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Original Article

Subgingivally delivered coenzyme Q10 in the treatment of chronic periodontitis among smokers: A randomized, controlled clinical study

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ABSTRACT

Background: Coenzyme Q10 is an antioxidant whose efficacy in periodontal diseases is well known. However studies regarding its efficacy in smokers with periodontitis are few. Coenzyme Q10 serves as an endogenous antioxidant and its increased concentration in the diseased gingiva effectively suppresses advanced periodontal inflammation.

Objectives: The aim of this study is to evaluate the efficacy of coenzyme Q10 as an adjunct to scaling and root planing in smokers with chronic periodontitis.

Methods: Total of 40 patients were enrolled for the study. The subjects were divided into control (Scaling and root planing only) and test group (Coenzyme Q10 plus Scaling and root planing). Clinical parameters such as plaque index, modified sulcular bleeding index, probing pocket depth and clinical attachment level. These were assessed at baseline, at 1 month and 3 month. The results were subjected to appropriate statistical analysis.

Results: There was a significant improvement in all clinical parameters in the test sites seen at the end of the 1 month and 3 month period.

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

1. Introduction

Periodontitis is a chronic infectious disease affecting supporting tissues of the teeth. Bacterial infection leads to inflammation of periodontal tissues and their slow destruction due to inflammatory process. If left untreated, teeth lose their ligamentous support to the alveolar bone, alveolar bone itself is resorbed, and the teeth become mobile and are finally lost.[1] Variety of molecules are considered to mediate the inflammatory response at one time or another. Amongst these free radicals and reactive oxygen species like superoxide anion radicals, hydrogen peroxide, hydroxyl radicals and hypochlorous acid are also known to cause destruction. All these molecules are capable of damaging either cell membranes or associated bio-molecules. Periodontal pathogens can induce reactive oxygen species overproduction and thus may cause collagen and periodontal cell breakdown.[2]

Smoking is recognized as an important risk factor for periodontal disease, and it has been suggested that it increases the risk of periodontal disease by two-to-six times. Research has shown that smoking might lead to the production of reactive oxygen species. One puff of cigarette smoke contains up to 1017 oxidant molecules.[3] Reactive oxygen species play an important role in periodontal pathogenesis. They are important for intracellular bacterial killing but can also cause destruction of extracellular tissues. This tissue destruction can be direct, via increased oxidative stress, or indirect, by inducing a proinflammatory state. Literature suggests that there is increased generation of reactive oxygen species.[4]

Reactive oxygen species are scavenged by antioxidants, there is a reduction of collagen degradation. Hence, antioxidants are emerging as prophylactic and therapeutic agents. Antioxidants delivered by the diet, systemically, locally, and through a dentifrice have been shown to cause significant improvements in the measures of gingivitis, periodontitis, and oxidative injury.[5]

Coenzyme Q10 is one such antioxidant being evalauted recently. It was discovered in beef heart mitochondria at the University of Wisconsin.[6] Coenzyme Q10 is also known as ubiquinone because of its ubiquitous presence in nature and its quinone structure (similar to that of vitamin K).[7] 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.[8] The effects and mechanisms of action of

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coenzyme Q10 include stabilization of calcium-dependent channels, inhibition of intracellular phospholipases, prostaglandin metabolism, free radical scavenging and direct membrane stabilization.[9] Coenzyme Q10 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 ubiquinole, the reduced form, which are the basis for its antioxidant properties.[10] Coenzyme Q10 functions as an intercellular antioxidant by acting as a primary scavenger of free radicals and reactive oxygen species. It serves as an endogenous antioxidant, and its increased concentration in the diseased gingiva effectively suppresses advanced periodontal inflammation.[10]

To the best of our knowledge, no study in the literature has demonstrated the effect of locally delivered co-enzyme Q10 in the treatment of smokers with chronic periodontitis. Thus, the current study was designed as a randomized, controlled clinical trial to evaluate the efficacy of a co-enzyme Q10 local drug delivery as an adjunct to scaling and root planing for the treatment of smokers with chronic periodontitis in comparison with scaling and root planing.

2. Materials and methods

40 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 20–60 (37.4 + 9.76) years who were diagnosed with moderate to severe chronic periodontitis clinically and radiographically were included in the study.[11,12]

2.1. Selection criteria

Systemically healthy patients with chronic periodontitis with sites having probing depth (PD) $\geq$ 5 mm or clinical attachment level (CAL) $\geq$ 4 mm with no history of periodontal therapy or use of antibiotics in the preceding 6 months were included. Questionnaire was used to obtain smoking history. No biochemical investigations such as serum cocitine levels were investigated to validate the smoking history. Only current smokers with a habit of smoking 10 cigarettes/day for a minimum of 5 years were included.[13] Exclusion criteria was smokers who had stopped their habit, patients with known systemic disease, patients with aggressive periodontitis, users of tobacco in any other form than cigarettes, alcoholics, immunocompromised patients were excluded from the study, patients who received scaling and root planing within 6 months prior to the study, presence of periapical or pulpal infections on qualifying teeth, use of systemic or subgingival antimicrobials microbials within 6 months prior to baseline examination and ongoing drug therapy that could affect the clinical features of periodontitis or the response to periodontal treatment.

2.2. Clinical parameters

Clinical parameters were evalauted at baseline, 1 month and 3 months. These included modified sulcus bleeding index (mSBI),[14] Plaque index(PI),[15] Probing depth (PD), and clinical attachment level (CAL). Modified sulcular bleeding index is an indicator of inflammatory processes occurring in a subject and thus it was selected in present study.[14] Plaque index was also evaluated to check whether patients are compliant with the study are or not by evaluating their oral hygiene.[15] In addition whether the test sites had any beneficial effect over plaque reduction or not was also one of the factor for its inclusion.[15] Probing depth and clinical attachment level are the indicators of the destructive process occurring in the periodontitis patients and thus were evaluated to check whether test site had any added advantage after drug placement on stopping the disease progression and preventing further attachment loss.

All pre- and post-treatment clinical parameters were recorded by one examiner who was masked to the type of treatment received by the patients while another clinician provided treatment to both groups.

2.3. Randomization and examiner calibration

Patients were randomly divided into two groups using computer generated random number sequence.

1 Control Group: Scaling and root planing only (20 patients)
2 Test Group: Scaling and root planing plus co-enzyme Q10 (20 patients)

After randomization intra-examiner calibration was achieved by examination of 20 patients twice, 1 h apart. Calibration was accepted if measurements at baseline and 1 h were similar to 1 mm at the 95% level.

2.4. Local drug delivery gel

Coenzyme Q10 (Perio Q10 gel Manufactured by Perio Q Inc., Manchester, USA) [Fig. 1] was used as locally delivered antioxidant gel. It is supplied as a pack of gel, contains a mixture of Coenzyme Q10 and vegetable glycerine 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.

2.5. Treatment procedure

At the baseline, scaling and root planing were performed in all the groups. In control group only scaling and root planing was performed. In test group local application of Co-enzyme Q10 gel was performed using special needles designed to deliver gel in the pocket. (Figs. 1 & Figure 2)

After application of gel periodontal pack placement was done to avoid flowing away of the gel and for its sustained release into the periodontal pocket. Patients were recalled after 7 days for removal of pack and 1 month for follow-up. No antibiotics or anti-inflammatory agents were prescribed after treatment.

3. Statistical analysis

Power analysis calculations were performed before the study was initiated. To achieve 90% power and detect mean differences of the clinical parameters between groups, 30 sites in each group were required. Normality assumption was tested using Shapiro-Wilk's W test. Within the treatment group, a comparison was carried out using Student's *t*-test if the continuous variable followed a normal distribution. Statistical significance was defined as p-value < 0.05. Statistical analysis was performed with statistical software (SPSS version 10.5, SPSS, Chicago, IL, USA).

4. Results

All 40 patients initially enrolled completed the study (Fig. 3). No complications or adverse reactions were reported.

4.1. Probing depth

On intergroup comparison, probing depth which was 6.33 + 0.66 and 6.42 + 0.60 in control and test group respectively showed statistically non-significant (p-value = 0.418) difference at baseline. At 1-month follow-up probing depth was reduced to 5.46 $\pm$ 0.60 an d 4.56 + 0.64 in control and test group which was statistically significant (p-value < 0.001). Statistically significant difference was seen at 3 months when test group showed mean probing depth of 4.38 $\pm$ 0.59 whereas control, group showed probing depth of 3.59 $\pm$ 0.67 (p-value < 0.001). The mean reduction was 2.87 $\pm$ 0.80 in the test as

Fig. 1. Coenzyme Q10 Gel.

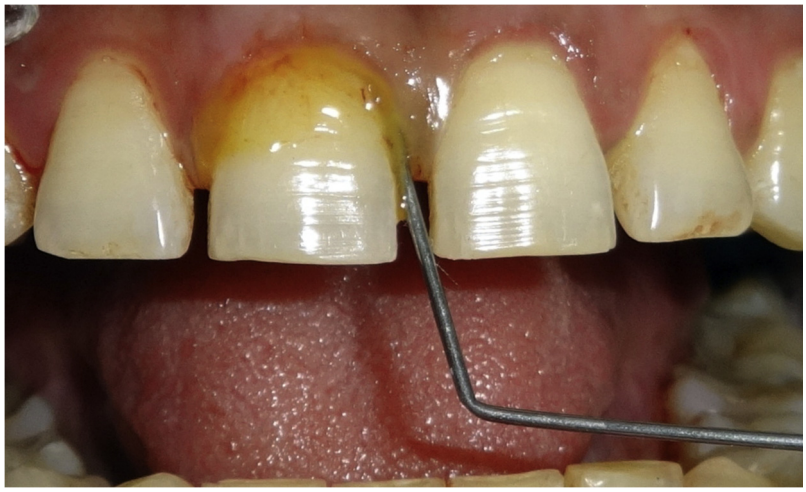

Fig. 2. Subgingival delivery of coenzyme Q10 Gel.

compared to 1.94 ± 0.64 in the control group (p-value < 0.001). [Tables 1 and 2]

Intragroup comparison revealed statistically significant difference at 1-month and 3-month follow up respectively from baseline in both the test group (p-value < 0.001) and the control group (p-value < 0.05). However the result was highly significant in test group as compared to the control group.

4.2. Clinical attachment level

At baseline the clinical attachment level was 5.46 + 0.60 and 5.59 ± 0.63 in the control group and the test group respectively. On inter-group comparison this difference was statistically non-significant (p-value +0.960). At 1-month follow-up clinical attachment level scores were 4.59 ± 0.67 an d 3.97 + 0.84 in the control group and the test group which was statistically significant (p-value < 0.001). Statistically significant difference was seen at 3 months when test group showed mean clinical attachment level scores of 3.07 ± 0.73 whereas control group showed clinical attachment level scores of 3.71 ± 0.64 (p-value < 0.001). [Tables 1 and 2]

Intragroup comparison revealed statistically significant difference at 1-month and 3-month follow up respectively from baseline in both the test group (p-value < 0.001) and the control group (p-value < 0.05). However, the results similarly to probing depth reduction were highly significant in test group as compared to the control group.

4.3. Plaque index (PI)

At baseline examination plaque index scores were 2.05 ± 0.51 and 1.85 ± 0.48 in the control group and the test group. Statistical analysis of the data revealed non-significant difference. (P-value = 0.421). At 1-month follow-up plaque index scores were 1.45 ± 0.60 and 1.25 + 0.63 in the control group and the test group which was statistically non- significant (p-value = 0.103). Statistically non-significant difference was seen at 3 months when test group showed mean plaque index scores of 0.60 ± 0.50 whereas control showed scores of 0.55 ± 0.51 (p-value = 0.329). [Tables 1 and 2]

Intragroup comparison revealed statistically significant difference at 1-month and 3-month follow up respectively from baseline in both the test group (p-value < 0.001) and the control group (p-value < 0.05). This results indicated that both groups maintained comparable levels of oral hygiene throughout the study. (Tables 1 and 2).

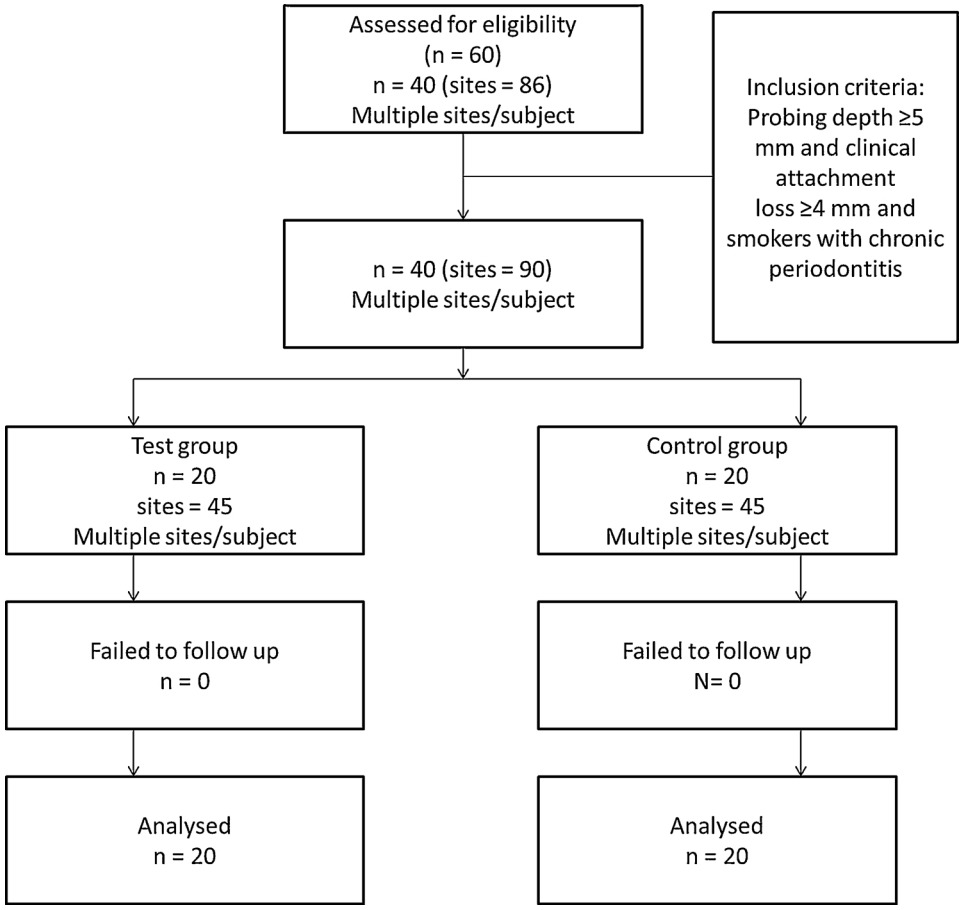

Fig. 3. Study flowchart.

Table 1
Intergroup comparison of mean ± standard deviation of all clinical parameters at baseline, 1 month and 3 months.

Parameter	Time interval	Control group (n = 20)	Test group (n = 20)	P value†
PD (mm)	Baseline	6.33 + 0.66	6.42 + 0.60	0.418*
	1 month	5.46 + 0.60	4.56 + 0.64	< 0.001***
	3 month	4.38 + 0.59	3.59 + 0.67	< 0.001***
CAL (mm)	Baseline	5.46 + 0.60	5.59 + 0.63	0.960*
	1 month	4.59 + 0.67	3.97 + 0.84	< 0.001***
	3 month	3.71 + 0.64	3.07 + 0.73	< 0.001***
PI	Baseline	2.05 + 0.51	1.85 + 0.48	0.421*
	1 month	1.45 + 0.60	1.25 + 0.63	0.103*
	3 month	0.55 + 0.51	0.60 + 0.50	0.329*
mSBI	Baseline	2.05 + 0.55	2.41 + 0.50	0.082*
	1 month	1.25 + 0.62	1.17 + 0.63	0.02**
	3 month	1.35 + 0.49	0.70 + 0.58	0.0004**

n: Sample size.
† Student's *t*-test.
* P-value > 0.05 considered non-significant.
** P-value < 0.05 considered significant.
*** P-value < 0.001 considered highly significant.

Table 2
Intragroup comparison mean + standard deviation of clinical parameters at baseline, 1 month and 3 months using repeated measures of ANOVA.

Parameters	Groups	Baseline	1 month	3 month	P- value
PD	Control	6.33 + 0.66	5.46 + 0.60*	4.38 + 0.59*	< 0.05
	Test	6.42 + 0.60	4.56 + 0.64*	3.59 + 0.67**	< 0.001
CAL	Control	5.46 + 0.60	4.59 + 0.67*	3.71 + 0.64*	< 0.05
	Test	5.59 + 0.63	3.97 + 0.84*	3.07 + 0.73**	< 0.001
PI	Control	2.05 + 0.51	1.45 + 0.60*	0.55 + 0.51*	< 0.05
	Test	1.85 + 0.48	1.25 + 0.63*	0.60 + 0.50*	< 0.05
mSBI	Control	2.05 + 0.55	1.25 + 0.62*	1.35 + 0.49*	< 0.05
	Test	2.41 + 0.50	1.17 + 0.63*	0.70 + 0.58**	< 0.001

* p- value < 0.05 considered significant compared to baseline.
** p-value < 0.001 considered highly significant compared to baseline.

4.4. Modified sulcus bleeding index (mSBI)

The gingival index as assessed by modified sulcus bleeding index revealed scores of 2.05 ± 0.55 and 2.41 ± 0.50 in the control group and in the test group respectively. On intergroup comparison this difference was statistically non-significant (p-value = 0.082). At 1-month follow-up modified sulcus bleeding scores were reduced to 1.25 ± 0.62 in the control group and 1.17 ± 0.63 in the test group. This difference was statistically significant (p-value = 0.02). Modified sulcus bleeding scores were 1.35 ± 0.49 and 0.70 ± 0.58 in the control group and the test group which was statistically significant (p-value < 0.0004).

Intragroup comparison revealed statistically significant difference at 1-month and 3-month follow up respectively from baseline in both the test group (p-value < 0.001) and the control group (p-value < 0.05). However the results were highly significant in test group as compared to the control group.

5. Discussion

In the current study, we evaluated the clinical efficacy of Co-enzyme Q10 gel as an adjunct to SRP for the treatment of chronic periodontitis in smokers. Smokers often present a poorer response to periodontal treatment when compared to non-smokers.[16,17] New therapeutic

approaches are therefore investigated for these patients. The present study was designed to clinically evaluate the use of locally delivered co-enzyme Q10 as an adjunctive treatment to scaling and root planing in smokers.

Periodontal diseases are considered infections of the periodontium because of bacterial etiology, an immune response, and tissue destruction. There is a complex bidirectional series of host-microbial interaction involving cellular and humoral factors and networks of cytokines, chemokines, and growth factors. The majority of periodontal tissue destruction is caused by an inappropriate host response to periodontopathogens and their product which includes overproduction of free radicals and reactive oxygen species, matrix metalloproteinases during the inflammatory process causing collagen and periodontal cell breakdown.[7] Moreover smoking is also known to produce reactive oxygen species which might further cause periodontal destruction.[3,4] Thus, antioxidant therapy has gained popularity in recent years due to their ability to scavenge free radicals

It has been suggested that co-enzyme Q10 have antioxidant action which may also be important in the case of periodontal infection. The antioxidant nature of coenzyme Q10 is derived from its energy carrier function. As an energy carrier, the co-enzyme Q10 molecule is continuously going through an oxidation-reduction cycle. Co-enzyme Q10 inhibits lipid peroxidation by preventing the production of lipid peroxyl radicals. In addition, the reduced form of co-enzyme Q10 effectively regenerates vitamin E from the α-tocopheroxyl radical. Furthermore, during oxidative stress, interaction of hydrogen peroxide (H_2O_2) with metal ions bound to DNA generates hydroxyl radicals and co-enzyme Q10 efficiently prevents the oxidation of bases, particularly in mitochondrial DNA.[18] In the present study there was decreased gingival bleeding index from baseline to 3 months, suggesting an anti-inflammatory and immunomodulatory effect of co-enzyme Q10. A similar effect was observed in a clinical study done Raut and Sethi in patients with chronic periodontitis where they found significant there was significant reduction in gingival bleeding in sites delivered with co-enzyme Q10.[19]

There was significant improvement in clinical parameters like probing depth and clinical attachment level in test group as compared to control group at both 1 month and 3 months interval. These results are in agreement with the previous study conducted by Sale et.al (2014)[20] wherein they found that local application of co-enyme Q10 either intrasulcularly or topically both resulted in significant improvement. However in contrast Manthena et al.,[21] reported no significant difference between the co-enzyme Q10 and scaling and root planing group in relation to probing depth reduction and clinical attachment level gain.

Results showed that there was a statistically significant reduction in the mean Plaque index scores during the study periods in both groups as compared with baseline values and there was no significant difference between them. The reduction in plaque scores could be attributed to the proper oral hygiene maintenance after SRP. These results are consistent with the clinical study conducted by Sharma et al.[22] who found that there was no difference in plaque index scores in sites receiving co-enzyme-Q10. This suggests that co-enzyme Q10 might not have any additional benefit in reducing plaque formation.

Current study was focused on evaluating the adjunctive benefits of coenzyme Q10 with scaling and root planing in smokers with chronic periodontitis. To best of our knowledge no study has been conducted evaluating the same. Thus the results of the present study cannot be directly compared to the previous study as there is clearly a difference in response to therapy provided in smokers as compared to non-smokers. However the positive results obtained from the present study suggests that co-enzyme Q10 used as an adjunctive to SRP in smokers may provide added therapeutic benefits. Thus, further studies evaluating the same are recommended.

Present study had certain limitations like short follow up period of 3 months and lack of knowledge about the substantivity of the drug used whether sustained release or a controlled release. Moreover, no biochemical investigation were done to validate anti-oxidant effect of the drug. And also for the inclusion of the smokers. Hence we recommend further studies to be conducted with longer follow up and biochemical investigations.

6. Conclusion

Within the limits of this study, it can be concluded that the application of locally delivered coenzyme Q10 with scaling and root planing may provide additional benefits to periodontal treatment of smokers. However, a longitudinal follow up study is necessary to confirm the long-term advantages of this adjunctive therapy.

Conflicts of interest

None.

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