



From the Desk of Dr. Stephen Sinatra

Coenzyme Q₁₀ in Patients with End-Stage Heart Failure Awaiting Cardiac Transplantation: A Randomized, Placebo- Controlled Study

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Letters

Coenzyme Q10 in Patients with End-Stage Heart Failure Awaiting Cardiac Transplantation: A Randomized, Placebo-Controlled Study

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To the Editor:

In the May 2004 article by Marcus Berman *et al.*,¹ researchers discussed the appropriateness of oral coenzyme Q10 (CoQ10) administration for those awaiting heart transplantation. Participants taking 60 mg of a highly bioavailable form of CoQ10 per day appreciated significant improvements in clinical symptoms, functional status, and quality of life, despite a lack of an objective measurable change in cardiac status. Considering the tenuous nature of the waiting period, this finding has great potential for intervening in severe heart failure suffered by those qualifying for this surgical intervention.

Their documentation of severe low blood levels of CoQ10 (0.22 mg/l in the experimental group and 0.18 mg/l in the placebo group) is consistent with earlier findings correlating heart failure with CoQ10 deficiencies. Usual levels of this nutrient range from 0.5 mg/l to 1 mg/l in healthy individuals.

The relatively large size of the CoQ10 molecule can impede tissue absorption, and is a likely reason for disappointing findings in two previous studies^{2,3} that failed to show improvement in left ventricular systolic function and quality of life with only doubling of the blood levels of CoQ10. The CoQ10 molecule containing a quinone ring and 10 isoprenoid units is oftentimes poorly absorbed in oral form, so highly bioavailable preparations are required to raise blood and tissue levels in severely compromised patients.^{1,4}

The experimental group in the study by Berman *et al.* did show an approximately 3½- to 4-fold increase in CoQ10 blood levels over the severely depleted baselines. The improvement in exercise tolerance as measured by 6-min walk test, dyspnea, fatigue, and New York Heart Association classification after only three months is remarkable. The lack of change in echocardiographic evidence of contractility or atrial natriuretic factor and tumor necrosis factor levels was a discrepancy warranting further investigations, although the time-frame of three months may have been too short to impact these parameters.

What this study does support is more routine usage of CoQ10 for those with heart failure, even when it is advanced, as it is in transplant candidates. Coenzyme Q10 is a vital component of the mitochondrial respiratory chain supporting intramyocardial energy at the cellular level. Cardiologists who treat patients on a day-to-day basis must think of congestive heart failure as an “energy-starved heart.” Since endocardial biopsy samples taken from patients with chronic congestive heart failure have shown a decrease in adenosine triphosphate

concentration and impaired myocardial contraction, serious defects of metabolism in myocytes are present in congestive heart failure.⁵ It behooves us to consider CoQ10 as a first-line approach for a metabolic cardiology solution that in some way positively impacts cellular dynamics, even though it may take more research to fully appreciate the physiology behind the clinical improvements. For example, in a recent rodent model, we showed that improved energy and increased locomotor activity in mice taking oral CoQ10 may have been related to a possible central nervous system effect.⁶

I have been using CoQ10 in my own practice for a wide array of cardiac situations and have been pleasantly surprised to learn that two patients came off transplant lists as a result of this unique, non-toxic and simple nutrient. A whole new emerging field in “metabolic cardiology” will most likely be realized by those who choose to treat the “energy-starved” heart at the mitochondrial level.

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Authors' reply:

We appreciate the comments of Dr. Stephen T. Sinatra regarding our study of the use of coenzyme Q10 (CoQ10) in severe heart failure patients—candidates for cardiac transplantation.

Most of the agents currently in use for heart failure treatment have limitations and potential side effects. These agents are targeted towards the neurohumoral derangements occurring in the presence of the failing heart and do not correct the molecular dysfunction of myocardium. It is not unusual that the passion and enthusiasm with which new drugs are greeted are subsequently tempered with the appearance of reports on adverse effects.

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Energy starvation of the myocardium due to mitochondria dysfunction may play a dominant pathophysiologic role in heart failure. There are similarities between the failing heart and the aged heart: several mitochondria functions decline with age, and of all the organs, the heart is the most susceptible to premature aging. Coenzyme Q10 may counterattack the insult to the failing heart by virtue of its potential to serve as an electron carrier in the adenosine triphosphate chain reaction and its potent antioxidant action. In an elegant review of the current data on heart failure and CoQ10 treatment, Mortensen¹ noted biochemical evidence that myocardial deficiency or depletion of CoQ10 in failing hearts was higher with increasing severity of disease and was reduced by oral therapy. These findings correlate with the positive outcome of CoQ10 adjunctive therapy (dose 100–200 mg/day) for chronic heart failure documented in 10 (out of 13) double-blind studies. All confirmed the safety of CoQ10 and the general alleviation of symptoms and improved functional capacity and quality of life. The improved myocardial function supports the hypothesis that mitochondria dysfunction and energy starvation are prominent in heart failure and that exhausted bioenergetics—and decreased efficiency of the utilization of oxygen—are corrected by CoQ10 replenishment.

As mentioned in our report, we used a new Q10 technological delivery system (Ultrasome™, Herbamed Ltd., Rehovot, Israel). We believe the best way to assess bioavailability is by measuring blood levels of Q10.

The lack of a severe adverse reaction raises the question of whether in daily practice we should not first give a “loading dose” followed by a maintenance dose, considering that some groups administered up to 600 mg/day of CoQ10.

In our group of patients, despite the fact that few of them improved significantly, we had to adhere to the signed Helsinki informed consent, and we did not exclude them from the waiting list or from transplantation. Nevertheless, their quality of life undoubtedly changed for the better during the waiting period.

The results of the multinational trial “Q-symbio,”¹ which will be available in 2005, will shed further light on the clinical utility of CoQ10 in the routine treatment of heart failure.

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