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A comparative evaluation of topical and intrasulcular application of coenzyme Q10 (Perio Q™) gel in chronic periodontitis patients: A clinical study

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Abstract

Background and Objectives:

Coenzyme Q10 is a well-studied antioxidant in the medical literature, but studies regarding its efficacy in periodontal diseases are few. Coenzyme Q10 serves as an endogenous antioxidant and its increased concentration in the diseased gingiva effectively suppresses advanced periodontal inflammation. The aim of this study is to evaluate the efficacy of coenzyme Q10 (Perio Q™) as an adjunct to scaling and root planing in patients with chronic periodontitis.

Materials and Methods:

A total of 18 patients were enrolled for the study. The selected subjects were treated in three different quadrants randomly. The control quadrant was treated by scaling and root planing only, while the other two test quadrants were treated by intra-pocket application of gel combined with scaling or root planing and topical applications combined with scaling and root planing, respectively. Clinical parameters such as plaque index, gingival index, gingival bleeding index and probing pocket depth were assessed at baseline and at the 2nd week and 4th weeks. The results were subjected to statistical analysis.

Results:

There was a significant improvement in all clinical parameters in the test sites seen at the end of the 4-week period. Sites with bleeding on probing were reduced more in the test group than in the control group.

Conclusion:

Coenzyme Q10 can be said to have a beneficial effect on periodontitis when used as an adjunct to scaling and root planing.

Keywords: Antioxidants, coenzyme Q10, chronic periodontitis, inflammation, reactive oxygen species

INTRODUCTION

Periodontitis is an immuno-inflammatory disease process resulting from the interaction of a bacterial attack and host inflammatory response, causing inflammation of the supporting tissues of the teeth leading to tissue destruction and tooth loss. Arrays of molecules are considered to mediate the inflammatory response at one time or another, among these is free radicals (FRs) and reactive oxygen species (ROS) like superoxide anion radicals, hydrogen peroxide, hydroxyl radicals and hypochlorous acid. All these molecules are capable of damaging either cell membranes or associated bio-molecules. Periodontal pathogens can induce ROS overproduction and thus may cause collagen and periodontal cell breakdown. When ROS are scavenged by antioxidants, there is a reduction of collagen degradation.^[1] Oxidative stress arises within tissues when the normal balance between ROS generation and antioxidant defense shifts in favor of the former, a situation arising

from either an excess of ROS and/or a depletion of antioxidants.

There has been a tremendous expansion in dental research concerned with free radicals, ROS and anti-oxidant defense mechanisms. These are essential to many normal biological processes and low doses of certain radicals or radical-derived species can stimulate the growth of fibroblasts and epithelial cells in culture. A low FR/ROS often behaves as an inductor stimulus, whereas higher levels may result in injury. It may be necessary to deliver anti-oxidants selectively to specific cell types and to define the concentrations suitable for blocking inappropriate cell responses but leaving the unimpaired physiological levels of FR/ROS activity necessary for normal cell function.[2]

Coenzyme Q10 was discovered in beef heart mitochondria at the University of Wisconsin.[3] coenzyme Q10 is also known as ubiquinone because of its ubiquitous presence in nature and its quinone structure (similar to that of vitamin K).[4] It is also called as “coenzyme” because of its unique ability to participate in chemical reactions but remain at steady-state levels in the cell, and plays a central role in energy metabolism. It has a positive inotropic effect.[5]

The effects and mechanisms of action of CoQ10 include stabilization of calcium-dependent channels, inhibition of intracellular phospholipases, prostaglandin metabolism, free-radical scavenging and direct membrane stabilization.[6]

CoQ10 is also known to play a crucial role in the generation of adenosine triphosphate (ATP) and cellular respiration. It exists in two molecular forms, ubiquinone, the oxidized form, and ubiquinol, the reduced form, which are the basis for its antioxidant properties.[7] Co-Q10 functions as an intercellular antioxidant by acting as a primary scavenger of FRs and ROS. It serves as an endogenous antioxidant, and its increased concentration in the diseased gingiva effectively suppresses advanced periodontal inflammation.

A deficiency of coenzyme Q10 in the gingival tissue may exist independently of and/or because of periodontal disease. If a deficiency of coenzyme Q10 existed in the gingival tissue for nutritional causes and independently of periodontal disease, then the advent of periodontal disease could enhance the gingival deficiency of coenzyme Q10. In such patients, oral dental treatment and oral hygiene procedures can remove the local factors only but cannot correct the deficiency of CoQ10 due to systemic cause. Thus, mechanical periodontal therapy along with the adjunctive use of CoQ10 can be included for an overall improvement of the gingival health in periodontal disease.[8] The present study was designed with the aim to evaluate the efficacy of coenzyme Q-10 gel application in the treatment of chronic periodontitis.

MATERIALS AND METHODS

This was a randomized, controlled, clinical trial with a split-mouth design. A total of 18 patients were selected from the Outpatient Department of Periodontology. Ethical clearance was obtained from the institutional ethical committee. Systemically, healthy patients in the age group of 20-55 years of both the genders (mean age 33.8 years) who were diagnosed with chronic periodontitis by their clinical and radiographic findings were included in the study. Written and verbal consent was obtained from the sample recruited for the study.

Patients suffering from chronic periodontitis and having a probing pocket depth of ≥ 5 mm in different quadrants (having a minimum of six permanent teeth in each quadrant) of the mouth with radiographic evidence of bone loss were included in the study [Figures 1–3].

Patients with a history of any systemic diseases, any apparent oral infection like herpes or candida, patients who had taken antibiotic therapy in the past 3 months or undergone any periodontal therapy in the past 6 months, smokers, pregnant women and lactating mothers were excluded from the study.

Perio Q gel (Perio Q™) is a mixture of CoQ10 in a vegetable oil base in ratio of 1:9 and is supplied as a pack of gel [Figure 4], and was stored at a temperature between 4 and 8°C to maintain its shelf-life.

In this study, three quadrants were assigned randomly in each patient: Group I: Scaling and root planning only (Control group); Group II: Scaling and root planing and topical application of Perio Q gel (Test group A); Group III: Scaling and root planing and intrapocket Perio Q gel application (Test Group B) [Figures 5 and 6].

All the clinical parameters, i.e. plaque index,[9] gingival index,[10] modified sulcular bleeding index and probing pocket depth were recorded at baseline and at the 2nd week and 4th week after treatment.

At the baseline, scaling and root planing were performed in all the groups and in Group II, the topical application of gel was performed with the tip of the applicator completely soaked in gel. Intrapocket application was performed in Group III using special needles designed to deliver gel in the pocket. Patients were recalled every alternate day for the application of gel for 1 week. Eating, spitting and drinking were restricted for 1 h after application. Patients were recalled at the 2nd and 4th weeks after treatment to record all the clinical parameters [Figure 7].

RESULTS

The ANOVA test was employed for plaque index, gingival index, gingival bleeding index and probing pocket depth. A comparison of the mean plaque index, gingival index, gingival bleeding index and probing pocket depth among all the three groups at the observational period of 2nd and 4th weeks showed statistically significant results ($P < 0.01$) [Tables 1–4].

Plaque index

There was a statistically significant improvement in the plaque index from baseline to the 4th week revaluation in Groups I-III [Table 1]. For Group I, the plaque index was reduced from the baseline value of 1.72 ± 0.492 to 0.96 ± 0.274 ($P < 0.0001^*$), and for Groups II and III, it was reduced from 1.93 ± 0.468 to 0.61 ± 0.230 and 1.69 ± 0.424 to 0.48 ± 0.148 ($P < 0.0001^*$), respectively.

Gingival index

The gingival index scores were significantly improved from baseline to the 4th week revaluation [Table 2]. For Group I, the gingival index scores was reduced from 1.64 ± 0.422 to 0.63 ± 0.366 ($P < 0.0001^*$), and for Groups II and III, it was reduced from 1.82 ± 0.391 to 0.5 ± 0.227 and 1.96 ± 0.57 to 0.57 ± 0.397 ($P < 0.0001^*$), respectively.

Gingival bleeding index

Similarly, for Group I, the bleeding scores were improved significantly from 1.93 ± 0.329 to 1.06 ± 0.107 ($P < 0.0001^*$), and for Groups II and III, it was reduced from 1.88 ± 0.261 to 1.01 ± 0.059 and 1.82 ± 0.341 to 1 ± 0 ($P < 0.0001^*$), respectively [Table 3].

Probing pocket depth

Improvement in probing pocket depth from baseline to the 4th week was also significant. For Group I [Table 4], it was reduced from 5 ± 0.84 to 3.66 ± 0.686 ($P < 0.0001^*$), and for Groups II and III, it was reduced from 5.72 ± 0.57 to 3.72 ± 0.826 and 6.33 ± 1.085 to 3.72 ± 0.826 ($P < 0.0001^*$), respectively.

Thus, there was a more significant improvement in all the clinical parameters among Groups II and III as compared with Group I at the 2nd - and 4th -week revaluations.

DISCUSSION

Periodontal disease affects 60% of the young adults and 90% of individuals over the age of 65 years. Healing and repair of periodontal tissue requires efficient energy production, and the metabolic functions of the periodontal tissues depend on an adequate supply of CoQ10.[3] Gingival biopsies revealed subnormal tissue level of CoQ10 in 60–96% patients with periodontal disease, indicating that periodontal disease is frequently associated with CoQ10 deficiency.[3]

Physiologically, CoQ10 plays four major roles. It has an essential role in mitochondrial energy (ATP) production through redox activity in the respiratory chain, transporting electrons between enzymes. Second, it plays a role in extra-mitochondrial redox activity in the cell membrane and endo-membranes. CoQ10 also functions as an antioxidant, inhibiting lipid peroxidation and scavenging FRs. Finally, it plays an important role in membrane stabilization and fluidity.[4]

The antioxidant nature of CoQ10 is derived from its energy carrier function. As an energy carrier, the CoQ10 molecule is continuously going through an oxidation–reduction cycle. CoQ10 inhibits lipid peroxidation by preventing the production of lipid peroxyl radicals. In addition, the reduced form of CoQ10 effectively regenerates vitamin E from the α -tocopheroxyl radical. Furthermore, during oxidative stress, interaction of H_2O_2 with metal ions bound to DNA generates hydroxyl radicals and CoQ10 efficiently prevents the oxidation of bases, particularly in mitochondrial DNA.[8]

Data show that a high respiration rate is positively correlated with an increased amount of mitochondrial CoQ10, suggesting that its supplementation can play an important role in diseases related to CoQ10 deficiency. The mitochondrial respiratory chain organization plays an important role in the increase of respiratory activity.[11,12] Currently, two models have been proposed: The random collision model and a super complex organization called respirasome.[13]

In the first model, electron transfer through the respiratory chain is assured by free diffusion of each component within the inner mitochondrial membrane. In this scenario, CoQ10 forms a pool used by all the CoQ-dependent respiratory complexes (mainly Complex I, II and III). On the other hand, the respirasome requires a solid state organization in which only bound CoQ10 is involved in electron transfer. This last hypothesis seems to be in contrast with a dose-dependent effect of CoQ10 addition on the respiratory rate. However, it may be possible that the bound ubiquinone should be in equilibrium with the

pool. This hypothesis explains the beneficial effect of exogenous CoQ10 supplementation.[14]

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 the immune-enhancing effects of CoQ10 or its analogues. These effects included the increased phagocytic activities of macrophages, increasing the proliferation of granulocytes in response to infection.[8] Patients with a decreased level of serum CoQ10 were at an increased risk of disease progression, [15,16] and application of CoQ10 would improve the clinical parameters.

Our study has shown a significant decrease in the plaque index, gingival index and gingival bleeding index in Groups II and III (test group) as compared with Group I (control group), thereby corroborating the added advantage of coenzyme Q10 gel. On comparison between Groups II and III, there was a more significant improvement in the plaque index, gingival index and gingival bleeding index in Group III as compared with Group II. There was a significant decrease in the probing pocket depth in Groups II and III (test groups) at the end of the 4th week as compared with Group I (control group). The *P*-value, 0.001, was statistically significant at the 4th week for the test groups. All the parameters as well as the clinical indices indicate that coenzyme Q10 (Perio Q gel) when used with scaling and root planing gave an added advantage as compared with sites treated with scaling and root planing alone. The results were more significant in the group treated with intra-pocket gel delivery along with scaling and root planing.

One problem encountered during the study was the substantivity of the gel, as it was neither a sustained release nor a controlled release formulation. The bioavailability of the gel was not known. During the study, some patients gave the statement of improved subjective feeling of the disease condition and less bleeding from the gums, indicating the effectiveness of the gel. No adverse reactions were reported.

Our research was focused on the adjunctive use of Q gel in patients with chronic periodontitis. On intragroup comparison, more significant results were seen in the sites treated with Scaling and root planing and Perio Q gel combination as compared with the sites treated with SRP alone. However, in this study, because of the lack of further follow-up of 3–6 months, the long-term effect of the Perio Q gel cannot be commented upon. Thus, this study necessitates further detailed, long-term evaluation of the effect of the Perio Q gel in a bigger population with chronic periodontitis, along with follow-up of up to 3 months.

Our study has shown decreases in the clinical parameters scores, which are consistent with the earlier studies performed by Hans *et al.*,[3] Wilkinson *et al.*[15] and Chatterjee *et al.*[17] A study conducted by Matthews *et al.* in 2007 showed that coenzyme Q10 with vitamin E has a beneficial effect on the periodontal tissue.[18] A split-mouth trial conducted by Hanioka demonstrated improved periodontal scores along with gingival scores when Co-Q10 was applied alone or as an adjunct to scaling and root planing.[19] A study was conducted by Figuero (2006) to evaluate the potential oxidant/antioxidant interactions of nicotine with antioxidant coenzyme Q10 in smokers who were diagnosed with periodontitis, suggesting that the catabolic effects of nicotine could be reversed by the addition of antioxidants such as CoQ10.[20]

A study reported deficiency of CoQ10 in patients with periodontal disease by conducting a series of trials on succinate dehydrogenase–CoQ10 reductase enzyme, which is found in the mitochondrial complex II of the cell.[5] This study was later supported by the works of Nakamura[8] and Matsumura.[21]

Clinical trials showed a positive relation between Co-Q10 administration and improved periodontal health and immune response.[22] Other than antioxidant action, it has also been shown in the literature that CoQ10 acts as an immune enhancer and also accelerates tissue healing.[23,24] Thus, the result of our study could probably be due to the cumulative effects of Perio Q gel as an antioxidant, immune enhancer and tissue healer.

CONCLUSION

Intrapocket and topical application of Perio Q gel along with mechanical debridement has improved the clinical parameters. The results of the research were encouraging and suggested the possibility to use the gel as a topical agent to support standard treatment procedures in periodontitis. In our research, the clinical parameters significantly improved in the phase of periodontal treatment, indicating that CoQ10 opens new treatment options by improving the host response to disease activity. The results were more significant and encouraging in the group treated with intrapocket gel application. Thus, this study necessitates further long-term clinical trials of Perio Q gel in larger sample sizes with long-term reevaluation, along with other antioxidants agents with various doses and durations for designing a strategy for their use in routine supportive periodontal therapy.

Footnotes

Source of Support: Nil

Conflict of Interest: None declared.

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Figures and Tables

Figure 1



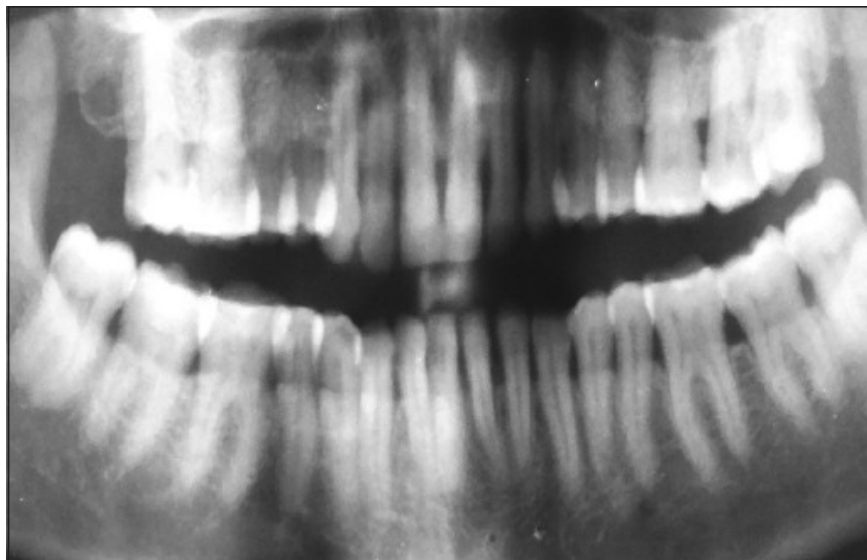
Preoperative photograph

Figure 2



Probing pocket depth

Figure 3



Radiograph of chronic periodontitis patient

Figure 4



Perio Q gel

Figure 5



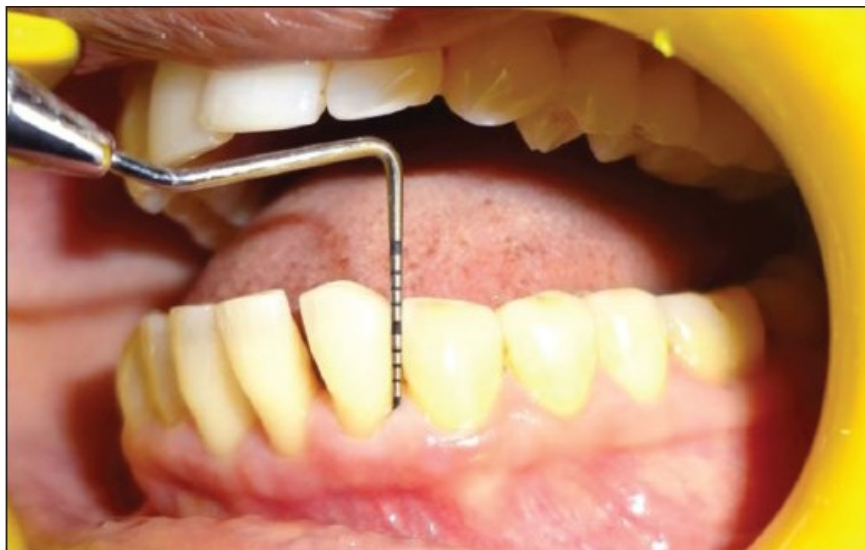
Topical application of Perio Q gel

Figure 6



Intrasulcular application of Perio Q gel

Figure 7



Photograph showing probing pocket depth at 4weeks reevaluation

Table 1

Plaque index (Silness and Loe 1964)

Groups	Mean±SD			F value	P value
	Baseline	2 nd week	4 th week		
I	1.72±0.492	0.722±0.256	0.96±0.274	38.341	<0.0001*
II	1.93±0.468	0.83±0.297	0.61±0.230	74.992	<0.0001*
III	1.69±0.424	0.53±0.189	0.48±0.148	106.612	<0.0001*
F value	1.441	6.580	22.206		
P value	0.246	0.003*	<0.0001*		

P<0.05, *P*<0.01. Significant one-way ANOVA; F – Between-group variance/
within-group variance

Table 2

Gingival index (Loe and Silness 1963)

Groups	Mean±SD			F value	P value
	Baseline	2 nd week	4 th week		
I	1.64±0.422	0.89±0.23	0.63±0.366	40.697	<0.0001*
II	1.82±0.391	1.14±0.456	0.5±0.227	57.063	<0.0001*
III	1.96±0.57	0.99±0.378	0.57±0.397	43.884	<0.0001*
F value	2.119	2.118	0.666		
P value	0.131	0.131	0.518		

P<0.05, *P*<0.01. Significant one-way ANOVA; F – Between-group variance/
within-group variance

Table 3

Gingival bleeding index (Ainamo and Bay 1975)

Groups	Mean±SD			F value	P value
	Baseline	2 nd week	4 th week		
I	1.93±0.329	1.26±0.201	1.06±0.107	70.036	<0.0001*
II	1.88±0.261	1.42±0.192	1.01±0.059	94.310	<0.0001*
III	1.82±0.341	1.26±0.234	1±0	55.441	<0.0001*
F value	0.560	3.490	3.737		
P value	0.575	0.038*	0.031*		

P<0.05, *P*<0.01. Significant one-way ANOVA; F – Between-group variance/
within-group variance

Table 4

Probing pocket depth

Groups	Mean±SD			F value	P value
	Baseline	2 nd week	4 th week		
I	5±0.84	4±0.84	3.66±0.686	13.923	<0.0001*
II	5.72±0.574	4.61±0.608	3.72±0.826	39.248	<0.0001*
III	6.33±1.085	4.72±1.27	3.72±0.826	26.966	<0.0001*
F value	10.819	3.022	0.035		
P value	<0.0001*	0.058	0.965		

P<0.05, *P*<0.01. Significant one-way ANOVA; F – Between-group variance/
within-group variance

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