cell membranes (4), from oxidative damage by preventing lipid peroxidation. Since congestive heart failure is often accompanied by oxidative damage to the myocardium (5), and since CoQ10 levels are often decreased in the myocardial cells of advanced heart failure patients (6), it is possible that supplementing CoQ10 levels could help alleviate the severity of heart disease. This hypothesis is bolstered by the fact that myocardial CoQ10 deficiency correlates with heart failure severity (6,7). To test the validity of this idea, let us examine the effects of CoQ10 in treating hypertrophic cardiomyopathy and congestive heart failure.

Hypertrophic Cardiomyopathy (HCM)

HCM is characterized primarily by a thickening of the left ventricle walls (usually the septal), as well as by significant impairment of left ventricular filling. Although standard disease treatment calls for negative inotropic drugs, this regimen relieves pain and palpitations without decreasing wall thickness, and generally leads to worse fatigue and dyspnea. Given the decreased CoQ10 levels in diseased heart tissue, it is possible that the heart wall thickens in response to decreased myocardial energy production, such that cells become larger to compensate for reduced contractile efficiency.

Logsojoen et al. (8), explore this possibility in a study of seven patients with HCM. After being placed on a mean dose of 200mg of CoQ10/day (mean blood level 2.9ug/ml), in addition to current digitalis and diuretics medications, subjects were examined before starting therapy, 3-6 months afterwards and once a year subsequently by electrocardiogram. At final assessment, all seven patients noted improvement in fatigue and dyspnea symptoms, along with a mean interventricular septal thickness reduction of 24% ($P < 0.002$).

Although this improvement suggests a potential therapeutic effect for CoQ10 in HCM, design flaws of the study severely limit the strength of such a conclusion. First of all, the lack of a negative control group and the concurrent medications prevent one from definitively concluding that the observed responses are due to CoQ10 treatment. Furthermore, the small study size with no defined patient selection criteria, no subject randomization and no clearly defined study endpoint allow the results to be influenced by bias and confounding. Given these problems, a randomized double-blind study, addressing all of the limitations of this study, needs to be conducted.

Congestive Heart Failure (CHF)

A number of clinical trials have been conducted to find supporting evidence for CoQ10 use in treating CHF. One of the most recent by Soja and Mortensen (9). uses a statistical aggregation method, known as meta-analysis, to congregate the data from several studies, in order to analyze a number of CHF related variables with respect to CoQ10 treatment. The specific parameters examined include stroke volume (SV), cardiac output (CO), ejection fraction (EF), cardiac index (CI), end diastolic volume index (EDVI), systolic time intervals (PEP/LVET) and total work capacity (Wmax). Of these indicators, SV, CO, EF, CI and EDVI were found to have improved significantly in the CoQ10 group compared to placebo.

Although the total number of subjects was of acceptable size (n=356), the manner in which the study was carried out casts shadows of doubt on the findings. First of all, the basic premise of the study is questionable, in that the authors combine the data from several studies without regard to the individual variations occurring in each (i.e. the assumption of homogeneity is unsubstantiated). Furthermore, there is no specific patient selection criteria, no standardization of experimental protocol, no attempt to standardize the data, and no common diagnostic criteria. The authors also introduce bias into their study by selectively choosing which primary studies to analyze. Given these flaws, the findings of this analysis need to be corroborated by additional primary studies before they are to be believed.

Up until recently, most of the clinical trials have supported the effectiveness of CoQ10 in treating CHF. The study by Khatta et al. (10). however, disputes this association. Measuring changes in ejection fraction, peak oxygen consumption, and exercise duration, the group found no difference between patients receiving CoQ10 and placebo. Since the study design included specific inclusion and exclusion criteria, objective and subjective baseline testing, consistent CoQ10 administration and a set measurement time frame, in addition to being randomized, double-blinded and placebo-controlled, these results are more believable than the studies described previously. However, the conclusions of the authors may be limited by the fact that the subjects were predominantly male and were non-uniformly taking concurrent additional medications.

Localization of Administered CoQ10 to the Heart

In many clinical trials of CoQ10, results from the experimental and placebo groups are compared to blood serum levels of the substance to determine if the observed effects are in fact due to CoQ10 administration. The assumption is that the elevated blood levels correspond to a proportional elevation in myocardial CoQ10 or antioxidant effect of CoQ10. While the latter may be true, Ibrahim et al. (11). have shown that when rats are fed 500mg of CoQ10/day, the only locations (besides serum) of significant elevated supplement are in the total and mitochondrial extracts of liver and spleen. Although there may be some variation in humans, these results suggest that any observed effects of orally administered CoQ10 on heart disease in the previous studies were unlikely to be due to elevated levels in myocytes.

This finding, however, does not rule out the possibility that elevation of CoQ10 in myocytes may help to alleviate problems associated with heart failure. Whitman et al. (12). used DMSO and liposomes as delivery vehicles for CoQ10 in a study of myocardial ischemia reperfusion injury in rats. Their findings indicate that elevated CoQ10 levels in heart tissue are associated with greater protection of endothelial dependent and independent vasodilation after ischemia reperfusion.

Discussion

In recent years, there has been a great deal of excitement over CoQ10 as a health supplement. It has been touted as having beneficial effects for a number of illness and disorders, advertised by some as a virtual panacea. In the case of heart disease, however, it appears that many of these claims as of yet lack substantial proof. Of the studies supporting the supplement, poor experimental design and small subject number limit the reliability of their conclusions. Conversely, recent trials showing conflicting evidence involve relatively well thought out designs with sound conclusions, although these too have their limitations. Given the state of research on CoQ10, it is advisable for additional randomized, double-blinded, placebo-controlled studies to be performed to provide more in-depth information on the subject.

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