Original Research

Clinical and immunological evaluation of Coenzyme Q10 as an adjunct to nonsurgical periodontal therapy in chronic periodontitis patients

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Abstract:

Background: Periodontal pathogens can induce overproduction of free radicals and reactive oxygen species (ROS) that may increase periodontal tissue breakdown. Coenzyme Q10 (CoQ10) serves as potent endogenous antioxidant that act as a scavenger to ROS and may be suppress the periodontal inflammation.

Aim: The present study was aimed to evaluate the clinical and immunologic effects of intrapocket application of CoQ10 as an adjunct to nonsurgical periodontal therapy.

Materials and methods: Twenty eight mild to moderate chronic periodontitis patients with age ranged from 29 to 46 years. All individuals were carried out to scaling and root planning (SRP) and classified into group 1 (G1, treated by SRP only) and group 2 (G2, treated by COQ10 gel plus SRP). Clinical parameters; plaque index (PI), gingival index (GI), pocket depth (PD) and clinical attachment loss (CAL), in addition to gingival crevicular fluid (GCF) samples were obtained at baseline and 30 days after treatment. Tumor necrosis factor- (TNF-) levels were evaluated by ELISA technique at both time intervals of periodontal therapy.

Results: Clinical evaluation of both groups revealed a high significant improvement in all parameters at baseline and 30 days of treatment (P≤0.01). Whereas, more clinical improvement in G2 at 30 days compared to G1, but the difference was non-significant (P≥0.05). TNF- levels were significantly high reduced at 30 days versus to baseline in both groups (P≤0.01), in comparison between groups at 30 days TNF- levels reduced in G2 compared to G1, but there is no significant difference (P≥0.05).

Conclusions: Topical application of CoQ10 as an...
adjunct to non-surgical periodontal therapy improve the clinical and immunologic findings, but it is not considered a significant adjunct modality for periodontal therapy. Further studies needed to clarify clinical and immunological outcomes.

Keywords: chronic periodontitis, non surgical therapy, host response

Introduction:
Chronic Periodontitis is a term used to describe an inflammatory process, initiated by the plaque biofilm, that leads to loss of periodontal attachment to the root surface and adjacent alveolar bone and which ultimately results in tooth loss. It can be defined as a chronic infection that results from the interaction of periodontopathogenic bacteria and host inflammatory immune responses.¹

Coenzyme Q10 (CoQ10) belongs to a homologous series of compounds that share a common benzoquinone ring structure but differ in the length of the isoprenoid side chain. In humans and a few other mammalian species, the side chain is comprised of 10 isoprene units. Also, CoQ10 is similar to vitamin K in its chemical structure.² CoQ10 is considered as an antioxidant, so that it is essential for the health of virtually all human tissue and organs.³ It is also known to play a crucial role in the generation of adenosine triphosphate (ATP) and cellular respiration, and act as a primary scavenger of free radicals (FRs) and reactive oxygen species (ROS).⁴

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% of patients with periodontal disease and low levels of CoQ10 in leukocytes in 86% of cases. These findings indicate that periodontal disease is frequently associated with CoQ10 deficiency.⁵ Many clinical trials with oral administration of CoQ10 to patients with periodontal disease have been conducted. The results have shown that oral administration of CoQ10 increases the concentration of CoQ10 in the diseased gingiva and effectively suppresses advanced periodontal inflammation and periodontal microorganisms.⁶,⁷,⁸

Topical application of CoQ₁₀ to the periodontal pocket was evaluated with and without subgingival mechanical debridement. In the first three-week period, significant reduction in gingival crevicular fluid flow, probing depth and attachment loss were found and significant improvements in modified gingival index, bleeding on probing and peptidase activity derived from periodontopathic bacteria were observed only at experimental sites which treated CoQ10 with subgingival mechanical debridement.⁹ A study on clinical evaluation of topical application of the Perio-Q gel (Coenzyme Q10) in chronic periodontitis patients. The results represented that intra-pocket gel application in combination with scaling and root planning (SRP) showed significant reduction (P<0.05) for plaque index (PI), gingival index (GI), gingival bleeding index (GBI), and clinical attachment loss (CAL) in comparison to intra-pocket gel alone. On the other hand, sub-gingival mechanical debridement only and with CoQ10 (Perio-Q gel) showed almost similar clinical results without any statistically significant differences.¹⁰ Moreover, coenzyme Q10 can be said to have a beneficial effect clinically on gingivitis and slight periodontitis when used as adjunct to scaling and root planning.¹¹
Raut and Sethi 2016 performed a comparative study on the efficacy of Coenzyme Q10 and tea tree oil gel as an adjunct to scaling and root planing in the treatment of chronic periodontitis. They concluded that Coenzyme Q10 and tea tree oil gel proved to be effective in the treatment of chronic periodontitis.\textsuperscript{12}

TNF-α is a proinflammatory cytokine that plays a role in the development and maintenance of inflammatory diseases, its mediating effects on the development, progress, and maintenance of periodontal diseases would be expected to occur.\textsuperscript{13}

The effect of oral administration of coenzyme Q10 on the levels of tumor necrosis factor-α(TNF-α) and interleukin-10 (IL-10) in gingival tissue of experimental periodontitis in rats was studied by. They reported that Coenzyme Q10 inhibits the expression of TNF-α and promotes the expression of IL-10 in periodontal tissues of experimental periodontitis rats. Coenzyme Q10 may play a role in treating periodontitis.\textsuperscript{14}

Hence, the aim of the present study was to evaluate the intrapocket application of Coenzyme Q10 in nonsurgical periodontally treated chronic periodontitis patient to assess of clinical outcomes and the changes in gingival crevicular fluid (GCF)–TNF- levels.

Materials and methods:

Patients: Twenty eight patients of both sex (18 females and 10 males) ranged in age from 29-46 years with a mean of 38 ± 60 years with mild to moderate chronic periodontitis. All subjects were selected from patients attending at the out-patient clinic, Oral Medicine and Periodontology Department, Faculty of Dental Medicine, Al-Azhar University, Assiut Branch. A clinical examination was done to all patients participate in the study, and patients gave their agreement.

All patients were categorized into two groups:

Group I: It includes 14 chronic periodontitis patients were treated by conventional periodontal therapy alone (scaling and root planning).

Group II: It includes 14 chronic periodontitis patients were treated by conventional periodontal therapy with intrapocket and topical application of coenzyme Q 10.

Selection of patients: The inclusion criteria include the following:

1- All subjects were free from any systemic diseases according to the criteria of Modified Cornell Medical Index.\textsuperscript{15}

2- All subjects were not receiving antibiotics and non-steroidal anti-inflammatory for at least three months prior to sample collection.

3- All subjects were non-smokers and cooperative.

4- All subjects were suffering from chronic periodontitis with pocket depth not more than 6 mm and clinical attachment level (CAL) not more than 4 mm.

5- All subjects were not subjected to previous periodontal therapy during at least 6 months.

6- All subjects were not receiving vitamin supplements.

7- All Subjects were not regularly using mouth wases.

Periodontal examination: The periodontal conditions were evaluated for all subjects for baseline and 30 days using following parameters: Plaque Index (PI), Gingival index (BI), Pocket depth (PD) and Clinical attachment loss (CAL).\textsuperscript{16-19}

Periodontal therapy: All individuals were carried out to nonsurgical periodontal treatment include; scaling and root planning (SRP) that done through 3 visits and the patient became maintained on plaque control measures. Fig (1,3)
GCF samples collection: GCF samples were obtained from all patients. The site which showed the highest probing depth and CAL (range 4-6 mm) score was selected for GCF sampling. The teeth selected for sampling was isolated with cotton roll, and supragingival plaque was removed without touching the marginal gingiva. The crevicular site was then dried gently with an air syringe. Samples of GCF were obtained before probing into the site by placing paper point. Sterilized paper point size #30 was carefully inserted to the maximum depth of the periodontal pocket and held in position for 30 seconds. The site that did not express any volume of GCF, and paper point which were contaminated with blood and saliva, were excluded from the study. The collected GCF was immediately transferred into plastic vials containing phosphate buffer saline (PBS) and the samples were frozen at -70°C till they were assayed for TNF-α.

Application of Coenzyme Q10: In patients of the Group 2 after treatment with conventional periodontal therapy the teeth isolated by cotton rolls for intrapocket and topical application of Perio-Qgel® (PERIOQ INC, Manchester, USA). It is a mixture of CoQ10 in a vegetable oil base in a ratio of 1:9. It is supplied as a pack of gel and was stored at a temperature between 4°C and 8°C for maintaining its shelf-life.

The periodontal pocket was dried with paper points before subgingival administration of Perio-Q gel. Intrapocket application of gel with bunted needle tip, eating, spitting and drinking was restricted for 1 hour after application, teeth brushing and flossing for 4 hours after application. Patients were instructed for plaque control regimen, and the oral hygiene instructions were provided at each appointment. Topical application was repeated after 7 & 15 days. (Fig 2)

TNF-α ELISA Assay: The samples were assayed for TNF-α levels using commercially available enzyme-linked immunosorbent assay (ELISA). The assay was conducted according to the manufacturer's instructions. Highly sensitive ELISA kit (Shanghai Sunred Biological Technology Co., Ltd) was used to detect the TNF-α level in the sample of Human serum, blood plasma, GCF and other related tissue liquid.

Statistical analysis: The results were recorded and statistically analyzed using Statistical Package for Social Science (SPSS Version 22, IBM Inc, Chicago, IL, USA). P < 0.05 was defined as statistically significant. The tables and figures were done by Microsoft word 10.
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Fig (1): Group 2 female 41 aged patient before treatment.

Fig (2): Intrapocket application of CoQ10 gel

Fig (3): Patient at 30 days after treatment
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**Fig (4): Illustrate the clinical parameters at baseline in both groups.**

- G1 = Treated by SRP only
- G2 = Treated by SRP and CoQ10 application
- PI = Plaque index
- GI = Gingival index
- PD = Pocket depth
- CAL = Clinical attachment loss

**Fig (5): Illustrate the clinical parameters at 30 days in both groups.**

- G1 = Treated by SRP only
- G2 = Treated by SRP and CoQ10 application
- PI = Plaque index
- GI = Gingival index
- PD = Pocket depth
- CAL = Clinical attachment loss
Results:
Twenty eight patients suffering from mild to moderate chronic periodontitis with probing pocket depth 4-6 mm and CAL not more than 4 mm. The patients were divided into two groups: Group 1 (G1) treated by scaling and root planning (SRP) only, and group 2 (G2) treated by SRP plus topical and intrapocket application of Coenzyme Q10 gel. The clinical outcomes of periodontal parameters and levels of GCF-TNF- were assessed at baseline and 30 days after treatment.

Clinical findings: The results of mean values of PI, GI, PD and CAL among both groups at baseline and 30 days showed high statistically significant differences (P<0.01). (Table 1, Fig 4,5) Table 2 showed independent t-test for comparing Means, Standard deviations, t values and p-values among the two groups at baseline and 30 days representing an improvement in G2 versus G1. The statistical comparison revealed that no statistical significant difference in G2 compared with G1 (P≥0.5).

TNF-alpha assaying: The mean values, Standard deviations, t values and p-values records were expressed in (Table 3, Fig 6). The statistical comparisons between the baseline and 30 days for both groups, the differences were highly significant (P<0.01). The statistical comparisons between both groups at baseline and 30 days were revealed in (Table 3), the statistical results were represented a reduction of TNF- levels at 30 days in both groups. The levels of TNF-more decreased in G2 than G1 at day 30, while, the statistical differences were non-significant (P≥0.5).
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Table (1): Demonstrate the statistical comparisons of clinical parameters at baseline compared to 30 days in both groups.

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>30 Days</th>
<th>T Value</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1</td>
<td>PI</td>
<td>2.69±0.480</td>
<td>1.23±0.43</td>
<td>6.789</td>
</tr>
<tr>
<td></td>
<td>GI</td>
<td>2.36±0.275</td>
<td>0.85±0.16</td>
<td>23.739</td>
</tr>
<tr>
<td></td>
<td>PD</td>
<td>4.27±0.436</td>
<td>3.55±0.39</td>
<td>5.269</td>
</tr>
<tr>
<td></td>
<td>CAL</td>
<td>2.33±0.473</td>
<td>1.83±0.36</td>
<td>6.059</td>
</tr>
<tr>
<td>G2</td>
<td>PI</td>
<td>2.68±0.470</td>
<td>1.15±0.37</td>
<td>10.690</td>
</tr>
<tr>
<td></td>
<td>GI</td>
<td>2.32±0.249</td>
<td>0.80±0.32</td>
<td>13.056</td>
</tr>
<tr>
<td></td>
<td>PD</td>
<td>4.22±0.364</td>
<td>3.32±0.30</td>
<td>7.831</td>
</tr>
<tr>
<td></td>
<td>CAL</td>
<td>2.35±0.962</td>
<td>1.70±0.39</td>
<td>6.150</td>
</tr>
</tbody>
</table>

G1 = Treated by SRP only  G2 = Treated by SRP and CoQ10 application
PI = Plaque index  GI = Gingival index
PD = Pocket depth  CAL = Clinical attachment loss
** = High significant (P = 0.01)

Table (2): Show the statistical comparisons of clinical parameters at 30 days in both studied groups.

<table>
<thead>
<tr>
<th></th>
<th>Comparison</th>
<th>Mean ± Sd</th>
<th>T Value</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PI</td>
<td>G1 Vs G2</td>
<td>G1 (1.23±0.43)  G2 (1.15±0.37)</td>
<td>0.480</td>
<td>0.635</td>
</tr>
<tr>
<td></td>
<td>G1 Vs G2</td>
<td>At 30 days  G1 (0.85±0.16)  G2 (0.80±0.32)</td>
<td>0.530</td>
<td>0.601</td>
</tr>
<tr>
<td>GI</td>
<td>G1 Vs G2</td>
<td>G1 (3.55±0.39)  G2 (3.32±0.30)</td>
<td>1.696</td>
<td>0.103</td>
</tr>
<tr>
<td>PD</td>
<td>G1 Vs G2</td>
<td>G1 (1.83±0.36)  G2 (1.70±0.39)</td>
<td>1.032</td>
<td>0.312</td>
</tr>
<tr>
<td>CAL</td>
<td>G1 Vs G2</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

G1 = Treated by SRP only  G2 = Treated by SRP and CoQ10 application
PI = Plaque index  GI = Gingival index
PD = Pocket depth  CAL = Clinical attachment loss
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Table (3): Revealed the statistical comparisons of GCF - TNF-χ (Pg lk j’ jct cj q) of both studied groups.

<table>
<thead>
<tr>
<th>Comparisons</th>
<th>Mean±Sd</th>
<th>T Value</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1 Baseline</td>
<td>319.90±30.699</td>
<td>3.941</td>
<td><strong>0.01</strong></td>
</tr>
<tr>
<td>30 days</td>
<td>281.67±46.089</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G2 Baseline</td>
<td>322.48±49.223</td>
<td>12.710</td>
<td><strong>0.003</strong></td>
</tr>
<tr>
<td>30 days</td>
<td>278.85±52.329</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G2 Vs G1 Baseline</td>
<td>322.48±49.223</td>
<td>1.179</td>
<td>0.249</td>
</tr>
<tr>
<td>30 days</td>
<td>278.85±52.329</td>
<td>-2.702</td>
<td>0.062</td>
</tr>
<tr>
<td>30 days</td>
<td>281.67±46.089</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

G1 = Treated by SRP only   G2 = Treated by SRP and CoQ10 application
** = High significant (P=0.01)

Discussion:
Chronic Periodontitis is an inflammatory process, initiated by the plaque biofilm, which leads to loss of periodontal attachment to the root surface and adjacent alveolar bone that result from the interaction of perio-pathogens and host inflammatory immune responses. It is considered as one of the most common bacterial infection worldwide with prevalence in mild to moderate forms ranging from 13% to 57% in different populations depending on oral hygiene and socio-economic status.

Periodontal pathogens can induce reactive oxygen species (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 Q10) serves as an endogenous antioxidant which increases the concentration of CoQ10 in the diseased gingiva and effectively suppresses advanced periodontal inflammation.

A deficiency of CoQ10 at its enzyme sites in gingival tissue may exist independently of and/or because of periodontal disease. If a deficiency of CoQ10 expressed in gingival tissue for nutritional causes and independently of periodontal disease, then the advent of periodontal disease could enhance the gingival deficiency of CoQ10. 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.

On exogenous CoQ10 administration, an increase in the specific activity of this mitochondrial enzyme was found in deficient patients. The periodontal scores were also decreased concluding...
that CoQ10 should be considered as an adjunct for the treatment of periodontitis in current dental practice.\textsuperscript{6}

The purpose of this study was to evaluate the clinical and immunologic efficacy of topically applied CoQ10 as an adjunct to basic conventional therapy in treatment of mild to moderate chronic periodontitis. The local application of chemotherapeutic agents into periodontal pocket could be beneficial, both in terms of rising drug concentration directly in the active site, and in preventing systemic side effects.\textsuperscript{24}

About 20\%-30\% of all chronic periodontitis cases do not respond favorably to conventional periodontal treatment. Many factors may contribute to that response, such as improper removal of bacterial deposits and calculus, poor plaque control, systemic conditions leading to an impaired immune response, defective restorations, occlusal dysfunction, periodontal-endodontic involvement and others. In these cases, other treatment approaches.\textsuperscript{25}

The present study aimed to use a new modality in the periodontal therapy by topical application of antioxidant as adjunctive to basic conventional therapy to overcome the unresponsive cases treated by conventional periodontal therapy alone.

In the resent study, there is a highly significant reduction of clinical parameters in patients treated by CoQ10 plus SRP and patient treated by SRP only. These findings were in accordance to several studies.\textsuperscript{6,9,10,12} On the other hand, when comparing the mean values of clinical parameters after treatment at 30 days between both groups more reduction was seen in patients treated by CoQ10 but the statistical differences was non-significant. This results in consistent with Sale et al. 2014\textsuperscript{26} whereas our results in contrary with findings of Hans et al. 2012\textsuperscript{10}, they reported that intra-pocket gel application in combination with SRP showed significant reduction (P<0.05) for PI, GI, GBI, and CAL in comparisons to sites treated by SRP only.

Therefore, the effect of CoQ10 locally may be not enough to provide a significant effect than SRP only due to deficiency of CoQ10 in the periodontal tissues, this concept is supported by some studies.\textsuperscript{6,23}

The mean values of GCF- TNF-\(\alpha\) levels compared among both groups at baseline, and 30 days showed marked decrease in level of TNF-\(\alpha\) (highly significant difference) in both groups at 30 days when compared to the baseline this is in agreement with the finding of Heralgi et al. 2011\textsuperscript{28} who found that the severity of inflammation increases, there is a significant increase in the TNF-\(\alpha\) level suggesting that there is a direct relationship between TNF-\(\alpha\) level in GCF and periodontal destruction proved thatTNF-\(\alpha\) may be used as a potential biochemical marker for assessment of periodontal disease activity in chronic generalized periodontitis.

In a study done by Aditi et al.2013\textsuperscript{29} determined uric acid level as an antioxidant in patients with chronic periodontitis treated with topical antioxidants predicting that with the improvement of the periodontal tissue inflammation the antioxidants level will raise so uric acid level will increase. This direct indicator may give a false diagnosis with many factors as any food, drink or...
any other supplement contains antioxidants that may raise the GCF uric acid level. TNF-α was chosen in this study as an indirect indicator to the response of the periodontal tissue to CoQ10 antioxidant in treatment of chronic periodontitis.

TNF-α level was high at baseline before the treatment with SRP and CoQ10gel this level was decreased in further session with a significant improvement in periodontal tissue and significant difference in periodontal parameters confirmed that there was increase in antioxidant level and its balance with ROS was regain, these could be attributed to Chapple et al.2007 who mentioned that loss of balance between ROS and antioxidant defense has been implicated as an etiological factor for periodontal diseases that may manifested as an increase in oxidative stress or decrease in individual antioxidant level.

For elucidation, why the levels of TNF- not significantly reduced at 30 days of treatment in G2 (SRP plus CoQ10) versus G1 (SRP only), this may be related to the deficiency of endogenous CoQ10 that reduce ROS which induce periodontal inflammation. This explanation supported by an experimental study on the effect of oral administration of CoQ10 on the expression of tumor necrosis factor-α and interleukin-10 in gingival tissue of experimental periodontitis in rats.14 They concluded that the CoQ10 inhibits the expression of TNF-α and promotes the expression of IL-10 in periodontal tissues of experimental periodontitis rats. Regarding to that result, the CoQ10 may play a role in treating periodontitis. Periodontal condition after oral applications of CoQ10 with vitamin E was studied by Brzozowska et al. 2007, they concluded that CoQ10 with vitamin E had a beneficial effect on the periodontal tissue.

Based on suggestion of previous studies, the oral administration plus topical application of CoQ10 gel may be more beneficial to diseased periodontal tissues through reducing the Levels of TNF- and improvement the clinical outcomes of periodontal therapy. So that, the systemic and local adminstration of CoQ10 may be may an interest scientific point of research.

In conclusions, the topical application of CoQ10 as an adjunct to non-surgical periodontal therapy improve the clinical and immunologic outcomes, but it not considered a strong modality for periodontal therapy. Tumor Necrosis Factor- α could be considered as strong laboratorymarker for periodontal disease activity. In addition, conventional periodontal therapy remains the cornerstone as basicand initial periodontal therapy.

References:


26. Sale S, Parvez H, Yeltiwar R, Vivekanandan G,


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