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Coenzyme Q10

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Continuing Education Activity

Coenzyme Q10 (CoQ10), also known as ubiquinone, is a fat-soluble, vitamin-like molecule naturally present in every cellular membrane within our bodies. This enzyme is a regular component of our diet, although it is also synthesized endogenously. CoQ10 is crucial for efficiently transferring electrons within the mitochondrial oxidative respiratory chain and producing adenosine triphosphate (ATP). CoQ10 can potentially increase the production of vital antioxidants, such as superoxide dismutase, an enzyme that effectively mitigates vascular oxidative stress in individuals with hypertension. In addition, CoQ10 lowers lipid peroxidation levels by diminishing pro-oxidative compounds. Furthermore, CoQ10 can improve blood flow and safeguard blood vessels by preserving nitric oxide. Although CoQ10 lacks approval from the United States Food and Drug Administration (FDA) for treating any medical condition, it is readily accessible as an over-the-counter dietary supplement and is often recommended by both primary care clinicians and specialists.

Certain conditions such as fibromyalgia, diabetes, cancer, heart failure, and neurodegenerative, mitochondrial, and muscular diseases are linked to reduced circulating levels of CoQ10. Statin drugs inhibit the production of an intermediate in the mevalonate pathway—a biochemical route leading to CoQ10 synthesis. Researchers theorize that statin drugs may contribute to CoQ10 depletion. Given that muscle pain and cramping are frequent adverse effects of statins, they attribute these symptoms to the diminished levels of CoQ10. This activity emphasizes the mechanism of action, adverse event profile, recent research findings, and pertinent interactions related to CoQ10, providing interprofessional healthcare team members with essential information for effectively treating patients with relevant conditions.

Objectives:

- Identify patients at risk of coenzyme Q10 deficiency, considering factors such as medical history, medication use, and specific health conditions.
- Implement screening protocols to assess coenzyme Q10 levels in patients with conditions linked to its deficiency, such as fibromyalgia, neurodegenerative diseases, and heart failure.
- Select appropriate coenzyme Q10 formulations and dosages based on individual patient needs, ensuring optimal therapeutic outcomes.
- Collaborate with interprofessional healthcare professionals to integrate coenzyme Q10 supplementation into a comprehensive patient care plan, especially in conditions with known coenzyme Q10 deficiency associations.

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Indications

Coenzyme Q10 (CoQ10), also known as ubiquinone, is a fat-soluble, vitamin-like molecule naturally present in every cellular membrane within our bodies. This enzyme is a regular component of our diet, although it is also synthesized endogenously. Although CoQ10 lacks approval from the United States Food and Drug Administration (FDA) for treating any medical condition, it is readily accessible as an over-the-counter dietary supplement and is often recommended by both primary care clinicians and specialists. Conditions such as fibromyalgia, diabetes, cancer, heart failure, and neurodegenerative, mitochondrial, and muscular diseases are associated with decreased circulating levels of CoQ10.[1][2] Several studies have been conducted to determine whether increasing systemic CoQ10 levels would enhance bodily function.[3][4][5]

Primary CoQ10 deficiency is a rare autosomal recessive disorder caused by gene defects involved in CoQ biosynthesis with clinical features of steroid-resistant nephrotic syndrome (SNHL), optic atrophy, retinopathy, and encephalopathy. CoQ10 replacement therapy is indicated for this rare disorder.[6]

According to 2022 ACC/AHA/HFSA (American College of Cardiology/American Heart Association/The Heart Failure Society of America), guidelines for (2022) supplementation with CoQ10 effectively reduced vascular mortality, all-cause mortality, and hospital stays for heart failure at 2 years. However, long-term supplementation is needed.[7]

A recently published systematic review showed that supplementation with CoQ10, in addition to standard therapy in patients with moderate-to-severe heart failure, is associated with symptom reduction and reduction of major adverse cardiovascular events.[4][8] CoQ10 may improve functional capacity, endothelial function, and left ventricle contractility in congestive heart failure patients.[4][9]

Supplementation shows promising results in improving endothelial function in several subsets of patients. CoQ10 can improve endothelial function in patients with ischemic left ventricular systolic dysfunction and heart failure.[10][11] Likewise, compared with placebo, CoQ10 improves endothelial function in the peripheral circulation of patients with type 2 diabetes mellitus and hyperlipidemia.[12] Routine use of CoQ10 in patients with coronary artery disease apart from congestive heart failure is still inconclusive.[13][10]

There is also evidence that combined with selenium, CoQ10 supplementation in healthy older patients and older patients with diabetes, hypertension, and ischemic heart disease may decrease cardiovascular mortality risk.[14] Data are conflicting on whether CoQ10 may play a role in treating high blood pressure.[15] CoQ10 shows the potential to decrease pain, fatigue, and morning tiredness compared to a placebo in patients with fibromyalgia.[16][17] Some data suggest that supplementation with moderate-to-high dose CoQ10 may influence bicycle exercise aerobic capacity in patients with mitochondrial disorders.[18]

Supplementation with CoQ10 in men with Peyronie disease may decrease penile plaque size, reduce penile curvature, and improve erectile function.[19] Statin drugs inhibit the production of an intermediate in the mevalonate pathway—a biochemical route leading to CoQ10 synthesis.[20] Therefore, many researchers theorize that statin drugs may contribute to CoQ10 depletion in the body. Given that muscle pain and cramping are frequent adverse effects of statins, they attribute these symptoms to the diminished levels of CoQ10.[21]

Although most studies have used patients with preexisting medical conditions, one study of healthy participants did show that oral supplementation improved fatigue and physical performance during bicycle exercise routines.[22]

CoQ10 has also shown promise in migraine prophylaxis. A cohort study of 1550 children and adolescents with headaches found that this population has low CoQ10 levels.[23] Supplementation appeared to decrease headache frequency.[23] A recent study indicated that CoQ10 is beneficial for the prophylactic treatment of migraine headaches in children without significant adverse effects.[24] Interestingly, CoQ10 levels may be decreased in those with acute influenza infection.[25]

However, studies on supplementation in this subset of patients have yet to be done. A recent study showed promising results of CoQ10 supplementation for long COVID syndrome. However, significant research is needed.[26] When supplemented alongside standard psychiatric medical therapy, CoQ10 appears to lessen symptoms of depression in patients with bipolar disorder.[27] In patients with polycystic ovary syndrome, supplementation may improve fasting blood glucose, insulin levels, and total testosterone levels.[28]

Mechanism of Action

CoQ10, also called ubiquinone, is a fat-soluble, vitamin-like molecule found naturally in every cellular membrane in our bodies and a normal part of our diet, though endogenously synthesized. CoQ10 is crucial for efficiently transferring electrons within the mitochondrial oxidative respiratory chain and producing adenosine triphosphate (ATP).[29] CoQ10 can potentially increase the production of vital antioxidants, such as superoxide dismutase, an enzyme that effectively mitigates vascular oxidative stress in individuals with hypertension.[30] In addition, CoQ10 lowers lipid peroxidation levels by diminishing pro-oxidative compounds.[31] Furthermore, CoQ10 can improve blood flow and safeguard blood vessels by preserving nitric oxide.

Supplements offer CoQ10 in either the oxidized form (ubiquinone) or the reduced form (ubiquinol). The bioavailability of a given CoQ10 supplement depends on the lipid carrier it is immersed in and any added preservatives.[32]

Pharmacokinetics

Absorption: CoQ10 is a hydrophobic (lipophilic) molecule with a high molecular weight; absorption of dietary CoQ10 is slow but is improved in the presence of fatty meals. Solubilized CoQ10 formulations provide improved bioavailability, with peak plasma concentrations typically ranging from 5.80 to 8.10 hours, depending on the specific formulation. Various formulations such as liposome, nanocapsule, and nanoemulsion are being explored to improve bioavailability. A second plasma peak may also be observed due to the enterohepatic recycling and redistribution from the liver to the circulation.

Distribution: CoQ10 is primarily absorbed from the small intestine, and CoQ10 is incorporated into chylomicrons and is redistributed via the bloodstream, primarily within VLDL, LDL, and HDL. Preclinical studies indicate that CoQ10 in large doses is taken up by all tissues, including heart and brain mitochondria; consequently, a beneficial effect is observed in cardiovascular and neurodegenerative diseases. The highest levels of CoQ10 in human tissues exist in the heart, liver, kidneys, and muscles (high energy requirements).[33]

Metabolism: CoQ10 is metabolized in all tissues, and the resulting metabolites are phosphorylated in the cells and transported through the plasma. CoQ10 is reduced to ubiquinol during or after absorption in the small intestine, and the reduced form represents approximately 95% of the circulating CoQ10 in humans.

Elimination: The primary route of elimination is biliary and fecal. A small fraction is eliminated in the urine.[34]

Administration

Available Dosage Forms and Strengths

Most human studies on CoQ10 have focused on its oral supplementation. Available in various forms, such as tablets, capsules, soft gels, and liquid formulations, these oral supplements range from 30 to 600 mg per unit and are easily accessible over the counter. While topical over-the-counter preparations are also available, research on this mode of administration is limited. For instance, one study explored the effectiveness of a topical treatment for age-related skin oxidative damage.[35]

Meat has the highest amount of CoQ10, followed by dairy, eggs, and plant-based food sources (oils and legumes). CoQ10 extracted from living tissues is more expensive than produced in the laboratory by fermentation, yielding

consistent quality and cheaper supplements.[36]

- Supplementation with 50 mg twice daily has decreased statin-related mild-to-moderate myalgias, resulting in an increased ability to perform daily activities.[21] The meta-analysis of RCTs indicated that CoQ10 supplementation (100 to 600 mg/d) decreased the Statin-Associated Muscle Symptoms (SAMS).[37]
- Supplementation with 300 mg daily for 24 weeks in men with Peyronie disease may decrease penile plaque size, reduce penile curvature, and improve erectile function.[19]
- A double-blind, randomized controlled trial showed 300 mg daily to be safe and superior to a placebo for migraine prevention.[38] Another randomized, double-blind, placebo-controlled trial in adult women showed that 400 mg of supplementation decreased migraine frequency, severity, and duration.[2] One study showed that only 100 mg daily reduced the severity of headaches and the number of headaches per month in migraine sufferers.[39]
- The meta-analysis of RCTs indicated that CoQ10 supplementation (100 to 600 mg/d) decreased the SAMS.
- In patients with primary CoQ10 deficiency, early treatment with high-dose supplementation (ranging from 5 to 50 mg/kg/day) can limit disease progression.[40] A recent study of CoQ10 supplementation (20 mg/kg) demonstrated promising results in patients with primary CoQ10 deficiency with nephrotic syndrome and SNHL.[6][41]

Specific Patient Populations

Hepatic impairment: CoQ10 supplementation reduces systemic inflammation and biochemical parameters in nonalcoholic fatty liver disease (NAFLD). However, as mentioned in pharmacokinetics, CoQ10 is excreted in bile. Hence, the use is not advised in patients with biliary obstruction.[34]

Renal impairment: According to a recent article on Kidney Disease Improving Global Outcomes (KDIGO 2022), CoQ10 supplementation may benefit patients with nephrotic syndrome due to primary CoQ10 deficiency. However, studies of CoQ10 in patients with renal impairment are lacking; CoQ10 supplements should be avoided in patients with renal impairment and used only for the indications mentioned in KDIGO guidelines.[42]

Pregnancy considerations: According to the manufacturer, CoQ10 is not advised during pregnancy. However, a recent meta-analysis demonstrated that supplementation with CoQ10 may benefit clinical pregnancy rates (CPR) in assisted reproductive technologies (ART).[43]

Breastfeeding considerations: According to the manufacturer, CoQ10 is not advised during breastfeeding. Ubiquinone is endogenously synthesized and is a standard component of human milk. Concentration CoQ10 is slightly low in the breast milk of mothers with preterm infants. CoQ10 has no specific lactation-related uses; safety data is lacking during lactation. Therefore, use is usually not recommended. [44]

Older patients: No specific dosing recommendations for older or pediatric patients are available.

Adverse Effects

The common adverse effects of CoQ10 are listed below.

- CoQ10 is present naturally in the human body. CoQ10 supplements are generally well-tolerated with only minor and infrequent adverse effects, including stomach upset, nausea, vomiting, and diarrhea.[44][45]
- Dosages of 100 mg/d or higher have been associated with mild insomnia in some individuals.[46]

- Liver enzyme elevation is seen in some patients taking 300 mg or more daily, but no liver toxicity is reported. Caution is required in bile duct obstruction.[46]
- Supplementation is well tolerated, up to 1200 mg/d.[5]
- Other rare adverse effects have included dizziness, photophobia, irritability, headache, heartburn, increased involuntary movements, and fatigue.[44][45][47]

The FDA does not strictly regulate dietary supplements such as CoQ10, nor are manufacturers required to prove their safety and purity before and after market release. However, several independent agencies test supplements for purity, composition, and strength and issue certifications to manufacturers that meet testing criteria. However, these agencies do not test every batch they manufacture nor guarantee therapeutic value. Manufacturers who have received approval will advertise on their product packaging.

Drug-Drug Interactions

CoQ10 is chemically similar to vitamin K, and some reports are available in the literature for potential warfarin and CoQ10 interaction. There are chances of warfarin treatment failure when patients are taking CoQ10 supplements with warfarin therapy. This interaction is reversible.[48][49][50]

Contraindications

Patients administering chemotherapeutic drugs should also avoid CoQ10, as there is insufficient data on its interaction with these drugs. As CoQ10 lowers fasting blood glucose in some patients, it should be used cautiously in those with diabetes and patients prone to hypoglycemic episodes. CoQ10 is contraindicated in patients with known hypersensitivity reactions to CoQ10 or excipients. Some supplements contain silicon dioxide, which may be responsible for hypersensitivity reactions.[51]

Monitoring

Many studies have monitored blood levels of CoQ10 to assess the efficacy of supplementation. Average plasma concentrations appear to be about 0.34 to 1.65 $\mu\text{g/mL}$. [5] A toxic blood CoQ10 level has not been determined, mostly because CoQ10 toxicity is absent at the highest oral supplementation levels.[5][52]

Periodic urinalysis (for proteinuria) and renal function tests, neurologic evaluation, ophthalmologic evaluation, and audiometry are required for primary CoQ10 deficiency.[6][40][53]

Toxicity

CoQ10 is safe as a dietary supplement. Toxicity is unlikely up to a daily intake of 1200 mg/d, although typical dosages have been 100 to 200 mg/d.[52] In preclinical studies, ubiquinol's No-Observed-Adverse-Effect Level (NOAEL) is 300 to 600 mg/kg (Sprague Dawley rats).

The human supplementation dose of CoQ10 is generally 100 to 300 mg/d. Assuming the human dose is 300 mg/day (5 mg/kg body weight), the safety factor is 60 to -120 times. The study indicated that chronic use of ubiquinol as a dietary supplement in humans is safe.[54]

Enhancing Healthcare Team Outcomes

CoQ10 is a safe, popular dietary supplement that is continuously being studied as an adjunctive treatment for several medical conditions. With the broad commercial base of the supplement industry and widespread interest in complementary and alternative medicine in the United States, many healthcare professionals will inevitably encounter patients interested in using this and other dietary supplements.

As data on this promising supplement continue to grow, clinicians, pharmacists, and other interprofessional healthcare team members must continue to update themselves on the potential as an adjunctive treatment for various medical conditions. With proper education and open communication regarding the patient's condition and use of supplements, including CoQ10, the chances for better outcomes are enhanced and potential adverse events minimized.

Potential Level 1: This evidence for CoQ10 includes adjunctive treatment for patients with moderate-to-severe congestive heart failure.[4]

Potential Level 2: This evidence includes CoQ10 supplementation for the below-mentioned indications.

- To improve endothelial function in patients with ischemic left ventricular systolic dysfunction heart failure.[10]
- To improve endothelial function in the peripheral circulation of patients with type-2 diabetes mellitus with hyperlipidemia.[12]
- To decrease pain, fatigue, and morning tiredness in patients with fibromyalgia.[16][17]
- To improve aerobic capacity in patients with mitochondrial disorders.[18]
- To decrease penile plaque size, reduce penile curvature, and improve erectile function in patients with Peyronie disease.[19]
- To decrease statin-related mild-to-moderate myalgias.[21]
- To improve subjective fatigue and physical performance during bicycling exercise routines in healthy patients. [22]
- To lessen symptoms of depression in patients with bipolar disorder alongside conventional pharmacologic therapy.[27]
- To improve fasting blood glucose, insulin levels, and total testosterone levels in patients with polycystic ovary syndrome.[28]
- To decrease migraine frequency in adult migraine sufferers.[2][38]

Potential Level 3: This evidence for the use of CoQ10 includes the below-mentioned indications.

- To reduce cardiovascular mortality risk along with selenium administration in healthy older patients.[14]
- To decrease the severity of headaches and the number of headaches per month in adult and pediatric migraine sufferers.[23][39]
- To attenuate disease progression in patients with primary coQ10 deficiency.[55]

Review Questions

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