

CoQ10 a Valuable Ally for Male Fertility

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Oxidative stress is one of the main factors responsible for DNA fragmentation in human spermatozoa, and a key contributor to male infertility, which is on the rise in the US.

According to several recent studies, supplementation with Coenzyme Q10 can attenuate this oxidative damage and improve multiple parameters of sperm health, making it a valuable tool in the care of infertile couples.

Infertility affects roughly 15% of couples in the United States (Thoma ME, et al. *Fertil Steril*. 2013; 99(5): 1324–1331). In about half of them, the problem is attributable to a male factor. While genetic conditions and structural issues may be the root cause of male infertility, one-third of all cases are classified as “idiopathic” or unexplained.

A review of data published world-wide between 1938 and 1990 reveals that sperm density in the population has decreased by 50% in 50 years (Carlsen E, et al. *Br Med J*. 1992; 305(6854): 609–613). These changes happened so rapidly that genetics alone could not account for them. Researchers postulate that environmental and lifestyle factors might be to blame.

DNA fragmentation has been implicated as the most important indicator of fertility problems, even more so than traditional semen parameters (Wright C, et al. *Reprod BioMed Online*. 2014; 28(6): 684–703).

An excess of oxidative stress generated from the products of oxygen metabolism can contribute to DNA damage, sperm cell membrane damage, and reduced sperm motility (Tesarik J. *Non-Invasive Sperm Select for In Vitro Fertil*. 2015; 138).

Crippled Motility

As reactive oxygen species (ROS) are produced during natural cellular functions, the body must use its antioxidants to neutralize them. Poor diet can lead to antioxidant depletion, and the condition is exacerbated by inflammatory conditions and immune system over-activation.

ROS can oxidize lipids found in sperm membranes in a way that can degrade or permeate them and cripple motility (Makker K, et al. *Indian*

J Med Res. 2009; 129: 357–367). Since sperm cells contain minimal amounts of cytoplasm, they do not have the cytoplasmic enzymes necessary to repair the damage. Once they are crippled, there is little that can be done.

Infertile men often have high levels of ROS, whereas fertile men do not (Kumalic IK, Pinter B. *BioMed Res Intl*. 2014; 2014: 1–11). The total antioxidant network contained within the seminal fluid is crucial for the neutralization of these free radicals and for the maintenance of sperm integrity. Poor diet, stress, sickness, chemical exposure, chronic inflammation and other circumstances typical of modern living contribute to depletion of antioxidants in semen.

Over the years, a number of research teams have looked at antioxidant supplementation for enhancing male fertility.

High Energy Demand

CoQ10 is the most commonly studied single antioxidant used for this purpose. It is unique in that it also plays a key role in cellular energy production and is found in high concentrations in tissues with substantial energy needs. This is especially important for sperm, since their motility has a large energy requirement. Low motility can be caused by a depletion of intracellular energy or ATP (Nakata K, et al. *Med Gas Res*. 2015; 2 [doi:10.1186/s13618-014-0023-x]).

CoQ10 has been found to impact all three of the basic semen parameters (morphology, concentration, motility) and seems to have the greatest overall effect on motility.

Clinical studies of CoQ10 have yielded varied results. One study published in 2011 showed that 200 mg daily of CoQ10 for 12 weeks reduced oxidative stress, but did not significantly improve semen parameters (Nadjarzadeh A, et al. *J Endocrinol Invest*. 2011; 34(8): e224–e228).

However, three years later, the same research group found that 200 mg of CoQ10 over a 3-month period not only reduced oxidative stress, but also improved semen parameters and positively correlated with an increase in superoxide dismutase (SOD) and catalase, two other essential antioxidants found in semen (Nadjarzadeh A, et al. *Andrologia*. 2014; 46(2): 177–183).

The majority of CoQ10 studies have indicated positive outcomes on semen parameters

and/or pregnancy rates. Safarinejad showed significant improvement in sperm motility, density, and morphology in men taking 300 mg of CoQ10 anywhere from 6 to 12 months (Safarinejad MR. *J Urol*. 2009; 182(1): 237–248; *Intl Urol and Nephrol*. 2012; 44(3): 689–700).

In the 12-month study, sperm concentration, motility, and morphology were improved by 113.7%, 104.8%, and 78.9%, respectively. There was an overall pregnancy rate of 34.1% within the first 8 months (Safarinejad MR. *Intl Urol and Nephrol*. 2012; 44(3): 689–700).

A 2014 review of clinic trials on oral antioxidants used for male fertility listed CoQ10 as the antioxidant most often proved to be effective in every category of sperm health (Kumalic IK, Pinter B. *BioMed Res Intl*. 2014; 2014: 1–11).

A Combination Approach

One company that has capitalized on the antioxidant research into male infertility is Fairhaven Health (fairhavenhealth.com). This small, family-owned company based out of Washington State was founded in the early 2000s in an attempt to bring natural alternatives to couples with fertility issues.

Suzanne Munson, Director of Product Development at Fairhaven Health, told *Holistic Primary Care* that the company emerged out of a partnership she created with Dr. Amos Grunebaum, a prominent OB/GYN and fertility expert from New York, who helped them develop their FertilAid supplement.

The Fairhaven team reviewed numerous supplement studies prior to formulation of this product, which includes a “motility-enhancing dose” of CoQ10. The FertilAid formula also includes Maca (*Lepidium meyenii*), a root indigenous to the Andes, which has been shown to enhance sperm count, and carnitine for improving sperm quality.

In 2009, Fairhaven helped to fund a small pilot study of their product. Fourteen infertile men participated in a 90-day randomized, double-blind, placebo-controlled trial. FertilAid boosted the number of healthy sperm significantly in the 8 men that took it compared with those in the placebo group (Clifton GD, Ellington JE. *J Androl Annual Proceedings*. 2009; (S25): 41). While further studies are needed on

a larger scale to verify these results, the initial findings are promising.

FertilAid includes a modest 15 mg of CoQ10. This is considerably lower than the 200 to 300 mg typically given in the male infertility studies. However, FertilAid also includes a high dose of vitamin B6, which helps the body to synthesize CoQ10 on its own.

A combination of antioxidants seems to work better to enhance fertilizing capability than any antioxidant alone (Lanzafame FM, et al. *Reprod BioMed Online*. 2009; 19(5): 638–659). This is because antioxidants work together to neutralize ROS and reduce the free radical burden. They form a network with the ability to recycle one another and thus extend their lifespan and capacity.

The FertilAid product includes other ingredients shown to be effective for enhancing sperm parameters including Vitamins C and E and the minerals selenium and zinc.

Fairhaven Health has separate CountBoost and MotilityBoost products that are formulated to work with the FertilAid supplement.

According to Ms. Munson, there are other things men can do to promote fertility. She recommends avoiding smoking, alcohol, and recreational drugs as these things all increase oxidative stress and reduce sperm count and quality.

Moderate exercise is important, but excessive exercise can be detrimental. Eating a clean diet filled with fruits and vegetables (high in antioxidants) is important, as is maintaining a healthy weight (obesity has been linked to infertility). Finally, prevent overheating of the genitals by avoiding saunas, hot tubs, and other situations with extreme temperatures. There is even a company called Snowballs (we kid you not) that makes underwear with an ice pack to prevent overheating.

Keep in mind that fertility is a reflection of overall health. Lifestyle choices are integral to optimal fertility. Eating well, drinking enough fluid, getting adequate sleep, exercising in moderation, and minimizing stress are all part of an integrative plan to promote wellness, decrease oxidation, and increase the potential for conception.

As a stand-alone supplement, CoQ10 is one of the best. In combination with other antioxidants, it is even better. Given the low risk and high benefit potential of using antioxidants, it makes sense to include them as part of a comprehensive strategy toward improving male fertility. ☺

Citicoline Reduces Cocaine Use in Bipolar Patients

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A readily available over-the-counter nutritional supplement may help reduce illicit drug dependency in patients with psychiatric illness, according to researchers at the University of Texas Southwestern Medical Center.

In a study published over the summer in the *American Journal of Psychiatry*, the Texas researchers showed that supplementation with citicoline was effective at lowering cocaine use in individuals dually-diagnosed with bipolar I disorder and cocaine dependence.

Citicoline, a naturally occurring exogenous form of cytidine 5'-diphosphate choline, seems to support brain health in a number of ways. It plays a key role in the biosynthesis of membrane phospholipids and modulates neurotransmitter levels. It appears to improve cognition in some central nervous system disorders and has been shown to be neuroprotective in animal models (Dávalos et al. *Lancet*. 2012; 380(9839): 349–357).

The new findings suggest that citicoline holds great promise as a safe alternative therapy for an often difficult-to-treat population.

Bipolar & Substance Abuse

Substance abuse is remarkably common in patients with psychiatric disorders. Rates are particularly high in individuals with bipolar disorder, among whom cocaine use is especially prominent.

Drug dependence further complicates an already complex illness. Previous studies have documented increased hospitalization rates, higher incidence of aggression and violence, lower rates of recovery during hospitaliza-

tion, and poorer medication adherence in patients with both bipolar and substance abuse disorders.

Scientists aren't entirely sure why the rates of drug abuse are so high in people with bipolar disorder, though there are many possible explanations. The classic features of bipolar disorder—such as impulsivity—might lead to a greater risk of abuse. Exposure to substances being sold or used in a patient's living environment or elsewhere may be a factor as well. It's also possible that an underlying genetic vulnerability may contribute to substance abuse.

Having a diagnosis of bipolar disorder is associated with poor response to drug dependency treatment, which typically consists of prescription pharmaceuticals combined with counseling and behavioral therapy. But some researchers, like the group at the University of Texas, are now exploring novel treatment options for this vulnerable patient population.

Citicoline for Drug Users

E. Sherwood Brown, MD, PhD, professor of psychiatry at the UT Southwestern Medical Center and lead researcher of the citicoline study, notes that when he first entered the field, the literature clearly indicated that a majority of patients with bipolar disorder also had longstanding substance abuse issues.

Despite this striking correlation, “most clinical trials excluded people with substance abuse, and there was little research on the treatment of patients with both bipolar disorder and substance dependence.”

Recognizing an unmet need, he and his colleagues conducted a pilot study to investigate the efficacy of citicoline in preventing cocaine relapse in bipolar patients. The hypothesis was based on earlier work

suggesting that citicoline might decrease cocaine dependency.

The initial data showed that citicoline was more effective than placebo at decreasing the risk of relapse to cocaine use. These findings set the stage for the current study, which involved active cocaine users with bipolar diagnoses.

A cohort of 130 adult outpatients with bipolar I disorder and current cocaine dependence were recruited for this randomized, double-blind, placebo-controlled trial. All had self-reported cocaine use within the seven days prior to the study's onset. Additionally, they all had cocaine-positive urine screens at baseline (Brown ES, et al. *Am J Psych*. 2015; 172(10): 1014–1021).

Over the course of 12 weeks, patients received either *Cognizin*® citicoline (*Jarrow*® Formulas) or placebo add-on therapy. In the first week, participants in the citicoline group took 500 mg/day of the substance, or an identical placebo. The dose was increased to 1,000 mg/day at week two, 1,500 mg/day at week four, and 2,000 mg/day at week six. The researchers monitored adherence using a Medication Event Monitoring System cap, and collected urine samples from all participants three times per week.

In order to improve retention, participants also engaged in manual-based cognitive behavioral therapy (CBT) designed specifically for patients with bipolar and substance use disorders. They received CBT twice weekly in the first four weeks followed by weekly sessions for the duration of the study, for a total of 16 sessions.

“A Useful Choice”

After 12 weeks, the researchers found that, based on participants' urine screens, cocaine use had decreased significantly in the citicoline group. They reported significant treat-

ment group ($F = 5.2$, $df = 1,1351$, $p = 0.022$) and group-by-time effects ($F = 5.9$, $df = 1,1351$, $p = 0.015$).

Citicoline was safe and well tolerated, with no significant differences in side effects or treatment retention between the citicoline and placebo groups.

Its “favorable safety profile and absence of known drug-drug interactions may make citicoline a useful choice in bipolar disorder and cocaine-dependent patients who are taking a variety of concomitant medications,” the authors suggest.

Furthermore, the reduction in cocaine use appeared to occur without affecting participants' mood. This suggests that the decreased drug dependence was not contingent upon the initial stabilization of patients' moods, Dr. Brown notes.

He adds that while the participants' lack of mood change during treatment could be a result of the study's design, it may also indicate a deeper and yet unknown mechanism through which citicoline reduces cocaine dependence.

The study included patients who were generally depressed with “rather mild manic symptoms, so there really wasn't much opportunity to see a change in manic symptoms,” Brown explains. “But there was potential to see a change in depressive symptoms, and we just didn't see it. So it looks like whatever mechanism citicoline is decreasing cocaine use with is probably not a secondary effect of an improvement in mood.”

“In terms of the broader generalizability of the study,” Dr. Brown continues, “this may be a positive finding,” suggesting that the efficacy of citicoline could extend beyond the dual-diagnosed study group to a much broader population. In other words, it might also be effective in treating pure cocaine use