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COENZYME Q10 LOCAL DELIVERY AS AN ADJUNCT TO NON-SURGICAL PERIODONTAL TREATMENT: A RANDOMIZED CONTROLLED CLINICAL STUDY WITH BIOCHEMICAL ASSESSMENT OF IL-1B AND IL-10 LEVELS IN THE GINGIVAL CREVICULAR FLUID

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ABSTRACT

Aim: The present study was performed to evaluate the effect of locally delivered Coenzyme Q10 when used as an adjunct to conventional non-surgical mechanical periodontal treatment regarding the periodontal clinical parameters (Primary objective) and the biochemical gingival crevicular fluid levels of IL-1β and IL-10 (secondary objective).

Subjects and methods: Thirty periodontitis patients were recruited. Patients were randomly allocated into two groups. Group I (test group) involved fifteen patients who received mechanical periodontal debridement, then single application of 0.2 ml of CoQ10 gel after 48 hours. Group II included fifteen patients who received mechanical periodontal debridement only. Changes in Plaque index, Gingival index, Probing depth, Clinical attachment level, Gingival crevicular fluid IL-1β and IL-10 were assessed after treatment.

Results: Regarding CoQ10 effect on GCF level of IL-1β, intergroup comparison of percentage of change after treatment showed significant difference in favor of the test group. The same result was found for IL-10.

Conclusion: CoQ10 can be used successfully in conjunction with mechanical plaque control in management of deep pockets in stage II and III periodontitis and could enhance both clinical and GCF biochemical parameters.

KEYWORDS: CoQ10, IL-1β, IL-10, local delivery

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INTRODUCTION

Periodontitis is a chronic disease characterized by being multifactorial in origin, associated with microbial dysbiosis and leading to destruction of the periodontium **(Papapanou et al., 2018)**.

Resident oral microorganisms share in dental biofilm helping in resistance of exogenous pathogenic bacteria colonization and stimulating the immune system but at a level which is compatible with health. Microbial dysbiosis plays a significant role in etiopathogenesis of periodontitis and results from disturbance in the microbial homeostasis **(Marsh et al., 2015)**.

In the healthy state, the activity of reactive oxygen species (ROS) is usually counteracted by antioxidants reaching a state of balance **(Waddington et al., 2000, Palwankar et al., 2015)**.

Reactive oxygen species (ROS) play an important role in periodontal disease pathogenesis and many biologically active agents have been reported to counteract their destructive effect **(Imlay & Fridovich, 1991; Mates, 2000)**.

Coenzyme Q10 (CoQ10) is an endogenous antioxidant that is present in the cells of living organisms. It scavenges the ROS and protects cellular membrane phospholipids thus can aid in suppressing periodontal inflammation **(Shahla, 2000)**.

CoQ10 (ubiquinone) structure is similar to vitamin K and is present in veal, chicken and fish in large amounts **(Ercan & El, 2010; Soni et al., 2012)**.

Local periodontal levels and systemic levels of CoQ10 have been reported to be decreased in periodontal disease and in nutritional deficiencies **(Bentinger et al., 2010; Soni et al., 2012)**.

Previous studies reported that adding dietary supplement of CoQ10 to mechanical periodontal treatment, could enhance the outcomes of the treatment clinically **(Saini, 2014; Pandav et al., 2021)**. On the other hand, other studies found no additional benefits for adding CoQ10 to the conventional mechanical therapy **(Attia & Alghriany, 2017, Pranam et al., 2020)**.

To the best of our knowledge, this conflict has not been resolved yet. Moreover, no previous studies were carried out to explore the biochemical effect of CoQ10 on gingival crevicular fluid level of IL-1β and IL-10 beside the periodontal clinical effect when used as an adjunct to non-surgical mechanical therapy in the form of a locally-delivered chemotherapeutic.

AIM OF THE STUDY

The present study was performed to evaluate the effect of locally delivered Coenzyme Q10 when used as an adjunct to conventional non-surgical mechanical periodontal treatment regarding the periodontal clinical parameters (Primary objective) and the biochemical gingival crevicular fluid levels of IL-1β and IL-10 (secondary objective).

SUBJECTS AND METHODS

Sample size calculation:

A power analysis was designed to have adequate power to apply a 2-sided statistical test of the research hypothesis (Null hypothesis) that there was no difference between tested groups. An effect size 1.20 was calculated based on the results of Hugar et al 2016 and by adopting an alpha level of 0.05(5%) and a beta level of 0.20 (20%); power =80%; the predicted sample size (n) was a total of 24 cases (12 for each group). Sample size calculation was performed using G*power version 3.1.9.4. For each group 3 cases were added to compensate for any dropouts: thus, the total is 30 patients.

Study design

Thirty periodontitis cases were recruited from the outpatient clinic of Oral Medicine, Periodontology and Oral Diagnosis department, faculty of Den-

tistry, Ain Shams University. Ethical committee of the faculty of dentistry Ain Shams University approved the study protocol and the approval number is (99 /29.1.2020). All patients were informed with full details regarding the study and they all signed the informed consent for approval. Cases were randomly distributed among two equal groups according to computer program (quickCalcs): Group I included fifteen cases; sites received mechanical periodontal debridement, then single application of 0.2 ml of CoQ10 gel (Perio Q gel)* after 48 hours. Group II included fifteen patients; sites received mechanical periodontal debridement only. Allocation concealment was followed using sequentially numbered opaque sealed envelopes. Inclusion criteria included Both genders aged from 30-50 years, systemically healthy patients according to Burket's oral medicine health history survey **(Glick et al., 2008)**, cases diagnosed with periodontitis stage II or III periodontitis, test site criteria: depth of Probing pocket ≥ 5 mm and CAL ≥ 4 mm, lack of previous periodontal treatment or use of antimicrobial in the preceding 6 months and capability of attending the therapy sessions and comply with the procedures, the recall visits and protocol of oral hygiene. Exclusion criteria included smokers, breast feeding, pregnant women, vulnerable individuals (Diabetic, mentally retarded, having hematological diseases), alcoholics, patients taking antioxidant therapy and immunocompromised patients.

Treatment protocol

In the first visit after diagnosis of patients who had fulfilled inclusion criteria, all cases underwent conventional periodontal treatment which included mechanical periodontal debridement, performed using ultra-sonic scaler** and hand instruments*** for the whole dentition in a single visit. Following treatment, no anti-inflammatory or antibiotic medications were administered, and each patient received comprehensive instructions on how to self-manage plaque reduction, which included brushing and interdental cleaning. In the second visit (baseline visit) after forty-eight hours **(Han et al., 2012)**, the test site was dried using oil free air syringe, and then cotton rolls were used to isolate the site for contamination prevention by saliva for initial biochemical assessment (GCF sampling using size #30 paper point) and clinical assessment. After GCF sampling, in group 1 patients, 0.2% *perio Q* gel was locally delivered to the periodontal pocket (test site) using a plastic syringe with a plastic blunt tip to prevent injury to the pocket lining. Following the placement of the gel, cases were instructed to refrain from aggressive brushing, chewing sticky or hard food on the test site for 1 week. Follow up was scheduled for clinical and biochemical assessment.

Clinical assessment

The clinical assessment was performed at baseline and 3 months postoperatively involving Plaque index (PI), Gingival index (GI), Probing depth (PD) and Clinical attachment level (CAL).

Biochemical assessment

Gingival crevicular fluid (GCF) samples were collected to detect IL-1β & IL-10 levels at the baseline visit and after one month of treatment. This was performed by placing one size #30 paper-point in the orifice of the pocket for 30 seconds **(Makeudom. et al., 2014; Shimada et al., 2013)**, Paper point was transferred to eppendorf tube, then 0.5ml of 7.4 PH phosphate buffer saline were added, after that stored in -20˚C till analyzed in the lab. The concentration level of IL-1β & IL-10 was estimated using Enzyme linked immunosorbent assay (ELISA)**** in Global Labs, Cairo, Egypt.

* PERIO Q INC., 37 Hamilton St., Leominster, MA. 01453, USA.

** NSK, Multifunction Ultrasonic Scaler, Kanuma, Japan.

*** Gracey curettes Hu-Friedy, Chicago. IL, USA.

**** Fine Test, Wuhan Fine Biotech, Wuhan, China.

Statistical analysis

Analysis was done using SPSS 20®*, Graph Pad Prism®** and Microsoft Excel 2016***. Varaibles were presented as means ±standard deviation (SD). Periodontal and biochemical evaluation had been recorded at fixed time intervals for group I and group II. Paired t-test evaluated the level of significance between dependent parameters (time intervals for intragroup comparison) while independent t-test evaluated the level of significance between different independent variables (group I & II for intergroup comparison). In addition, percentage of total change were calculated for further statistical analysis, according to formula

$$\frac{(\text{Baseline}) - (\text{Postoperative})}{(\text{Baseline})} \times 100$$

The significant level was set at $P \leq 0.05$.

RESULTS

The study was performed on a total of 30 patients. All the patients completed the whole study steps without complications. Thus, no dropouts were found and statistical analysis was performed on the whole 30 participants

Clinical Parameters Evaluation:

Evaluation of Coenzyme Q10 Effect on Plaque Index

Plaque index of the selected patients was evaluated among three months for group I (Coenzyme Q10) and group II (Control). Regarding group I (CoQ10), mean and standard deviation of plaque index at baseline and after three months were (1.00±.53) and (1.07±.46) respectively while for group II (control) were (1.12±.51) and (1.20±.41) respectively, as listed in table (1).

Intragroup comparison using Paired t-test revealed that group I showed insignificant change by (7%) while for group II showed also insignificant change by (7.14%) as P-value > 0.05, listed in table (1).

TABLE (1) Intragroup Comparison between Different Time Intervals for Effect of Time Evaluation for Each Group on Plaque Index:

Intragroup						
	Plaque Index (M ± SD)				% Change	P-value
	Baseline		3 months			
	M	SD	M	SD		
Group I (CoQ10)	1.00	.53	1.07	.46	7%	0.702 (ns)
Group II (Control)	1.12	.51	1.20	.41	7.14%	0.6395 (ns)

M; Mean, SD; Standard Deviation, %; Percentage of change, P; Probability Level

ns; Insignificant Difference using Paired T-test

Intergroup comparison between group I and II at baseline and after three months were done by using independent t-test for independent variables which revealed insignificant difference, and there was insignificant variation between both groups regarding percentage of change as P-value >0.05, as listed in table (2).

TABLE (2) Intergroup Comparison between Group I and Group II for Plaque Index Evaluation:

Intergroup					
Time	Plaque Index (M ± SD)				P-value
	Group I (CoQ10)		Group II (Control)		
	M	SD	M	SD	
Baseline	1.00	.53	1.12	.51	.7801 (ns)
3 months	1.07	.46	1.20	.41	.2575 (ns)
% Change	7%	.92	7.14%	.98	0.6897 (ns)

M; Mean, SD; Standard Deviation, %; Percentage of change, P; Probability Level ns; Insignificant Difference using Independent T-test

* *Statistical Package for Social Science, IBM, USA.*

** *Graph Pad Technologies, USA.*

*** *Microsoft Co-operation, USA.*

Evaluation of Coenzyme Q10 Effect on Gingival Index

Gingival index of the selected patients was evaluated among three months for group I (Coenzyme Q10) and group II (Control). Regarding group I (CoQ10), mean and standard deviation of Gingival index at baseline and after three months were (2.47±.52) and (1.27±.46) respectively while for group II (control) were (2.53±.52) and (1.33±.49) respectively, as listed in table (3).

Intragroup comparison using Paired t-test revealed that group I showed significant decrease by (-48.583%) while for group II showed also significant decrease by (-47.4308%) as P-value <0.05, listed in table (3).

TABLE (3) Intragroup Comparison between Different Time Intervals for Effect of Time Evaluation for Each Group on Gingival Index

Intragroup						
	Gingival Index (M ± SD)				% Change	P-value
	Baseline		3 months			
	M	SD	M	SD		
Group I (CoQ10)	2.47	.52	1.27	.46	-48.583%	0.000*
Group II (Control)	2.53	.52	1.33	.49	-47.4308%	0.000*

M; Mean, SD; Standard Deviation, %; Percentage of change, P; Probability Level *; Significant Difference using Paired T-test

Intergroup comparison between group I and group II at baseline and after three months were performed by using independent t-test for independent variables which revealed insignificant difference as P-value > 0.05, and there was insignificant difference between both groups regarding percentage of change as P-value >0.05, as listed in table (4).

TABLE (4) Intergroup Comparison between Group I and Group II for Gingival Index Evaluation:

Intergroup					
Time	Gingival Index (M ± SD)				P-value
	Group I (CoQ10)		Group II (Control)		
	M	SD	M	SD	
Baseline	2.47	.52	2.53	.52	.726 (ns)
3 months	1.27	.46	1.33	.49	.702 (ns)
% Change	-48.583%	1.86	-47.4308%	1.32	0.0604 (ns)

M; Mean, SD; Standard Deviation, %; Percentage of change, P; Probability Level ns; Insignificant Difference using Independent T-test

Evaluation of Coenzyme Q10 Effect on Pocket Depth

Pocket depth of the selected patients was evaluated among three months for group I (CoQ10) and group II (Control). Regarding group I (CoQ10), mean and standard deviation of pocket depth at baseline and after three months were (5.87±.92) and (3.53±1.25) respectively while for group II (control) were (5.93±.70) and (4.20±1.01) respectively, as listed in table (5).

Intragroup comparison revealed that group I showed significant decrease by (-39.8637%) while for group II showed also significant decrease by (-29.1737%) as P-value < 0.05, listed in table (5).

TABLE (5) Intragroup Comparison between Different Time Intervals for Effect of Time Evaluation for Each Group on Pocket Depth:

Intragroup						
	Pocket Depth (M ± SD)				% Change	P-value
	Baseline		3 months			
	M	SD	M	SD		
Group I (CoQ10)	5.87	.92	3.53	1.25	-39.8637%	0.000*
Group II (Control)	5.93	.70	4.20	1.01	-29.1737%	0.000*

M; Mean, SD; Standard Deviation, %; Percentage of change, P; Probability Level

****; Significant Difference using Paired T-test***

Comparison between the two groups at baseline and after three months were done which revealed insignificant difference, while there was considerable variation between both categories regarding percentage of change as P-value <0.05, as listed in table (6).

TABLE (6) Intergroup Comparison between Group I and Group II for Pocket Depth Evaluation:

Intergroup					
Time	Pocket Depth (M ± SD)				P-value
	Group I (CoQ10)		Group II (Control)		
	M	SD	M	SD	
Baseline	5.87	.92	5.93	.70	.825 (ns)
3 months	3.53	1.25	4.20	1.01	.120 (ns)
% Change	-39.8637%	0.092	-29.1737%	0.067	<0.0001*

M; Mean, SD; Standard Deviation, %; Percentage of change, P; Probability Level

ns; Insignificant Difference using Independent T-test

****; significant Difference using Independent T-test***

Evaluation of Coenzyme Q10 Effect on Clinical Attachment Level

Clinical attachment level of the selected patients was evaluated among three months for group I (Coenzyme Q10) and group II (Control). Regarding group I (CoQ10), mean and standard deviation of Clinical attachment level at baseline and post three months were (3.73±1.03) and (1.93±1.10) respectively while for group II (control) were (3.87±.99) and (2.53±1.25) respectively, as listed in table (7).

Intragroup comparison using Paired t-test for significance evaluation for dependent variables of each group, it was revealed that group I showed significant decrease by (-48.2574%) while for group II showed also significant decrease by (-34.6253%) as P-value < 0.05, listed in table (7).

TABLE (7) Intragroup Comparison between Different Time Intervals for Effect of Time Evaluation for Each Group on Clinical Attachment Level:

Intragroup						
	Clinical Attachment Level (M ± SD)				% Change	P-value
	Baseline		3 months			
	M	SD	M	SD		
Group I (CoQ10)	3.73	1.03	1.93	1.10	-48.2574%	0.000*
Group II (Control)	3.87	.99	2.53	1.25	-34.6253%	0.000*

M; Mean, SD; Standard Deviation, %; Percentage of change, P; Probability Level

****; Significant Difference using Paired T-test***

Intergroup comparison revealed insignificant difference as P-value > 0.05, while there was significant difference between both groups regarding percentage of change as P-value <0.05, as listed in table (8).

TABLE (8) Intergroup Comparison between Group I and Group II for Clinical Attachment Level Evaluation:

Intergroup					
Time	Clinical Attachment Level (M ± SD)				P-value
	Group I (CoQ10)		Group II (Control)		
	M	SD	M	SD	
Baseline	3.73	1.03	3.87	.99	.721 (ns)
3 months	1.93	1.10	2.53	1.25	.173 (ns)
% Change	-48.2574%	0.11	-34.6253%	0.08	<0.0001*

M; Mean, SD; Standard Deviation, %; Percentage of change, P; Probability Level

ns; Insignificant Difference using Independent T-test

****; significant Difference using Independent T-test***

Biochemical Evaluation:

Evaluation of Coenzyme Q10 Effect on GCF Level of IL-1β

GCF Level of IL-1β of the selected patients was evaluated among one month for group I (Coenzyme Q10) and group II (Control). Regarding group I (CoQ10), mean and standard deviation of IL-1β at baseline and after one month were (98.78±36.57) and (54.20±8.41) respectively while for group II (control) were (102.23±29.05) and (75.32±15.12) respectively, as listed in table (9).

Intragroup comparison using Paired t-test for significance evaluation for dependent variables of each group, it was revealed that group I showed significant decrease by (-45.1306%) while for group II showed also significant decrease by (-26.323%) as P-value < 0.05, listed in table (9).

TABLE (9) Intragroup Comparison between Different Time Intervals for Effect of Time Evaluation for Each Group on GCF Level of IL-1β:

Intragroup						
	Concentration Level of IL-1β (M ± SD)				% Change	P-value
	Baseline		1 month			
	M	SD	M	SD		
Group I (CoQ10)	98.78	36.57	54.20	8.41	-45.1306%	0.000*
Group II (Control)	102.23	29.05	75.32	15.12	-26.323%	0.000*

M; Mean, SD; Standard Deviation, %; Percentage of change, P; Probability Level

****; Significant Difference using Paired T-test***

The comparison between both groups at baseline and after one month were done for independent variables which revealed insignificant difference as P-value > 0.05 for baseline and significant difference after one month, and there was considerable difference between groups regarding percentage of change, table (10).

TABLE (10) Intergroup Comparison between Group I and Group II for GCF Level of IL-1β Evaluation:

Intergroup					
Time	Concentration Level of IL-1β (M ± SD)				P-value
	Group I (CoQ10)		Group II (Control)		
	M	SD	M	SD	
Baseline	98.78	36.57	102.23	29.05	.777 (ns)
1 month	54.20	8.41	75.32	15.12	.000*
% Change	-45.1306%	0.1	-26.323%	0.061	<0.0001*

M; Mean, SD; Standard Deviation, %; Percentage of change, P; Probability Level

****; Significant Difference using Independent T-test***

ns; Insignificant Difference using Independent T-test

Evaluation of Coenzyme Q10 Effect on GCF Level of IL-10:

GCF Level of IL-10 of the selected patients was evaluated among one month for group I (Coenzyme Q10) and group II (Control). Regarding group I (CoQ10), mean and standard deviation of IL-10 at baseline and after one month were (21.49±10.88) and (64.16±25.55) respectively while for group II (control) were (52.72±9.89) and (81.30±7.11) respectively, as listed in table (11).

Intragroup comparison using Paired t-test for significance evaluation for dependent variables of each group, it was revealed that group I showed significant increase by (198.557%%) while for group II showed also significant increase by (54.2109%) as P-value < 0.05, listed in table (11).

TABLE (11) Intragroup Comparison between Different Time Intervals for Effect of Time Evaluation for Each Group on GCF Level of IL-10:

	Intragroup					
	Concentration Level of IL-10 (M ± SD)				% Change	P-value
	Baseline		1 month			
	M	SD	M	SD		
Group I (CoQ10)	21.49	10.88	64.16	25.55	198.557%	0.000*
Group II (Control)	52.72	9.89	81.30	7.11	54.2109%	0.000*

M; Mean, SD; Standard Deviation, %; Percentage of change, P; Probability Level

****; Significant Difference using Paired T-test***

Intergroup comparison between group I and group II at baseline and after one month were performed by using independent t-test for independent variables which revealed significant difference as P-value < 0.05, and there was significant difference between both groups regarding percentage of change as P-value <0.05, as listed in table (12).

TABLE (12) Intergroup Comparison between Group I and Group II for GCF Level of IL-10 Evaluation:

	Intergroup				
Time	Concentration Level of IL-10 (M ± SD)				P-value
	Group I (CoQ10)		Group II (Control)		
	M	SD	M	SD	
Baseline	21.49	10.88	52.72	9.89	.000*
1 month	64.16	25.55	81.30	7.11	.018*
% Change	198.557%	0.46	54.2109%	0.12	<0.0001*

M; Mean, SD; Standard Deviation, %; Percentage of change, P; Probability Level

****; Significant Difference using Independent T-test***

DISCUSSION

Reactive oxygen species (ROS) overproduction can be induced by periodontal pathogens, which may lead to the breakdown of periodontal tissue. Collagen breakdown is decreased when antioxidants scavenge ROS **(Sale et al., 2014)**.

When ROS production and antioxidant defense become out of balance, as they often do, either because of an overabundance of ROS or because antioxidant reserves are being depleted, oxidative stress occurs inside the tissues **(Nita & Grzybowski, 2016)**. Antioxidant therapy is widely applied nowadays to manage many inflammatory diseases **(Mathur et al., 2013)**.

The use of adjunctive chemical treatment modalities to the standard mechanical methods help in modifying the environment for the surrounding bacteria and stimulate the host tissue to regenerate **(Karde et al., 2017)**.

Periodontal pocket acts as a natural reservoir which is easily accessible by a local delivery device. Since periodontal diseases are confined to the pocket's immediate surroundings, periodontal pocket is an ideal location for local delivery systems used in conjunction with mechanical periodontal therapy **(Garala et al., 2013; Bibi et al., 2021)**.

CoQ10 is a naturally occurring substance **(Ercan & El, 2010; Soni et al., 2012)** . It is essential for cellular respiration, ATP production and involved in the proper functioning of the circulatory system **(Sumien et al., 2009, Saini, 2011, Saini, 2014)**

Tissue levels of CoQ10 as a protective measure are elevated with certain diseases, such as diabetes, liver diseases and infections to maintain the ratio between ROS and antioxidants **(Guan et al., 1996)**.

In recent years, CoQ10 has drawn a lot of attention from researchers in the medical literature due to its function **(Attia & Alghriany, 2017)**. Our study was performed to demonstrate the

clinical and biochemical effect of CoQ10 as a local delivery chemotherapeutic agent in the treatment of periodontitis.

Evaluation of levels of various biomarkers is one tool that can be used as a supplementary measurement for correct diagnosis **(Gurlek et al., 2017)**.

According to power analysis, the sample size was a total of 24 patients, 12 patients in each group while we decided to include 30 patients to accommodate for patients who may not be committed to the treatment or follow-up visits.

This study was performed on 30 systemically healthy patients since systemic diseases have been associated with low tissue levels of CoQ10 **(Saini, 2011)**. Patients aged between 30-50 years. since aging can be a cause of decreased levels of CoQ10 in serum or tissue **(Lopez-Lluch et al., 1999)**.

Smokers were excluded from the current study as the use of nicotine would have undesirable effects on healing of gingival tissues. Nicotine causes increased collagenase production, TNF-α, and PGE2 in GCF which in turn elevates the inflammatory state of the periodontal tissues. Moreover, it reduces GCF flow, bone mineral and impairs fibroblast formation **(Holliday et al., 2019)**.

Furthermore, smoking may affect the serum level of coQ10 increasing its demand as a result of free radicals present in cigarettes causing oxidative damage to macromolecules such as proteins, lipids and DNA **(Niklowitz et al., 2016)**.

Regarding selection of cases diagnosed as periodontitis stage II or III with probing pocket depth ≥ 5 mm and CAL ≥ 4 mm in the test site, these are considered the common stages most periodontitis patients suffer from with moderate to severe rate of disease progression and mechanical therapy maybe not be sufficient for pocket reduction which may need adjunctive use of a local delivery drug or surgical intervention **(Papapanou et al., 2018, Sanz et al., 2020)**.

It was found that a period of 3 months is suitable for the primary clinical evaluation of initial non-surgical periodontal therapy, according to previous studies **(Rylander, 1997, Egelberg, 1999)**.

ELISA was used for biochemical analysis of GCF to quantify IL-1β and IL-10 levels as it showed the marked diagnostic accuracy, sensitivity, reliability, ease of use that makes it more adaptable to office settings than other assays **(Ince et al., 2015; Baeza et al., 2016)**.

IL-1β was selected in our study, as it was proved by previous studies that IL-1 which is a potent pro-inflammatory cytokine associated with tissue destruction and inflammation in periodontitis **(Delima et al., 2002)**. Regarding IL-10, **Al-Hamoudi et al.,** in **2020** highlighted its anti-inflammatory effect in periodontitis as they found a significant elevation of GCF level of IL-10 after periodontal treatment.

A study found that GCF level of IL-1β was markedly reduced after 6 weeks of mechanical non-surgical periodontal therapy then GCF level seemed to return after that period to reach almost the same baseline level after 6 months following periodontal therapy. GCF level of IL-10 was increased only after 6 weeks with no significant changes after this period **(Goutoudi et al., 2004)**. Thus ELISA was done at baseline and after one month follow-up.

Regarding Plaque index (PI) both groups showed no statistical significant difference at baseline and follow-up, and this could be attributed to the effective patient education and enhanced plaque control performed by the patients throughout the whole study period.

Regarding Gingival index (GI) there was no statistical significant difference between group I and group II at baseline and after three months of treatment. This could be attributed to the decrease of the bacterial load inside the pocket and also due to the process of soft tissue healing that occurs post

non-surgical periodontal therapy **(Rylander, 1997; Egelberg, 1999; Graziani et al., 2017)**.

Regarding probing depth (PD) results, the current study showed that both groups showed a statistical significant reduction at 3 months compared to baseline. This reduction in PD is due to reduction of inflammation and gain of attachment after periodontal therapy **(Rylander, 1997; Egelberg, 1999; Graziani et al., 2017)**.

Results demonstrated no statistical significant difference in PD at baseline, while there was a statistical significant difference in mean percentage change between the two groups as group I showed pocket reduction by (39.86%) followed by group II which showed a (29.17%) pocket reduction. This result was in accordance with study done by **Sale et al.,** in **2014** which revealed that adjunctive use of coenzyme Q10 resulted in a more significant PD reduction than sites received non-surgical periodontal therapy alone.

Contrary to the current study **Attia & Alghriany,** in **2017** showed that intra pocket applicaton of coenzyme Q10 as an adjunct to non surgical periodontal treatment yielded no significant difference between both groups regarding PD. This result maybe due to that post operative PD evaluation was performed after one month in this study not 3 months like our study.

Considering Clinical attachment level (CAL) as a clinical outcome, both groups of the present study showed a statistical significant CAL reduction at 3 months postoperatively compared to baseline. This reduction maybe due to decreased bacterial load within the periodontal pocket after mechanical periodontal therapy and oral hygiene measures leading to reduction of inflammation and periodontal repair **(Rylander, 1997; Egelberg, 1999; Graziani et al., 2017)**.

Comparing mean percentage change of CAL post 3 months between both groups, group I showed a statistical significant CAL gain by (48.26%) more than group II which showed a (34.63%) CAL gain. This result may be due to action of coenzyme Q10 as an intercellular antioxidant by scavenging of free radicals and ROS providing a suitable environment for normal cell function and reduction of collagen degradation **(Prakash et al., 2010; Matsumura et al., 2015; Morsy et al., 2015)**.

This result was in accordance with study done by **Barakat & Attia** in **2019** which revealed that adjunctive use of coenzyme Q10 with periodontal dressing resulted in significant CAL gain after one month of healing than sites which received non-surgical periodontal therapy alone.

On the contrary another study revealed no significant gain of CAL after non-surgical periodontal treatment with the adjunctive use of coenzyme Q10 **(Salih, 2016)**. This result may be due to early placement of Q10 gel on the same day of non-surgical procedure where tissues may not be ready for gel application because of postoperative bleeding.

Regarding biochemical analysis of IL-1β within the GCF in the treated sites of this study, there was a statistical significant decrease in both groups after one month postoperatively. This result may be due to mechanical treatment and strict oral hygiene measures **(Tsang et al., 2018)**.

There was no significant difference at baseline in IL-1β level in both groups which ensure that the baseline was the same for the two groups, thus any change will be attributed to the effect of adjunctive use of coQ10. While after one month postoperatively, there was a marked statistical significant decrease in both groups. The mean percentage change of IL-1β level in group I (45.13%) which was statistical significantly different than group II (26.32%), this can be explained on the basis that coenzyme Q10 as an antioxidant is capable of calcium-dependent channels stabilization , intracellular phospholipases inhibition, inhibition of prostaglandin biosynthesis, free-radical scavenging and direct stabilization

of membrane resulting in down regulation of inflammatory state **(Morsy et al., 2015)**. In particular the decreased activity of IL-1β will diminish the production of prostaglandin E2 (PGE2) which explains the anti-inflammatory effect of CoQ10 **(Abiri & Vafa, 2021)**.

Regarding IL-10 present within the GCF in the treated sites of this study, there was a statistical significant increase in both groups after one month postoperatively. There was a marked statistical significant difference between the mean percentage change of IL-10 level in both groups as group I (198.56%) showed more increase in IL-10 level than group II (54.21%). This effect may be attributed to the ability of CoQ10 to stimulate anti-inflammatory and antioxidant activities to defeat the damage caused by free radicals and through transcriptional inactivation of inflammation signaling pathways **(Alam & Rahman, 2014)**. This result is in agreement with **Jin et al., 2013** who revealed that IL-10 level increased significantly in sites treated with coenzyme Q10 in his study on rats.

CONCLUSION

CoQ10 is a successful adjunctive modality that can be used in conjunction with mechanical plaque control in management of deep pockets in stage II and III periodontitis and can enhance both clinical and GCF biochemical parameters.

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