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CO ENZYME Q_{10} –AN ADJUNCTIVE IN THE PERIODONTAL MANAGEMENT OF TYPE II DIABETIC PATIENTS

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ABSTRACT

Aim: The term diabetes mellitus (DM) describes a metabolic disorder characterized by chronic hyperglycemia with disturbances in the carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both. Periodontitis is an inflammatory disease of the supporting tissues of the teeth caused by specific microorganisms or group of microorganisms resulting in progressive destruction of the periodontal ligament and alveolar bone with pocket formation, recession or both. Periodontitis is stated to be the sixth complication of diabetes. Prevalence of periodontitis in diabetic patients is higher as compared to non-diabetic patients. When periodontitis occurs, reactive oxygen species, which are overproduced mostly by hyperactive neutrophils, could not be balanced by antioxidant defense system and cause tissues damage especially in case of systemic diseases. Coenzyme Q_{10} functions as an intercellular antioxidant by acting as a primary scavenger of FRs and ROS. The purpose of the study was to evaluate the effect of Co Q_{10} in patients with chronic periodontitis with and without type 2 diabetes mellitus. **Materials and Methods**: 60 patients were included in the study and divided into three groups. Group I comprises of chronic periodontitis (CP) without any systemic diseases. Group II comprises of CP with type II diabetes mellitus(DM) with HbA1c less than 7%.Group III comprises of CP with type II DM with HbA1c greater than 7%. All the groups were received SRP along with Coenzyme Q_{10} at baseline, after 3,6,9 weeks. Clinical parameters like plaque index (PI), Gingival index (GI), Probing pocket depth (PPD), Clinical attachment level (CAL) were recorded at baseline, after 3, 6, 9 weeks. **Results:** Results showed that there was a statistically significant reduction in the mean PI, GI

scores during the study in all the three groups compared with baseline values. There was statistically significant reduction in PPD and CAL in all the three groups compared to baseline values. There was statistically significant difference seen in group I and II in comparison to group III in terms of PPD and CAL. There was no statistically significant difference seen at baseline3 weeks, 6 weeks, 9 weeks values in Group I and II regarding PD and CAL. **Conclusion:** The topical application of coenzyme Q_{10} in periodontitis patients has shown improvement in GI, PI, and reduction in pocket depth and gain attachment level. In patients with periodontitis, oral hygiene combined with therapy using CoQ_{10} could provide improved clinical parameters and long term benefits. But application of antioxidant could not overcome the TOS in group III patients with chronic periodontitis and uncontrolled type II DM.

KEYWORDS: Chronic periodontitis(CP), Diabetes mellitus(DM), CoenzymeQ_{10}(Co Q_{10}). Total oxidative stress(TOS).

INTRODUCTION

The term diabetes mellitus describes a metabolic disorder characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both.[1] Periodontitis is an inflammatory disease of the supporting tissues of the teeth caused by specific microorganisms or group of microorganisms resulting in progressive destruction of the periodontal ligament and alveolar bone with pocket formation, recession or both. Periodontitis is stated to be the sixth complication of diabetes. Prevalence of periodontitis in diabetic patients (59.6%) is higher as compared to non-diabetic patients (39%).[2] People with diabetes are more likely to have periodontitis and with increased severity when diabetes is uncontrolled or poorly controlled. The goal of periodontal therapy is to preserve the natural dentition, periodontium and peri-implant tissue to improve the health, comfort, esthetics and function. Mechanical debridement procedures like scaling and root planing (SRP) is considered as gold standard, but this alone may fail to eliminate the pathogens from the pockets completely because of the invasion of the organisms within the gingival tissue or in the deeper areas inaccessible to periodontal instrumentation and thus, results in recurrence of periodontal diseases. Therefore, selective removal or inhibition of pathogenic microbes with systemic or locally delivered antimicrobial, in combination with SRP, is often considered as an effective approach at specific disease active sites.[3] When periodontitis occurs, reactive oxygen species, which are

overproduced mostly by hyperactive neutrophils, could not be balanced by antioxidant defense system and causes tissues damage. This is characterized by increased metabolites of lipid peroxidation, DNA damage and protein damage. Local and systemic activities of antioxidants can also be influenced by periodontitis. Under normal physiological conditions, there is a balance between ROS and antioxidants. Oxidative stress happens only when the antioxidant defense system could not neutralize the elevated ROS production. Antioxidants present a strong defense function against ROS. Coenzyme Q_{10} is a chemical compound which has antioxidant properties and can be used as local drug delivery agent. Coenzyme Q_{10} (also known as Ubiquinone) was discovered by Crane and his colleagues in 1957 in beef heart mitochondria. It was first isolated from the mitochondria of bovine hearts in 1957 at the University of Wisconsin. Because of its Quinone structure (similar to that of vitamin K), coenzyme Q_{10} is also known as Ubiquinone.[4] Exogenous administration of CoQ_{10} showed improved specific activity of enzymes against to oxidative damage. Because of these anti-inflammatory properties, therapeutic use of coenzyme Q_{10} recently came into existence in the treatment of patients with chronic periodontitis.[5] The topical application of coenzyme Q_{10} in adult periodontitis patients has shown reduced gingival crevicular fluid flow, pocket depth and attachment loss. Results have shown that Coenzyme Q_{10} can have a beneficial effect on periodontitis when used as an adjunct to scaling and root planing. However there is lack of literature demonstrating the efficacy of coenzyme Q_{10} in chronic periodontitis patients with type II DM. Hence the present study proposes to compare the effect of coenzyme Q_{10} in periodontitis patients with and without type 2 diabetes mellitus.

MATERIALS AND METHODS

SOURCES OF DATA

Out patients visiting the Department of Periodontics, D.A.P.M.R.V Dental College, Bangalore.

INCLUSION CRITERIA

1. Age between 31 and 55 years.
2. Patient should have more than 20 teeth remaining.
3. Patients diagnosed with chronic periodontitis without Diabetes mellitus.
4. Patients diagnosed with chronic periodontitis with well controlled type 2 Diabetes mellitus and glycated hemoglobin level (HbA1c $\leq$ 7%).

5. Patients diagnosed with chronic periodontitis with uncontrolled type 2 Diabetes mellitus and glycated haemoglobin levels (HbA1c > 7%).
6. Following Phase I therapy probing depth of 5mm-7mm should be remnant.

EXCLUSION CRITERIA

1. Patients diagnosed with chronic periodontitis with type 1 diabetes mellitus.
2. Patients aged below 30 years.
3. Patients diagnosed with other systemic disorders.
4. Subjects who have received periodontal flap / regenerative therapy within the past 1 year.
5. Subjects with habits like smoking, pan chewing and other personal habits.
6. Patients who demonstrate poor oral hygiene maintenance, with a Gingival index score ≥2.1 after 2weeks of Phase I therapy.
7. Pregnant and lactating patients.
8. Patients diagnosed with known coenzyme Q_{10} allergy.
9. Patients who have received antibiotic and NSAIDS therapy from past 6 months.

METHOD OF COLLECTION OF DATA

60 Subjects were selected from OPD, Dep of periodontics, DAPM R V Dental College, Bangalore, diagnosed as with chronic periodontitis (based on the 1999 Classification of Periodontal Diseases and Conditions). These subjects were categorized into three different groups (systemically healthy group, well controlled diabetic group, uncontrolled diabetic group) and each group consists of 20 subjects with probing pocket depth of ≥ 5mm. After completion of phase I periodontal therapy. The nature of the study was explained verbally in a language comprehensible to the patient, information sheet was given and informed consent was obtained from the patient. Group I comprised of patients diagnosed with chronic periodontitis without any systemic diseases.20 patients were included in the study. First complete case history was recorded. Plaque index (Silness and Loe) and Gingival indices (Loe and Sillness) were measured. Impressions were taken from each patient by using alginate material. Customized occlusal stents prepared from cold cure acrylic material.

Following measurements were recorded

Stent to cement-enamel junction -A

Stent to gingival margin -B

Stent to deepest probing depth at test sites –C

Following parameters were calculated

Probing pocket depth = Stent to deepest probing depth at test sites(C) - Stent to gingival margin (B).

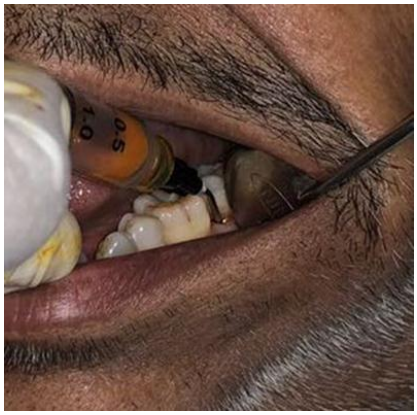
Clinical attachment level = Stent to deepest probing depth at test site(C) -Stent to cement enamel junction(CEJ) (A)

Group II comprised of patients diagnosed with chronic periodontitis and 20 patients were included. Medical history revealed that patients diagnosed with type II Diabetes mellitus and under medication. Patients were categorized into controlled diabetes through HbA1c investigation which was less than ≤ 7%. Complete case history was recorded. PI and GI were measured for each patient. Probing pocket depth (PPD) and CAL was measured for each patient by using acrylic stent.

Group III comprised of patients diagnosed with chronic periodontitis and 20 patients were included. Medical history revealed that patients diagnosed with type II Diabetes mellitus and under medication. Patients were categorized into uncontrolled diabetes through HbA1c investigation which was more than ≥8%. Complete case history was recorded. PI and GI was measured. Probing pocket depth (PPD) and clinical attachment level (CAL) was measured for each patient by using acrylic stent.

TREATMENT PROCEDURE

Initially scaling and root planing was done. One week after scaling, probing pocket depth was measured using acrylic stent. Coenzyme Q10 obtained from commercially available (iOTH coenzyme Q10) product which contain capsules. Each Capsule contains 100mg of ubedecarenone (coenzyme Q 10) and capsule is made up of gelatin and glycerine. Capsule was placed in the saline for 15 mins. Capsule containing coenzyme Q 10 loaded into disposable syringe. It was placed in the deepest pocket by blunt tipped cannula. Periodontal dressing was placed .Same Procedure was followed at, 3 6,9 weeks in all the three groups. Clinical parameters including Plaque index (PI) and Gingival index (Loe and Silness) (GI), probing pocket depth (PPD) and clinical attachment levels (CAL) were recorded using customized acrylic stent at baseline, 3,6,9 weeks. Values were subjected to statistical evaluation.



POSTOPERATIVE PROTOCOL

Oral hygiene instructions were given. Periodontal dressing was removed after 7-10 days. Postoperative evaluation was done at 3 weeks, 6 weeks, and 9 weeks. Gingival and plaque index was measured at 3 weeks, 6 weeks, and 9 weeks. Probing Pocket Depth, Clinical Attachment levels were measured at 3 weeks, 6 weeks, and 9 weeks with the previously used acrylic stents and values were subjected to statistical evaluation. Statistical test used was One way ANNOVA.

RESULTS

PI-In group I, plaque index scores at baseline, 3 weeks, 6 weeks, and 9 weeks were 1.52 ±0.16, 1.32±0.12, 1.26±0.17, 1.12±0.2 respectively. The mean difference in the values between baseline & 3weeks, base line and 6 weeks & base line and 9 weeks were 0.2, 0.26, and 0.4 respectively. The difference in the mean PI was found to be statistically significant between all the time intervals (P<0.05). It showed the same trend in group II and group III.**GI-**In group I, gingival index scores at baseline, 3 weeks, 6 weeks, and 9 weeks were 1.44 ±0.12, 1.22±0.23, 1.19±0.3, 1.08±0.12 respectively. The mean difference in the values between baseline & 3weeks, base line and 6 weeks & base line and 9 weeks were 0.2, 0.26, and 0.36 respectively. The difference in the mean PI was found to be statistically significant between all the time intervals (P<0.05). It showed the same trend in group II and III. **PD-**In group I, pocket depth at baseline, 3 weeks,6 weeks, and 9 weeks were 6.23 ±0.21 4.86±0.22, 3.96±0.3, 3.67±0.`2 respectively. The mean difference in the values between baseline & 3weeks, base line and 6 weeks & base line and 9 weeks were 1.4,2.21 and 2.5 respectively. The difference in the mean PI was found to be statistically significant between all the time intervals (P<0.05). It showed the same trend in group II and III. **CAL-**In group I, CAL at baseline, 3 weeks, 6 weeks, and 9 weeks were 6.72 ±0.21 4.92±0.22, 4.12±0.3, 3.8±0.2

respectively. The mean difference in the values between baseline & 3weeks, base line and 6 weeks & base line and 9 weeks were 1.8,2.4 and 2.9 respectively. The difference in the mean PI was found to be statistically significant between all the time intervals ($P<0.05$). It showed the same trend in group II and III. There was statistically no significant difference seen in baseline, 3 weeeks, 6 weeks, 9 weeks values in Group I and II regarding PD CAL. There was statistically significant difference seen in group III and II and group III and group I at 6 weeks and 9 weeks regarding PPD and CAL.

DISCUSSION

When periodontitis occurs, reactive oxygen species, which are overproduced mostly by hyperactive neutrophils. ROS are effectively neutralized by antioxidants, which prevent ROS-mediated tissue damage. They can cause direct damage to the tissues resulting in a variety of metabolites of lipid peroxidation, DNA damage, and protein damage and cause periodontitis. It is more severe in patients with systemic diseases like Diabetes mellitus. Under normal physiological conditions, there is a balance between ROS and antioxidants. Oxidative stress happens only when the antioxidant defence system could not neutralize the elevated ROS production. Antioxidants present a strong defence function against ROS; The antioxidant system is highly complex and total antioxidant capacity (TAOC) is important in the diagnosis. Brock et al., 2004; Chapple et al. suggested that periodontitis is associated with compromised local TAOC. TAOC associated with periodontitis can be affected by systemic conditions like gender, smoking, pregnancy, and systemic diseases like Diabetes mellitus. Pendyala et al showed that both periodontitis and diabetes mellitus could contribute to lower TAOC in saliva, and decreased TAOC in saliva. Mechanical debridement procedures like scaling and root planing (SRP) is considered as gold standard, but this alone may fail to eliminate the pathogens from the pockets completely because of the invasion of the organisms within the gingival tissue or in the deeper areas inaccessible to periodontal instrumentation and thus, results in recurrence of periodontal diseases. Therefore, selective removal or inhibition of pathogenic microbes with systemic or locally delivered antimicrobial or antioxidants in combination with SRP, is often considered as an effective approach at specific disease active sites. Hence, antioxidants are emerging as prophylactic and therapeutic agents along with the SRP. Antioxidants delivered by the diet, systemically, locally, and through a dentifrice have been shown to cause significant improvements in the measures of gingivitis, periodontitis, and oxidative injury. Coenzyme Q_{10} (CoQ_{10}) was discovered in beef heart mitochondria at the University of Wisconsin. The mechanisms of action of CoQ_{10}

include stabilization of calcium-dependent channels, inhibition of intracellular phospholipases, prostaglandin metabolism, FR scavenging, and direct membrane stabilization. CoQ_{10} functions as an intercellular antioxidant by acting as a primary scavenger of FRs and ROS. It serves as an endogenous antioxidant, and its increased concentration in the diseased gingiva effectively suppresses advanced periodontal inflammation. In the present study, Commercially available coenzyme Q_{10} was placed in all three groups at baseline, 3,6,9 weeks. Clinical parameters like Probing pocket depth(PD),clinical attachment loss, PI,GI were measured at baseline,3,6,9 weeks. It showed that subgingival application of coenzyme Q_{10} along with SRP yielded beneficial results in both systemically healthy patients as well as well controlled type II DM patients. Coenzyme Q_{10} primarily act as antioxidant. Application of Coenzyme Q_{10} along with good plaque control measures serves as scavenger of free radicles formation. Studies has shown that: In periodontitis there is excess amount of free radicle formation due to hyperactive active neutrophils which cause tissue damage. Application of antioxidants showed beneficial results in chronic periodontitis patients. Matsumura et al showed that in patients with periodontitis, oral hygiene when combined with therapy using CoQ_{10} provided improved clinical parameters and longterm benefits. Hanioka et al. evaluated the effect of subgingival debridement with topical application of CoQ_{10} to periodontal pocket and showed that sites that received CoQ_{10} topical application along with subgingival debridement showed significant improvements the clinical parameters when compared to sites that received only subgingival debridement. Priya Jain et al has done study on comparative evaluation of intrasulcular application of coenzyme Q_{10} (Perio Q TM) gel in chronic periodontitis patients. Results have shown that Coenzyme Q_{10} can have a beneficial effect on periodontitis when used as an adjunct to scaling and root planing.

But in intergroup comparison of PPD, CAL in group III (Uncontrolled Type II DM) did not show significant results when compared to other two groups. A Clinical study was done by Vidya S. Patil et al in CP with uncontrolled DM has shown that significant increase in ROS levels and significant decrease in TAOC when compared to healthy controls. Another clinical study was done by Vincent et al has shown that there was significant increase in TOS and OHI scores and significant decrease in TAOC in uncontrolled DM patients compared to healthy controls. External application of antioxidant could not overcome the TOS in chronic periodontits with uncontrolled type II DM. It is also influenced by oral hygiene status as in group III patients with poor oral hygiene status showed persistent periodontal pockets and gingival inflammation**.**

CONCLUSION

CoQ_{10} functions as an intercellular antioxidant by acting as a primary scavenger of FRs and ROS. It serves as an endogenous antioxidant, and its increased concentration in the diseased gingiva effectively suppresses advanced periodontal inflammation. Sub gingival application of coenzyme Q_{10} along with SRP yielded beneficial results in both systemically healthy patients as well as well controlled type II DM patients. External application of antioxidant could not overcome the TOS in chronic periodontits with uncontrolled type II DM. It is also influenced by oral hygiene status as in group III patients with poor oral hygiene status showed persistent periodontal pockets and gingival inflammation.

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