Evaluation of the Efficacy of Coenzyme Q_{10} in the Management of Chronic Periodontitis: A Clinical Study

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Abstract

Aim The present study was aimed to clinically evaluate the effectiveness of coenzyme Q_{10} (CoQ_{10}) in the management of chronic periodontitis.

Materials and Methods A total of 60 patients aged between 30 and 60 years with bleeding on probing and probing pocket depth (PPD) of 3 to 5 mm were selected and divided into three groups, with group I receiving scaling and root planing, group II CoQ_{10} formulation for 6 weeks, and group III receiving both scaling and root planning, followed by coenzyme Q_{10} administration for 6 weeks. PPD, relative attachment level (RAL), and gingival index were recorded in all the groups at baseline, 6 weeks, and 3 months, respectively. The data was statistically analyzed using Kruskal–Wallis, Mann–Whitney, and Wilcoxon signed rank tests.

Result Intragroup comparison showed statistically significant difference ($p \leq 0.05$) between the clinical parameters of all the groups at all time intervals, whereas intergroup comparison of all the parameters showed high statistically significant difference ($p \leq 0.001$) in group III at various time intervals followed by group I and group II.

Conclusion It was concluded from the study that CoQ_{10} is a useful adjunct in treating chronic periodontitis by boosting the host resistance to periodontal disease.

Keywords
- antioxidants
- chronic periodontitis
- coenzyme Q_{10}

Introduction

Chronic periodontitis is an inflammatory disease resulting from the interaction of bacteria and the host inflammatory response.[1] The neutrophils play a vital role in host defense, causing destruction of periodontal pathogens by both oxygen-dependent and oxygen-independent mechanisms.[2] Excessive production of reactive oxygen species (ROS) by neutrophils results in tissue damage due to oxidation of DNA, lipids, and proteins, stimulating proinflammatory cytokine release by monocytes and macrophages.[3]

Physiologically, an equilibrium exists between ROS and antioxidant defense mechanism. Elevated intracellular levels of ROS results in oxidative stress.[2]

Most of the periodontal therapies attempt to arrest the progression of periodontal destruction by causing an

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alteration of the subgingival environment, which in most instances is sufficient to improve the periodontal health. Systemic pharmacological agents such as antibiotics, antioxidants, and chemical plaque control agents tend to reinforce the mechanical periodontal treatment and enhance the host defense mechanism.[4] Provision of antioxidants, either through endogenous or exogenous sources, causes significant reduction in periodontal disease.[5] Antioxidants such as coenzyme Q_{10} (CoQ_{10}), vitamin C, vitamin E, carotenoids, and reduced glutathione protect cells and tissues from damage caused by free radicals.

CoQ_{10} is a naturally occurring lipid-soluble antioxidant discovered by Frederick Crane and colleagues in 1957. Human cells synthesize CoQ_{10} through a cascade of eight aromatic precursors, which require adequate levels of vitamins such as folic acid, niacin, riboflavin, vitamins B6, B2 and B12, pyridoxine, and pantothenic acid.[4]

CoQ_{10} plays an important role in energy coupling by oxidative phosphorylation within mitochondria and also acts as a primary scavenger of free radicals. It also has an anti-inflammatory role because of its ability to repress inflammatory gene expression. CoQ_{10} is an important lipid-soluble antioxidant which helps in protecting cellular membrane and lipoproteins from free radical-induced oxidative damage.[4,6]

Deficient levels of CoQ_{10} can result due to various reasons such as nutritional deficiencies, genetic or acquired defects, increased tissue needs, and declining levels of CoQ_{10} in advancing age.[7] Deficiency in CoQ_{10} levels are associated with development and progression of periodontal disease. Hence, ROS-induced tissue destruction has led to the search of an appropriate complimentary antioxidant therapy, useful in the treatment of numerous diseases including chronic periodontitis.

Keeping these views in mind, the present study was aimed to clinically evaluate the effectiveness of CoQ_{10} in the management of chronic periodontitis.

Materials and Methods

A total of 60 systemically healthy individuals aged between 30 and 60 years with bleeding on probing and probing pocket depth (PPD) of 3 to 5 mm were selected among the patients visiting the Department of Periodontology and Oral Implantology. Subjects who were on antibiotics for last 3 months; smokers and pregnant or lactating women were not included in the study.

Test Material

- Ubidecarenone (CoQ_{10}) capsules (Recharje Forte manufactured by Troikaa Pharmaceuticals Ltd. Uttarakhand, India) containing 30 mg of CoQ_{10} was given in the dosage of one capsule two times daily for 6 weeks.

Method

Patients were selected by simple random sampling technique (using table of random numbers) with 20 patients in each group. Selected patients were divided into three groups with group I receiving scaling and root planing, group II CoQ_{10} formulation for 6 weeks, and group III receiving both scaling and root planing, followed by CoQ_{10} administration for 6 weeks.

Ethical clearance was obtained from the Institutional Review Board, and all the participants were informed about the study procedure by taking verbal and written informed consent.

Parameters like PPD, relative attachment level (RAL) and gingival index (GI)[8] were recorded in all the groups at baseline, 6 weeks, and 3 months, respectively. At baseline, GI, PPD, and RAL were recorded among all the patients in three groups.

All patients were instructed to use only tooth brushing with toothpaste, and no use of mouth rinse was permitted.

Statistical Analysis

Statistical analysis was done using statistical package for social sciences (SPSS) software version 17. The quantitative data was presented as mean and standard deviation (SD). As the data was not normally distributed, nonparametric tests (Kruskal–Wallis, Mann–Whitney, and Wilcoxon signed rank) were applied to represent qualitative data. A *p*-value of ≤ 0.001 was considered to be statistically highly significant.

Results

The results are presented in the ►**Tables (1–7)**. ►**Table 1** and ►**Fig. 1** show the baseline comparisons of various parameters in different groups. ►**Tables 2–4** and ►**Figs. 2–4** show the intragroup comparisons of all the parameters (PPD, RAL, and GI) at various time intervals in groups I, II, and III, respectively, using Wilcoxon signed rank test. ►**Tables 5–7** and ►**Figs. 5–7** shows the intergroup comparisons between group I and group II, group I and group III, and between group II and group III, respectively, for mean change in PPD, RAL, and GI at various time intervals.

Table 1 Comparison of various parameters in different groups at baseline

Parameters	Group I	Group II	Group III	*p*-Value	Significance
PPD	3.5 ± 0.36	3.5 ± 0.62	3.6 ± 0.68	0.853	NS
RAL	6.72 ± 0.92	6.77 ± 1.05	6.70 ± 0.96	0.779	NS
GI	1.81 ± 0.20	1.69 ± 0.21	1.74 ± 0.30	0.218	NS

Abbreviations: GI, gingival index; NS, nonsignificant; PPD, probing pocket depth; RAL, relative attachment level.

Table 2 Intragroup comparison of the parameters at various time intervals in group I (Wilcoxon signed rank test)

Parameters	Time interval	Mean ± SD	*p*-Value	Significance
PPD	Baseline–6 weeks	0.50 ± 0.16	< 0.001	HS
	Baseline–3 months	1.05 ± 0.27	< 0.001	HS
	6 weeks–3 months	0.55 ± 0.27	< 0.001	HS
RAL	Baseline–6 weeks	0.50 ± 0.28	< 0.001	HS
	Baseline–3 months	0.87 ± 0.48	< 0.001	HS
	6 weeks–3 months	0.37 ± 0.35	< 0.001	HS
GI	Baseline–6 weeks	0.61 ± 0.32	< 0.001	HS
	Baseline–3 months	0.64 ± 0.33	< 0.001	HS
	6 weeks–3 months	0.03 ± 0.10	0.157	NS

Abbreviations: GI, gingival index; HS, highly significant; NS, not significant; PPD, probing pocket depth; SD, standard deviation; RAL, relative attachment level.

Table 3 Intragroup comparison of the parameters at various time intervals in group II (Wilcoxon signed rank test)

Parameters	Time interval	Mean ± SD	*p*-Value	Significance
PPD	Baseline–6 weeks	0.20 ± 0.25	0.005	HS
	Baseline–3 months	0.40 ± 0.30	0.005	HS
	6 weeks–3 months	0.20 ± 0.25	< 0.001	HS
RAL	Baseline–6 weeks	0.12 ± 0.22	0.025	S
	Baseline–3 months	0.40 ± 0.38	0.001	HS
	6 weeks–3 months	0.27 ± 0.25	0.001	HS
GI	Baseline–6 weeks	0.18 ± 0.20	0.004	HS
	Baseline–3 months	0.38 ± 0.24	0.001	HS
	6 weeks–3 months	0.19 ± 0.16	< 0.001	HS

Abbreviations: GI, gingival index; HS, highly significant; PPD, probing pocket depth; RAL, relative attachment level; S, significant; SD, standard deviation.

Table 4 Intragroup comparison of the parameters at various time intervals in group III (Wilcoxon signed rank test)

Parameters	Time interval	Mean ± SD	*p*-Value	Significance
PPD	Baseline–6 weeks	0.65 ± 0.28	< 0.001	HS
	Baseline–3 months	1.35 ± 0.43	< 0.001	HS
	6 weeks–3 months	0.70 ± 0.34	< 0.001	HS
RAL	Baseline–6 weeks	0.52 ± 0.44	< 0.001	HS
	Baseline–3 months	1.22 ± 0.65	< 0.001	HS
	6 weeks–3 month	0.67 ± 0.37	< 0.001	HS
GI	Baseline–6 weeks	0.53 ± 0.36	< 0.001	HS
	Baseline–3 months	0.71 ± 0.31	0.014	S
	6 weeks–3 months	0.18 ± 0.31	< 0.001	HS

Abbreviations: GI, gingival index; HS, highly significant; PPD, probing pocket depth; RAL, relative attachment level; S, significant; SD, standard deviation.

Discussion

Chronic periodontitis is the result of abnormal host response and alterations in the complex microflora of subgingival plaque biofilm. This microflora causes tissue destruction directly by the formation of toxic products and indirectly by activating the host defense mechanisms, that is, inflammation. Inflammation results in tissue infiltration by polymorphonuclear leukocytes and monocytes, subsequently followed by

Table 5 Intergroup comparison of mean change in PPD at various time intervals (Mann–Whitney test)

Time interval	Group	Mean ± SD	*p*-Value	Significance
Baseline–6 weeks	Group I	0.50 ± 0.16	< 0.001	HS
	Group II	0.20 ± 0.25		
	Group I	0.50 ± 0.16	0.049	S
	Group III	0.65 ± 0.28		
	Group II	0.20 ± 0.25	< 0.001	HS
	Group III	0.65 ± 0.28		
Baseline–3 months	Group I	1.05 ± 0.27	< 0.001	HS
	Group II	0.40 ± 0.30		
	Group I	1.05 ± 0.27	0.018	S
	Group III	1.35 ± 0.43		
	Group II	0.40 ± 0.30	< 0.001	HS
	Group III	1.35 ± 0.43		
6 weeks–3 months	Group I	0.55 ± 0.27	< 0.001	HS
	Group II	0.20 ± 0.25		
	Group I	0.55 ± 0.27	0.147	NS
	Group III	0.70 ± 0.34		
	Group II	0.20 ± 0.25	< 0.001	HS
	Group III	0.70 ± 0.34		

Abbreviations: GI, gingival index; HS, highly significant; NS, not significant; PPD, probing pocket depth; RAL, relative attachment level; S, significant; SD, standard deviation.

Table 6 Intergroup comparison of mean change in RAL at various time intervals (Mann–Whitney test)

Time interval	Group	Mean ± SD	*p*-Value	Significance
Baseline–6 weeks	Group I	0.50 ± 0.28	< 0.001	HS
	Group II	0.12 ± 0.22		
	Group I	0.50 ± 0.28	0.964	NS
	Group III	0.52 ± 0.44		
	Group II	0.12 ± 0.22	0.002	HS
	Group III	0.52 ± 0.44		
Baseline–3 months	Group I	0.87 ± 0.48	0.003	HS
	Group II	0.40 ± 0.38		
	Group I	0.87 ± 0.48	0.153	NS
	Group III	1.20 ± 0.65		
	Group II	0.40 ± 0.38	< 0.001	HS
	Group III	1.20 ± 0.65		
6 weeks–3 months	Group I	0.37 ± 0.35	0.422	NS
	Group II	0.27 ± 0.25		
	Group I	0.37 ± 0.35	0.016	S
	Group III	0.67 ± 0.37		
	Group II	0.27 ± 0.25	0.001	HS
	Group III	0.67 ± 0.37		

Abbreviations: GI, gingival index; HS, highly significant; NS, not significant; PPD, probing pocket depth; RAL, relative attachment level; S, significant; SD, standard deviation.

Table 7 Intergroup comparison of mean change in GI at various time intervals (Mann–Whitney test)

Time interval	Group	Mean ± SD	*p*-Value	Significance
Baseline–6 weeks	Group I	0.61 ± 0.32	< 0.001	HS
	Group II	0.18 ± 0.20		
	Group I	0.61 ± 0.32	0.532	NS
	Group III	0.53 ± 0.36		
	Group II	0.18 ± 0.20	0.003	HS
	Group III	0.53 ± 0.36		
Baseline–3 months	Group I	0.64 ± 0.33	0.010	HS
	Group II	0.38 ± 0.24		
	Group I	0.64 ± 0.33	0.489	NS
	Group III	0.71 ± 0.31		
	Group II	0.38 ± 0.24	0.001	HS
	Group III	0.71 ± 0.31		
6 weeks–3 months	Group I	0.03 ± 0.10	0.001	HS
	Group II	0.19 ± 0.16		
	Group I	0.03 ± 0.10	0.053	S
	Group III	0.18 ± 0.31		
	Group II	0.19 ± 0.16	0.194	NS
	Group III	0.18 ± 0.31		

Abbreviations: GI, gingival index; HS, highly significant; NS, not significant; PPD, probing pocket depth; RAL, relative attachment level; S, significant; SD, standard deviation.

phagocytosis, leading to nonmitochondrial O_2 consumption. This phenomenon, in turn, generates free radicals (FR) and ROS capable of damaging cellular membranes.

The oxidative damage is controlled by the antioxidant defense mechanisms of the surrounding tissues but plaque microflora responsible for periodontitis tend to alter this equilibrium. These findings, therefore, led to a search for an efficient "antioxidant therapy" in inflammatory periodontal disease.[9]

CoQ_{10} was evaluated first in animal models of periodontitis and was shown to be capable of producing significant reduction in PPD and GI.[10]

Various clinical trials of Coenzyme Q_{10} have been conducted so far and the results showed that it is an effective intracellular antioxidant and its increased concentration in the diseased gingiva effectively suppresses advanced periodontal inflammation.[4,11–14]

On the basis of new concepts of synergism with nutritional supplements and host response, the present study is intended to compare the following three treatment modalities: scaling and root planing, administration of CoQ_{10} orally, and scaling and root planing combined with CoQ_{10} in patients suffering from chronic periodontitis.

In our study, CoQ_{10} was given in the dosage of 30 mg twice daily for 6 weeks, which was in accordance with the study conducted by Brzozowska et al.[15] Different authors have used different dosages of the drug for different time periods.[12,13,16,17] In our study, the time period for drug

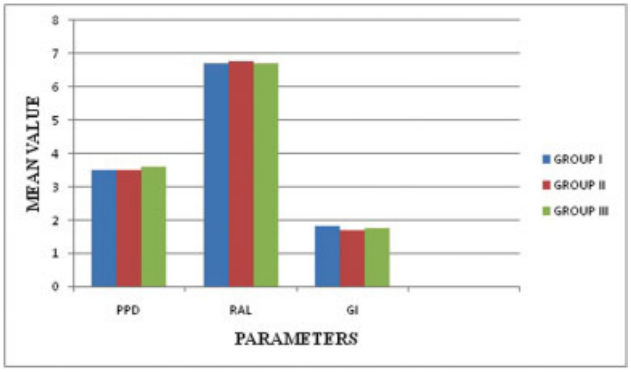

Fig. 1 Baseline comparison of the different groups for various parameters.

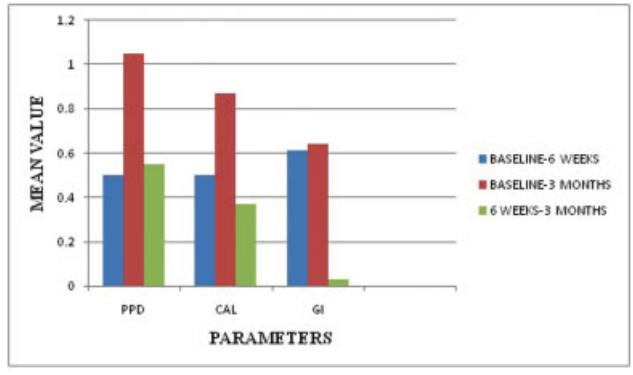

Fig. 2 Intragroup comparison of the parameters at various time intervals in group I (Wilcoxon signed rank test).

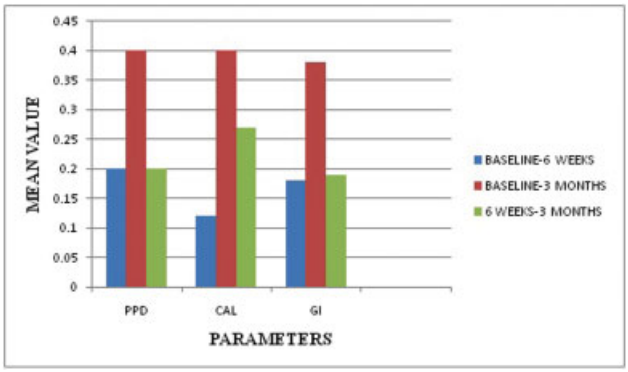

Fig. 3 Intragroup comparison of the parameters at various time intervals in group II (Wilcoxon signed rank test).

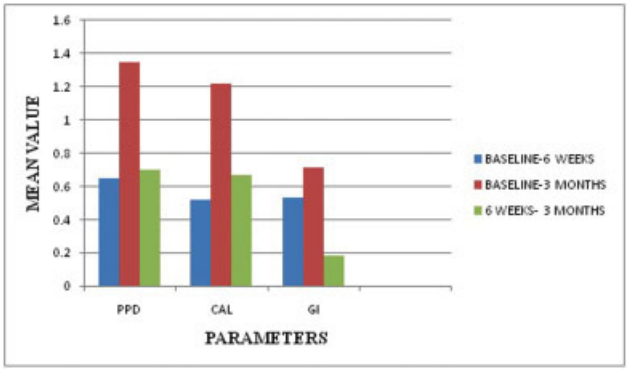

Fig. 4 Intragroup comparison of the parameters at various time intervals in group III (Wilcoxon signed rank test).

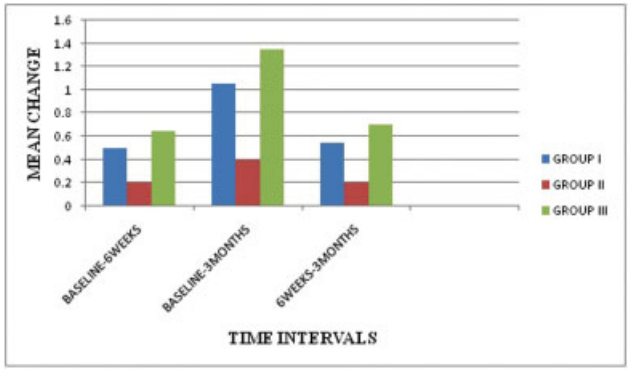

Fig. 5 Intergroup comparison of mean change in probing pocket depth (PPD) at various time intervals (Mann–Whitney test).

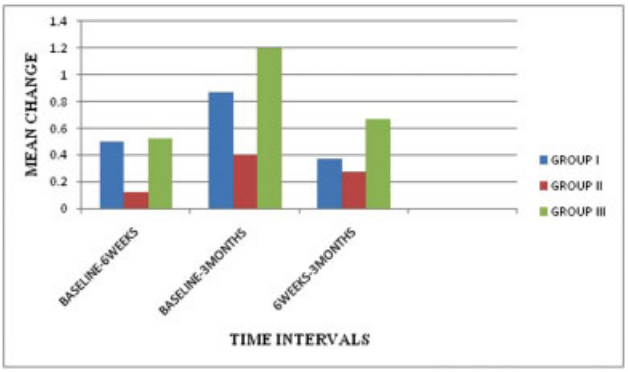

Fig. 6 Intergroup comparison of mean change in relative attachment level (RAL) at various time intervals (Mann–Whitney test).

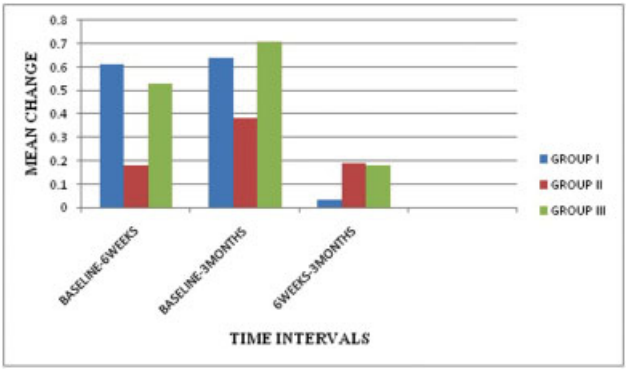

Fig. 7 Intergroup comparison of mean change in gingival index (GI) at various time intervals (Mann–Whitney test).

administration was 6 weeks, owing to the fact that a complete healing of the soft tissues takes at least 6 weeks, whereas maturation and remodeling can continue up to 6 months.[18]

The intragroup comparison of all the parameters at various time intervals showed significant improvement in all the three groups. Improvement in group I can be attributed to the fact that scaling and root planing causes gradual reduction in inflammatory cells and crevicular fluid flow, causing repair of connective tissue, which results in decreased inflammatory response in the periodontal tissues.[19] A similar improvement in the parameters was seen in group II, which can be attributed to the fact that CoQ_{10} decreases the bacterial peptidase activity specific for periodontopathic bacteria like Porphyromonas gingivalis, Bacteroides forsythus and Treponema denticola, as proposed in the study conducted by Ishihara et al.[20] Wilson et al[21] and McRee et al [13] in their study showed that topical application of a redox agent to the periodontal pocket shifted subgingival microbiota from Gram-negative anaerobes, spirochetes and motile bacteria to facultative anaerobes and cocci, causing improvement in periodontal health. Similarly, significant improvement was also seen in our study in group III due to the combined effect of scaling and root planing along with CoQ_{10} administration. The results of our study are also in accordance with the study conducted by Hanioka et al.[22]

Intergroup comparison of the mean change in PPD was significantly higher in group III, followed by group I and group II. Hence, it was seen that scaling and root planing along with CoQ_{10} in group III caused greatest reduction in PPD. These findings were in conjunction with study conducted by Sale et al[23] and Saini.[24] Scaling and root planing reduces the number of subgingival plaque microorganisms significantly and produces a shift in its composition, with increase of Gram-negative anaerobes to one dominated by

Gram-positive facultative bacteria.[25–31] It also leads to profound reduction in the number of spirochetes, motile rods and putative pathogens such as Actinobacillus actinomycetemcomitans, Porphyromonas gingivalis and Prevotella intermedia and an increase in coccoid cells.[26,28,30,32–34] These changes are accompanied by either reduction or elimination of the signs of clinical inflammation.[35–42] CoQ_{10}, used as an adjunct to scaling and root planing, tends to lower the gingival lipid peroxidation at an advanced rate than scaling and root planing alone, thus causing greater improvement in periodontal health, as shown in the study conducted by Kuru et al,[10] which can be the possible reason for improvement seen in PPD in group II and group III in our study. Also, the oral administration of CoQ_{10} increases the succinate dehydrogenase-coenzyme Q_{10} reductase enzyme activity in gingiva, which contributes to the extraordinary effective healing and could be the reason for the results seen in groups II and III.[11]

The intergroup comparison of mean change in RAL showed significantly higher improvement in group III followed by group I and group II. Studies conducted by Hans et al, Sale et al, and Saini showed similar results.[23,24,43] Possible reason for such an improvement, according to Matsumura et al,[44] is that the administration of CoQ_{10} restores the elevated blood-citrate and serum-calcium levels, leading to significant improvement in alveolar bone porosity, myelofibrosis, and atrophy of periodontal membrane. It also profoundly effects citric acid metabolism and consequently prevents the decreased activity of osteoblasts and fibroblasts. According to Schmelzer et al,[45,46] CoQ_{10} is an efficient anti-inflammatory molecule that decreases the lipopolysaccharide (LPS)-induced secretion of proinflammatory cytokine tumor necrosis factor-α (TNF-α). CoQ_{10} regulates the functioning of interleukin-5 (IL-5), thrombin, vitronectin, vitronectin receptor, and C-reactive proteins (CRP) via transcription factor NFkappaB1. The study concluded that CoQ_{10} exerts an anti-inflammatory property via NFkappaB1-dependent gene expression. Fischer et al[47] concluded in their study that CoQ_{10} played a significant role in the reduction of the expression of proinflammatory genes CXCL2, PMAIP1, and MMD, thus limiting the periodontal disease process. These can be the other possible reasons for the improvement seen in the parameters in our study.

On comparing the three groups for the GI at baseline, 6 weeks, and 3 months, group I and III showed similar results and group II showed least reduction in the GI. At 6 weeks to 3 months, highest mean change in GI was seen in group II. Studies conducted by Iwamoto et al,[48] Denny et al,[49] Brzozowska et al,[15] Babbush et al,[50] Chatterjee et al,[51] Hans et al,[43] and CoQ_{10}[52] were in accordance with the results shown in our study. Elevated levels of CoQ_{10} are significantly responsible for improvement in GI scores. The oral administration of CoQ_{10} enhanced the restoration of the metabolic energy required for the diseased tissue and also led to increased activity of CoQ_{10}-dependent enzymes and oxygen utilization in inflamed human gingiva.[12,53] CoQ_{10}, used as an adjunct to scaling and root planing, tends to lower the gingival lipid peroxidation, causing greater improvement, which can be the possible reason for improvement seen in GI score in groups II and III in our study.[8] Hansen et al[54] and Shizukuishi et al[55] concluded in their studies that CoQ_{10} deficiencies in gingiva and leucocytes could predispose the tissues to periodontitis which, in turn, further augment the deficiency, as inflamed gingiva needs increased bioenergetics for proliferative and reparative changes. The present study showed improvement in clinical parameters like PPD, RAL, and GI score, which can be attributed to the fact that once the deficiency of CoQ_{10} is met with its oral administration, significant improvement in periodontal health results.

In the light of our study and available literature, it can be concluded that use of CoQ_{10} as an adjunct to scaling and root planing gives promising results in the treatment of plaque-induced gingivitis, significantly reduces PPD, and also causes improvement in clinical attachment level.

Conclusion

It was concluded from the study that CoQ_{10} is a significant factor in boosting host resistance to periodontal disease, not only improving the periodontal status but also enhancing the quality of life. Further studies are required with other antioxidant agents for their use in clinical practice and opening new treatment options by strengthening the host side of the disease interaction. Additional studies are needed to define the precise role of CoQ_{10}, keeping in mind its appropriate dose, effectiveness, and bioavailability in the treatment of periodontal diseases. Further role of CoQ_{10} also needed to be substantiated not only as an adjunct but also as a major therapeutic agent in the treatment of various diseases.

Conflict of Interest
None declared.

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