Gingival Lipid Peroxidation and Glutathione Redox Cycle Before and After Periodontal Treatment with and without Adjunctive Coenzyme Q_{10}¶

KOENZİM Q_{10} İLE DESTEKLENEN PERİODONTAL TEDAVİ ÖNCE VE SONRASINDA DİŞ ETİ LİPİD PEROKSİDASYONU VE GLUTATYON REDOKS SİKLÜSÜ

Bahar KURU*, Yıldız DİNÇER**, Ülkü NOYAN*, Leyla KURU***,
Selçuk YILMAZ****, Refik KAYALI*****, Tülay AKÇAY******

* Prof., Department of Periodontology, Faculty of Dentistry, Marmara University,
** Assoc. Prof., Department of Biochemistry, Cerrahpaşa Faculty of Medicine, İstanbul University,
*** Assist. Prof., Department of Periodontology, Faculty of Dentistry, Marmara University
**** Prof., Department of Periodontology, Faculty of Dentistry, Yeditepe University
***** Dr. Department of Biochemistry, Cerrahpaşa Faculty of Medicine, İstanbul University,
****** Prof., Department of Biochemistry, Cerrahpaşa Faculty of Medicine, İstanbul University, İSTANBUL

Summary

Purpose: The objective is to evaluate lipid peroxidation and glutathione redox cycle in gingival tissues sampled from periodontal sites treated with scaling/root planing (SRP) in comparison with non-treated inflamed gingiva in chronic periodontitis. The adjunctive use of Coenzyme Q_{10} (CoEQ) was further evaluated.

Material and Methods: Levels of thiobarbituric acid reactive substance (TBARS), an end product of lipid peroxidation, reduced glutathione (GSH) and the activity of glutathione-peroxidase (GSH-per) and-reductase (GSH-red) were investigated using biochemical methods. Gingival samples were collected from 10 patients before and after SRP and SRP + CoEQ treatments performed in sequence providing 2 different treatment groups in each individual. Patients, who had at least 2 teeth with 4-7 mm periodontal pockets in each quadrant, were given oral hygiene instructions before treatment and measurements of plaque, probing depth and bleeding were performed before each sampling.

Results: All clinical parameters ($p< 0.01$) and the levels of TBARS ($p< 0.01$) after SRP and SRP + CoEQ reduced. The changes in the levels of GSH, GSH-per and GSH-red were insignificant. Although intergroup changes were not significant, the adjunctive use of CoEQ to SRP tended to lower the gingival lipid peroxidation more than SRP alone.

Conclusion: Within the limits of this study, both clinical and biochemical results revealed a marked decrease in gingival lipid peroxidation and clinical resolution of infection in both groups, however, did not provide enough evidence to support the additive effect of CoEQ.

Key Words: Lipid peroxidation, Coenzyme Q_{10}, periodontitis, periodontal treatment

Özet

Amaç: Bu çalışmanın amacı, kronik periodontitisli hastalarda diş ve kök yüzeyi temizliği (SRP) önce ve sonrasında diş eti dokusu lipid peroksidasyon ve glutatyon seviyelerini değerlendirmektir. SRP'ye ilave olarak kullanılan Koenzim Q_{10} (KQ) etkisi de ayrıca incelenmiştir.

Materyal ve Metod: Lipid peroksidasyonun son ürünü olan "Thiobarbituric Acid Reactive Substance (TBARS)" ve glutatyon (GSH) seviyeleri ile glutatyon peroksidaz (GSH-per) ve glutatyon redüktaz (GSH-red) enzim aktiviteleri biyokimyasal yöntemLerle araştırıldı. Her kadranında 4-7 mm sondalanabilir cep derinliğine sahip en az 2 dişi olan kronik periodontitisli hastalara ağız hijyeni eğitimi verildi, plak indeks (Pİ), sondalanabilir cep derinliği (SCD) ve sondalamada kanama (SK) değerleri ölçüldü. Her hastanın birbirini takip eden 2 farklı tedavi grubunu oluşturduğu bu çalışmada, diş eti örnekleri 10 bireyden SRP ve SRP + KQ uygulamasından önce ve sonra elde edildi.

Bulgular: Tüm klinik parametrelerde ($p< 0.01$) ve TBARS seviyelerinde ($p< 0.01$), SRP ve SRP + KQ tedavilerinden sonra azalmalar görüldü. Her iki grupta da tedavi öncesi ile sonrası arasındaki GSH, GSH-per ve GSH-red seviyelerindeki değişiklik anlamLı bulunmadı. Gruplar arasındaki farkların anlamLı olmamasına rağmen SRP'ye ilave kullanılan sistemik KQ'nun diş eti lipid peroksidasyon seviyesini tek başına SRP'ye kıyasla daha fazla azalttığı görüldü.

Sonuç: Bu çalışmanın sınırları dahilinde, her iki grupta da diş eti lipid peroksidasyonda belirgin azalma ve klinik iyileşme gözlendi, ancak KQ'nun ilave etkisini destekleyecek yeterli kanıt elde edilmedi.

Anahtar Kelimeler: Lipid peroksidasyon, Koenzim Q_{10}, periodontitis, periodontal tedavi

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Periodontal diseases are inflammatory disorders that give rise to tissue damage, as a result of the complex interactions between pathogenic bacteria and the host response. Bacteria cause the observed periodontal tissue destruction characterized by attachment and alveolar bone loss, directly by toxic products and indirectly by activating host defense systems, i.e., inflammation (1). Infiltration, an event characteristic of mammalian inflammation, is usually present in the connective tissues and junctional epithelium of periodontium with mononuclear phagocytes, lymphocytes, and polymorphonuclear leukocytes (PMN) comprising the majority of the infiltrate (2). A variety of

molecular species such as free oxygen radicals (FOR)/reactive oxygen species (ROS) and proteolytic enyzmes, which have the potential to mediate bacterial killing as well as host tissue destruction, appears in the inflamed tissues (3). Especially an increased generation rate of FOR mainly related to the PMN cells was observed in periodontitis patients (4). FOR cause tissue damage in terms of oxidative damage by peroxidation of membrane phospholipids leading to changes in permeability and loss of membrane integrity (5). On the other hand, the organism is also endowed with various endogenous antioxidant defense systems that are mainly of 3 kinds: Preventive antioxidants, radical scavenging antioxidants and finally enzymes that repair the damage and reconstitute the membranes. Reduced glutathione (GSH) is one of the most important intracellular antioxidants and is present in all mammalian cells (6). GSH protects the cell against free radicals, hydrogen peroxide and organic peroxides. Glutathion-peroxidase (GSH-per) eliminates organic peroxides in the presence of GSH. During the reaction, GSH is oxidized to GSH disulfide which is then reduced to GSH by the reaction catalyzed by glutathion-reductase (GSH-red) (5,7). They altogether play an important role in minimizing oxidative damage.

The organism's welfare depends on the activity of efficient defense systems against oxidative damage induced by FOR/ROS. The balance between these factors affects the extent of periodontal damage, and a decrease in the oxidation of host tissues may be a factor in the resolution of inflammatory changes. Therefore, besides elimination of etiological factors by mechanical approaches, complementary antioxidant treatment strategies aiming at suppressing oxidative damage and improving the energy dependent processes of healing and tissue repair have been proposed in periodontal therapy (7,8).

Coenzyme Q_{10} (CoEQ), a vitamin-like substance existed naturally in the mitochondria of all cells in the human body, has indispensible functions in the bioenergetics of human tissues, including the gingiva (9). It also functions as an antioxidant and acts to inhibit lipid and protein peroxidation (10). Because of the antioxidant properties and the central role in mitochondrial oxidative phosphorylation, its adjunctive use has received a particular attention in the prevention and treatment of cardiovascular diseases and non-cardiac conditions including cancer, compromised immune systems or periodontal diseases (7,11,12). A deficiency of CoEQ has been suggested in the serum and gingiva of patients with periodontal disease (13). Periodontitis may itself lead to localized CoEQ deficiency. A limited number of clinical trials with adjunctive local and systemic administration of CoEQ to patients with periodontal disease have been conducted and the authors have claimed that CoEQ suppresses periodontal inflammation and improves clinical condition (13-16).

The present study attempted to evaluate the lipid peroxidation and GSH redox cycle of gingival tissues sampled from periodontal sites treated with subgingival scaling/root planing (SRP) alone and SRP plus adjunctive systemic use of CoEQ (SRP + CoEQ) in comparison with non-treated inflamed gingival tissue. Thus, the gingival tissue levels of thiobarbituric acid reactive substances (TBARS) which is an end-product of lipid peroxidation, GSH and the activity of GSH-red and GSH-per were investigated in chronic periodontitis (CP) patients before and after periodontal treatment.

Material and Methods

Patient Selection

Ten patients (6 males and 4 females; ranging in age from 34-47) were selected from those referred to the Department of Periodontology, Faculty of Dentistry, Marmara University and included in the study. The criteria for entry were:

- Clinical and radiographic evidence of moderate to advanced CP
- No history of periodontal treatment
- No use of antibiotics or complementary antioxidative agents within the previous 6 months
- No systemic disease or special requirements that would affect the participation

- No smoking
- In each quadrant, the presence of at least 2 teeth with comparable root anatomy and interproximal periodontal sites having probing depths (PD) of 4-7 mm combined with bleeding on probing (BOP).

Informed consent was obtained from all subjects, and gingival sampling and surgical procedures were fully explained before the study.

Clinical Examination

Plaque index (PI) was assessed according to Silness and Löe (17). PD was measured to the nearest mm from the gingival margin to the base of the pocket with a calibrated William's periodontal probe (PQ-OW, Hu-Friedy Instrument Co., Chicago, IL, USA). BOP was recorded at the time of pocket probing.

Experimental Design

All patients were thoroughly educated in oral hygiene routines 2 weeks before the start of the research to maintain a high level of oral hygiene throughout the experimental period. Subjects were asked to brush twice daily using modified Bass method. Interdental brushes and/or dental floss were employed for the proximal cleaning. The experimental design is illustrated in Figure 1.

All teeth in the mouth were treated according to a randomized block design using either the maxilla or the mandible for separate treatments applied in sequence. So, all patients were entered into a clinical protocol consisting of 2 stages each representing two different treatment groups of (SRP) and (SRP+ CoEQ).

Following the whole mouth baseline clinical measurements and site selection for sampling, the non-treated inflamed gingival tissue specimens were obtained from maxilla or mandibula. For the first stage, maxillary or mandibular 2 quadrants were selected randomly for treatment by SRP alone. SRP was performed with an ultrasonic instrument (Dentsply®, Cavitron® TF1-10 tip) and with curettes (Hu-Friedy), and was completed in one session under local anesthesia. Three weeks after the completion of SRP (18), scaled and root planed half of the mouth was assessed clinically and accessed surgically by conventional flaps where indicated (unresolved sites). Samples representing the gingival tissues of periodontal sites treated with SRP were obtained during the surgery.

At the start of the second stage, the remaining untreated half of the dentition underwent a second clinical assessment to ascertain that the clinical condition of the selected sites in these 2 quadrants was similar to the baseline values. Systemic administration of CoEQ was performed (2x daily for 3 weeks; 10 mg Coenzyme Q_{10}, Natural Wealth) and the subjects received SRP involving these untreated 2 quadrants. Three weeks after the completion of SRP, clinical measurements were repeated and the patients underwent surgical procedure (unresolved sites) during which the gingival samples representing the tissues of periodontal sites treated with SRP + CoEQ were obtained.

Measurements for clinical and biochemical variables were made by two different researchers blind to the treatment procedures.

Gingival Tissue Specimens

The pooled samples of non-treated inflamed gingival tissues were obtained from one interproximal site (PD of 4-7 mm combined with BOP) at one of the selected teeth in each quadrant of maxilla or mandibula by excision. The samples

Subjects: Chronic periodontitis patients
Pretreatment: Oral hygiene instructions
↓2 weeks
- Clinical measurements and teeth/site selection
- Baseline gingival tissue sampling (2 interproximal sites in maxilla or mandibula)

STAGE 1 (maxillary or mandibular 2 quadrants)
- Treatment: SRP

↓ 3 weeks
- Post-SRP clinical measurements
- Post-SRP gingival tissue sampling during flap surgery (2 interproximal sites)

↓3 weeks

STAGE 2 (remaining 2 quadrants)
- Clinical measurements
- Treatment: SRP + systemic administration of CoEQ

↓3 weeks
- Post-SRP + CoEQ clinical measurements
- Post-SRP + CoEQ gingival tissue sampling during flap surgery (2 interproximal sites)

Figure 1. Experimental design.

representing periodontal sites treated with SRP and SRP + CoEQ were taken at the end of stage 1 and 2, respectively, during flap surgery which was performed on half of the dentition (as maxilla or mandibula) at one time. Post-treatment gingival tissue samples were obtained from sites requiring flap surgery due to unresolved pockets.

Tissue Preparation

Gingival tissue specimens were washed in saline, blotted dry and stored at -80°C prior to use. For biochemical measurements, tissues were homogenized in 10 mM potassium phosphate buffer (1:10, v/v) with 140 mM KCL (pH 7.4) at 4°C by using a mechanic teflon piston homogenizer (RZR 2021, Heidolph Instruments GmbH & Co., Schwabach, Germany). The homogenate was centrifuged for 10 min at 400x g by using a refrigerated centrifuge (Christ II KS, Heraeus, Hanau, Germany). The resultant supernatant was used for the measurement of TBARS, GSH and GSH-related antioxidant enzyme activities (19).

TBARS assay

For the measurement of the TBARS level, 0.1 mL of the homogenate was added to a mixture of 0.2 mL 81% sodium dodecyl sulfate, 1.5 mL of 20% acetic acid and 1.5 mL of 0.8% 2-thiobarbituric acid. This mixture was heated in an oil bath at 95°C for 60 min. After cooling with tap water, 1 mL of distilled water and 5 mL of n-butanol/pyridine (15:1, v/v) were added and shaken vigorously. After centrifugation at 2000 x g for 10 min, the absorbance of the organic layer was measured spectrophotometrically at 532 nm. TBARS level was calculated using 1.56×10^5 M^{-1} cm^{-1} as molar absorption coefficient and expressed as nmol TBARS/mg protein. The protein concentration of homogenate was measured with the folin phenol reagent (19,20).

Measurement of GSH

A modified method of Beutler et al. (21) was used for the measurement of the GSH levels (20). Briefly, 1.5 mL of 1.15% KCl was added to 0.5 mL of homogenate. The mixture was deproteinized with the precipitating solution containing 1.67 g meta phosphoric acid, 0.2 g EDTA and 30 g NaCl per 100 mL and centrifuged at 400xg for 10 min. A volume of 0.5 mL supernatant was added to 2 mL of 0.3 M sodium phosphate solution. After 0.5 mL of 0.4 mg/mL dithiobis-nitrobenzoic acid was added, absorbance was measured at 412 nm. The GSH level was calculated using 1.36×10^4 M^{-1} cm^{-1} as molar absorption coefficient and expressed as nmol GSH/mg protein.

Measurement of GSH-per and GSH-red activities

GSH-per and GSH-red activities of gingival tissues were measured by using commercially available kits, RS 504 and GR 2368, respectively (Randox Lab. Ltd., Co. Antrim, UK). Enzyme activity was expressed as Unit/mg protein.

Data analysis

All tested parameters were evaluated only at periodontal sites with an initial PD of 4-7 mm. Interproximal sites sampled initially by gingival excision were excluded from clinical evaluation. Thus, a total of 113 periodontal sites (8-20 sites per patient) in the SRP group and 125 sites (7-20 sites per patient) in the SRP+ CoEQ group constituted the final clinical data. For all variables the arithmetic means and standart deviations ($x \pm SD$) were determined in each patient. The statistical analyses were performed using the NCSS statistics package program on an IBM compatible microcomputer. The statistical analysis of the changes of baseline and post-treatment values and intergroup (SRP versus SRP+ CoEQ) differences was performed using the Wilcoxon matched pairs signed ranks test.

Result

Clinical findings

In all patients the self-performed plaque control program, given 2 weeks prior the experimental period, resulted in improved oral hygiene. Full mouth scoring of plaque was renewed at every visit for oral hygiene reinforcement. PI scores of ≥2 were less than or equal to 10% of whole mouth throughout the study period (data not shown).

Both periodontal treatment modalities resulted in significant improvements in both PD and BOP between the baseline and post-treatment values (Table 1). The mean differences in PD and BOP from baseline were 1.73 mm and 69.02%, respectively, in the SRP group and a similar of 1.71 mm and 67.74%, respectively, in the SRP + CoQE group. The difference between these 2 groups was below the 0.05 level of significance (Table 1).

Biochemical Findings

The mean initial value for TBARS level representing the nontreated inflamed gingival tissues was 2.05 ± 0.88 nmol/mg protein. There were significant decreases in TBARS levels of gingival tissues after SRP ($p< 0.01$) and SRP + CoEQ treatments ($p< 0.01$) (Table 2). On the other hand, the GSH levels tended to increase but did not reach statistical significance ($p> 0.05$). Decreases in both GSH-red and GSH-per levels were of similar magnitude in both treatments. Intergroup changes were not significant in all parameters tested ($p> 0.05$).

Table 1. Probing depth (PD) and bleeding on probing (BOP) (%) values before and after treatments.

	SRP		SRP + CoEQ	
	PD (mm)	BOP (%)	PD (mm)	BOP (%)
Baseline (x±SD)	5.05 ± 0.54	88.68 ± 10.02	5.25 ± 0.79	84.08 ± 12.58
Post-treatment (x±SD)	3.32 ± 0.49	19.66 ± 10.98	3.44 ± 0.51	16.04 ± 9.82
Change (x±SD)	1.73* ± 0.32	69.02* ± 9.93	1.71* ± 0.42	67.74* ± 10.54

intragroup changes,*$p< 0.01$
intergroup changes were not significant

Discussion

FOR/ROS are essential to many normal biological processes, however, high levels of certain radicals or radical-derived species may result in tissue injury (22). It is likely that the oxidation of gingival tissues enhanced by increases in FOR/ROS production occurs during inflammation (7). Pathological alterations, produced by FOR/ROS actions, depend on a disequilibrium between increased FOR/ROS production and decreased antioxidant levels or activities. A decrease in the oxidation of host tissues may be a factor in the resolution of inflammatory changes. This concept has led to search for an appropriate complementary antioxidant therapy in the treatment of numerous diseases including inflammatory periodontal diseases.

The treatment of periodontal diseases is primarily based on mechanical debridement that removes subgingival plaque and plaque retaining factors in pockets such as calculus, irregularities and endotoxin deposits of cementum. The objective of mechanical therapy is to eliminate subgingival pathogens and to change the environment such that recolonization by the pathogens is unlikely, rendering the tooth surface biologically acceptable to the soft tissue (11,12). This approach reduces bacterial aggression and

Table 2. TBARS, GSH, GSH-per, GSH-red values before and after treatments.

	TBARS (nmol/mg protein)	GSH (nmol/mg protein)	GSH-per (U/mg protein)	GSH-red (U/mg protein)
Baseline (x ± SD)	2.05 ± 0.88	43.46 ± 20.31	49.14 ± 14.41	42.10 ± 5.87
Post-treatment (SRP) (x ± SD)	0.78* ± 0.63	51.26 ± 23.65	47.34 ± 13.50	35.99 ± 19.14
Post-treatment (SRP + CoQE) (x ± SD)	0.41* ± 0.39	59.08 ± 23.49	47.23 ± 10.86	36.02 ± 21.95

Intragroup changes, *$p< 0.01$ Intergroup changes were not significant

inhibits the tissue destruction directly by reducing bacterial toxic effects and indirectly by preventing the activation of host defense system.

The evidence for the therapeutic use of antioxidant agents either alone or as an adjunct to mechanical debridement in periodontal treatment exists in the literature (8). The use of exogenous antioxidants can interfere with the deteriorating activities of FOR in inflammatory diseases. CoEQ is a radical scavenging antioxidant which is thought to stabilize cell membranes (10). The reaction of FOR with CoEQ usually terminates the radical chain reaction (23). Other proposed mechanisms of actions for CoEQ include its essential function in cellular energy production and immune system stimulation (9). CoEQ has been evaluated first in animal models of periodontitis and shown to be capable of producing significant reductions in pocket depths and gingival indices when compared with controls (24). However, there is limited data on the use of CoEQ in the treatment of human periodontal diseases. Wilkinson et al (15) in a controlled study have evaluated calculus, plaque and pocket depths. Authors of this study have indicated a clinical improvement, however, no details are given of these measurements. Iwamoto et al (16) in their double-blind trial have administred adjunctive CoEQ or placebo and suggested a beneficial clinical effect in terms of tooth mobility/PD whereas McRee et al (25) have reported an antibacterial effect on subgingival microorganisms using a phase contrast microscopy. Hanioka et al (14) have recorded the beneficial effects of CoEQ administration on the immune system of periodontitis patients and subsequently they have shown significant reductions of gingival indices, BOP and microbial peptidase activity when topical CoEQ is combined with mechanical subgingival debridement in the pockets deeper than 4 mm (13). In contrast, Watts (26) have commented on the research data in the dental literature and also remarked that most of the present papers suffered from inadequate evaluation methods whose results are either inconclusive or open to question. As a matter of fact, although CoEQ has been written about in the lay literature extensively since the early 80s, there are also insufficient data to form any firm conclusions about its administration in periodontal disease, dosage and therapeutic plasma concentrations. At present, there is still a paucity of information avaible on the use of CoEQ in periodontal treatment and continued scientific and clinical validation is needed.

This study focused on investigating the levels of gingival tissue TBARS and GSH and the activity of GSH-related antioxidant enzymes in CP patients before and after initial periodontal therapy consisting of subgingival mechanical debridement. An antioxidant agent, CoEQ, used as an adjunct to mechanical debridement was further evaluated in terms of its additive clinical and biochemical effects. The clinical data indicated that both treatments improved the clinical conditions of the patients and the changes in all tested parameters were of similar magnitude in both treatment modalities. The measurement of TBARS revealed significant reductions in both groups without any significant intergroup differences. GSH levels were slightly increased after the treatments accompanied by slight reductions in GSH-related enzyme activities.

The detection and measurement of lipid peroxidation is the evidence most frequently cited to support the involvement of FOR reactions to cause cellular damage in many of the pathologic disorders and inflammatory conditions (5). Lipid peroxidation give rise to several end products. One of them is alkalans, typified by malondialdehyde which is a TBARS used as an indicator of lipid peroxidation (27). The most common approach for measuring FOR activity is to measure the end or intermediate products of lipid peroxidation (28). Within the scope of this study, it has been shown that TBARS levels in the inflamed gingival tissues are statistically greater than in post-SRP ($p< 0.01$) and post-SRP + CoEQ values ($p< 0.01$). These findings indicate the inhibitory effect of subgingival mechanical debridement either alone or together with systemic use of CoEQ on lipid peroxidation in inflamed gingival tissues collected from CP patients. Clinical resolution of

inflammation is accompanied by reductions in lipid peroxidation. Lipid peroxides are considered as one of the most important causes of periodontal diseases (29). Tüter et al (30) in a recent study showed that disease activity markers in gingival crevicular fluid (GCF) and TBARS levels in gingival tissues are closely related with periodontal status. A part of the anti-inflammatory effect of these two treatments could be due to the inhibition of FOR/ROS activity which is supported by the clinical results and TBARS level changes of our patient samples. CoEQ given as an exogenous antioxidant agent in this study, which has antioxidant activity in mitochondria and cellular membranes, protecting against peroxidation of lipid membranes was tested with regards to its additive effects on the clinical and biochemical parameters. Although the intergroup difference revealed a limited superior effect, this difference (1.27 ± 1.13 versus 1.53 ± 0.76) may imply the potential additive effect of CoEQ in periodontal treatment and needs to be substantiated with further studies. A different dosage recommendation based upon a person's weight remains to be tested.

GSH is one of the most important cellular thiol which acts as an intra-cellular antioxidant by scavenging FOR and through enzymatic reactions. High concentrations of GSH was reported in GCF in health (28). In this study, there were insignificant increases in the gingival levels of GSH together with insignificant decreases in peroxidase and reductase activities after both types of treatments compared to baseline value. Possible relations between antioxidant systems and oxidative damage at the tissue level have been widely discussed recently (7). It is suggested that the lower GSH levels found in inflamed gingival tissues do not necessarily imply its involvement in antioxidant activity, since its free thiol (-SH) may simply have been used by oral bacteria to form hydrogen sulfide (31). Thus, slightly increasing levels of GSH after two types of initial periodontal treatment in this study (43.46 ± 20.31 versus 51.26 ± 23.65 and 59.08 ± 23.49), may reveal a limited increase in antioxidant potential and/or a possible suppression of periodontal bacteria since following the completion of initial periodontal therapy there were still unresolved sites in the patients requiring further periodontal surgical access. However, the detection of higher post-treatment GSH levels in the SRP + CoEQ group (59.08 ± 23.49) than the SRP group (51.26 ± 23.65) warrants further studies to clarify the possible positive influences of the complementary use of CoEQ on antioxidant systems.

Conclusion

The conclusion within the limits of this study is that, in CP patients, subgingival mechanical debridement with and without systemic application of CoEQ showed similar clinical and biochemical effects without statistically significant differences. The results of the present study evaluated on a short-term basis, confirmed the primary role of basic mechanical approaches in periodontal therapy and did not provide enough clinical and laboratory support for the superiority of adjunctive CoEQ use during initial periodontal treatment. However, it appears that CoEQ may have a potential additive effect, although a low dose administration was used in this study. This report which is an early proof of principle studies, necessitates further studies with other antioxidant agents for designing a strategy for their use in clinical practice. Furthermore, the long-term clinical significance of CoEQ with various doses needs to be clarified on larger group of patients.

REFERENCES

1. Page R, Kornman KS: The pathogenesis of human periodontitis: An introduction. Periodontol 2000 14: 9, 1997
2. Schroder HE, Pedrazolli SM, Page R: Correlated morphometric and biochemical analysis of gingival tissue in early chronic gingivitis in man. Archs Oral Biol 18: 899, 1973
3. Kimura S, Yonemura T, Kaya H: Increased oxidative product formation by peripheral blood polymorphonuclear leukocytes in human periodontal diseases. J Periodontal Res 28: 197, 1993
4. Gustafsson A, Asman B: Increased release of free oxygen radicals from peripheral neutrophils in adult periodontitis after Fcγ-receptor stimulation. J Clin Periodontol 23: 38, 1996
5. Kakkar R, Mantha SV, Radhi J, Prasad K, Kalra J: Increased oxidative stress in rat liver and pancreas during progression of streptozotocin-induced diabetes. Clin Sci 94: 623, 1998

6. Sido B, Hack V, Hochlehnert A, Lipps H, Herfarth C, Droge W: Impairment of intestinal glutathione synthesis in patients with inflammatory bowel disease. Gut 42: 485, 1998
7. Battino M, Bullon P, Wilson M, Newman H: Oxidative injury and inflammatory periodontal diseases: The challenge of anti-oxidants to free radicals and reactive oxygen species. Crit Rev Oral Biol Med 10: 458, 1999
8. Leggott PJ, Robertson PB, Jacob RA, Zambon JJ, Walsh M, Armitage GC: Effects of ascorbic acid depletion and supplementation on periodontal health and subgingival microflora in humans. J Dent Res 70: 1531, 1991
9. Crane FL, Sun IL, Sun EE: The essential functions of coenzyme Q. Clin Investig 71: 55, 1993
10. Ernster L, Forsmark-Andree P: Ubiquinol: An endogenous antioxidant in aerobic organisms. Clin Investig 71: 60, 1993
11. Halliwell B: Commentary oxidative stress, nutrition and health. Experimental strategies for optimization of nutritional antioxidant intake in humans. Free Radic Res 25: 57, 1996
12. Judy WV, Stogsdill WW, Folkers K: Myocardial preservation by therapy with coenzyme Q10 during heart surgery. Clin Investig 71: 155, 1993
13. Hanioka T, Tanaka M, Ojima S, Shizukuishi S, Folkers K: Effect of topical application of Coenyzme Q_{10} on adult periodontitis. Mol Aspects Med 15: 241, 1994
14. Hanioka T, McRee JT, Xia L-J, Shizukuishi S, Folkers K: Therapy with Coenyzme Q_{10} for patients with periodontal disease. 2. Effect of Coenyzme Q_{10} on the immune system. J Dent Health 43: 667, 1993
15. Wilkinson EG, Arnold RM, Folkers K: Bioenergetics in clinical medicine. VI. Adjunctive treatment of periodontal disease with coenzyme Q_{10}. Res Commun Chem Pathol Pharmacol 13: 715, 1976
16. Iwamoto Y, Watabane T, Okamoto H, Ohata N, Folkers K: Clinical effect of coenyzme Q10 on periodontal disease. In: Folkers K, Yamamura Y, eds. Biomedical and Clinical Aspects of Coenyzme Q_{10}. Amsterdam, Elsevier, 1981, p. 109
17. Silness J, Löe H: Periodontal disease in pregnancy II. Correlation between oral hygiene and periodontal condition. Acta Odontol Scand 22: 121, 1964
18. Caton J, Proye M, Polson A: Maintenance of healed periodontal pockets after a single episode of root planing. J Periodontol 53: 420, 1982
19. Ohkawa H, Ohishi N, Yagi K: Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. Anal Biochem 95: 351, 1979
20. Akçay T, Dinçer Y, Kayalı R, Çolgar U, Oral E, Çakatay U: Effects of hormone replacement therapy on lipid peroxides and oxidation system in postmenopausal women. J Toxicol Environ Health A 59: 1, 2000
21. Beutler E, Duran O, Duarte BMK: Improved method for the determination of blood glutathione. J Lab Clin Med 51: 882, 1963
22. Winrow VR, Winyard PG, Morris CJ, Blake DR: Free radicals in inflammation: second messengers and mediators of tissue destruction. Br Med Bull 49: 506, 1993
23. Marubayashi S, Dohi K, Ochi K: Role of free radicals in ischemic rat liver cell injury: Prevention of damage by α-tocopherol administration. Surgery 99: 184, 1986
24. Shizukuishi S, Inoshita E, Tsunemitsu A, Takahashi K, Kishi T, Folkers K: Therapy by Coenyzme Q10 of experimental periodontitis in a dog-model supports results of human periodontitis therapy. In: Folkers K, Yamamura Y, eds. Biomedical and Clinical Aspects of Coenyzme Q10. New York, Elsevier, 1984, p.153
25. McRee JT, Hanioka T, Shizukuishi S, Folkers K: Therapy with coenzyme Q_{10} for patients with periodontal disease. Effects of coenzyme Q_{10} on sub-gingival micro-organisms. J Dent Health 43: 659, 1993
26. Watts, TL: Coenyzme Q_{10} and periodontal treatment: is there any beneficial effect? Br Dent J 178: 209, 1995
27. Noyan A, Dincer Y, Ural S, Lynem H, Akcay T: Effect of pentoxyfilline on tourniquet damage in hand injuries. Med Sci Res 27:671, 1999
28. Chapple IL, Brock G, Eftimiadi C, Matthews JB: Gluthatione in gingival crevicular fuid and its relation to local antioxidant capacity in periodontal health and disease. Mol Pathol 55: 367, 2002
29. Sheiki M, Bouhafs RK, Hammarstrom KJ, Jarstrand C: Lipid peroxidation caused by oxygen radicals from Fusobacterium-stimulated neutrophils as a possible model for the emergence of periodontitis. Oral Dis 7: 41, 2001
30. Tüter G, Kurtiş B, Serdar M: Interleukin-1B and thiobarbituric acid reactive substance (TBARS) levels after phase 1 periodontal therapy in patients with chronic periodontitis. J Periodontol 72: 883, 2001
31. Carlsson J, Larsen JT, Edlund MB: Peptostreptococcus micros has a uniquely high capacity to form hydrogen sulfide from glutathione. Oral Microbiol Immunol 8: 42, 1993

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Correspondence: Bahar KURU, MD
Marmara University, Faculty
of Dentistry, Department
of Periodontology, İSTANBUL
btkuru@superonline.com

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