

The Role of Coenzyme Q₁₀ in Clinical Medicine: Part I

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Abstract

This review discusses the potential role of coenzyme Q₁₀ in the treatment of acquired immunodeficiency syndrome (AIDS), cancer, periodontal disease, gastric ulceration, obesity, muscular dystrophy, and allergy. The effect of coenzyme Q₁₀ (CoQ₁₀) on immune function and physical performance is also reviewed. Controlled trials have demonstrated a beneficial effect of CoQ₁₀ in the treatment of periodontal disease. Promising (although anecdotal) clinical results have been reported for cases of cancer, AIDS, and muscular dystrophy. CoQ₁₀ is of theoretical value as a treatment for gastric ulceration and allergies; however, CoQ₁₀ treatment of these conditions has not been tested in humans. There is limited evidence that CoQ₁₀ may enhance immune function and improve physical performance in certain circumstances. The value of CoQ₁₀ as a treatment for obesity remains speculative.

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Coenzyme Q₁₀ (CoQ₁₀) is a compound found naturally in the human body. Because of its ubiquitous presence in nature and its quinone structure (similar to that of vitamin K), CoQ₁₀ is also known as ubiquinone. The primary biochemical action of CoQ₁₀ is as a cofactor in the electron-transport chain, the series of redox reactions that are involved in the synthesis of adenosine triphosphate (ATP; the body's major form of stored energy). Since most cellular functions are dependent on an adequate supply of ATP, CoQ₁₀ is essential for the health of virtually all human tissues and organs.

Although CoQ₁₀ can be synthesized "in vivo", situations may arise in which the body's synthetic capacity is insufficient to meet CoQ₁₀ requirements. Susceptibility to CoQ₁₀ deficiency appears to be greatest in cells that are metabolically active (such as those in the heart, immune system, gingiva, and gastric mucosa), since these cells presumably have the highest requirements for CoQ₁₀. Tissue deficiencies or subnormal serum levels of CoQ₁₀ have been reported to occur in a wide range of medical conditions, including cardiovascular disease, hypertension, periodontal disease, and acquired immunodeficiency syndrome (AIDS). In addition, CoQ₁₀ levels decline with advancing age, and this decline might contribute in part to some of the manifestations of aging.

A need for supplemental CoQ₁₀ could theoretically result from (1) impaired CoQ₁₀ synthesis due to nutritional deficiencies, (2) a genetic or acquired defect in CoQ₁₀ synthesis or utilization, or (3) increased tissue needs resulting from a particular illness. Since oral administration of CoQ₁₀ can increase tissue levels of the nutrient,¹ it is possible to correct CoQ₁₀ deficiency

and its associated metabolic consequences by supplementation.

The optimal dose of CoQ₁₀ is not known, but it may vary with the severity of the condition being treated. For example, 30 mg/day of CoQ₁₀ was reportedly effective in the treatment of mild congestive heart failure; 90 mg/day resulted in improvements in some cases of cancer; and 390 mg/day was associated with complete regression of liver metastases in a patient with breast cancer.

Part I of this two-part article will review research on the relationship between CoQ₁₀ and immune function, cancer, periodontal disease, gastric ulceration, obesity, physical performance, allergy, and muscular dystrophy. Part II will discuss the effect of CoQ₁₀ on cardiovascular disease, hypertension, diabetes mellitus, and infertility, as well as CoQ₁₀-drug interactions.

Immune Function

Cells and tissues that play a role in immune function are highly energy-dependent and therefore require an adequate supply of CoQ₁₀ for optimal function. Several studies have demonstrated immune-enhancing effects of CoQ₁₀ or its analogues.²⁻⁴ These effects included increased phagocytic activity of macrophages; increased proliferation of granulocytes in response to experimental infections; and prolonged survival in mice infected with *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, or *Candida albicans*. Inoculation of animals with Friend leukemia virus reduced CoQ₁₀ levels in the blood and spleen,⁵ whereas treatment of infected animals with CoQ₁₀ increased the survival rate and decreased the severity of hepatomegaly and splenomegaly.⁶

Immune function tends to decline with advancing age. In a study of elderly mice, suppression of the immune response was associated with a marked decline of CoQ₁₀ levels in thymic tissue.⁷ This immune suppression was

partly reversed by treatment with CoQ₁₀.⁸ In a study of eight chronically ill patients, administration of 60 mg/day of CoQ₁₀ was associated with significant increases in serum levels of immunoglobulin G (IgG) after 27-98 days of treatment.⁹ These studies suggest that CoQ₁₀ may help prevent or reverse the immunosuppression that is associated with aging or chronic disease.

Treatment of Acquired Immunodeficiency Syndrome (AIDS)

AIDS is a complex disease that is associated with a wide range of nutritional deficiencies and immunological disorders. While correction of nutritional deficiencies will not cure AIDS, appropriate nutritional interventions may help prevent weight loss and enhance overall immune function. In addition, since oxidative stress is believed to be involved in the pathogenesis of AIDS-related diseases, the antioxidant activity of CoQ₁₀¹⁰ may be of value for individuals with AIDS.

In one study,¹¹ blood levels of CoQ₁₀ were significantly lower in patients with AIDS-related complex (ARC) than in a control group, and were significantly lower in patients with AIDS than in those with ARC. Six patients with AIDS or ARC were treated with 200 mg/day of CoQ₁₀. T-cell helper/suppressor ratios increased in three patients, becoming normal in one case. Five patients reported symptomatic improvement, which was dramatic in some cases. Furthermore, none of the patients developed opportunistic infections during a 4-7 month follow-up period. This study demonstrates that CoQ₁₀ deficiency is common in patients with HIV infection, and that supplementation with CoQ₁₀ may improve immune function and reduce the incidence of opportunistic infections.

Treatment of Cancer

Because of its role in enhancing immune function, CoQ₁₀ has been considered as a possible anti-cancer agent. Administration of CoQ₁₀ reduced tumor size and increased survival in mice exposed to a chemical carcinogen.¹² Preliminary studies in humans, though uncontrolled, are promising. In one study, 32 women with breast cancer who were classified as “high risk” because of tumor spread to the axillary lymph nodes received daily 90 mg of CoQ₁₀, along with vitamin C, vitamin E, beta-carotene, and essential fatty acids. In six of these cases, the tumor became smaller. During the 18-month treatment period, none of the patients died (the expected number of deaths was four), and none showed signs of further distant metastases. Six patients had an apparent partial remission. In addition, patients receiving CoQ₁₀ required fewer pain killers.¹³

In another report, two women with metastatic breast cancer received 390 mg/day of CoQ₁₀. One of the patients was a 44-year-old woman with numerous liver metastases. After treatment with CoQ₁₀ for 11 months, all of the liver metastases had disappeared and the patient was reported to be in excellent health. The other patient was a 49-year-old woman with breast cancer that had metastasized to the pleural cavity. After six months of CoQ₁₀ therapy, the pleural fluid had completely resolved and the patient was reported to be in excellent health.¹⁴

Although these reports are anecdotal, the results are far better than would normally be expected. Considering that CoQ₁₀ is virtually free of side effects, empirical treatment of breast cancer with CoQ₁₀ seems justified.

Periodontal Disease

Periodontal disease affects about 60% of young adults and 90% of individuals over the age of 65. Although proper oral hygiene is helpful, many people suffer from intractable

gingivitis, often requiring surgery and resulting in eventual loss of teeth. Because periodontal disease is so common, the costs of periodontal surgery and other treatments contribute a significant amount to the overall cost of health care in the United States.

Healing and repair of periodontal tissues requires efficient energy production, which depends in part on an adequate supply of CoQ₁₀. Gingival biopsies revealed subnormal tissue levels of CoQ₁₀ in 60% to 96% patients with periodontal disease and low levels of CoQ₁₀ in leukocytes in 86% of cases.¹⁵⁻¹⁸ These findings indicate that periodontal disease is frequently associated with CoQ₁₀ deficiency.

Eighteen patients with periodontal disease received either 50 mg/day of CoQ₁₀ or a placebo in a 3-week, double-blind trial.^{19,20} Results were assessed according to a “periodontal score,” which included gingival-pocket depth, swelling, bleeding, redness, pain, exudate, and looseness of teeth. All eight patients receiving CoQ₁₀ improved, compared to only three of ten receiving the placebo ($p < 0.01$). The treating dentists, who were unaware that a study was being conducted, consistently remarked about the “very impressive” rate of healing in patients treated with CoQ₁₀. One prosthodontist commented that the amount of healing that took place in three weeks in patients receiving CoQ₁₀ would normally require about 6 months.

In an open trial, administration of CoQ₁₀ produced “extraordinary post-surgical healing (2-3 times as fast as usual) in 7 patients with advanced periodontal disease.²¹ The beneficial effect of CoQ₁₀ has also been confirmed in dogs, where it reduced the severity of experimentally induced periodontal disease.²²

Gastric Ulcer

Susceptibility to gastric ulceration is related to the balance between ulcer promoting factors (such as excessive gastric acidity and infection with *Helicobacter pylori*), and resis-

tance factors (such as tissue integrity, production of protective mucus, and repair mechanisms). Free-radical damage is believed to be one of the primary mechanisms by which external factors induce gastric injury²³ and peptic ulceration.²⁴ Since CoQ₁₀ possesses antioxidant activity, it might be capable of preventing ulceration by reducing the amount of free-radical damage. In addition, the production of protective mucus and the rapid cell turnover of gastric mucosa are highly energy-dependent processes, which require the presence of adequate amounts of CoQ₁₀.

The efficiency of these protective and reparative processes may be compromised in some patients with gastric ulcers. With advancing age, the fundic mucosa and its rich blood supply are gradually replaced by pyloric tissue, which has poor vascularity. This change in cell type may result in hypoxia in certain portions of the stomach. The hypoxic state of gastric tissue could explain why gastric ulcers frequently become intractable in elderly patients or in those with chronic heart or lung disease.

The importance of CoQ₁₀ for healing of gastric ulcers has been demonstrated in animals.²⁵ Gastric ulcers were induced in mice by application of acetic acid. The mice were then maintained either in room air (20% oxygen) or under mild hypoxic conditions (17% oxygen). Ulcers healed normally in mice exposed to room air, but increased in size under hypoxic conditions. However, in hypoxic mice treated with CoQ₁₀ (50 mg/kg/day) the ulcers healed normally.

This study demonstrates that hypoxia has an adverse effect on the healing of gastric ulcers in animals, and that the effect of hypoxia can be prevented by administration of CoQ₁₀. Although human studies have not been done, empirical use of CoQ₁₀ seems like a reasonable option for elderly patients with intractable gastric ulcers, particularly those who also have diseases likely to produce hypoxia.

Obesity

The tendency to become overweight is associated in some cases with impaired energy production. This abnormality may be in part genetically determined. Individuals with a family history of obesity have a 50% reduction in their thermogenic response to meals, suggesting the presence of an hereditary defect in energy output. Since CoQ₁₀ is an essential cofactor for energy production, it is conceivable that CoQ₁₀ deficiency is a contributing factor in some cases of obesity.

Serum levels of CoQ₁₀ were found to be low in 14 (52%) of 27 morbidly obese patients.²⁶ Nine of these 27 individuals (five with low CoQ₁₀ levels) received 100 mg/day of CoQ₁₀ along with a 650 kcal/day diet. After 8-9 weeks, the mean weight loss in the CoQ₁₀-deficient group was 13.5 kg, compared with 5.8 kg in those with normal levels of CoQ₁₀.

One possible interpretation of this study is that about 50% of obese individuals are deficient in CoQ₁₀ and that replacement therapy accelerates weight loss during calorie restriction. However, it is also possible that CoQ₁₀ treatment had nothing to do with the accelerated weight loss. Obese individuals with low CoQ₁₀ levels may have other metabolic abnormalities which are more directly related to their obesity. A low CoQ₁₀ level might therefore have been an effect, rather than a cause, of the abnormalities that caused obesity. Until a controlled study is done to evaluate the effectiveness of this therapy, the potential value of CoQ₁₀ as a treatment for obesity remains speculative.

Physical Performance

Because CoQ₁₀ is involved in energy production, it is possible that supplementation might enhance aerobic capacity and muscle performance. In one study,²⁷ six healthy, sedentary men (mean age, 21.5 years) performed

a bicycle ergometer test before and after taking CoQ₁₀ (60 mg/day) for 4-8 weeks. CoQ₁₀ treatment improved certain performance parameters, including work capacity at submaximal heart rate, maximal work load, maximal oxygen consumption, and oxygen transport. These improvements ranged from 3-12% and were evident after about four weeks of supplementation. This study suggests that administration of CoQ₁₀ improves physical performance in sedentary individuals. The effect of CoQ₁₀ on the performance of trained athletes has not been studied.

Muscular Dystrophy

Biochemical evidence of CoQ₁₀ deficiency was found in cardiac and skeletal muscle of animals with hereditary muscular dystrophy.²⁸ In addition, treatment with CoQ₁₀ or its analogues increased survival and improved the performance of dystrophic mice, rabbits, and monkeys, as determined by a reduction of creatinuria, regaining of righting reflex, and weight gain.²⁹⁻³²

Deficiency of CoQ₁₀ has been found in muscle mitochondria of humans with muscular dystrophy.³³ This deficiency could conceivably be involved in the pathogenesis of cardiac disease, which occurs in virtually every form of muscular dystrophy and myopathy. In a double-blind study, 100 mg of CoQ₁₀ was given daily for three months to 12 patients with progressive muscular dystrophy. CoQ₁₀ treatment resulted in significant improvements in cardiac output and stroke volume, as well as increased physical well being in four of eight patients.³⁴ Subjective improvements included increased exercise tolerance, reduced leg pain, better control of leg function, and less fatigue. The mechanism of action of CoQ₁₀ is probably related to improved energy production in muscle cells.

Allergy

When passively sensitized guinea pig lung tissue was pre-incubated with CoQ₁₀, release of both histamine and slow-reacting substance of anaphylaxis induced by antigen challenge was markedly inhibited.³⁵ This study raises the possibility that CoQ₁₀ might be of value in the treatment of various allergy-related disorders. However, no clinical trials have been performed in this area.

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