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Omega 3 Fatty Acids as a Host Modulator in Chronic Patients: A Randomized, Double Blind, Placebo-Controlled, Clinical Study

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Abstract: ***Introduction*: chronic periodontitis as "an infectious disease resulting in inflammation within the supporting tissues of the teeth, progressive attachment loss, and bone loss." Omega-3 fatty acids (ω-3 FAs) have anti-inflammatory properties. In present study we aimed to evaluate the effect of dietary supplementation with ω-3 FAs as a host modulating agent in patients with chronic periodontitis. *Methods*: Sixty otherwise healthy subjects with moderate and severe chronic periodontitis were selected divided randomly in test group (TG) and control group(CG) ,this study was double blind. In both the group scaling and root planing is done in control group placebo is given while in test group omega -3 fatty acid tablet is given. Periodontal clinical parameters and serum C-reactive protein (CRP) levels were evaluated in all patients at baseline, a 6-week and 12- week period after treatment. *Results*: A significant reduction in the gingival index, pocket depth, and clinical attachment level was found in the TG compared to the CG at a 12-week period. However, no statistically significant changes in serum CRP levels were found. *Conclusions*: Dietary supplementation with ω-3 FAs may have potential benefits as a host modulatory agent in the management of chronic periodontitis.***

Keywords: Generalized chronic periodontitis, omega-3 fatty acid (omega-3FA), c-recative protein (CRP), Test group (TG), Control group (CG)

1. Introduction

Chronic periodontitis as "an infectious disease resulting in inflammation within the supporting tissues of the teeth, progressive attachment loss, and bone loss." Periodontitis is caused by gram-negative periodontal microorganisms along with a disproportional unchecked host-mediated response to the dental biofiim. it is a major public health concern as it is among the most prevalent human diseases. Once the healthy periodontal architecture is lost, is cannot be completely or predictably restored. There has been a constant search for agents that can dampen the exaggerated host-mediated response. The term "Host Modulation Therapy (HMT) was introduced, to describe the emerging concept of managing the periodontal patents in part, by the use of pharmaceutical or biological agents to modify the patients host response to bacterial irritants. A variety of different drug classes have been evaluated as host modulation agents including the nonsteroidal anti inflammatory drugs (NSAIDs), bisphosphonates, tetracyclines, cytokine antagonists,- nitric oxide synthase inhibitors, enamel matrix proteins, growth factors and bone morphogenic proteins. These drugs have their own limitations and adverse effects . However, omega-3 polyunsaturated fatty acids (ω-3 PUFAs), including docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), were shown to have therapeutic value and anti-inflammatory effects in rheumatoid arthritis, cystic fibrosis, ulcerative colitis, asthma, atherosclerosis, cancer, cardiovascular disease, and periodontitis . At first, the beneficial effects of ω-3 PUFAs were attributed to a decrease in the production of classic inflammatory mediators such as AA-derived eicosanoids (prostaglandin E2) and inflammatory cytokines[1]. . However, later work revealed that a novel series of lipid mediators, resolvins and protectins, is enzymatically converted by ω-3 PUFAs, which serve as substrates for the reaction [2,3]. Hence this study was undertaken to evaluate the effect of omega-3 fatty acids as host modulating agent on chronic periodontitis patients as an adjunct to scaling and root planning.

C-reactive protein (CRP) is a serological marker of systemic inflammation that has been associated with an increased risk of various systemic diseases, including cardiovascular disease[4] and adverse pregnancy outcomes[5]. Serum CRP levels were shown to be higher in patients with periodontal disease and positively correlated with clinical parameters, including bleeding on probing (BOP), clinical attachment level (CAL), and the percentage of sites with pocket depths (PDs) ±4 mm. Thus, CRP might be a possible mediator for the association between periodontitis and systemic diseases[6].Hence in this study Clinical outcome of active versus placebo therapies were measured in addition to the quantification of serum CRP biomarkers.

2. Material and Method

The study was undertaken at the outpatient Department of Periodontology at Government Dental College and Hospital, Ahmedabad Prior to the commencement of the study the patients were explained about the study protocol and an informed written consent was obtained from them. The study was reviewed and approved by the Ethical Committee of the institution.

Criteria for Selection

Sixty patients with moderate (≥2 interproximal sites with a CAL ≥4 mm on different teeth or ≥2 interproximal sites with PDs ≥5 mm on different teeth) or severe (≥2 interproximal sites with a CAL ≥6 mm on different teeth and ≥1 interproximal site with PDs ≥5 mm) chronic periodontitis, were selected for this study. Patients who were nonsmokers,

between the age of 30 to 60 years, and without any systemic illnesses, allergies, current pregnancy, history of drug intake, and periodontal treatment in past 6 months were eligible for participation.

Patients were randomly divided into two groups - Group I (test) and Group II (control). This is a double blind study so the patients and examiner both were not aware about the drug administered. After the patient allocation, periodontal parameters such as plaque index (PI), gingival index (GI), oral hygiene index-simplified (OHIS), BOP, PD, Serum CRP and CAL were recorded at baseline (before treatment). Initial therapy was performed on all patients at baseline and consisted of a full-mouth SRP. The protocol called for SRP to be completed within a 14-day interval. After the completion of scaling and root planing test group patient has given 300 mg omega-3 fatty acids capsule twice daily for 12 weeks and the control group received a 300mg of sugar containing gelatin capsule once daily for 12 weeks as a placebo. The same clinical and laboratorial parameters were recorded at a 6-week and 12-week period after treatment in both the Test group and Control Group.

3. Statistical Analysis

The mean values and SD of all parameters (PI, GI, OHI-S, PPD, RAL and CRP) were estimated at baseline, after 3 weeks and after 12 weeks. Two tailed, unpaired (independent) Student *t*-tests were used to investigate the significance of study parameters on a continuous scale between the two groups (intergroup variability) and two tailed, paired(dependent) Student *t*-tests were used to determine the significance of study parameters on a continuous scale within each group (intragroup variability).A p value <0.05 is considered statistically significant.

Parameters	Control group (mean±SD)	Test group (mean±SD)
OHI-S		
Baseline	5.03±0.11	5.09±0.45
6 weeks	2.10±0.08	1.97±0.36
12 weeks	2.14±0.82	1.99±0.37
Gingival Index		
Baseline	2.13±0.17	2.05±0.24
6 weeks	1.31±0.24	1.31±0.13
12 weeks	1.3±0.21	1.3±0.13
Plaque Index		
Baseline	2.39±0.21	2.32±0.24
6 weeks	1.28±0.27	1.31±0.24
12 weeks	1.31±0.27	1.36±0.24
Pocket Depth		
Baseline	4.86±0.39	4.89±0.31
6 weeks	3.84±0.44	3.34±0.28
12 weeks	3.77±0.44	3.24±0.25
Relative attachment level		
Baseline	9.53±1.06	9.89±0.41
6 weeks	8.41±1.02	7.61±0.5
12 weeks	8.37±102	7.53±0.5
C-reactive protein		
Baseline	2.44±0.58	2.42±0.55
6 weeks	2.08±0.43	1.72±0.51
12 weeks	1.52±0.37	1.1±0.44
Plaque index		
Baseline	2.39±0.21	2.32±0.24
6 weeks	1.28±0.27	1.31±0.24
12 weeks	1.31±0.27	1.36±0.24

As previously stated, all clinical and biochemical parameters were assessed in both groups at the baseline and again in 6 and 12 weeks after treatment. At baseline, no significant differences between the groups were found among any of the clinical parameters and serum CRP levels .Throughout the study, plaque accumulation was minimal with no significant differences between the two groups. OHI-S index score also has no significant difference between test and control group. significant difference has been seen for gingival index, pocket depth and relative attachment level at 6 weeks and 12 weeks.

4. Discussion

periodontal disease is a periodic, progressive disease associated with tissue host response to bacterial antigens and stimuli. Host response to bacterial invasion in the form of subgingival plaque plays, an important role in which is also influenced by the genetic, systemic and environmental factors. Until the 1970s, treatment strategies for periodontal disease were based on the understanding that plaque bacteria and their products primarily mediated the issue. This concept changed when investigators began to document the host's contribution to disease pathogenesis. Scaling and root planing decrease the bacterial count while host modulators affect host-bacterial interactions. It has been confirmed that tissue destruction is due to the host response to microorganisms. HMT modulates excessive inflammatory response to allow wound healing and periodontal stability. The beneficial actions of dietary omega-3 (ω-3) PUFA supplementation were demonstrated in various inflammatory conditions in humans including rheumatoid arthritis, cardiovascular disease, and inflammatory bowel disease and in a wide variety of animal models of inflammatory disease[7,8]. dietary supplementation with omega 3 PUFAs in humans is known to increase the circulating level of resolvins[9] Which suggests a potential therapeutic modality.

Considering the above facts, in this study Host Modulation Therapy using dietary omega-3 PUFA supplementation in humans as an adjunct to nonsurgical treatment of periodontitis was performed. The present study consisted of 60 patients (males and females) having 41.3years (30 to 50 years) divided equally into the test and control.

C-reactive protein (CRP) is a serological marker of systemic inflammation that has been associated with an increased risk of various systemic diseases, including cardiovascular disease and adverse pregnancy outcomes. Serum CRP levels were shown to be higher in patients with periodontal disease and positively correlated with clinical parameters. Hence in this study Clinical outcome of active versus placebo therapies were measured in addition to the quantification of serum CRP biomarkers.

Subjects were randomly divided into the following groups-
Group A: Case group (SRP +omega 3 fatty acid capsule)
Group B: Control group (SRP + placebo)

All the examinations were performed for all the participants at baseline, 6 weeks and 12 weeks recall.

After the statistical analysis the 2nd investigator disclosed which patients were included in the case group and which patients in control group.

In the present study the plaque score at baseline in the test and control is insignificant. For intragroup comparison in the test and control group the plaque score reduced significantly from baseline to 6 weeks and 12 weeks. But showing an insignificant increase from 6 weeks to 12 weeks in the test as well control groups. Significant improvement in plaque control was seen throughout in the present study, in agreement with study of Ricardo et al in 2006[10]and with study by Suzan Ali Salmanet al in 2014[11].

Oral hygiene index is also calculated in this study additionally evaluates the patient's oral hygiene maintenance. The OHI score for test and control at baseline was insignificant. After 6 weeks and 12 weeks OHI scores decreased significantly as compared to baseline in both the groups.

The Gingival index score for test and control at baseline was insignificant. But at 6 weeks and 12 weeks there was a significant difference is seen between test and control group gingival index score.Similar observation is seen in study by **Campan et al**,he observed that using omega-3 (ω-3) fatty acids is effective in reducing gingival inflammation in human models with gingivitis.

The mean reduction in probing depth from baseline to 12 weeks was 1.09 mm in control group and 2.76 mm in test group. Reduction in probing depth was significant from baseline to 6 weeks and from baseline to 12 weeks and from 6 weeks to 12 weeks more reduction is seen in test group compare to control group.

This study finding are also in accordance with study by EL Sharkawy et al. In which he evaluated adjunctive treatment of chronic periodontitis with daily dietary supplementation with omega-3 fatty acids and low-dose aspirin in which statically significant reduction in pocket probing depth has seen after 3 and 6 month in test group compare to control group[12].

The difference of RAL in both the groups was statistically not significant when observed at baseline; however the attachment gain was significantly greater test group compare to control group at 6 weeks and 12 weeks. . In a clinical trial on patients with chronic periodontitis, PD and RAL were significantly improved after omega-3 (ω-3) PUFAs were administered compared to the placebo these findings have been corroborated by Elkhouli et al[13].

Reduction in C Reactive Protein was significant from baseline to 6 weeks and at after 12 weeks. However the C Reactive Protein reduction from 6 weeks to 12 weeks was insignificant. C Reactive protein level at baseline was statistically insignificant for the test and control groups. The reduction in the C-Reactive Protein from baseline to the 6 weeks and 12 weeks was significantly higher the in the test group as compared to the control group. **Montebugnoli et al** showed that the CRP level in and severe periodontitis patients decreased significantly after periodontal moderate therapy (form baseline to 12 weeks) in both the groups.

5. Conclusion

In conclusion, among the many methods available to treat periodontitis, host modulation by means of dietary therapy as an adjunct to conventional nonsurgical therapies (SRP) may be important in controlling deteriorative effects of the host response. Observed improvements in the TEST GROUP could have been attributed to the host modulating phenomenon of Omega-3 PUFAs in patients with chronic periodontitis. However, these beneficial results were only observed within the clinical parameters, but not within the biochemical parameter (serum CRP level). Hence, more randomised controlled trials with a larger sample size and longer duration of the follow-up are warranted to validate the usage of ω-3 PUFAs as an adjunctive dietary therapy option to treat chronic periodontitis. If effective, this therapeutic modality may be a cheaper and safer adjunctive therapy option than currently available ones for the prevention and treatment of periodontitis.

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