Coenzyme Q10 and chronic fatigue syndrome

Ubiquinol-10 supplementation improves autonomic nervous function and cognitive function in chronic fatigue syndrome.

Introduction

Think back to a period in your life when you were utterly exhausted. Not just "tired," but walking around like a zombie, wanting to lay down on the couch and instantly fall asleep at any time of the day. Now imagine feeling like this for six months straight, or even longer. This is what people dealing with chronic fatigue syndrome (CFS) experience. CFS is known by many names, including systemic exertion intolerance disease (SEID), myalgic encephalomyelitis, and chronic fatigue and immune dysfunction syndrome (CFIDS), none of which should be confused with the mythical diagnosis of adrenal fatigue. CFS is thought to afflict 0.26 to 0.78% of the U.S. population, roughly 800,000 to 2.5 million people. The causes of this syndrome have been hotly debated.

One proposed hypothesis suggests that CFS is influenced by how well the hypothalamic–pituitary–adrenal axis (HPA) is functioning. All three of these organs, the hypothalamus (a region of your brain), the pituitary gland (attached to the base of the hypothalamus) and the adrenal glands (which sit on top of your kidneys) play a role in regulating the stress response. Ramp this system up too high and you will feel anxious all the time. Turn it down too low and you feel constantly lethargic and become susceptible to illness. Another hypothesis suggests that some sort of immune abnormality is causing a pro-oxidative inflammatory response. This could interfere with CoQ10 production, which the body uses to help produce energy. These are just two of many theories. No one knows for certain what the causes of CFS are.

To date, reviews of treatment options have suggested that cognitive behavioral therapy and graded exercise treatment can reduce fatigue. Neither of these treatments are curative, but are centered around symptom management and improvement. Since the exact mechanisms of CFS are, as of yet, unknown, researchers are testing various hypotheses about the root causes of the disease. One such line of research has investigated the use of supplemental coenzyme Q10 (CoQ10).

CoQ10 is an antioxidant that can influence the production of ATP, the body's energy currency. Our bodies are able to synthesize most of the CoQ10 we need, but we also get some from food, such as beef, broccoli, and eggs. The CoQ10 content of selected other foods is shown in Figure 1. Researchers conducting previous studies have observed markedly lower levels of CoQ10

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in people with CFS, so it stands to reason that these low CoQ10 levels may be preventing the body from producing adequate amounts of ATP, and thus causing fatigue. One other study noted an improvement in CFS fatigue symptoms when CoQ10 was added to the diet, but may have been confounded by addition of supplemental NADH as well. The study under review extends this line of research by examining the effects of ubiquinol-10, a lipid-soluble form of CoQ10, on clinical outcomes in patients with CFS.

Chronic fatigue syndrome is a condition of excessive fatigue lasting longer than six months. While the precise causes of CFS are unknown, one line of research has observed low levels of CoQ10 in patients with CFS. One study has shown symptom improvement with supplemental CoQ10, and the present study is furthering this research by examining the effects of ubiquinol-10, a form of CoQ10, in patients with CFS.

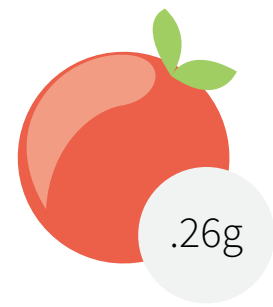
Who and what was studied?

Two separate studies were reported in this paper. Both only included patients who had been diagnosed with CFS. In each study, pre- and post-evaluations were comprised of a "questionnaire to assess fatigue and depression symptoms; blood samples to measure CoQ10 concentrations, oxidation activity, and antioxidant activity; an arithmetic task, a sleep-wake cycle study, and an autonomic nervous function test". Autonomic nervous function was estimated in this study by recording the participant's heart rate variability, which assesses the differences between heart beats.

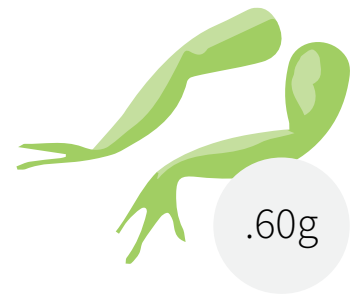
Study 1 was an open-label study made up of 20 participants, both male and female. In open-label trials, there is no blinding and both the researchers and participants know which intervention is being delivered. There was no control group, so all participants took 150 milligrams of ubiquinol (3 capsules of 50 mg ubiquinol each) with a meal once a day for 8 weeks. Supplementation timing was left up to each patient, they just had to consume all three pills each day. Participants were told to abstain from taking any CoQ10 supplements 14 days prior to the beginning of the trial.

Study 2 was a randomized, double-blinded, placebo-controlled trial. Forty-three male and female patients were enrolled and randomized to either take 150 milligrams of ubiquinol or placebo daily with a meal for 12 weeks. All who had been previously supplementing with CoQ10 were allowed to participate only after a four-week washout.

Figure 1: CoQ10 content in food (per 120g serving)



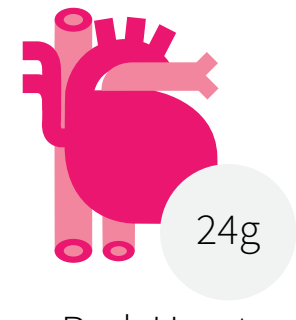
Orange



Frog leg

Trout

Chicken Leg



Pork Heart

Adapted from: Crane FL. J Am Coll Nutr. 2001 Dec.

There were participants in both groups who were taking vitamin C and/or psychoactive medications. While participants taking either of these were not evenly distributed between the placebo and intervention groups, baseline ubiquinol concentrations of those taking either in the intervention group were assessed and no significant differences were seen when compared with those taking either in the control group.

Ubiquinol is the most common form of CoQ10 found circulating in your body at any given time. About 95% of serum CoQ10 is ubiquinol. When taking an oral CoQ10 supplement, your body will convert it from the oxidative form, ubiquinone, to the reduced form, ubiquinol-10, a potent antioxidant. Supplementing with this reduced form may be more effective at increasing total CoQ10 levels as the body would not need to convert it before putting it to use.

Two trials were reported in this paper. Study 1 was a non-blinded trial with no control group where all participants took 150 milligrams of ubiquinol daily for 8 weeks. Study 2 was a randomized, double-blinded, placebo-controlled trial where patients took either 150 milligrams of ubiquinol or placebo daily for 12 weeks. Pre- and post-evaluations focused on changes in fatigue level, depression symptoms, CoQ10 concentrations, mental acuity, sleep cycles, and autonomic nervous function.

What were the findings?

Study 1 - Open-label study

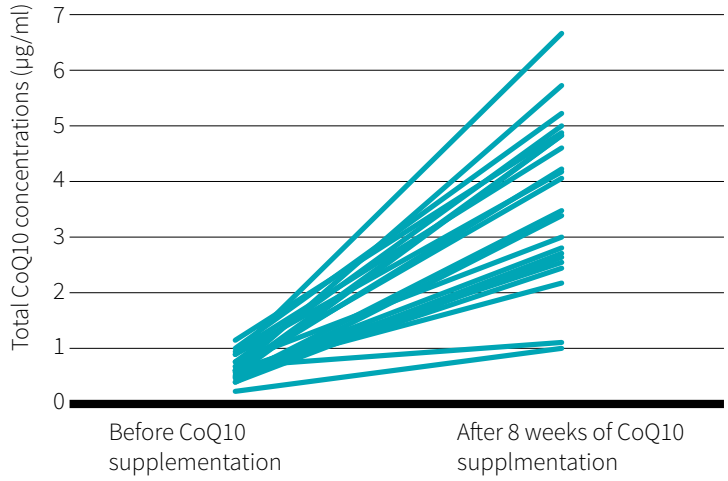
Some of the main results from the first study are shown in Figure 2. About 95% of participants had lower than average ubiquinol levels. Supplementing with ubiquinol produced increases in total CoQ10 concentrations in all participants, although two participants only experienced marginal increases. The researchers observed that higher increases in total CoQ10 levels were associated with improvements in depressive symptoms and improved performance on the arithmetic task. However, neither of these were reported to have reached statistical significance. The more directly relevant outcomes, pre- and post-fatigue scores and oxidative stress levels in the body, also did not differ significantly.

Study 2 – Randomized controlled trial

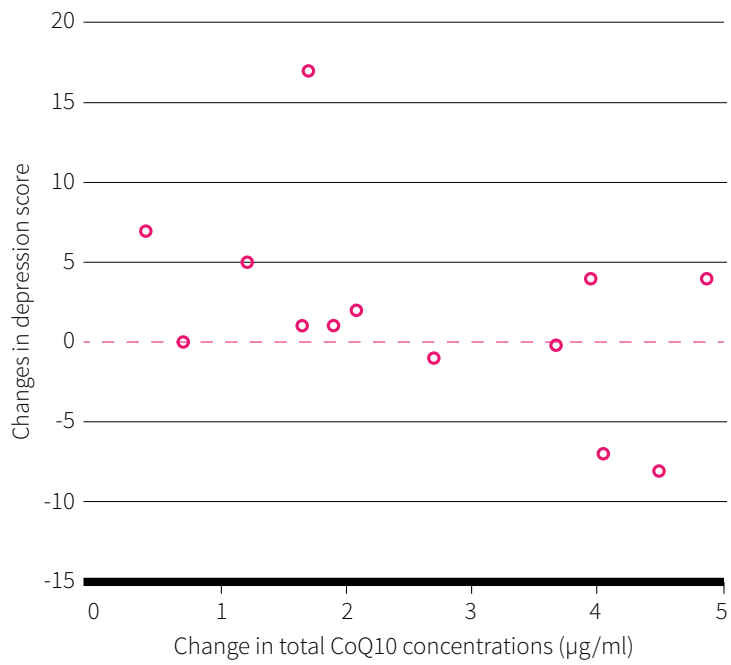
Of the 43 participants originally randomized in the trial, only 31 completed the study (27.9% dropout rate). The high dropout rate was due to a number of reasons. Some participants withdrew their consent to be in the

Figure 2: Study 1 results

Effects of 8-week ubiquinol supplementation on CoQ10 concentrations



Correlation between changes in CoQ10 concentrations and depressive symptoms



study, while others failed to adhere to the supplementation rules. There was a higher dropout rate in the placebo group, so the final sample sizes were 14 participants for placebo and 17 for CoQ10. The placebo group's total CoQ10 levels stayed largely flat between pre- and post-testing (from 0.67 µg/ml to 0.63 µg/ml) while the supplementation groups levels rose significantly (from 0.76 µg/ml to 2.96 µg/ml).

Some mild improvements were noted in the CoQ10 group. Namely, performance in the arithmetic task improved (including both a greater number of correct responses and total number of responses), the number of times participants awoke during the night and the duration for which they awoke decreased, and their autonomic nervous function improved. Similar to Study 1, increases in ubiquinol concentrations were associated with decreased fatigue, depression, and oxidation. However, no significant results were seen in any of these three measures when comparing the intervention to control group.

While both studies found associations between CFS symptom improvement and higher levels of circulating CoQ10, all of these improvements were very small or mild and did not change symptoms enough to be considered clinically meaningful. Perhaps most important of all was that fatigue symptoms did not consistently improve with CoQ10 supplementation.

What does the study really tell us?

All participants in this study met the CDC criteria for CFS and all had lower than normal levels of ubiquinol. Supplementation was effective at raising total circulating CoQ10 levels. Overall, testing results were improved with supplementation, but in most cases these improvements were moderate to minimal, and thus of questionable practical relevance. A small handful of participants did not respond to treatment or experienced a very mild worsening of depressive symptoms. This may be within normal symptom variation, but at the very least shows an inconsistent response to treatment with ubiquinol.

Ubiquinol did not significantly improve symptoms of fatigue, but researchers observed that there was a weak positive trend in symptom improvement that was correlated with the increase in ubiquinol blood concentrations. The higher the concentration, the more likely a participant would experience improvements in their fatigue level. The same relationship was observed in Study 1 with arithmetic task performance and depression symptoms. Of note, the high dropout rate in the second study may have influenced its ability to find significant differences between groups, due to a loss of statistical power.

It should be noted that the study was partially funded by the company Kaneka, Inc. which sells CoQ10 under the brand name Kaneka Ubiquinol™ and provided the supplements for this study. Additionally, the large dropout rate (nearly ⅓ of participants) in study 2 may have affected the ability for researchers to accurately detect positive, negative, or neutral outcomes.

Ubiquinol was not able to produce consistent real-world relevant symptom improvement. What improvements were observed in depressive and fatigue symptoms were moderate to minor. Some participants did not respond to the treatment at all. Those who had higher increases of blood CoQ10 from supplementation were more likely to see positive results.

The big picture

Including the present paper, two studies have now looked at the use of CoQ10's effect on ameliorating

fatigue in people diagnosed with CFS. A paper published in 2015 examined the effects of CoQ10 plus NADH supplementation in an eight-week randomized, double-blind placebo-controlled trial on 73 patients with CFS. NADH is a naturally-occurring chemical in the body that aids in energy production. The dosing in that study was 50 milligrams higher, coming in at 200 milligrams per day of CoQ10 plus 20 milligrams per day of NADH. Researchers also observed a moderate reduction in fatigue symptoms with supplementation compared to placebo. Like in the present study, it was a modest to weak effect. It should be noted that both of these studies were funded by nutraceutical companies. CoQ10 supplementation aside, current research has indicated that more intensive treatment options like cognitive behavioral therapy and graded exercise therapy tend to show better results for CFS symptom management.

The authors of this study put forth a hypothesis as to why CoQ10 may be causing these mild improvements. As mentioned before, CFS patients commonly have low CoQ10 levels and CFS may be caused by certain oxidative pathways that can reduce energy production in the mitochondria, the power plant of our cells. The addition of the antioxidant CoQ10 would, in theory,allow the mitochondria to function better. But as the effects of supplemental CoQ10 have so far been consistently minor, it would appear there is more to CFS than what the mere the addition of CoQ10 can fix. With a difficult condition such as CFS, no one treatment is likely to be curative for most people, so even something with minor-to-moderate results like CoQ10 could be worth trying.

Two studies have shown a minor reduction in fatigue symptoms in people with CFS. This may be, in part, due to the antioxidant effect that CoQ10 has in the body. Reduction of oxidation via CoQ10 supplementation may allow energy production pathways to function more normally, resulting in the contaminant fatigue reductions.

Frequently asked questions

Why were so many of the participants taking vitamin C?

Vitamin C is commonly marketed to consumers for its ability to fight fatigue. However, vitamin C supplementation for alleviating symptoms of CFS is not well-studied. Two studies have looked at oral supplementation in adults with obesity undergoing an exercise and diet intervention, and intravenous supplementation in healthy volunteer office workers. Both resulted in moderate decreases in fatigue, but in the case of the intravenous study this effect was only observed in people whose baseline vitamin C was already low. Neither of these studies had direct applicability to people with CFS and it remains unknown if there would be potential benefit or harm to supplementation.

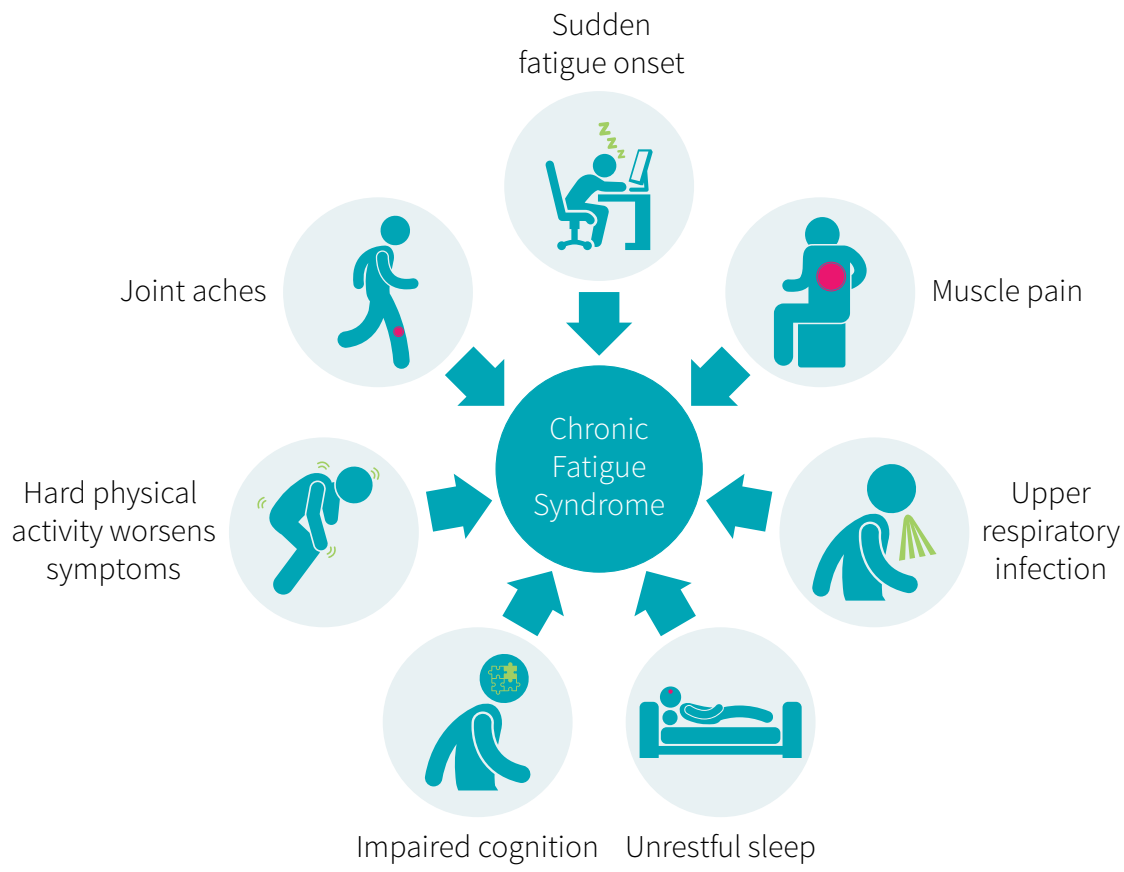
Can CoQ10 increase my energy level even if I don't have CFS?

CoQ10 has been investigated as a potential anti-fatigue supplement for exercise and for those with fibromyalgia, mitochondrial disorders, and in female breast cancer patients reporting treatment-related fatigue. The results have usually suggested minor or no beneficial effects. When supplemented by women undergoing chemotherapy, no improvements were observed. In patients with mitochondrial disorders, 1,200 milligrams per day was able to elicit minor fatigue improvement. Two studies looking at CoQ10 and fibromyalgia were able to also produce mild fatigue reduction.

Three trials (here, here, and here) looking at the potential for CoQ10 to stave off fatigue during exercise showed that it may be able to reduce self-reported symptoms of fatigue in a dose-dependent manner in long-duration exercises. In one study, a dose of 300 milligrams per day was able to reduce exercise related fatigue while the 100 milligrams per day dose was not. These results have not been observed in short duration/high intensity exercises, though.

What else is CoQ supplementation used for?

Figure 3: Symptoms of CFS



Perhaps most famously, CoQ10 was suggested as an adjunct therapy to be taken with statins, drugs that are used to lower cholesterol levels. Certain statins can interfere with the body's synthesis of CoQ10. It was hypothesized that a reduction of CoQ10 may lead to statin-induced muscle damage and that supplementation may ameliorate this. A 2015 meta-analysis (which called for longer, larger trials) concluded that current studies "do not suggest any significant benefit of CoQ10 supplementation in improving statin-induced [muscle damage]."

How do I know if I have CFS or am just fatigued?

The Institute of Medicine (IOM) published a new set of diagnostic criteria for CFS in 2015. The symptoms, which are summarized in Figure 3, include a significant reduction in the ability to engage in daily activities compared to pre-symptom levels, feeling uneasy after exercise, and not being able to achieve restful sleep. These feelings must persist for more than six months, and you would likely be experiencing concurrent feelings of great fatigue during this time.

What should I know?

Results of this study should be considered cautiously. CoQ10 may play a role in helping to reduce CFS symptoms in those with low ubiquinol levels. Two studies looking at this research question had small to moderate sample sizes and showed a weak effect of CoQ10 supplementation to alter patient symptoms.

The positive effects seen in the present study were mostly in participants who had the highest blood levels of CoQ10 at the end of the study. But even then the changes in symptoms were small. This study suggests that CoQ10 could improve symptoms through modulating energy metabolism and reducing oxidative stress. Nevertheless, these results are preliminary and current data indicate treatments like cognitive behavioral therapy and graded exercise therapy are more effective for CFS symptom management. However, use of CoQ10 as an adjunct to primary therapies is still a possibility that could be explored in future research. ◆

Having CFS doesn't just mean you're tired. It's a life-altering condition that's usually very difficult to treat. Discuss the treatment potential of CoQ10 over at the ERD Facebook forum.