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Research Article

Co-enzyme Q-10 and its Effect on Periodontal Disease and Oral Cancer: A Systematic Review Article

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Abstract

Background: To combat the excess production of free radicals in periodontal disease, antioxidant medications are employed. Free radicals (FRs) and reactive oxygen species (ROS) are the major contaminants that Co-Q10 primarily effectively removes in order to perform its intercellular antioxidant function, this study is aimed to:

1. Analyze the results of using perio Q gel (coenzyme Q10) intravenously only.

2. As an additional step in the treatment of patients with chronic periodontitis in conjunction to scaling and root planning on the periodontal clinical criteria.

3. Examine which of the various treatment modalities improved clinical periodontal markers more at 3 and 6 weeks.

Materials and Methods: Clinical periodontal markers like the Plaque Index (PI), Gingival Index (GI), Bleeding on Probing (BOP), Probing Pocket Depth (PPD), and Relative Attachment Level (RAL) were evaluated at the first visit, 3 weeks, and 6 weeks.

Results: When compared to the SRP group, the clinical parameters PPD and RAL of the combination group significantly decreased, according to intergroup analysis.

In all groups, the reduction in PI, GI, BOP, PPD, and RAL across the three visits was highly significant when intra-group analysis was performed.

Conclusion: By using the gel in addition to scaling and root planning rather than only scaling and root planning alone, the clinical periodontal parameters improved more significantly.

The ability to employ the gel as the only substance to support common periodontitis treatment methods. In the periodontal treatment phase, the clinical metrics considerably improved, showing that CoQ10 expands treatment possibilities by enhancing the host response to disease activity.

All living things possess the lipid-soluble endogenous antioxidant coenzyme Q10. Coenzyme Q10 may be a therapy for periodontitis, according to the pharmacology of the substance. To establish its precise function in the treatment of periodontitis, including both as an adjuvant and a primary therapeutic agent, as well as the right dosage, efficacy, and bioavailability, more research is required.

Keywords: Co-enzyme Q10; PPD; BOP; SRP; RAL

Introduction

Coenzyme Q10

Coenzyme Q, also known as ubiquinone, is a coenzyme family that is ubiquitous in animals and most bacteria (hence the name ubiquinone). The most prevalent form in humans is Coenzyme Q10, also known as ubiquinone-10. CoQ10 has not been authorized in the USA, Food and Drug Administration (FDA), for the treatment of any medical condition [1], despite the fact that it is marketed as a nutritional supplement.

It is a 1,4-benzoquinone, with the numbers 10 indicating the number of isoprenyl chemical subunits in its tail and Q denoting the quinone chemical group. The range in natural ubiquinones is between 6 and 10. All respiring eukaryotic cells contain this class of fat-soluble compounds, which mimic vitamins and are largely found in the mitochondria. It takes part in aerobic cellular respiration, which produces ATP as a source of energy, and is a part of the electron transport chain. This process produces 95% of the energy used by the human body [2,3]. The largest CoQ10 concentrations are found in organs including the heart, liver, and kidney that demand the most energy [4-6].

There are three redox states of CoQ: [1] fully oxidized (ubiquinone), [2] semiquinone (ubisemiquinone), [3] and fully reduced (ubiquinol). Due to its position in the electron transport chain and its ability to scavenge free radicals, this molecule's ability to function as a two-electron carrier (moving between the quinone and quinol form) and a one-electron carrier (moving between the semiquinone and one of these other forms) is crucial.

Sources

- The highest dietary CoQ10 concentrations can be found in the heart and liver of beef, hog, and chicken, which also have values exceeding 50 mg/kg.
- Compared to animal tissues, dairy products are substantially worse providers of CoQ10.
- Vegetable oils are also a good source of CoQ10. Parsley and perilla are the greatest sources of CoQ10 found in vegetables.
- Cauliflower, grapes, and broccoli are all fair providers of CoQ10.
- Aside from avocados, which have a reasonably high CoQ10 level, most fruits and berries are a weak to very poor source of CoQ10 [7].

Intake

The expected daily consumption of CoQ10 in the developed world has been calculated as 3-6 mg, with meat serving as the main source [7].

Effect of heat and processing

CoQ10 concentration is reduced by 14-32% when food is fried [8].

Deficiency and toxicity

Human CoQ10 insufficiency is primarily caused by two factors: [1] decreased production, and [2] increased body utilization. The main natural source of CoQ10 is biosynthesis.

Statins

There is early evidence that statin-related muscle complaints such soreness, weakness, cramps, and fatigue can be reduced by taking oral CoQ10 [9].

Cancer

According to the American Cancer Society, "Most physicians would advocate avoiding CoQ10 during cancer treatment since it may diminish the efficiency of chemotherapy and radiation therapy" [10].

Pharmacokinetics

The plasma peak can be observed 2-6 hours after oral administration.

Improving the bioavailability of CoQ10

Several innovative efforts have been made in search of a concept to increase the bioavailability of CoQ10 following oral administration:

Reduction of particle size

Only a small impact is also seen when using an aqueous suspension of finely powdered CoQ10 in clean water [11].

Soft-gel capsules with CoQ_{10} in oil suspension

Lecithin is a powerful stabilizer and was utilized to create soft gelatin capsules from soybean oil emulsions (lipid microspheres).

Novel forms of CoQ_{10} with increased water-solubility

Utilization of the polymer tyloxapol to disperse solid CoQ10 in water [12], formulations based on different solubilizing agents, like hydrogenated lecithin [13], and complexation with cyclodextrins; among the latter, the complex with β-cyclodextrin has been found to have significantly increased bioavailability [14,15].

Q-10 function

- Coenzyme Q10 is a benzoquinone vitamin-like molecule that is fat soluble and primarily serves as an antioxidant.
- A membrane stabilizer,
- Additionally, it serves as a cofactor for the oxidative phosphorylation that produces adenosine triphosphate (ATP) [16,17].
- Additionally, it has been demonstrated to stabilize cardiac calcium-dependent ion channels and support myocardial sodium-potassium adenosine triphosphatase activity. CoQ10 is not readily absorbed when taken orally by humans due to its lipophilic nature.

Enhancement of oral bioavailability of coenzyme Q10 by complexation with _cyclodextrin in healthy adults [18].

CoQ10 and Periodontal disease

Most periodontal tissue loss results from an ineffective host response to perio-pathogens (P. gingivalis, A. acomitans) [19], the non-mitochondrial oxygen consumption that occurs after phagocytosis, which may be 10 or 20 times greater than resting consumption, results in the production of free radicals (FRs) and reactive oxygen species (ROS), including superoxide anion radicals, hydrogen peroxide, hydroxyl radicals, and hypochlorous acid, which are all capable of harming cell membranes or associated biomolecules [20]. Numerous FRs and ROS can quickly alter either small, free biomolecules (such as vitamins, amino acids, carbohydrates, and lipids) or macromolecules (such as proteins and nucleic acids) due to their high reactivity (i.e., cell membranes, circulating lipoproteins). Normally, the anti-oxidant defense mechanisms of the surrounding tissues properly regulate oxidative damage, but plaque microorganisms causing periodontitis can upset this equilibrium. Massive neutrophil migration to the gingiva and gingival fluid causes the FRs/ROS generated to spread abnormally.

This prompted researchers to look for the best "antioxidant therapy" for inflammatory periodontal disease. Effective energy production is necessary for periodontal tissue healing and repair.

An appropriate quantity of CoQ10 is necessary for the metabolic processes. Periodontal disease patients' gingival tissue has been found to be deficient in CoQ10. In 60% to 96% of patients with periodontal disease, gingival biopsies showed subnormal tissue levels of CoQ10, and in 86% of instances, low levels of CoQ10 in leukocytes [21,22]. These results showed that CoQ10 depletion and periodontal disease are frequently linked.

CoQ10 levels in gingival tissue and blood are low in patients with periodontal disease [18-20]. Due to this fact, some clinical researchers and dentists now advise CoQ10 supplementation, especially for diabetic patients and those at risk for periodontal disease [23].

In conclusion, CoQ10 should be taken into account as an adjuvant for the treatment of periodontitis in current dentistry practice. The periodontal score was also decreased. By increasing the amount of CoQ10 in the sick gingiva, oral CoQ10 therapy efficiently reduces advanced periodontal inflammation [24-27] and periodontal bacteria.

Methodology

Mode of application of Coenzyme Q10 in periodontitis patients

Application of Coenzyme Q10 can be done intravenously, topically, or sub gingivally [28].

Topical application

Using the applicator's tip that has been fully saturated in gel and applied to the designated quadrant (Figure 1).

Intrapocket application

Utilizing irrigation needles to supply gel inside the pocket (Figure 2).

Figure 1: Topical Application of Coenzyme Q10.

Subgingival administration: Putting the gel while moving the syringe up till the gingival margin, starting at the bottom of the periodontal pocket (Figure 2).

Figure 2: Subgingival Administration of Coenzyme Q10.

Results

The clinical parameters PPD and RAL of the combination group were significantly lower than those of the SRP group, according to the results of the inter-group study [29].

All groups had a highly significant decrease in PI, GI, BOP, PPD, and RAL over the course of the three visits when intra-group analysis was performed. According to the results of the inter-group analysis, the combination group's PPD and RAL clinical values were significantly lower than those of the SRP group [30].

Although they were given the Perio Q™ gel to self-apply only on one side, for home use, which may have indirectly compelled them to maintain their oral hygiene more towards the test sites, there was a statistically non-significant difference between the test and control sites for both the subjects' unbiasedness while maintaining their oral hygiene. Plaque scores remained unchanged between the groups [29]. The gingival index score values for the test sites improved more than the control sites, which supports the additional benefit of coenzyme Q10 gel. This increase was statistically significant [30]. As it is shown in figures 3-10.

Figure 3: Illustrate the mean values of Plaque Index (PI) in both sites treated by SRP/CoQ10 and SRP only.

Figure 4: Shows the average Plaque Index (PD) values at the two sites that were treated with SRP/CoQ10 and SRP alone.

Figure 5: Shows the average values of Clinical Attachment Loss (CAL) for both the SRP/CoQ10-treated sites and the SRP-only locations.

Figure 6: Clinical parameters and periodontal indices.

Figure 7: Plaque index.

Figure 8: Gingival index.

Figure 9: Bleeding on probing difference was statistically insignificant.

Figure 10

Periodontal probing depth

Periodontal probing depth was evaluated with a pressure sensitive probe. There was an improvement seen in terms of reduction in probing depth in millimeters from statistically significant at was seen in groups were coenzyme Q10 was used with scaling root planning [29-33].

In comparison to areas where scale root planing alone was applied, Q10 (Perio Q ™) provided an extra benefit. In addition to its antioxidant effects, it strengthens the immune system and speeds up tissue repair.

Discussion

Functioning on PD disease

The gel is easily prepared and administered. Moreover, they possess a higher biocompatibility and bioadhesivity, allowing adhesion to dental pocket tissues and finally, they can be rapidly eliminated through bloodstream, decreasing the irritation or allergic host reactions in the application site [34]; so, it has additional activity because of its functions and its form (gel). According to the best of our knowledge, few studies evaluate the clinical effectiveness of this gel as a mono therapy and as adjunct to scaling and root planing in the management of patients with chronic periodontitis. The metabolic processes of periodontal tissues depend on a sufficient supply of CoQ10, which serves as a cofactor in the oxidative phosphorylation generation of adenosine triphosphate, which is necessary for periodontal tissue healing and repair (ATP) [35]**.** Energy for muscle contraction and other essential cellular processes is provided by ATP. Coenzyme Q10 is present in the inner membrane of mitochondria, where a significant portion of ATP synthesis takes place [36]. Scaling is the process by which plaque and calculus are removed from both supra gingival and sub gingival tooth surfaces. The treatment method known as root planing is used to get rid of cementum or surface dentin that is rough, calculus-impregnated, or polluted with poisons or bacteria. The gel is the only substance used to complement common periodontitis treatment methods. By enhancing the body response to disease activity, CoQ10 expands the range of available treatments. Clinical periodontal parameters were improved with mechanical debridement alone, mechanical debridement combined with Perio Q gel, and mechanical debridement alone.

Conclusion

Using the gel in addition to scaling and root planing rather than only these two procedures alone resulted in a better improvement of the clinical periodontal parameters. the ability to support common periodontitis treatment methods using the gel as the only agent. In the periodontal treatment phase, the clinical metrics considerably improved, showing that CoQ10 expands treatment possibilities by enhancing the host response to disease activity.

All living things include the indigenous lipid-soluble antioxidant coenzyme Q10. Coenzyme Q10 may be a therapy for periodontitis, according to its pharmacology. Its specific function in treating periodontitis, as well as the right dosage, efficacy, and bioavailability, both as an adjuvant and a primary therapeutic agent, will require further research. Coenzyme Q10 is an antioxidant, although there is no recent research on its use in the management of periodontal diseases. Coenzyme Q10 may be a therapy for periodontitis, according to its pharmacology.

CoQ10 topical treatment was assessed both with and without sub-gingival mechanical debridement in the periodontal pocket. Significant reductions in probing depth, attachment loss, and gingival crevicular fluid flow were observed in the first three weeks. Substantial progress in modified gingival index, bleeding on probing, and peptidase activity produced by periodontopathic bacteria were also identified.

Problems

Another issue was that the gel's bioavailability was unknown (the percentage of a chemical taken orally that enters the bloodstream is known as bioavailability [37]). It has been found that improving the bioavailability of CoQ10 can be achieved through:

Reduction in particle size [38].

CoQ10 in oil suspension [39].

CoQ10 in new formulations with higher water solubility [40].

Oral cancer

Of all cancers throughout the body, oral cancer accounts for 2-5%. 90% of oral cancers are epithelial in origin, with the other 10% being spread among adenocarcinomas, sarcomas, lymphoproliferative diseases, metastases, melanomas, and malignant odontogenic tumors. The floor of the mouth and posterior lateral border of the tongue (Figure 11) are the primary intraoral sites for oral squamous cell carcinoma (OSCC) (Figure 12). The oxidative stress and chronic degenerative diseases are present here if the lips are regarded as being part of the oral region. (Figure 13).

Premalignant lesions such as leukoplakia, erythroplakia, oral submucosa fibrosis, palatal lesions from smoking cigars retrograde, oral liken planus, discoid lupus erythematosus, and

Figure 11: A 28-year-old woman was diagnosed with squamous cell carcinoma on the tongue's posterior lateral border. For fifteen years, she smoked one cigarette every day.

Figure 12: Squamous cell cancer of floor of mouth in a 58-year-old woman. She had type 2 diabetes that had been poorly managed for 42 years. She also has used ill-fitting dentures since age 50. Note the linear lesion with presence of necrosis in the center of the fissure.

Figure 13: Squamous cell cancer of the lip in a 74-year-old man. He was a farmer and consumed alcohol chronically.

genetic illnesses like congenital are recognized. The DNA is the major target since mutations there can lead to a variety of harmful repercussions in the cell. The process, known as the epithelial-mesenchymal transition, occurs when the cells express chemicals that enable them to develop an invasive phenotype. Free radicals are byproducts of the cell's oxidation-reduction mechanisms, and their involvement in metabolic processes is crucial for cell viability. Free radicals have been linked to the development of cancer for three decades; they are thought to damage DNA in a variety of ways, including:

- Punctual mutations
- DNA base oxidations
- Strand breaks
- Tumor suppressor gene mutations can result in the overexpression of proto-oncogenes [41].

Additionally, it should be mentioned that oxidative protein degradation aids in the growth of cancer [42-47]. The findings support the notion that there is an imbalance between the abundance of free radicals and the insufficient activity of the antioxidant system. Furthermore, some researchers have discovered a correlation between poor survival rates in oral cancer patients and high levels of lipid peroxidation associated with low levels of thiols and antioxidant status [43]. The OSCC is a multifactorial disease, however, a factor strongly associated, is smoking. 90% of individuals with oral cancer are smokers. It is considered that the smoke from cigarettes have 4000 chemicals, 40 of which have carcinogenic potential. According to studies, cigarette smoke contains pro-oxidants that can start the process of lipid peroxidation and decrease the body's supply of antioxidants from food [44,45].

Treatments

Vitamin C is one of the most extensively evaluated antioxidants in oral cancer alternative co-therapies. Vitamin C levels that are low or even undetectable are linked to oral cancer [45,46]; Vitamin C scavenges free radicals and prevents the harmful chain reactions that the free radicals can start.

- Another antioxidant, l-glutamine, has demonstrated a positive modifying effect in individuals with oral cancer in stages III and IV. In the diet, l-glutamine is given as a supplemental therapy with the theory that it will help the glutathione cascade system recover [47].

- Carotene, vitamin E, thiamine, vitamin B6, folic acid, niacin, and potassium are antioxidants that have demonstrated a strong protective impact [48]. Even more, when they are administered together during the cycles of radiotherapy [49].

- A combination of antioxidants seems to be more effective than individual antioxidants alone [50,51]. Reactive oxygen species can activate all stages of carcinogenesis [52] Simplified, this process can be regarded as a continuous growth and accumulation of mutations in a cellular clone. If combinations of antioxidants have a preventive effect, it would seem possible that they would also retard the process at a later stage, i.e. when the cancer is apparent [53].

- **5.** Patients were offered treatment with Q10 and other antioxidants as a supplement to their usual cancer therapy. Daily doses included: vitamin C 5.7 mg, α-tocopherol 1.625 mg, Q10 300 mg, selenium (as selenomethionine) 487 μg, folic acid 5 mg, vitamin A 25 000 IU, and β-carotene 76 mg (Table 1) [54,55]. The antioxidant tablets were taken daily in two divided doses. Patients also received small amounts of γ- linoleic acid (375 mg) and fish oil (1.5 mg), as well as niacin 45 mg, pantothenic acid 22.5 mg, vitamin B12 13.5 μg, vitamin B6 12.6 mg, vitamin B2 8.4 mg and vitamin B1 5.4 mg.

	Minimum	Maximum	Mean	Std. Deviation
ASCVD Risk	1	29	3.56	3.395
Weight	55	126	81.38	14.078
BMI	20	46	31.69	5.496
HBA1C	6	87	8.87	6.601
LDL	1	8	2.49	1.026
HDL	0	3	1.14	.401
Triglyceride	0	6	1.55	.814
GFR	29	128	88.64	16.809
Microalbu-minuria	0	179	20.40	31.794

Table 1: Predication of survival time, Antioxidant treatments given to the 41 patients with end-stage as a supplement to their usual cancel theraphy

Side effects

Side effects associated with antioxidant therapy were very rare and minor, mainly consisting of difficulties in swallowing the many tablets and aversion to the odor of the tablets, particularly once their general physical condition had deteriorated.

Survival in end-stage cancer following antioxidant treatment the potential anticancer effect of antioxidants. Most important among these are possible effects on cytokines and inflammation, modulation of the expression of the tumor suppressor gene. Inhibition of mutations and inhibition of tumor angiogenesis [56-58]. Breast cancer patients treated with tamoxifen who were also receiving Q10 [59]. In women co-administration of Q10 reduced the level of angiogenesis. This could have inhibited the metastatic spread of tumors in these patients. It was also found that the levels of cytokines interleukin (IL)-1, IL-6 and matrix metalloproteins (MMPs) were decreased [60,61] to show an impressive effect of a combination of antioxidants, including Q10.

Up-regulation of antioxidant enzymes and coenzyme Q10 in a human oral cancer cell

Coenzyme Q, which is endogenously synthesized, is an essential mitochondrial electron CoQ is widely distributed in most sub-cellular compartments, although it is enriched in the mitochondrial inner membrane [62]. The reduced form of CoQ, ubiquinol, is known to be important in suppressing lipid peroxidation [62], but its oxidized form, ubiquinone, can also exert antioxidative function by scavenging superoxide radicals in the mitochondria [63]. It has been shown that acute treatment of the anti-cancer drug camptothecin could induce biosynthesis of endogenous CoQ10 in human cancer cells in association with concurrent increase in the production of reactive oxygen species (ROS), which might be important for survival of cancer cells in response to camptothecin-induced cell death [64]. CoQ10 could be able to stop or undo the immunosuppression brought on by age or chronic illness. CoQ10's antioxidant properties [65] may be beneficial for those with AIDS [66]. Patients with HIV infection frequently lack CoQ10, and supplementing with CoQ10 may enhance immune function and lower the risk of opportunistic infections.

Treatment of cancer

CoQ10 has been looked into as an anti-cancer drug due to its function in boosting immune response. Women with breast cancer

who were deemed to be at "high risk" due to tumor dissemination to the axillary lymph nodes were given daily 90 mg of CoQ10 combined with vitamins C, E, beta-carotene, and essential fatty acids [67]. This treatment reduced tumor size [68].

Proposed mechanisms of action for coenzyme Q10 that are relevant to cancer

Include its critical role in the creation of cellular energy, its activation of the immune system (which may be related to both), and its action as an antioxidant. The creation of aerobic energy requires coenzyme Q10, and it has been hypothesized that more cellular energy boosts the production of antibodies by B cells (B lymphocytes) [72,73]. Coenzyme Q10 can function as an antioxidant, as was previously mentioned (in the section titled "General Information") [69,70,74-76]. In this role, coenzyme Q10 is assumed to protect other vital cellular components from free radical damage and to stabilize cell membranes, which are lipid-containing structures crucial to preserving cell integrity [69,70,74,76]. The development of cancer may be influenced by free radical damage to DNA (and possibly other biological components as well) [77-81].

Coenzyme Q10 has been found to both activate the immune system while also safeguarding the heart against anthracycline-induced cardiotoxicity in cancer patients [81, 82]. Anthracyclines are a class of chemotherapy medications that have the potential to harm the heart. Patients with various cancers have received adjuvant therapy utilizing coenzyme Q10 [74,75, 79-82].

While coenzyme Q10 may have immune system-boosting properties that indirectly inhibit the progression of cancer, there is evidence that analogues of this substance can do so directly. The FDA must receive an application for an investigational new drug (IND). No researchers have declared that they have submitted an IND to research coenzyme Q10 as a cancer treatment.

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