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COENZYME Q10

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Coenzyme Q10

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Coenzyme Q10 (CoQ10) is a strong antioxidant and a key component of energy production in the electron transport chain. CoQ10 levels decrease with both age and cardiac disease in plasma and myocardium. After plasma CoQ10 concentrations decrease, dietary changes are generally unable to reestablish normal levels. CoQ10 supplementation is an inexpensive and safe therapy is able to reduce or prevent damage to cell membranes and vasculature by buffering reactive oxidative species. CoQ10 supplementation can decrease blood pressure in hypertensive patients as well as increase cardiac function and improve quality of life in cardiomyopathy and congestive heart failure patients. Additionally, CoQ10 supplementation is often able to reduce the dosage of expensive pharmaceutical interventions necessary to maintain the desired benefits. CoQ10 supplementation has no negative effects on cardiac medications but should be monitored closely while undergoing treatment with warfarin. Experimental research has shown that CoQ10 supplementation has no effect on warfarin treatment effectiveness but patients should be monitored closely if CoQ10 and warfarin are being taken simultaneously due to the severity of unwanted coagulation. Overall, Coenzyme Q10 is an inexpensive and safe dietary supplement that may be beneficial and cost effective as a cardiovascular therapy for older individuals with cardiac disease. CoQ10 is a strong antioxidant and it may be effective as a primary prevention for arteriosclerosis and heart disease.

Introduction

Coenzyme Q10, CoQ10, or ubiquinone, is an oil-soluble, vitamin-like substance present in most eukaryotic cells, primarily in the mitochondria. CoQ10 is a 1,4- benzoquinone, with a quinone chemical group, and 10 isoprenyl chemical subunits in its tail. It is a critical component of the electron transport chain (ETC) generating aerobic energy by converting ADP to ATP. Over 95 percent of human energy is produced aerobically and requires the ETC. The highest concentrations of CoQ10 are found in organs such as the heart, liver, and kidney with the highest energy requirements. Coenzyme Q10 is found in the highest concentrations in mitochondria due to its role in the ETC as well as in reacting with reactive oxygen species (ROS) (Crane, 2001; Langsjoen & Langsjoen, 1999). In the blood the normal concentration is around 2 micrograms/mL (Crane 2001; Mortensen et al., 2014).

Coenzyme Q10, CoQ10 or ubiquinone, is a relatively well known supplement today. It was discovered in 1940 by Moore et al. (Greenberg & Frishman, 1990). In 1957, Frederick Crane showed that CoQ10 was an important electron carrier in the electron transport chain (ETC)(Greenberg & Frishman, 1990; P. H. Langsjoen & Langsjoen, 1999). Folkers, Ho, and Yamamura found that Coenzyme Q10 levels were low in patients with heart disease in 1974 by taking cardiac muscle biopsies during open heart surgery (Folkers, Vadhanavikit, & Mortensen, 1985). Shortly after these discoveries, experimental trials began in which patients with essential hypertension were given Coenzyme Q10 to examine the effects CoQ10 supplementation had on blood pressure (Yamagami, Shibata, & Folkers, 1976). Coenzyme Q10 remains of great interest today in the areas of vitality, heart health, as an antioxidant, and in the various oxidation/reduction statuses that it exists in in the body.

I. Coenzyme Q10 Functions

Coenzyme Q10 serves many different roles throughout the body. A large portion of the research is focused on Coenzyme Q10's role in the Electron Transport Chain, its ability to be an effective antioxidant, and how it improves vascular function. The important quality of Coenzyme Q10 is its ability to be reduced and oxidized to various forms safely and easily. Coenzyme Q10 is responsible for accepting and donating electrons in all of its various roles it plays throughout the body.

Electron Transport Chain

Coenzyme Q10 is a key transporter in the ETC during the formation of adenosine triphosphate. ATP is regenerated from ADP when the ETC creates a proton gradient across the inner membrane of the mitochondria. This proton gradient is established by four complexes, located within the membrane, that use the energy of electrons donated by NADH and $FADH_2$ to pump the protons across the membrane into the intermembrane space. When the protons flow with the gradient across the membrane into the mitochondrial matrix, the energy is harnessed by specific channels to create ATP. Coenzyme Q10 is active in complex I and complex III (Crane, 2001).

CoQ10 in the oxidized form is called Ubiquinone. Ubiquinone can accept electrons and be reduced to ubiquinol. In complex I and III ubiquinone is partially reduced by NADH. When ubiquinone is oxidized, two protons are pumped into the intermembrane space of the mitochondria. This process in repeated twice in complex I and a total of four protons are pumped across the membrane. After the process in complex I is completed the electrons are accepted by another ubiquinone, which becomes reduced to ubiquinol. This ubiquinol travels through the membrane and delivers the electrons to complex III. In complex three the same mechanism as complex I is used to pump four protons across the membrane. At the end of this stage the CoQ10 will be in the ubiquinone form and will travel back to complex I to enter the cycle again (Crane, 2001) .

Antioxidant

Ubiquinol is the most commonly found form of Coenzyme Q10 (Crane, 2001). In the reduced form it is able to donate electrons, which makes it an antioxidant. Oxidative stress damages cell membranes and is known as lipid peroxidation. This oxidative stress is caused by Reactive Oxygen Species (ROS), formed during exercise or at very low levels during rest, stealing electrons from the lipid bilayers that make up the membranes of all cells. Ubiquinol is able to prevent the damage from occurring by donating electrons to the ROS (Hodgson & Watts, 2003; Rosenfeldt, Hilton, Pepe, & Krum, 2003; Schöpfer et al., 2000). Coenzyme Q10 has also been known to donate electrons to other antioxidants, such as Vitamin E, when necessary (Lass & Sohal, 2000). Large doses of Vitamin E are not recommended for supplementation as the results of a meta-analysis in 2005 that showed high doses of Vitamin E supplementation increased the rate of all-cause mortality (Miller et al., 2005). However Vitamin E is important in many functions in the body. An example is in the maintenance of nitric oxide to maintain vasodilation. Coenzyme Q10 is able to donate electrons and essentially recycle Vitamin E in the body to reduce the need to supplement with Vitamin E (Hodgson & Watts, 2003).

Vascular Function

Coenzyme Q10 is systematically important in vascular function via two pathways: 1) Vasodilation through the maintenance of nitric oxide and 2) prevention of an inflammatory response. Vasodilation and reduced inflammation are important as they may potentially lower total peripheral resistance, leading to decreased blood pressure in people with hypertension (Digiesi et al., 1994; Hodgson & Watts, 2003; Nakazono et al., 1991).

Oxygen is generally the final electron and proton acceptor in the ETC resulting in the formation of water (H_2O). Sometimes during exercise or in diseased states the electrons will be released out of complex I and III instead of complex IV. When the electrons are released out of complex I and III, the acceptor of the electrons is an oxygen molecule (O_2). However, without the protons to accompany the electrons superoxide (O_2^-) will be formed. Superoxide is a slightly reactive oxygen species that is known to react with nitric oxide to form peroxynitrate (ONOO-). Nitric oxide (NO) is a potent vasodilator that works throughout the body. When nitric oxide concentrations are lowered during the formation of peroxynitrate the vasodilation effect is reduced resulting in the constriction of blood vessels and potential for lipid peroxidation.

The formation of peroxynitrate starts a new sequence of events involving Q_{10}. Vitamin E (α-tocopherol) donates one Hydrogen molecule to superoxide changing it to hydroperoxyl (Lass & Sohal, 2000).

$$\alpha\text{-Toc-OH} + O_2^{\cdot-} \rightarrow \alpha\text{-Toc-O}^{\cdot} + HO_2^-$$

After the Vitamin E donates a Hydrogen molecule it becomes another radical species. This is where the reduced form of Coenzyme Q10, ubiquinol, is able to donate the necessary hydrogen molecule to vitamin E to recycle it (Sohal, Svensson, Sohal, & Brunk, 1989).

$$\alpha\text{-Toc-O}^{\cdot} + CoQH_2 \rightarrow \alpha\text{-Toc-OH} + CoQH^{\cdot}$$

Thus, in the presence of ubiquinol, the vitamin E is able to continue reacting with superoxide or preventing other reactive oxygen species from causing damage (Lass & Sohal, 2000).

Ubiquinol is also able to improve vascular function by preventing oxidative and nitrative damage from occurring once peroxynitrate($ONOO^-$) is already formed (Hodgson & Watts, 2003). Superoxide formation is increased after the oxidation of ubiquinol by peroxynitrate, which will react with vitamin E as mentioned above (Lass & Sohal, 2000). The ability of ubiquinol to be oxidized by peroxynitrate prevents damage to mitochondrial membranes and vasculature (Schöpfer et al., 2000). The increase in vascular function may provide a possible mechanism

for a decrease in blood pressure as well as the prevention of arteriosclerosis (Hodgson & Watts, 2003; Nakazono et al., 1991; Schöpfer et al., 2000; Tiano et al., 2007)

II. Coenzyme Q10 Supplementation

As explained previously, Coenzyme Q10 serves many functions throughout the body as an antioxidant, in energy production, and in improving vascular function. It is known that Coenzyme Q10 levels in the heart and systemically decrease with age and in many diseased states (Crane, 2001). Senescent rats have shown a decrease in coenzyme Q10 levels in the heart as well as a decrease in myocardial tolerance to exercise (Rowland, Nagley, Linnane, & Rosenfeldt, 1998). It has been shown that coenzyme Q10 levels are lower in patients with congestive heart failure (CHF) and decreased left ventricle function (P. H. Langsjoen & Langsjoen, 1999). Subjects with more severe CHF had lower levels of CoQ10 (Folkers et al., 1985; Molyneux et al., 2008). Along with a decrease in CoQ10 levels an increase in superoxide and peroxynitrate production is noted in patients with diabetes and hypertension (Hodgson & Watts, 2003). With supplementation, CoQ10 levels may increase in patients with cardiomyopathies (Folkers et al., 1985).

In light of the many studies that showed reduced concentrations of Coenzyme Q10 in the heart and blood from senescence and cardiac syndromes, CoQ10 has been extensively studied since the 1970's to evaluate possible therapeutic effects on hypertension, congestive heart failure, and vascular function (Yamagami et al., 1976).

Hypertension

Supplementation with coenzyme Q10 may have the ability to lower blood pressure in some subjects. Many studies have shown a decrease in blood pressure with supplementation of coenzyme Q10 in patients with hypertension (Table 1). The mechanism by which CoQ10 decreases blood pressure is not fully understood. Many of the earlier studies claimed that the decrease in blood pressure was due to increased ability to produce ATP that was previously inhibited by low CoQ10 levels in the patients with hypertension (H. Langsjoen, Langsjoen, Willis, & Folkers, 1994; P. Langsjoen, Willis, & Folkers, 1994; Yamagami et al., 1976). Another possible mechanism is that CoQ10 is able to decrease blood pressure through a decrease in total peripheral resistance through the maintenance of nitric oxide (Digiesi et al., 1994; Yamagami et al., 1986). Some of the studies did not offer a rationale for the decrease in blood pressure they observed (Burke, Neuenschwander, & Olson, 2001; Hodgson, Watts, Playford, Burke, & Croft, 2002). Table 1 shows the results of the studies reviewed in this paper listed in

chronological order. These studies were selected for this review because they are novel studies in the history of Coenzyme Q10 research. All of these studies showed an overall decrease in blood pressure in hypertensive patients with CoQ10 supplementation.

Researcher	Control	N	Dose (mg/day)	Time (Weeks)	Difference in Pre/post blood pressure (mmHg)	Statistical Significance
Yamagami et al. 1976	No	5		12-20	-16/-6.8	P<0.05
Yamagami et al. 1986	Yes	20	100	12	-15/-3	
Digiesi et al. 1994	No	26	100	10	-17.8/-12	P<0.001
Langsjoen et al. 1994	No	109	225	8-20	-12/-9	P<0.001
Singh et al. 1999		59	120	8	-14/-7	P<0.05
Burke et al. 2001	Yes	76	120	12	-17.8/ 0	P<0.01
Hodgson et al. 2002	Yes	80	200	12	-6.1/-2.9	P<0.05

Table 1. Experimental studies on the effect of supplementation with CoQ10 on blood pressure listed in chronological order.

Non-Placebo Controlled Trials

For this review I have chosen to report on three unique non-placebo trails. One of the first CoQ10 studies to involve humans was done by Yamagami et al. in 1976 (Yamagami et al., 1976). This study consisted of five subjects with decreased levels of CoQ10 and succinate dehydrogenase activity. Blood pressure and succinate dehydrogenase activity were measured. After 3-5 months of supplementation 4 out of 5 subjects showed a significant decrease in blood pressure. The succinate dehydrogenase activity increased in all of the subjects but only significantly in two of the subjects. The authors concluded that the increase in CoQ10 levels improved bioenergetics resulting in decreased blood pressures (Yamagami et al., 1976).

Digiesi et al. performed a non-placebo controlled trial in 1994. This study consisted of 26 hypertensive subjects. The subjects ceased their current hypertension treatments and began a 100 mg/day CoQ10 supplementation for 10 weeks. Blood pressure and plasma CoQ10 were evaluated in all 26 subjects. Total peripheral resistance was evaluated in five

patients. Mean systolic blood pressure decreased from 164.5 +/- 3.1 to 146.7 +/- 4.1 mmHg and mean diastolic blood pressure decreased from 98.1 +/- 1.7 to 86.1 +/- 1.3 mmHg ($P<0.001$). Plasma CoQ10 levels increased from 0.64 +/- 0.1 micrograms/ml to 1.61 +/- 0.3 micrograms/ml ($P<0.02$). Total peripheral resistance decreased from 2283 dyne·s/cm^5 to 1627 dyne·s/cm^5 ($P<0.002$). They concluded that the decrease in blood pressures were most likely due to the decrease in total peripheral resistance (Digiesi et al., 1994).

Langsjoen et al. also performed a non-placebo controlled trial in 1994. This study consisted of 109 subjects with diagnosed essential hypertension. Blood pressure, New York Heart Association (NYHA) functional class (Table 3), and number of hypertensive drugs used were evaluated. The average dosage of CoQ10 was 225 mg/day. The amount varied between subjects to achieve blood CoQ10 levels higher than 2.0 micrograms/ml. The subjects maintained their current regiment of hypertensive treatment. They were evaluated regularly in follow-up visits after beginning CoQ10 supplementation. Blood pressure medication was adjusted as necessary to maintain current values. Mean blood pressure before supplementation with CoQ10 was 159/94 mmHg. Post supplementation mean blood pressure was 147/85. The mean NYHA functional class increased from 2.40 to 1.36 ($P<0.001$). Fifty-one percent of patients were able to discontinue between 1-3 antihypertensive drugs. They concluded that the decrease in blood pressure was most likely due to improved diastolic function through the increased bioenergetics in myocardial tissue. Langsjoen et al. suggest that CoQ10 is a safe and more affordable technique of managing blood pressure and should be considered before administering pharmacological interventions(P. Langsjoen et al., 1994).

Randomized Controlled Trials

Yamagami et al. conducted a study in 1986 which consisted of 20 subjects who had hypertension and low CoQ10 levels. The subjects were instructed to continue their current medication regiment. The subjects in the experimental group were given 100 mg/day for a total of 12 weeks. The control group was given a placebo. Blood pressure, serum CoQ10 levels, and succinate dehydrogenase CoQ10 reductase's activity were monitored. The control group's blood pressure decreased from 168/96 mmHg to 164/93 mmHg. The experimental group's blood pressure decreased significantly ($P<0.01$) from 167/97 mmHg to 148/91 mmHg. This study recorded the changes in blood pressure every two weeks to demonstrate the effect of CoQ10 over time. Blood pressure did decrease during weeks 1-6 but did not decrease significantly until between 7 and 12 weeks (Table 2). This may be the only Q_{10} research evaluating change throughout the administration period. Serum CoQ10 levels increased from 0.704 microgram/ mL to 1.597 microgram/mL with supplementation of CoQ10 ($P<0.01$). The

placebo group saw no change in serum CoQ10 levels. The experimental group had a significant increase ($P<0.01$) of succinate dehydrogenase activity from 0.308 nmoles/mg/min to 0.942 nmoles/mg/min. Their conclusion is that supplementation with CoQ10 is able to increase CoQ10 levels, increase succinate dehydrogenase activity, and cause a decrease in blood pressure (Yamagami et al., 1986).

		SYSTOLIC mmHg	DIASTOLIC mmHg
COENZYME Q GROUP			
	Before	167 ± 2.6	97 ± 1.8
	After 2 w.	164 ± 3.7	94 ± 2.8
	4 w.	159 ± 6.3	95 ± 3.4
	6 w.	161 ± 3.7	96 ± 2.4
	8 w.	152 ± 6.2	89 ± 3.5
	10 w.	154 ± 5.4	90 ± 2.6
	12 w.	148 ± 4.4	91 ± 3.7
PLACEBO GROUP			
	Before	168 ± 4.8	96 ± 1.7
	After 2 w.	166 ± 6.4	95 ± 2.5
	4 w.	164 ± 4.6	94 ± 1.6
	6 w.	163 ± 4.3	95 ± 2.4
	8 w.	164 ± 4.4	94 ± 1.8
	10 w.	163 ± 5.3	91 ± 2.9
	12 w.	164 ± 5.7	93 ± 4.7

Table 2. Blood pressures recorded every two weeks. No change in the placebo group in systolic or diastolic. Decrease in CoQ10 group didn't happen until after 6 weeks of supplementation (Yamagami et al., 1986).

Burke et al. performed a randomized, double-blind, placebo-controlled study in 2001 with 76 subjects, all of whom had isolated systolic hypertension. There were two control groups within in this study. One control group consisted of 9 normotensive subjects who received 120 mg/day CoQ10 for 12 weeks. The second control group was made up of 39 isolated systolic hypertension subjects who received a placebo for 12 weeks. The experimental group had 32 subjects who received 120 mg/day CoQ10 for 12 weeks. Plasma CoQ10 levels and resting blood pressures were taken before and after 12 weeks. The experimental group had an average decrease in systolic blood pressure of 17.8 +/- 7.3 mmHg, whereas the control group saw almost no change in blood pressure. The study noted that within the experimental group there were responders and non-responders. They found that 55% saw a reduction of blood pressure greater than 4 mmHg while 45% did not. Within the responder group the average reduction in blood pressure was 25.9 +/- 6.4 mmHg. They found no statistical significance

between the experimental and control group (P=0.09). They felt that this was due to the non-responders. There was no change in the blood pressure in the subjects of the normotensive control group. The plasma CoQ10 levels increased in the experimental group from 0.47 mg/mL +/- 0.19 to 2.69+/- 0.54 mg/mL (P<0.01), whereas the placebo group saw no change. Even in the normotensive control group the plasma CoQ10 levels increased from 0.49 +/- 0.014 mg/mL to 2.50 +/- .61 (P<0.01). They concluded that CoQ10 is a safe, cheap, and well tolerated alternative or complementary treatment for hypertension (Burke et al., 2001).

In 2002, Hodgson et al. ran a random, double-blind, and placebo controlled study that consisted of 74 subjects who had type II diabetes and hypertension. This study also included supplementation with fenofibrate. Fenofibrate is a drug used to help control dyslipidemia. They found no effect on fenofibrate so their analysis focused on CoQ10. There were four groups in this experiment to control for both CoQ10 as well as fenofibrate. The control group (N=18) received a placebo for both CoQ10 and fenofibrate. One experimental group was administered 200 mg/day of both CoQ10 and fenofibrate (N=19). Another received 200 mg/day of CoQ10 and fenofibrate placebo (N=19). The last group was given a CoQ10 placebo and 200 mg/day of fenofibrate (N=18). All treatment periods lasted for 12 weeks. Pre/post 12 week treatment blood samples were collected to analyze cholesterol, triglycerides, plasma CoQ10, blood glucocse, serum insulin, and isoprostanes. They also measured blood pressures before and after treatment with CoQ10 and fenofibrate. Their main finding was that CoQ10 was able to significantly decrease blood pressures (P<0.05) and increase plasma CoQ10 (P<0.001). They reported blood pressure decrease of about 6 mmHg in systolic and 3 mmHg in diastolic blood pressure. This decrease was statistically significant, but was not as dramatic as previous studies have reported. The explanation for this is that the baseline systolic blood pressures were only slightly elevated around 130 mmHg. In studies that showed higher reductions in blood pressures the patients had a more exaggerated hypertension. The current authors also found a very large, significant increase in plasma CoQ10 levels from around 1.4 mmol/L to 4.8 mmol/L. Isoprotane is the only blood measurement mentioned in the discussion. The other blood measurements reacted to fenofibrate as predicted or were not significantly different, so they were not included in the discussion or conclusion. Isoprotane is a biomarker for lipid peroxidation. Oxidative stress is elevated in patients with type II diabetes (Bonnefont-Rousselot, Bastard, Jaudon, & Delattre, 2000), so one would expect isoprotane levels to be lower with CoQ10 supplementation. However, in this study they found no decrease in isoprotane levels. These results do not support the hypothesis that CoQ10 supplementation prevents oxidative stress. However, isoprotane is only one of many biomarkers for oxidative

stress. A different biomarker may have decreased that was not being measured. The conclusion for this study is that even though the results did not show a decrease in a lipid peroxidation biomarker, it was able to show a small but significant reduction in blood pressure in individuals with modest hypertension (Hodgson et al., 2002).

Both the placebo and non-placebo studies all showed a decrease in blood pressure with CoQ10 supplementation. The mechanism for blood pressure reduction with CoQ10 supplementation is not fully understood but the possible mechanisms are increased ability to produce energy in the myocardium, increased diastolic dysfunction, and decrease in total peripheral resistance through increased vascular function. All of these studies showed that supplementation with CoQ10 is safe and well tolerated. Some studies showed a responder/non-responder effect. This suggests that CoQ10 supplementation may not be effective for everyone but may potentially be beneficial for many individuals. These studies suggest that CoQ10 supplementation is a cheap alternative or additional treatment to hypertension. A long term study has shown that with supplementation of CoQ10 some individuals are able to decrease the amount of each or total number of cardiovascular drugs needed to achieve the same effects (H. Langsjoen et al., 1994). The potential to decrease the cost of treatment for hypertension may be very beneficial to many people.

Cardiomyopathy/Congestive Heart Failure

CoQ10 has been studied thoroughly since CoQ10 levels were discovered to be low in CHF and cardiomyopathy patients (Folkers et al., 1985). A longitudinal study by Molyneux et al. in 2008 expressed the importance of CoQ10 in 236 CHF patients. The study showed that morbidity was higher in CHF patients with low CoQ10 levels ($P=0.04$) and low total cholesterol ($P=0.08$). The authors concluded that lower CoQ10 levels in CHF patients increases the risk of morbidity (Molyneux et al., 2008). Experimental studies on CoQ10 supplementation in patients with cardiomyopathy and CHF have shown varied results, but overall the studies suggest that supplementation with CoQ10 with these conditions may be beneficial (Table 3). All of the experimental studies included in this review were placebo controlled and three of these included a crossover design.

Researcher	Crossover	N	Dose (mg/day)	Time (weeks)	Disease	Results
Langsjoen et al. 1985	Yes	19	100	12	CDMP	Increased EF (P<0.001) Increase Plasma CoQ10 (P<0.001)
Permanetter et al. 1989	Yes	25	100	16	DCDMP	No change in hemodynamic measurements No change in exercise tolerance
Morisco et al. 1994	Yes	6	150	4	CHF	No change in exercise tolerance Increase EF (P<0.05) Increase CO (P<0.05)
Hofman-Bang et al. 1995	No	69	100	12	CHF	Increase Plasma CoQ10 (P<0.01) Increase max exercise tolerance (P<0.05) Increase quality of life (P<0.05) No change in NYHA functional class
Munkholm et al. 1999	No	22	200	12	IH/CDMP	Increase Plasma CoQ10 (P<0.01) Increase Left Ventricular Function
Khatta et al. 2000	No	46	200	72	CHF	Increase Plasma CoQ10 (P<0.001) No change in max exercise tolerance No change in EF
Keogh et al. 2003	No	35	150	12	SHF	Increase Plasma CoQ10 (P=0.0001) Improvement in NYHA functional class (P=0.047) 6 MWT (P=0.047)
Mortensen et al. 2014	No	420	100-300	106	CHF	Improvement in NYHA functional class (P=0.028) Fewer Major Adverse Cardiovascular Events (P=0.028) Fewer Cardiovascular Deaths (P=0.039)

Table 3. Experimental studies on cardiomyopathy and heart failure arranged in chronological order.

Randomized, Double-Blinded, Placebo-Controlled, Non-Crossover Studies

Hofman-Bang et al. conducted a study in 1995 with 69 Coronary Heart Failure (CHF) subjects. The subjects supplemented with either 100 mg/day of CoQ10 or placebo for 3 months while maintaining their current medication regiment. The researchers evaluated ejection fraction, maximal exercise tolerance, quality of life, NYHA functional class, and plasma CoQ10 levels. Post intervention there was no significant change in NYHA functional class or submaximal exercise ejection fraction. However, there were significant increases in all of the other measurements. Maximum exercise tolerance increased from 94 watts to 100 watts ($P<0.05$). Quality of life, which was measured through a survey, showed a significant increase ($P<0.05$). Plasma CoQ10 levels increased from 1.07 microgram/mL to 2.30 microgram/mL ($P<0.001$) in the CoQ10 group but no change was seen in the placebo group. The authors concluded that more research should be done in this area as their results showed potential

benefits in quality of life and maximum exercise tolerance for CHF patients through supplementation with CoQ10 (Hofman-Bang, Rehnqvist, Swedberg, Wiklund, & Aström, 1995).

Munkholm et al. performed a study in 1999 with 22 subjects diagnosed with either ischemic heart disease or dilated cardiomyopathy. The subjects were given either 200 mg/day or placebo for 3 months. The subjects maintained their current medication regiment. The main measurements recorded in this study were left ventricular ejection fraction, cardiac output, pulmonary artery pressure, pulmonary artery wedge pressure, and plasma CoQ10 levels. Plasma CoQ10 levels increased from 1.09 microgram/mL to 3.25 microgram/mL in the CoQ10 group ($P<0.01$), but no change from baseline was observed in the placebo group. The authors reported no change in ejection fraction or cardiac output but used ejection fraction to calculate stroke index. The calculated stroke index, which is the ejection fraction indexed for body surface area, increased significantly at rest ($P<0.005$) and during exercise ($P<0.05$). The authors also reported a significant decrease in pulmonary artery pressure and pulmonary wedge pressure ($P<0.02$). Pulmonary hypertension is associated with CHF and is caused by smooth muscle dysfunction in the pulmonary arteries. Pulmonary hypertension causes a decrease in exercise capacity as well as worsens CHF. The increased pressure in the pulmonary artery causes hardening of the arteries and can lead to hypertrophy and ventricular dysfunction through increased preload of the left ventricle (Moraes, Colucci, & Givertz, 2000). Pulmonary hypertension is caused by a decreased availability of nitric oxide in the pulmonary arteries. Munkholm et al. did not discuss a mechanism of action for the decrease in pulmonary artery pressure, but the decrease may potentially be attributable to the nitric oxide protecting effects discussed previously. They concluded that the decrease in pulmonary arterial pressure and increase in stroke index suggest an increase in left ventricular function and that further studies should be done (Munkholm, Hansen, & Rasmussen, 1999).

Khatta et al. conducted a study in 2000 with 46 NYHA functional class III and IV CHF subjects. The subjects supplemented with either 200 mg/day of CoQ10 or placebo for 6 months while maintaining their current medication regiment. This study measured plasma CoQ10, ejection fraction, and maximum exercise tolerance. Plasma CoQ10 levels increased from 0.95 microgram/mL to 2.2 microgram/mL ($P<0.001$). They found no significant increase in ejection fraction or max exercise tolerance. In the discussion of this paper it strongly refutes the results of many studies done evaluating CoQ10 in CHF patients. They note that because the plasma CoQ10 concentration increased, but no effects were observed, that CoQ10 does not provide any benefits to CHF patients. This study did not discuss any possible reasons for why they saw none of the changes observed in other studies, aside from that their sample size was

relatively small. Munkholm et al. which was discussed, previously also did not see an increase in ejection fraction but did see a significant increase when normalized with body surface area which was not done in this study (1999). A meta-analysis in 2006 by Sander et al. showed that class I and II CHF patients show more benefits from CoQ10 than patients with class III and IV CHF. The other studies referenced in the discussion by Khatta et al.(2000) also had subjects in class II CHF, whereas their study had patients only in class III and IV. This may be a possible explanation for the lack of significant results in the Khatta study. The authors state,

> "In conclusion, our study shows no benefit to adding coenzyme Q10 to the standard treatment of heart failure. Chronic illnesses motivate patients to seek out alternative therapy, and it is not suprising that people have been willing to buy an expensive and unproven drug. However, patients should be made aware that coenzyme Q10 has been studied in randomized, blinded, and controlled studies and that these studies have found no detectable benefit (Khatta et al. 2000, p.639)."

In contrast, Langsjoen et al. (1994) showed in a long term, large study that patients were able to decrease the number and dosage of medications through supplementation with CoQ10(H. Langsjoen et al., 1994)(H. Langsjoen et al., 1994)(H. Langsjoen et al., 1994)(H. Langsjoen et al., 1994)(H. Langsjoen et al., 1994). It seems necessary when discussing the cost of treatment to mention the comparison of the cost of pharmaceuticals to CoQ10 as well as other research that evaluated the cost of various treatment.

Keogh et al. performed a study in 2003 consisting of 35 subjects with Class II and III systolic heart failure. These subjects received either 150 mg/day (50 mg TID) or placebo for 3 months. All subjects maintained their current medication regiment. This study evaluated NYHA functional class, 6 minute walk test distance, and plasma CoQ10 levels. There were no changes in any of these variables in the placebo group. NYHA functional class improved significantly in the CoQ10 group (P=0.012). Distance in the 6 minute walk test improved by 21 meters (P=0.047) and plasma CoQ10 levels increased from 0.7 microgram/mL to 2.1 microgram/mL (P=0.0001). They concluded that even though their sample population was small they did show benefits in exercise tolerance and functional class which may suggest that supplementation with CoQ10 may be beneficial for patients with CHF (Keogh et al., 2003).

The most recent and largest experimental study evaluating the efficacy of CoQ10 supplementation on CHF was conducted in 2014 by Mortensen et al. This study consisted of 420 subjects with class III and IV CHF. The subjects maintained their current medication regiment. The subjects supplemented with either 100-300 mg/day of CoQ10 or a placebo for over two years (106 weeks). The supplement amount was individualized to achieve 2

microgram/mL CoQ10 plasma levels. This study observed major adverse cardiac events, NYHA functional class, and deaths. Major adverse cardiac events decreased by 43% in the group that supplemented with CoQ10 compared to the placebo group (P=0.005). NYHA functional class improved significantly in the experimental group compared to the placebo group (P=0.028). There was a 43% decrease in cardiac deaths (P=0.039) and deaths from all cause (P=0.036) in the group that supplemented with CoQ10. This large scale and long duration study showed that supplementation with CoQ10, while continuing current medications can decrease the symptoms, risk of major adverse cardiac events, and risk of death in patients with CHF (Mortensen et al., 2014).

Randomized, Double-Blinded, Placebo-Controlled, Crossover Studies

The first study using the crossover design was performed by Langsjoen et al. in 1985. This study evaluated 19 subjects with class III and IV cardiomyopathy split into an experimental group receiving 100 mg/day of CoQ10 while the other group received a placebo. After 12 weeks the groups switched and received the other treatment. Outcome measures included plasma CoQ10 levels, stroke volume, and ejection fraction. Subjects showed a significant increase in CoQ10 levels when supplementing with CoQ10 (P<0.001). The group that received the placebo first saw no change in CoQ10 levels during the first 12 weeks, but after supplementing with CoQ10 for the second 12 weeks saw an increase. Likewise, the group that supplemented with CoQ10 in the first 12 weeks showed increased CoQ10 levels, but dropped back down to baseline during the second 12 weeks when receiving the placebo. Both stroke volume and ejection fraction increased significantly during the period of supplementation with CoQ10 (P<0.0001). When receiving the placebo they observed no changed in cardiac function. The authors concluded that improvement in cardiac function was most likely due to increased bioenergetics. The most interesting result is that cardiac function decreased upon cessation of supplementation with CoQ10 which shows that CoQ10 is a major component of the cardiomyopathy (P. H. Langsjoen, Vadhanavikit, & Folkers, 1985).

Permanetter et al. conducted a crossover study in 1989 with 25 subjects who had dilated cardiomyopathy. The experimental group received 100 mg/day (33.3 mg TID) for four months while the other group received a placebo. The groups were reversed after four months. This study measured cardiac function and found no significant increase in any of the measurements. A possible explanation for the lack of change in cardiac function could be that in patients with dilative cardiomyopathy the ability to pump blood is ineffective due to stretching of the left ventricle, ventricular hypertrophy, and possibly stiffening of the myocardium. CoQ10 may not

have as big of an effect on cardiomyopathy not associated with bioenergetics, vascular function, or blood pressure ((Permanetter et al., 1989).

The most recent crossover design study was in 1994 by Morisco et al. who evaluated short term effects of supplementation with CoQ10 in 6 subjects with CHF. The subjects discontinued their current medication for 3 weeks prior to beginning the study. When subjects were in the experimental phase they received 150 mg/day (50 mg TID) for 4 weeks. During the second four weeks they received a placebo. Ejection fraction, stroke volume, end diastolic volume, end systolic volume, stroke volume and maximum exercise capacity were evaluated in this study. The research team found no increase in max exercise capacity with CoQ10 supplementation or placebo. They did however see a significant increase in stroke volume ($P<0.05$), and cardiac output ($P<0.05$). The major drawback in this study was the small sample population. The authors noted that usually in CHF patients, the only way to increase cardiac output is to increase heart rate but with CoQ10 supplementation they observed an increase in stroke volume. They concluded is that CoQ10 can improve cardiac function in patients with CHF (Morisco et al., 1994).

Clinical Long-Term Studies

From 1985-1993 Langsjoen et al. conducted a long term study on the effects of supplementation with coenzyme Q10 in 424 patients with various cardiac diseases including ischemic cardiomyopathy, dilated cardiomyopathy, primary diastolic dysfunction, hypertension, mitral valve prolapse, and valvular heart disease. Throughout the study they measured NYHA functional class, number of cardiovascular drugs taken, left ventricular wall thickness, mitral valve ejection fraction, and blood CoQ10 levels. The CoQ10 dose administered to the subjects was varied to achieve a blood CoQ10 level of greater than 2 microgram/mL. Most subjects were enrolled in the study for a time of 1-12 months, but some subjects were evaluated up to 36 months. Overall, patients improved to a lower NYHA functional class with supplementation of CoQ10. Of 424 subjects, 5 subjects improved by three NYHA functional classes, 120 subjects improved two NYHA functional classes, 247 subjects improved 1 NYHA functional class, 51 subjects did not change NYHA functional classes, and 1 subject increased morbidity by one NYHA functional class. Left ventricular wall thickness decreased significantly ($P<0.03$) in all of the cardiac disease groups except for valvular heart disease. Mitral valve ejection fraction increased significantly in all groups ($P<0.02$) showing an increase in diastolic function. There was a significant decrease in the number and dose taken of cardiovascular drugs (Figure 1). Throughout the study they had 11 subjects drop out. Ten of the subjects were non-compliant and one subject quit due to nausea. The overall conclusion was that CoQ10 is a safe and

effective supplement that increases bioenergetics through the increased levels of CoQ10 that are deficient or in higher demand in many cardiac diseases. It was also noted that continued CoQ10 supplementation maintained the improved NYHA functional class and medication regiment (H. Langsjoen et al., 1994).

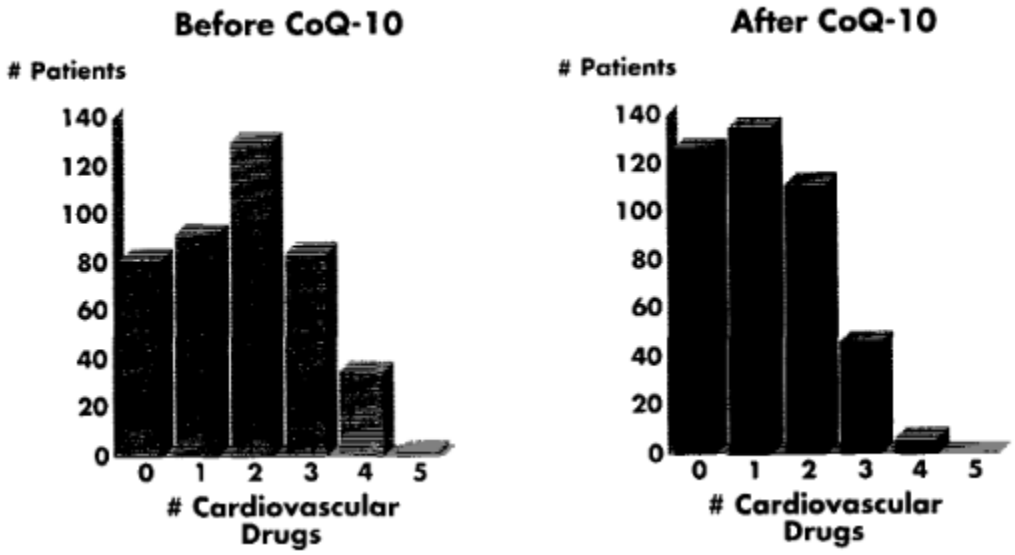

Figure 1. Number of cardiovascular drugs taken before and after supplementation with coenzyme Q10.

Class	Functional Capacity: How a patient with cardiac disease feels during physical activity
I	Patients with cardiac disease but resulting in no limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea or anginal pain.
II	Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea or anginal pain.
III	Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea or anginal pain.
IV	Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort increases.

Table 3. New York Heart Association Functional Classes. ("Classes of Heart Failure," 2014)

III. Supplementation Regiment

With senescence the ability of CoQ10 to move freely through membranes decreases due to degradation or changes in the membranes (Crane et al. 2013). In patients with

decreased levels of Coenzyme Q10, dietary intake is not generally enough to regain original levels of CoQ10 (Crane, 2001). Supplementation with CoQ10 will not increase CoQ10 tissue concentrations past the original levels. However, supplementation is able to increase CoQ10 in deficient subjects to original concentrations (Crane, 2001).

The recommended supplementation dosage for Coenzyme Q10 is 100-200 mg/day (100 mg twice daily) as this range has been shown to increase CoQ10 levels in the blood to 2 microgram/mL (Crane, 2001; Mortensen et al., 2014; Sander, Coleman, Patel, Kluger, & White, 2006).

Since coenzyme Q10 is a lipid soluble molecule, it is best ingested with a form of fat. In 1994, Langsjoen et al. found that capsules of Coenzyme Q10 were not able to achieve the desired blood CoQ10 levels of greater than 2 micrograms/mL but when chewed and consumed with peanut butter the levels were twice as high as the same dosage taken in the capsule form. More recent studies have evaluated various formulations with soluble forms of CoQ10, compressed tablets, or CoQ10 dissolved in oil in soft gel capsules, resulting in higher blood concentrations than when ingested as powder-capsules (Bhagavan & Chopra, 2007; Chopra, Goldman, Sinatra, & Bhagavan, 1998; Liu & Artmann, 2009). Also Coenzyme Q10 supplementation has been shown to be more effective at increasing CoQ10 levels in the ubiquinol form as opposed to the ubiquinone form (Bhagavan & Chopra, 2007; Chopra et al., 1998). In 1998, when Chopra et al. was studying the solubilized form of CoQ10 the hard powder-filled capsule was the main commercial product on the market. Today the standard on the market is soft solubilized gel tablets and chewable tablets.

There are over 100 different selections of CoQ10 supplements available at most pharmacies. Dietary supplements are not monitored by the Food and Drug Administration so when selecting a dietary supplement it is best to research the companies that produce them and choose a brand that has no negative incidence reports. CoQ10 is available in two forms ubiquinol and ubiquinone. Ubiquinol is more expensive per capsule; however the dosage is less with ubiquinol than with ubiquinone to achieve the same effects. Both forms increase CoQ10 levels, so the consumer can purchase whichever type they prefer.

IV. Drug Interactions

CoQ10 is safe with no side effects (H. Langsjoen et al., 1994). Most studies evaluating CoQ10 had subjects maintain their current medication regiment while supplementing with CoQ10 and showed no adverse reactions. While CoQ10 supplementation appears safe, individuals should be vigilant for any negative side effects which might occur as they start

CoQ10 supplementation as there are many possible drug interactions which have not yet been evaluated. Individuals with cardiac conditions may be on many different medications including statins, beta-blockers, ACE inhibitors, and anti-coagulants. Research has been done to understand possible effects of CoQ10 on the various classes of cardiac drugs.

Statins

Statins are common pharmaceutical drugs which reduce cholesterol in patients with hypercholesterolemia by inhibiting 3-hydroxy-3-methyl-glutaryl-CoA reductase (HMG-CoA reductase), an important enzyme in the production of both cholesterol and CoQ10 (Banach et al., 2015; Folkers et al., 1990). (Andalib, Shayanfar, Khorrami, Maleki-Dijazi, & Garjani, 2014; Young et al., 2007). Statins decrease CoQ10 levels significantly in patients with diseases that may already have reduced CoQ10 (Andalib et al., 2014; Folkers et al., 1990; Ghirlanda et al., 1993). While statins are very effective in lowering cholesterol, side effects include muscle pain and increased oxidative stress associated with decreased CoQ10 levels. Supplementation with CoQ10 is able to increase CoQ10 levels in patients taking statins to above baseline CoQ10 levels. This increase has been hypothesized as a method to potentially decrease statin-induced myalgia (Fedacko et al., 2013; Taylor, Lorson, White, & Thompson, 2015).

To date studies have shown mixed results in the ability of CoQ10 supplementation to reduce statin-associated myalgia. This may be attributable to small sample sizes or responder/nonresponder effect. All of these studies lasted longer than 8 weeks and used a CoQ10 supplementation dose that is known to significantly increase CoQ10 levels. Three experimental controlled studies showed that supplementation with CoQ10 was unable to decrease statin-associated myalgia significantly (Bookstaver, Burkhalter, & Hatzigeorgiou, 2012; Taylor et al., 2015; Young et al., 2007). Even with increased CoQ10 levels they found no decrease in muscle pain. However, other studies have shown a decrease in overall muscle pain and pain interference of daily living in subjects taking both statins and CoQ10 (Caso, Kelly, McNurlan, & Lawson, 2007; Fedacko et al., 2013; Skarlovnik, Janić, Lunder, Turk, & Šabovič, 2014).

Statin use increases malondialdehyde (MDA), which is a biomarker for lipid peroxidation, in the myocardium (Andalib et al., 2014; Nielsen, Mikkelsen, Nielsen, Andersen, & Grandjean, 1997). CoQ10 supplementation may help reverse this negative statin side effect. CoQ10 supplementation decreases MDA in the myocardium by increasing the activity of superoxide dismutase as well as increasing vitamin E availability, thus preventing the formation of reactive oxidative species (Andalib et al., 2014; Lass & Sohal, 2000; Lee, Tseng, Yen, & Lin, 2013).

In summary, CoQ10 supplementation while taking statins has shown a potential to decrease statin-associated muscle pain as well as prevent lipid peroxidation in the myocardium. Though the results are not consistent, some evidence suggests that CoQ10 supplementation while taking statins may be beneficial.

Beta Blockers

Beta blockers are a common cardiovascular drug that is used to treat congestive heart failure and high blood pressure. Beta blockers inhibit norepinephrine from binding to beta receptors that control heart rate, contractility, and constriction of blood vessels (Frishman, Cheng-Lai, & Nawarskas, 2005). These drugs have many frequent side effects such as dizziness, fatigue, dyspnea, upper respiratory tract infection, worsening heart failure, chest pain, hyperglycemia, diarrhea, cough, nausea, hypotension, bradycardia, and vomiting (Packer et al., 1996).

There is minimal research on the interaction between coenzyme Q10 and beta blockers. The only research found for this paper reported the effects of CoQ10 supplementation on the cardiovascular side effects of timolol maleate, which is used to decrease intraocular pressure in patients with glaucoma. Takahashi et al. performed a study in 1989 that showed CoQ10 supplementation 6 weeks before treatments with timolol maleate was able to decrease the adverse cardiac reactions from timolol maleate without reducing the intended effect of decreasing intraocular pressure. Timolol maleate causes bradycardia and a decrease in stroke index leading to a significant compensatory rise in total peripheral resistance. CoQ10 prevented the decrease in stroke index allowing cardiac output maintenance without the need for a compensatory increase in total peripheral resistance. Increased ATP availability and increased catecholamines both increase contractility, however the mechanism by which CoQ10 maintains contractility is not fully understood. Researchers suggest that CoQ10 supplementation may inhibit catecholamine release, thus the increased contractility with CoQ10 supplementation is not likely catecholamine related (Ursini & al., 1991). Also, it is unlikely that CoQ10 inhibits the beta blockers ability to block binding of catecholamines to Beta receptors as a concurrent result would be increased intraocular pressure (Takahashi et al., 1989). Therefore, the increase in contractility is most likely due to the increased availability of ATP via increased bioenergetics with increased CoQ10 levels.

To date, there is no literature discussing whether an increase in contractility, secondary to increased bioenergetics as opposed to increased catecholamine stimulation, is harmful to patients with CHF. It is plausible there may be a difference between the two mechanisms. Catecholamines stimulate the heart to beat harder and faster whether the myocardium can

tolerate it or not. Increased mitochondrial efficiencies with CoQ10 supplementation may increase ATP production with available oxygen, resulting in improved contractility. This could improve cardiac output and further improve both myocardial and systemic blood flow. Potentially the increase in contractility due to increased bioenergetics may be beneficial compared to direct stimulation from catecholamines.

Overall, the research suggests there may be some benefits with CoQ10 supplementation for patients using timolol maleate for glaucoma. Due to a lack of research of CoQ10 supplementation effect on beta blockers, patients should be monitored closely when taking beta blockers and CoQ10 simultaneously.

Warfarin

Warfarin is an anticoagulant that prevents blood clotting through the inhibition of the vitamin K reducing enzyme, vitamin K epoxide reductase. Vitamin K is a reducing agent that donates electrons to proteins in the cascade that leads to coagulation. Vitamin K becomes oxidized and warfarin prevents the reduction of Vitamin K back to its original state, thus inhibiting clotting after the initial oxidation of vitamin K (Ansell et al., 2008). The interaction between CoQ10 and warfarin is not fully understood and researchers have reported opposite results. CoQ10 is a vitamin like supplement thus it may inhibit the anticoagulation effect of warfarin, increasing the chance of clot formation. However, CoQ10 supplementation is also associated with increased self-report of bleeding in subjects being administered warfarin (Mousa, 2010).

Shalansky et al found that CoQ10 supplementation was associated with an increase in self report of bleeding in 2007, but the mechanism for increased bleeding was not discussed (Shalansky, Lynd, Richardson, Ingaszewski, & Kerr, 2007). A case study in 1998 reported that a woman became less sensitive to warfarin dosages when taking CoQ10 and a higher warfarin dosage was required to achieve the same results. When CoQ10 supplementation was ceased her responsiveness to warfarin returned (Landbo & Almdal, 1998). The mechanism was not discussed.

Other studies have shown that CoQ10 supplementation increases clearance of warfarin, leading to a decrease in warfarin blood concentration. While increased clearance should lead to decreased warfarin effectiveness, it may not. Warfarin is administered in two enantiomers, an S-enatiomer and an R-enantiomer. CoQ10 supplementation increases the clearance of both enantiomers, however the clearance rate is higher in the R-enantiomer, which is less potent than the S-enantiomer. Thus even though warfarin clearance is increased and CoQ10 is a vitamin K like substance, in contrast to the previous case study by landbo and research by

Shalansky et al., no inhibition of anticoagulation was observed with CoQ10 supplementation (Engelsen, Nielsen, & Hansen, 2003; Q. Zhou & Chan, 1998; S. Zhou & Chan, 2001).

In summary, CoQ10 supplementation may decrease the anticoagulation effect of warfarin in some patients through increased clearance or because of its similarities to vitamin K. However, research shows mixed results with more studies reporting no effect of CoQ10 supplementation on anticoagulation. Therefore, CoQ10 supplementation may be maintained while taking warfarin if responsiveness to warfarin is not inhibited. Patients should be monitored closely by their physicians because the formation of an embolism may be life threatening. Warfarin administration is normally monitored regularly and any effects caused by CoQ10 supplementation should be identified quickly. Upon beginning warfarin treatment the potential side effects of CoQ10 supplementation should be addressed by the physician and patients should be instructed to notify their physician they have begun CoQ10 supplementation.

Anthracycline Agents

Anthracycline agents are common potent chemotherapy drugs that treat cancer by preventing the replication and growth of cancerous cells (Conklin, 2005). An unwanted effect of anthracycline agents is cardiotoxicity as well as nephrotoxicity which can lead to CHF, cardiomyopathy, and renal failure (El-Sheikh, Morsy, Mahmoud, Rifaai, & Abdelrahman, 2012; Greenlee, Shaw, Lau, Naini, & Maurer, 2012; Minotti, Menna, Salvatorelli, Cairo, & Gianni, 2004). Acute effects of anthracycline-induced cardiotoxicity are cardiac conduction dysrhythmias as well as decreased cardiac function (Conklin, 2005; Judy, Hall, Dugan, Toth, & Folkers, 1984; Okuma & Ota, 1986). Cardiac output can decrease 25-40% after only two treatments with anthracyline agents (Folkers, Baker, Richardson, & al., 1980). Chronic effects of anthracycline agents are irreversible damage to mitochondria and CHF that do not respond to pharmaceutical treatments. Damage to the myocardium is caused by up to a 10 fold increase in reactive oxidative species and an inhibition of myocardial mitochondrial maintenance (Conklin, 2005; Greenlee et al., 2012; Solaini, Landi, Pasquali, & Rossi, 1987).

The cardiotoxicity from anthracycline agents is more severe in patients with low CoQ10 levels (Solaini et al., 1987). CoQ10 supplementation prior to administration of anthracycline agents may help prevent both cardiac dysfucion and damage to the myocardium and kidneys. This protective aspect of CoQ10 allows for higher doses of anthracycline agents to be tolerated without adverse effects (Judy et al., 1984). CoQ10 supplementation 3-7 days prior to anthracycline administration is able to reduce or prevent a number of problems including: lipid peroxidation, decrease in ejection fraction, decrease in stroke index, and cardiac conduction dysrhythmias (El-Sheikh et al., 2012; Folkers et al., 1980; Judy et al., 1984; Okuma & Ota,

1986). The reduction of reactive oxidative species by CoQ10 is the proposed mechanism for the decrease in adverse effects from anthracycline agents.

Overall, CoQ10 supplementation may be cardioprotective for patients being treated with anthracycline agents used in chemotherapy for cancer. CoQ10 supplementation prior to anthracycline administration is able to reduce or prevent severe damage to the myocardium and helps better preserve cardiac function. Most importantly CoQ10 supplementation does not interfere with the cancer fighting component of these drugs. CoQ10 supplementation may be safely recommended for patients prior to and during chemotherapy with anthracycline agents.

Conclusion

Coenzyme Q10 is important in many biological pathways throughout the body, especially in the myocardium. Research supports the many of the heart healthy/antioxidant claims for CoQ10. CoQ10 is safe, cheap, and effective with relatively no side effects. Although some research has not shown a positive effect with CoQ10 supplementation, most data shows a potential to decrease reactive oxidative species, blood pressure, and lipid peroxidation as well as increase cardiac function and NYHA functional class which supports that CoQ10 is a vital component in biological functions. Age, exercise, and disease increase reactive oxidative species which overtime will lead to membrane and vascular damage. As CoQ10 levels naturally decrease with age and disease, supplementation with CoQ10 may be beneficial for older individuals, older individuals who exercise, tobacco users, and patients with cardiac disease or undergoing chemotherapy. CoQ10 is generally shown to be a positive additive treatment to patients with diseases such as hypertension, CHF, and cardiomyopathy. Additionally, CoQ10 may also be effective in preventing the onset of cardiovascular diseases. Many studies had subjects maintain their current medication regiments and reported no negative side effects with CoQ10 supplementation. This would suggest that supplementing with CoQ10 can only benefit individuals or at worst have no negative effects. The cardiovascular system is one of the essential systems in the body and providing supplemental maintenance and protection seems logical. In conclusion, CoQ10 supplementation may be beneficial for older individuals who suffer from cardiac disease or are undergoing chemotherapy.

Since CoQ10 is a strong antioxidant, future research should evaluate the effects of CoQ10 supplementation in subjects without cardiac disease who are at risk for low CoQ10 levels and increased production of reactive oxidative species. Specifically, older individuals who use tobacco, consume alcohol, or exercise regularly.

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