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A REVIEW ON EFFECT OF COENZYME Q10 ON CARDIAC HEART FAILURE

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ABSTRACT

This article provides a comprehensive review of 30 years of research on the use of coenzyme Q10 in prevention and treatment of cardiovascular disease. This endogenous antioxidant has potential for use in prevention and treatment of cardiovascular disease, particularly hypertension, hyperlipidemia, coronary artery disease, and heart failure. It appears that levels of coenzyme Q10 are decreased during therapy with HMG-CoA reductase inhibitors, gemfibrozil, Adriamycin, and certain beta blockers. Further clinical trials are warranted, but because of its low toxicity it may be appropriate to recommend coenzyme Q10 to select patients as an adjunct to conventional treatment. Coenzyme Q10 (CoQ10) is an endogenous cofactor in the mitochondrial energy production. CoQ10 has been touted to improve heart failure, but its effect on systolic function is controversial. Several small, randomized controlled trials evaluating CoQ10 showed variable results and were largely underpowered. We conducted a meta-analysis of these trials to evaluate the impact of CoQ10 therapy on ejection fraction and cardiac output. Seventy-nine patients with stable chronic congestive heart failure were randomized into a double-blind, crossover placebo controlled study with 3-month treatment periods, where either 100 mg coenzyme Q_{10} (CoQ_{10}) or placebo was added to conventional therapy. Mean patient age was 61 ± 10 years, ejection fraction at rest was 22% ± 10%, and maximal exercise tolerance was 91 ± 30 W. The follow-up examinations included ejection fraction (primary objective), exercise test, and quality of life questions. Ejection fraction at rest, during a slight volume load, and during a submaximal supine exercise increased slightly compared with placebo: 24% ± 12% versus 23% ± 12% (NS), 25% ± 13% versus 23% ± 12% ($P < .05$), and 23% ± 11% versus 22% ± 11% (NS). Maximal exercise capacity increased from 94 ± 31 W during the placebo period to 100 ± 34 W during the CoQ_{10} period ($P < .05$). Total score for the quality of life assessment increased significantly from 107 ± 23 during the placebo period to 113 ± 22 during the CoQ_{10} period ($P < .05$). The results indicate that oral long-term treatment with 100 mg CoQ_{10} in patients with congestive heart failure only slightly improves maximal exercise capacity and the quality of life and that the clinical importance of this needs to be further evaluated.

Keywords: heart failure, coenzyme Q_{10}, clinical trial, statins.

INTRODUCTION

CARDIAC HEART FAILURE:

Chronic heart failure (CHF) is a major health problem whose incidence increases exponentially with age.[1] As a result of the aging population and of improved treatment of acute coronary syndromes, the prevalence of CHF has also dramatically increased in recent years.[1-3] Beyond being a cause of increased mortality, hospital readmissions, and medical visits, CHF is associated with disability,[4] reduced exercise tolerance,[5] and impaired health-related quality of life (HRQL).[6] It is a condition in which there is weakening of heart muscle function so that fluid or congestion backs up and causes swelling or edema in the liver, lungs, the lining of the intestine, and the lower legs and feet.[7]

Coenzyme Q10:

Scientific Names:

Ubiquinone, Ubidecarenone, Mitoquinone[1 -3]

Coenzyme Q10 (CoQ10), first isolated from beef heart mitochondria,[8] is an essential component of the mitochondrial respiratory chain, and also has antioxidant properties.[9]

The rationale for CoQ10 supplementation in CHF lies in at least two factors. One is the well-known role of CoQ10 in myocardial bioenergetics, and the second is its antioxidant property. CoQ10, an obligatory component of the mitochondrial electron transport chain, is essential for ATP generation. Its bioenergetic effect is believed to be of fundamental importance, particularly in cells with high metabolic demand such as cardiac myocytes. Previous reports have shown that CoQ10 concentration is decreased in myocardial tissue.[10] in CHF, and the greater its deficiency,the more severe is the cardiocirculatory impairment.[11] Plasma CoQ10 levels are also decreased in severe cardiocirculatory dysfunction[12] as well as in conditions of high oxidative stress, such as diabetes and liver disease.[13]

The objective of the present study was to determine whether, in patients with stable moderate CHF, oral CoQ10 supplementation given alone or in combination with ET may be more efficient in ameliorating endothelial dysfunction and functional impairment than standard therapy with or without ET. Moreover, we tested the hypothesis that, by raising plasma levels of CoQ10 after oral administration of doses three times higher than those used in the past, both LV contractility of dysfunctional myocardium and LV systolic function may be enhanced. CoQ10 has been investigated as an adjunctive agent in the treatment of both systolic and diastolic heart failure over the past 20 years. Research has demonstrated its effectiveness in increasing ejection fraction in patients with cardiomyopathy from 44% to 60% after six months[14] and decreasing incidence of serious complications of CHF such as hospital re-admission, cardiac asthma, and pulmonary edema.[15] Administering 100 mg of CoQ10 twice daily was found to help reduce exercise induced elevation of pulmonary artery pressure and pulmonary capillary wedge pressure in patients with serious heart failure.[16] Keogh *et al*. conducted a double-blind, placebo-controlled randomized clinical trial of CoQ10 in Class II-III SHF patients. Subjects taking CoQ10 had a significant improvement in exertional cardiac function.[17]

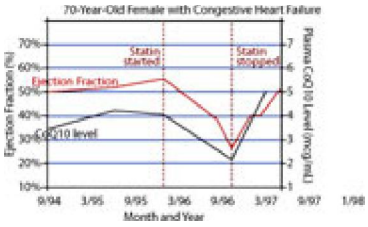


Figure 1. Statin Therapy, Plasma CoQ10, and Congestive Heart Failure

This demonstrates the simultaneous drop in plasma CoQ10 level and ejection fraction in a 70-year-old female patient started on statin therapy. Note that ejection fraction and CoQ10 level increased after statin therapy was discontinued

Coenzyme Q10 and Congestive Heart Failure

In the course of this six-year study, the 126 patients were followed very closely with measurement of blood CoQ10.

levels and heart function every three months.[18] We unexpectedly came across the detrimental effect of the cholesterol-lowering drugs known as HMG-CoA reductase inhibitors, or more simply as statins. The first statin drug, lovastatin (Mevacor®) came on the market in 1987, and five of our heart failure patients were started on this drug by their primary care physicians. All five of these stabilized patients had a significant decline in their blood CoQ10 levels and a decline in their heart function and clinical status. Their heart failure worsened to such a degree that two patients became critically ill and one went on to require a heart transplant. This clinical deterioration in our patients was particularly frightening at the time because we had no idea of the dramatic CoQ10-depleting effects of the newly released statin drugs. One patient in particular showed a simultaneous drop in plasma CoQ10 level and ejection fraction when started on statin therapy, with improvement after the statin was discontinued (see figure 1). My father first presented these data in Rome, Italy, in January of 1990.[19]Shortly after my father left the podium, a member of the audience shouted into one of the aisle microphones, "This is pharmaceutical terrorism!" To which my father calmly responded, "Yes, but who is the terrorist?" Later that year in May and in June of 1990, Merck went on to secure two patents that would combine CoQ10 with statin drugs in the same capsule to prevent muscle and liver damage.[20] The first of these patents was with co-inventor Michael Brown of Nobel Laureate fame for his work with low-density lipoprotein (LDL) receptors. Unfortunately, these patents have never been acted on and to this day, the vast majority of physicians and patients are completely unaware of statin-induced CoQ10 depletion.

The Trouble with Statins

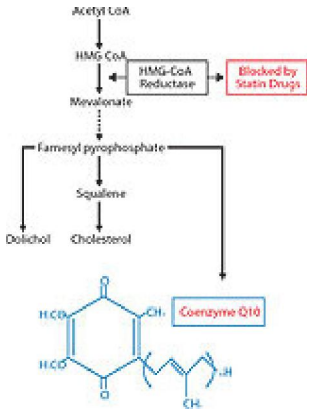
All statin drugs block the biosynthesis of both cholesterol and CoQ10, which explains statins' common side effects of fatigue, muscle pain and muscle weakness, and a worsening of heart failure (see figure 2)

When CoQ10 levels are lowered by statin drug therapy, one of the first changes to occur is a weakening of heart muscle function, known as diastolic dysfunction. This has nothing to do with diastolic blood pressure, but rather represents impairment in the relaxing or filling phase of the cardiac cycle. After heart muscle contracts, it takes a great deal of cellular energy, or ATP, to re-establish the calcium gradients such that muscle fibers may relax. Thus, if diastolic dysfunction is severe, it can result in congestive heart failure.

In 2004, a study published in the American Journal of Cardiology showed that diastolic dysfunction (heart muscle weakness) occurred in 70% of previously normal patients treated with 20 mg a day of Lipitor® for six months. This heart muscle dysfunction was reversible with supplemental CoQ10.7 Heart failure that develops after years of statin drug therapy can be termed statin cardiomyopathy and may well be playing a role in the epidemic of congestive heart failure in the United States.

It is important for the reader to be aware that for every adverse side effect caused by statin drug therapy, one can find a drug company-sponsored trial concluding that statins actually benefit the condition they may induce. Good examples are studies that suggest statins are useful in the treatment of cancer,[21] when in fact some studies suggest that they could be carcinogenic;[22,23] another study suggests that statin therapy may be helpful in dementia,[24] when other evidence indicates that statins impair mental function;[25,26] finally, studies that conclude statin therapy

Figure 2. Biosynthetic Pathway Leading to Cholesterol, Coenzyme Q10, and Dolichol



All statin drugs (HMG-CoA reductase inhibitors) block the biosynthesis of both cholesterol and CoQ10, which explains their common side effects of fatigue, muscle pain, and a worsening of heart failure.

improves heart failure,[27] when in fact it appears to weaken both skeletal muscle and heart muscle.[20,28]

In an effort to determine the prevalence of adverse effects from using statins, we studied 50 consecutive new patients, all of whom were taking a statin drug at the time of their initial visit.[29]

All 50 patients were found to have one or more side effects from statin therapy, so we discontinued their statin drugs and began supplemental CoQ10. Patients were followed for an average of 28 months with the following observations in the prevalence of adverse effects:

- A high prevalence of skeletal muscle pain and weakness at ***64%*** on initial visit was reduced to *6%* in follow-up.
- Fatigue decreased from *84%* to *16%***.**
- Shortness of breath went from *58%* down to *12%*.
- Memory loss was reduced from *8%* to *4%*.
- Peripheral neuropathy decreased from *10%* to *2%*.

There were no adverse effects from stopping statin drug therapy with no cases of heart attack or stroke during follow-up. Overall, there was an improvement in heart muscle function on discontinuation of statin therapy and addition of supplemental CoQ10. However, due to powerful propaganda surrounding both cholesterol and statin drug therapy, many patients and physicians are afraid to stop statin therapy.

ADJUNCTIVE THERAPY:

Lack of effect from treatment with coenzyme Q10 in congestive heart failure is not an objective title or conclusion for the study by Watson et al. [30] in which the main limitation obviously is their sample size and its lack of study patients. Even so, the investigators state in their introduction that previous studies with coenzyme Q10 "lack credibility because of small sample sizes, lack of controls, etc."

The majority of the 27 study patients, who were not classified according to the New York Heart Association (NYHA), were seemingly at late-stage disease (mean length of symptoms 3.4 years). Mean patient age was 55 years, which is compatible with predominantly ischemic origin. This was also recently confirmed at an International Conference in Sydney, Australia—"Oxidative Pathways in Health and Disease"—in a lecture by one of the co-authors, Nicholas Bett.[31] However, according to the Watson et al. 18 study, in the Patients' Demographics in Table 1, 77% of the patients were listed as having dilated cardiomyopathy. This is a patient clientele that is, at least partially, prone to respond either spontaneously or to medical intervention with subsequent improvement of myocardial function.

Conversely, it is well-known that changes—and not least improvements—in echocardiographic parameters of left ventricular (LV) function are minimal in late-stage disease, especially in heart failure due to ischemic heart disease. This is why the calculated number of patients necessary (n = 17) in this cross-over trial seems highly underestimated.

In a nearly threefold larger trial of 79 patients from Scandinavia, the same double-blind, cross-over design was used over two periods of three months on coenzyme Q10 100 mg/day or placebo. The beneficial results of this study were presented initially at The American College of Cardiology Meeting in 1992 (JACC 1992;19:216A, abstract 774–6) and later published in the *Journal of Cardiac Failure*.[32] Watson et al. [33] have not included this trial in their reference list.

In the Scandinavian Multicenter Study, a balanced randomization was used with respect to the diagnosis of ischemic versus nonischemic disease and the treatment with or without an angiotensin-converting enzyme inhibitor. There was a slight improvement on LV ejection fraction at volume load based on the results from the MUGA scans ($p = 0.025$). Maximal exercise capacity increased slightly but significantly ($p = 0.016$) and coenzyme Q10 mediated a significant decrease in the scoring for dyspnea ($p = 0.007$) and leg

fatigue ($p = 0.04$) at end-exercise (using the Borg-scale). According to the scoring from the Quality of Life Questionnaire, the total score ($p = 0.016$), the physical activity level ($p = 0.048$) and the life satisfaction ($p = 0.016$) increased significantly during the coenzyme Q10 period.

During the last 15 years, only 2 of 12 double-blind heart-failure trials have been "neutral" (i.e., without positive effect or side effects), whereas the remaining 10 studies have been positive and statistically significant with respect to improvement in clinical and or hemodynamic parameters.[34] In Watson and colleagues'"neutral study," adequate methods to assess myocardial function were used, but obviously the trial was insufficiently powerful to confirm or reject the hypothesized increase in LV function.

Mechanism of action

The possible therapeutic mechanisms of action of coenzyme Q10 in cardiovascular diseases are as follows: Improvement of cardiac bioenergetics Direct free radical scavenger and antioxidant effect Correction of coenzyme Q10 deficiency state Improved endothelial function and vasodilatory effect. Direct membrane-stabilizing activity due to phospholipid–protein Interactions Preservation of myocardial Na+K+ATPase activity Stabilization of integrity of Ca2+-dependent slow channels Correction of mitochondrial "leak" of electrons during oxidative respiration Induction of DT diaphorasePossible effects on prostaglandin metabolism Antiviscosity effect Altering the immune response (Greenberg & Frishman, 1990).[35]

1. Improvement of cardiac bioenergeticst

Cardiac contraction occurs after Ca2+ release from sarcoplasmic reticulum (SR) which activates the contractile proteins. During diastole, cytosolic Ca2+ re-sequesters into the SR. The cardiac contraction and the uptake of free cytoplasmic calcium into the sarcoplasmic reticulum is an energy-requiring mechanism (Kayo & Carsten, 2005).[36] Myocardial relaxation which is dependent on active Ca2+ uptake by the sarcoplasmic reticulum is not a passive process. Rather this latter step requires more energy. In cardiac

failure, changes in Ca2+ transport and metabolism have also been found (Marin-Garcia et al., 2001).[37]

2. Antioxidant action

Because of its ability to transfer electrons it acts as an antioxidant. The presence of CoQ10 in other membranes besides mitochondria, shows that its antioxidant effect may also be of physiological importance. In most membranes enzymes have been defined which can reduce the quinone and oxidize the quinol (Crane, 2001).[38]CoQ10 must be reduced to ubiquinol denoted QH2 to wield its maximum anti-oxidative function. In its reduced form (ubiquinol), the coenzyme Q10 molecule holds electrons loosely and will quite easily give up one or two electrons to neutralize free radicals. It is this form which displays its strongest antioxidant activity (Mellors & Tappel, 1966).[39]

3. Endothelial function

Endothelium-bound extracellular Superoxide Dismutase (ecSOD) activity is a major antioxidant enzyme system of the vessel wall which is reduced in patients with coronary artery disease. A recent study showed improvement in the endothelial relaxation with coenzyme Q10 administration. This might be related to its capability of enhancing endothelial function by counteracting nitric oxide oxidation. (Tiano et al., 2007; Belardinelli et al., 2008).[40]

4. Membrane stabilization and fluidity

The membrane-stabilizing property of CoQ10 has been postulated to involve the phospholipid–protein interaction that increases prostaglandin (especially prostacyclin) metabolism. It is thought that CoQ10 stabilizes myocardial calcium-dependent ion channels and prevents the depletion of metabolites essential for ATP synthesis. CoQ10 also decreases blood viscosity and improves blood flow to cardiac muscle in patients with ischemic heart disease (Kato & Yoneda, 1990).[41]

5. Reduction in proinflammatory cytokines

It is becoming increasingly apparent that inflammatory mediators play a crucial role in the development of congestive heart failure and acute myocardial infarction and several strategies to counterbalance the different aspects of inflammatory response are considered. The most important proinflammatory cytokines implicated in the progression of congestive heart failure are IL-6 and TNF-alpha. A doubleblind placebo-controlled randomized trial conducted on 31 patients of heart failure of mixed etiology for 12 weeks using 270 mg/day of ubiquinol along with oral carnitine showed marked reduction in IL-6 and TNF-alpha in the treated group as compared with the placebo. Thus CoQ10 also acts by altering the immune response (Kumar et al.,2007a,b).[42]

Role of Coenzyme Q10 in congestive heart failure (CHF)

Chronic heart failure represents a major public health burden and its prognosis is comparable to that of a malignant disease.

1. Deficiency in congestive heart failure

Heart failure is often characterized by an energy depletion status that has been associated with low endogenous CoQ10 levels. Its levels are depleted in both serum and myocardial tissue samples of patients with chronic heart failure (Folkers et al., 1970, 1985).[43] The possible usefulness of the CoQ10 in the treatment of CHF may be related to its ability to increase ATP synthesis with enhancement of myocardial contractility (Crane, 2001).[44] Recently it has been found to be an independent predictor of mortality in congestive heart failure (Molyneux et al., 2008a,b).[45]

2. Trials relating to congestive heart failure

Improvement in myocardial function with CoQ10 supplementation has been demonstrated in a variety of animal models. The first patients with heart failure were treated with coenzyme Q10 by Yamamura et al. (1967).[46]

3. Coenzyme Q10 in diastolic dysfunction

Diastolic dysfunction is one of the earliest identifiable signs of myocardial failure which accounts for 30–49% of heart failure cases. Patients with diastolic dysfunction have an

impairment of the filling phase of the cardiac cycle which causes a major limitation in their ability to increase cardiac output. It causes either decreased left ventricular end diastolic volume or a compensatory increased left ventricular end diastolic pressure and leads to pulmonary venous hypertension and the syndrome of 'diastolic heart failure.' In the process of relaxation a great deal of ATP is required to re-establish trans-membrane Ca2+ gradients which allow the uncoupling of actin/myocin and relaxation. Alterations in energy metabolism may lead to diastolic dysfunction and subsequently maladaptive cardiac remodelling.

4. HMG-CoA reductase inhibitors and Coenzyme Q10

Statins which are used to treat elevated blood cholesterol levels by blocking cholesterol biosynthesis also block CoQ10 biosynthesis (Folkers et al., 1990).[47] The resulting lowering of blood CoQ10 level is due to the partially shared biosynthetic mevalonate pathway of CoQ10 and cholesterol. Statins can reduce serum levels of coenzyme Q10 by up to 40% along with reduction in cholesterol/LDL levels by inhibiting HMG-CoA reductase. This depletes the CoQ10 in patients with heart failure using statins and produces significant harmful effects which can be negated by oral CoQ10 supplementation (Ghirlanda et al., 1993).[48]Recent studies have shown long term statin therapy to induce diastolic dysfunction in persons with initial normal cardiac function (Silver & Langsjoen., 2003).[49]

5. Role in dilated cardiomyopathy (DCM)

Dilated cardiomyopathy is a form of cardiac muscle disease characterized by ventricular dilatation, contractile dysfunction and eventual congestive heart failure. 143 cases of DCM, 98% of whom were in NYHA classes II and IV, were given 100 mg of coenzyme Q10 orally in addition to their conventional medical programme in an open-label long term study. Mean ejection fraction of 44% rose to 60% within 6 months and stabilized at that level with 84% of patients showing statistically significant improvement. Eighty-five percent of patients improved by one or two NYHA classes. Survival figures were also

encouraging (Langsjoen, 1990).[50]Other trials confirmed these findings, showing that CoQ10 administration significantly improved the cardiac function in dilated cardiomyopathy and resistant heart failure (Mortensen et al., 1985).[51]

TABLE 1: CONTROLLED CLINICAL TRIALS ON THE EFFICACY OF ORAL COENZYME Q10 IN HEART FAILURE [52]

Investigators	No. Of patients	Investigators Diagnosis	Results
Hashiba et al (1972)	197	CHF	Improved, NYHA class
Iwabuchi et al (1972)	38	CHF	Improved, NYHA class
Langsjoen et al (1985)	19	CHF	Increased EF
Vanfraechem et al (1986)	15	CHF	Increased EF, CO, SV
Judy et al (1986)	14	CHF	Increased EF, CO
Schneeberger et al (1986)	12	MVP,DD	Increased CO, SV
Oda (1990)	40	ICM	Improved DF
Rossi et al (1991)	20	ICM,IDCM	Increased ET
Poggesi et al (1991)	20	CHF	Increased EF
Judy et al (1991)	180	CHF	Increased survival
Rengo et al (1993)	60	CHF	Increased EF
Morisco et al (1993)	641	CHF	Fewer hospitalizations
Morisco et al (1994)	6	CHF	Increased EF, CO, SV
Hofman-Bang et al (1995)	79	CHF	Increased EF
Munkholm et al (1999)	22	CHF	Increased EF

Abbreviations: CHF – congestive heart failure, NYHA – NY Heart Association, EF – ejection fraction, CO – cardiac output, SV – stroke volume, MVP – mitral valve prolapse, DD – diastolic dysfunction, DF – diastolic function, ICM ischemic cardiomyopathy, IDCM – idiopathic dilated cardiomyopathy.

TABLE 2: CONTROLLED CLINICAL TRIALS ON THE LACK OF EFFICACY OF ORAL COENZYME Q10 IN HEART FAILURE

Investigators	No. of patients	Diagnosis	Results
Permanetter et al (1992)	25	IDCM	No improvement
Watson et al (1999)	30	CHF	No improvement
Khatta et al (2000)	55	CHF	No improvement

Dosage forms, recommended doses, duration:

Coenzyme Q10 capsules/tablets comes in different dosage formations: 25mg, 30 mg, 50 mg, 75 mg, and 100mg. Formulations containing soybean oil have superior bioavailability compared to other formulations.[53-55]

Recommended doses for common indications of coenzyme Q10 are:

• Congestive Heart Failure (CHF): 50 – 100 mg in two or three divided doses[53]

• Angina: 150 – 600 mg in two or three divided doses[53]

▪ HTN: 75-360mg/day in divided doses[57]

• Mitochondria Disorders: 400 – 600mg/day in divided doses[56]

▪ Coenzyme Q10 deficiency: 150mg/day[59]

▪ Migraines prophylaxis: 150mg/day[60]

▪ Gum disease: 25 mg two times a day[53]

• Parkinson Disease: 1200mg/day[58]

Safety of CoQ10

CoQ10 has an excellent safety record. It should be noted that CoQ10 is not a foreign substance but a naturally occurring nutrient that is synthesized in the body. Long-term safety of high dose CoQ10 supplementation has been very well documented in both

animals and humans (Langsjoen et al, 1990; Lampertico and Comis, 1993; Baggio et al, 1993, 1994; Sinatra, 1998; Williams et al, 1999).[52] The only side effects reported in a very small number of subjects are mild symptoms such as nausea and stomach upset. Daily dosage for up to eight years has not revealed any adverse effects and thus confirms the safety profile of CoQ10 in human subjects (Langsjoen et al, 1990a, 1990b, 1994; Overvad et al, 1999).[61]

Fuel for a healthy heart[62]

Deficient levels C0Q 10 have been most clearly established in the blood level of patients with congestive heart failure and cardiomyopathy. When the heart muscle is weakened, for whatever reason, it places an increased demand on the nutrients the heart cells need in order to create energy. Because of excessive utilization of these nutrients the heart muscle becomes depleted of CoQ10 which is the most important nutrient to create energy. Just correcting this deficiency makes a big difference. Even after a heart attack, CoQ10 can help repair heart tissue and help coach the heart into running properly again.

Falling short of CoQ10[62]

Our body peaks in CoQ10 production in twenties and it dwindles as we age. With age ourbody's natural ability to synthesize CoQ10 dwindles.

- Oral contraceptive pills too negatively impact the production of Co Q10.
- People suffering from asthma, cardiac diseases, type2 diabetes and Parkinson's have low levels of CoQ10 in their bodies. Clinical studies say CoQ10 improve glycemic control in people with type 2 diabetes
- Research studies say that cholesterol-lowering statin drugs also deplete CoQ10 by interfering with the body's ability to make the compound. This may be one reason for the muscle weakness sometimes associated with statins. In case you are on statins you may talk to your cardiologist about starting a CoQ10 supplement.

RECENT FINDINGS:[63-70]

Cardiovascular properties of coenzyme Q10 have been further addressed, namely regarding myocardial protection during cardiac surgery, end-stage heart failure, pediatric cardiomyopathy and in cardiopulmonary resuscitation. The vascular aspects of coenzyme Q10 addressing the important field of endothelial function are briefly examined. The controversial issue of the statin/coenzyme Q10 relationship has been investigated in preliminary studies in which the two substances were administered simultaneously. Work on different neurological diseases, involving mitochondrial dysfunction and oxidative stress, highlights some of the neuroprotective mechanisms of coenzyme Q10. A 4-year follow-up on 10 Friedreich's Ataxia patients treated with coenzyme Q10 and vitamin E showed a substantial improvement in cardiac and skeletal muscle bioenergetics and heart function. Mitochondrial dysfunction likely plays a role in the pathophysiology of migraine as well as age-related macular degeneration and a therapy including coenzyme Q10 produced significant improvement. Finally, the effect of coenzyme Q10 was evaluated in the treatment of asthenozoospermia.

CONCLUSIONS

There is sound scientific rationale for an important role for coenzyme Q10 in the maintenance of cardiovascular health in general and in the management of heart disease and in particular heart failure. Review of published literature in peer-reviewed journals on the use of coenzyme Q10 as an adjunct to conventional therapy in patients with congestive heart failure and cardiomyopathy shows that there is strong evidence in favor of significant clinical improvement with coenzyme Q10 supplementation. As a naturally-occurring nutrient that is produced in the body, coenzyme Q10 has an excellent safety record and no side effects. Therefore, coenzyme Q10 supplementation as supportive therapy for patients with or at risk for congestive heart failure or cardiomyopathy is justified and appropriate, since it can afford significant clinical benefit to the patients. Furthermore, by improving heart function and the quality of life in these patients, and by

reducing the number of hospitalizations, coenzyme Q10 supplementation also has the potential to reduce overall healthcare costs.

The weight of the evidence based upon an objective assessment of available scientific literature supports the following proposed health claims for coenzyme Q10:

- Coenzyme Q10 supplementation may help reduce the risk for congestive heart failure and cardiomyopathy.
- Coenzyme Q10 supplementation may help reduce the risk for heart failure.
- Coenzyme Q10 supplementation may help reduce the risk for certain types of heart diseases.
- Coenzyme Q10 supplementation may help reduce the risk for certain types of heart diseases such as congestive heart failure and cardiomyopathy.
- Coenzyme Q10 supplementation, as an adjunct to standard medical therapy, may help reduce the risk for certain types of heart diseases such as congestive heart failure and cardiomyopathy.

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