Coenzyme Q\textsubscript{10} GEL IN PERIODONTAL DISEASES - A WONDERFUL REMEDY

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I. INTRODUCTION

Coenzyme Q\textsubscript{10} is also known as ubiquinone.[1] Perio-Q gel (Coenzyme Q\textsubscript{10} gel manufactured by PERIOQ INC, Manchester, USA), supplied as a pack of gel, contained a mixture of coenzyme Q\textsubscript{10} and vegetable glycerin base in a ratio of 1:9. The gel should preferably be used within 48 months from the date of manufacture and stored in a dry area away from sources of light and heat.

Chemical and physical properties.

Ubiquinone, chemically is 2,3-dimethoxy-5-methyl-6-polysoprene parabenoquinone. It is in its natural form an orange lipophile powder, without odour and taste. Because CoQ10 has 10 isoprenoid units – its name is coenzyme Q10. (2) Molecular weight of CoQ10 is 863.34 g/mol. It is not very stable and deteriorates at temperatures of about 46°C (US Patent 2005). It is a biologically active quinone; it comprises a benzoquinone ring with an isoprenoid side chain, related in structure to vitamin K and vitamin E [2].

Historical background-

In 1955, Festenstein et al. (1955), the scientists in Morton’s Laboratory in Liverpool (England) isolated an unsaponifiable lipid with a striking ultraviolet absorption at 272 nm from the intestinal mucosa of horses [3]. As the new substance was identified as a quinone and was found to be widely distributed in animal tissues, Morton named it ubiquinone (ubiquitous quinone – everywhere present quinone). Two years later in David Green’s Laboratory at the University of Wisconsin (USA), Crane et al. (1957) observed a novel quinone in the lipid extracts of mitochondria and named it coenzyme Q because of its participation in the electron transport chain [4]. One year later, the chemical structure of coenzyme Q10 (CoQ10) was reported by Wolf (Olson 2001), under Dr. Folkers at Merck Laboratories.

In 1963, Professor Yamamura from Japan was the first to use coenzyme Q7 in the treatment of a human disease: congestive heart failure. (5) Ernst (1977) from Sweden enlarged upon the importance of CoQ10 as an antioxidant and free radical scavenger.

II. MECHANISM OF ACTION

Periodontal disease is an inflammatory disease process resulting from the interaction of a bacterial attack and host inflammatory response. Arrays of molecules are considered to mediate the inflammatory response at one time or another, among these are free radicals and reactive oxygen species (ROS). Periodontal pathogens can induce ROS overproduction and thus may cause collagen and periodontal cell breakdown. When ROS are scavenged by antioxidants, there can be a reduction of collagen degradation. Ubiquinol (reduced form coenzyme Q\textsubscript{10}) serves as an endogenous antioxidant which increases the concentration of CoQ\textsubscript{10} in the diseased gingiva and effectively suppresses advanced periodontal inflammation. Bacteria possess several structurally different quinones, among which ubiquinone (UQ), menaquinone (MK) and dimethylmenaquinone (DMK) are the most common. These quinones are found in the cytoplasmic membrane, where they participate as electron carriers in respiration and in the disulfide-bond formation. UQ participates in aerobic respiration, whereas MK and DMK have roles in anaerobic respiration. UQ molecules are classified based on the length (n) of their isoprenoid side chain (UQ-\textsubscript{n}). For example, the main UQ species in humans is UQ-10, in rodents it is UQ-9, in Escherichia coli it is UQ-8 and, in Saccharomyces cerevisiae, it is UQ-6 in varying amounts. [6]

Human cells synthesize CoQ\textsubscript{10} from the amino acid tyrosine, in an eight-step aromatic pathway, requiring adequate levels of vitamins such as folic acid, niacin, riboflavin, and pyridoxine. [7]

III. DOSAGE

The optimal dose of coenzyme Q\textsubscript{10} is not known, but it may vary with the severity of the condition being treated. [1] Coenzyme Q\textsubscript{10} is available as a dietary supplement in strengths generally ranging from 15 to 100 mg. In cardiovascular disease patients, CoQ\textsubscript{10} dosages generally range from 100 to 200 mg per day.

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Dosages of up to 15 mg/kg/day are being employed in the case of mitochondrial cytopathy patients. A dosage of 600 mg per day was used in the Huntington’s disease trial whereas a dosage of up to 1200 mg per day was employed in the Parkinson’s disease trial.[8]

**CoQ10 in periodontitis -**

Chronic periodontitis is the direct result of accumulation of subgingival plaque. The microflora of this plaque is extremely complex causing problems in establishing which organisms are responsible for tissue destruction associated with the disease. Despite these problems, there is one point on which investigators agree, the subgingival flora of healthy gingival crevice is sparse and consists largely of aerobic and facultative bacteria, while in diseased state there is an increase in the proportion of anaerobic bacteria. These bacteria cause the observed tissue destruction directly by toxic products and indirectly by activating host defense systems, i.e. inflammation.[9]

However, an event characteristic of mammalian inflammation, tissue infiltration by polymorphonuclear leukocytes and monocytes and subsequent phagocytosis features non-mitochondrial O2 consumption, which may be 10 or 20 times that of resting consumption ultimately ends in generating free radicals (FRs) and reactive oxygen species (ROS), such as superoxide anion radicals, hydrogen peroxide, hydroxyl radicals, and hypochlorous acid, all capable of damaging either cell membranes or associated biomolecules [9]. Because of their high reactivity, several FRs and ROS can rapidly modify either small, free biomolecules (i.e., vitamins, amino acids, carbohydrates, and lipids) or macromolecules (i.e., proteins, nucleic acids) or even supramolecular structure (i.e., cell membranes, circulating lipoproteins). The type and the extent of damage depend upon the site of generation. Usually, the oxidative damage is perfectly controlled by the antioxidant defense mechanisms of the surrounding tissues but plaque microorganisms promoting periodontitis can unbalance this equilibrium. A massive neutrophil migration to the gingiva and gingival fluid leads to abnormal spreading of FR/ROS produced. Consequently, this led to a search for appropriate “antioxidant therapy” in inflammatory periodontal disease.[10]

A deficiency of coenzyme Q10 at its enzyme sites in gingival tissue may exist independently of and/or because of periodontal disease. If a deficiency of coenzyme Q10 existed in gingival tissue for nutritional causes and independently of periodontal disease, then the advent of periodontal disease could enhance the gingival deficiency of coenzyme Q10 [11]. In such patients, oral dental treatment and oral hygiene could correct the plaque and calculus, but not that part of the deficiency of CoQ10 due to systemic cause; therapy with CoQ10 can be included with the oral hygiene for an improved treatment of this type of periodontal disease.[11]

The specific activity of succinic dehydrogenase–coenzyme Q10 reductase in gingival tissues from patients with periodontal disease against normal periodontal tissues has been evaluated using biopsies, which showed a deficiency of CoQ10 in patients with periodontal disease. On exogenous CoQ10 administration, an increase in the specific activity of this mitochondrial enzyme was found in deficient patients.[11] The periodontal score was also decreased concluding that CoQ10 should be considered as an adjunct for the treatment of periodontitis in current dental practice.[12]

It suggested that the research literature on coenzyme Q10’s periodontal effect does not extend to International English language dental literature. The review of available literature does not give any ground for the claims regarding benefit of coenzyme Q10 and has no place in periodontal treatment.[13] A study evaluated the periodontium condition after oral applications of coenzyme Q10 with vitamin E. The total antioxidant status (TAS) in the mixed saliva by the colorimetric method was determined twice. The average value of plaque index decreased from 1.0 to 0.36, average value of interdental hygiene index was reduced from 39.51–6.97%, gingival index values decreased from 0.68 to 0.18, and the values of sulcus bleeding index decreased from 7.26 to 0.87. Periodontal pockets also shallowed by 30%. The laboratory examination result improved by 20%. It concluded that coenzyme Q10 with vitamin E had a beneficial effect on the periodontal tissue.[14]

Because it is an antioxidant, coenzyme Q10 has received much research attention in the medical literature in the last several years. Although coenzyme Q10 may have been viewed as an alternative medication, it is used routinely, both topically and systemically, by many believing dentists and periodontists.

**Mode of application in periodontitis patients -**

Topical application with the tip of the applicator completely soaked in gel and applied to the assigned quadrant. Intrapocket application with help of irrigation needles to deliver the gel in the intrapocket. Subgingival administration by inserting the syringe to the base of the periodontal pocket first and then placing the gel while working the way up, until the gingival margin.
CoQ10 linked with systemic health:

**CoQ10 and cardiovascular diseases.** CoQ10 is known to be highly concentrated in the heart muscle cells due to the high energy requirements. Specifically, congestive heart failure (from a wide variety of causes) has been strongly correlated with significantly low blood and tissue levels of CoQ10. The heart failure was found to correlate with the deficiency of CoQ10, which may well be the primary etiologic factor in some types of heart muscle dysfunction, while in others it may be a secondary phenomenon. The treatment with CoQ10 significantly improved the heart muscle function while producing no adverse effects or drug interactions. There are many studies reporting positive results of oral administration of CoQ10 as adjunctive therapy in the treatment of congestive heart failure (Kaikkonen et al. 2002; Gazdik et al. 2003) [15]. In Japan and other countries, CoQ10 is an approved treatment for several cardiovascular conditions. CoQ10 may be useful in treating congestive heart failure as well as other heart conditions (Folkers et al. 1992 [16]).

**CoQ10 and hypertension.** Mortensen (1993) found that the addition of 120 mg/day of CoQ10 to conventional medical therapy for 8 weeks in patients with hypertension and coronary artery disease decreased systolic blood pressure by an average of 12 mm Hg and diastolic blood pressure by an average of 6 mm Hg as compared to a placebo containing B-complex vitamins. In patients with isolated systolic hypertension, the supplementation with 120 mg per day of coenzyme Q10 and 300 IU/day of vitamin E for 12 weeks resulted in an average decrease of 17 mm Hg in systolic blood pressure compared with 300 IU/day of vitamin E alone [17].

**CoQ10 and cancer.** CoQ10 may also have potential as an anticancerogenic and immune-stimulating agent. CoQ10 in conjunction with conventional medical treatment and other antioxidant nutrients showed an increased survival rate and regression of cancer incidence. Numerous studies have noted the incidence of CoQ10 deficiency in a variety of cancers including breast, lung, prostate, pancreatic, and colon cancer (Lockwood & Mosegaard 1994; Folkers & Osterborg 1997) [18].

**CoQ10 and bronchial asthma.** CoQ10 may be helpful in the treatment of respiratory diseases, especially asthma. Gazdik et al. (2002) described significantly decreased levels of CoQ10 and α-tocopherol both in plasma and blood in patients with bronchial asthma, as compared with healthy subjects [19].

**CoQ10 and diabetes.** The role of CoQ10 in the energy formation also relates to how the body uses carbohydrates. Preliminary research suggests that a close relative of this nutrient lowered blood sugar levels in a group of people with diabetes. People with type 2 diabetes were found to have significantly lower blood levels of CoQ10 as compared with healthy people (Miyake et al. 1999). [9]

**CoQ10 and renal failure.** CoQ10 was studied in a small pilot study involving 21 patients with chronic renal failure. Researchers administered CoQ10 to 11 of the subjects while 10 received placebo capsule. After 4 weeks the number of patients on dialysis was significantly lower in the CoQ10 group (36.2%) while 90.0% of patients in the placebo group were on dialysis at the end of the study (Singh et al. 2000). [20]

**CoQ10 and Parkinson disease.** CoQ10 showed some promise for slowing down the progression of Parkinson’s disease in the early stage (Muller et al. 2003). The research by Schultz showed that mitochondrial function is impaired in patients with Parkinson’s disease and CoQ10 levels are reduced in the mitochondria of Parkinsonian patients[21]

**CoQ10 and rheumatoid arthritis.** By a study of Bauerova and Bezek (1999) and that of Jaswal et al. (2003), oxidative stress is one of the primary factors involved in the pathogenetic changes during rheumatoid arthritis. Antiinflammatory treatment affecting the level of CoQ10 was found able to slowdown the progression of this disease (Comstock et al. 1997; Knekt et al. 2000). [22]

**IV. CONCLUSION**

The concept of ROS-induced destruction has led to search for an appropriate complimentary antioxidant therapy in the treatment of numerous diseases including inflammatory periodontal diseases. Because it is an antioxidant, there is a dearth of new information for coenzyme Q10 in the treatment of periodontal conditions. The pharmacology of coenzyme Q10 indicates that it may be an agent for treatment of periodontitis. Coenzyme Q10 has received much research attention in the medical literature in the last several years. Although coenzyme Q10 may have been viewed as an alternative medication, it is used routinely, both topically and systemically, by many dentists and periodontists.
More researches are needed to examine the appropriate dose, effectiveness, and bioavailability of orally-administered and topically-administered coenzyme Q10.

REFERENCES:


