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Subantimicrobial Dose Doxycycline as Adjunct to Non-Surgical Periodontal Therapy (NSPT)

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Abstract: MMPs play important role in the pathogenesis of periodontitis by degrading the extracellular matrix. A relatively new approach –host modulation therapy (HMT) may be beneficial in modulating the host response to these inflammatory mediators. Sub antimicrobial dose Doxycycline can be used to antagonize the activity of MMPs. The aim of the study was to evaluate the effectiveness of SDD as an adjunct to NSPT. 40 patients with chronic periodontitis were included in this randomized double blind parallel group clinical study. After fulfillment of inclusion criteria subjects were divided into two groups by simple random sampling; cases and controls. At baseline clinical parameters were recorded and NSPT was carried out in both groups. Cases were advised to take SDD 20mg for 3 months. Both the groups were again evaluated at 3 months and at the end of 6 months. Clinical parameters improved significantly in both the groups but significant reduction in PD, BOP and RAL was seen in NSPT+SDD group compared to control group. SDD can be regarded as effective adjunct to NSPT in treatment of chronic periodontitis as appreciated by improvement in clinical parameters.

Keywords: Non-surgical periodontal therapy (NSPT), Sub antimicrobial dose doxycycline (SDD), Host modulation therapy (HMT), Matrix metalloproteinase (MMPs), chronic periodontitis.

INTRODUCTION

Microbial challenge presented by subgingival plaque in periodontitis results in up regulation of host immune inflammatory response characterized by excessive production of inflammatory mediators viz cytokines (e.g.interleukins, tumor necrosis factor-a), prostanoids (e.g. prostaglandin E2) and enzymes [including matrix metalloproteinases (MMPs)] which are responsible for the majority of periodontal breakdown that occurs, leading to the clinical signs and symptoms of disease [1].

MMPs (including collagenase, gelatinase and elastase) are homologues Metallodependent enzymes, capable of degrading the extracellular matrix. Their destructive activities are balanced by their inhibitors, the tissue inhibitors of metalloproteinases. Imbalances between pro-inflammatory and anti-inflammatory activities in the periodontal tissues are a major determinant of periodontal destruction [2].

Non-surgical periodontal therapy (NSPT) is considered as the standard treatment for periodontitis with the aim to disrupt physically the subgingival biofilm and reduce the bacterial bioburden, while removing plaque and calculus to as large an extent as is achievable. The objective of this treatment is to reduce the chronic challenge presented by the subgingival

plaque bacteria, decreasing inflammatory responses, leading to resolution of inflammation and shrinkage of the gingival tissues, thus resulting in shallower pockets (with further gains in attachment possibly arising from the formation of a long junctional epithelium) which are easier to maintain for both the patient and the clinician, and favor a less pathogenic microflora. The results following NSPT are consistent. However complete removal of pathogenic load by root surface instrumentation is not achievable. Host modulation therapy can thus be used as an adjunct to NSPT. Various drugs are used as host modulators like non-steroidal anti-inflammatory drugs, bisphosphonates and tetracyclines. Sub antimicrobial dose of doxycycline is approved by US Food and Drug administration and was introduced under the trade name of "PERIOSTAT'' which inhibits the activity of MMPs and is independent of its antimicrobial activity[3].

The present study was carried out to evaluate the effectiveness of sub antimicrobial dose of doxycycline as an adjunct to NSPT in chronic periodontitis patients.

MATERIALS AND METHODS

A 6 month randomized, parallel group study was conducted compromising of 40 patients with chronic periodontitis. Inclusion criteria involves patients with atleast 20 teeth ,with pocket depth of 4mm to 6mm at more than 30% sites and the subjects who have not received periodontal treatment for past 6 months. Exclusion criteria involves lactation and pregnancy, systemic disease or hypersensitivity to any antibiotic from tetracycline family, history of using tetracycline antibiotic or any drug in previous 4 months ago, also history of smoking and alcoholism.

After fulfillment of inclusion criteria and signing the consent form, the patients were divided into two groups' cases and controls by lottery method.

At the baseline clinical parameters PDD, BOP and RAL were measured at 4 points (mesiobuccal, midbuccal, distobuccal and palatal) with UNC-15 probe. NSPT (scaling and root planing) was done in the both groups and oral hygiene instructions were given. In case group patients were advised to take SDD 20mg b.i.d for 3 months.

Patients were recalled every month for six months, inspected for any deposits and oral hygiene instructions were reinforced. Clinical parameters were again measured in both the groups at 3 months and at the end of 6 months.

RESULTS

Forty patients who met the inclusion criteria were included in the study. 26 were males (65%) and 14 were females (35%), with mean age of 52 years. Only 36 patients participated for whole study period and were randomly divided in two groups of cases and controls with 18 patients in each group. Cases were taking 20mg doxycycline capsules Bid daily.

In case group at baseline the mean probing depth was 3.82 mm and in the control group, 3.98 mm which at the first 3 months of study the mean probing depth in the case group reached to 2.02 mm and in the control group reached to 3.04 mm, at the end of 6 months decreased to 1.95 mm and 2.94 mm, respectively, in the case and control group. Comparison of these values showed significant reduction of probing depth in different time intervals (P-value>0.0001). At baseline of the study in the case group the mean BOP was 74.28 percent and in the control group was 75.80 percent which at 3 months decreased to 51.64% and 61.17% respectively, and at the end of 6 months decreased to 40.05% and 58.80%. Comparison of these values in the different groups, were statistically significant (P-value>0.0001). At baseline mean RAL in case group was 3.84 mm and 4.02 mm in the control group which after 3-month of the study, decreased to 2.64 mm in the case group and 3.01 mm in the control group, in the next 3 months decreased to 2.01 mm and 2.95 mm, respectively, in the case and control group. Comparison of these values in the 2 groups, were statistically significantly (P-value>0.0001).

DISCUSSION

In this double blind, parallel group study, the effect of SDD as an adjunct to NSPT in patients with chronic periodontitis was evaluated. Studies have shown Microbial challenge presented by subgingival plaque in periodontitis results in up regulation of host immune inflammatory response characterized by excessive production of inflammatory mediators viz cytokines (e.g.interleukins, tumor necrosis factor-a), prostanoids(e.g. prostaglandin E2) and enzymes [including matrix metalloproteinases (MMPs)] which are responsible for the majority of periodontal breakdown that occurs, leading to the clinical signs and symptoms of disease.

In new methods for the treatment of periodontitis, the etiopathologic factors involved in reaction chains provoked by bacteria in the host's immune system are being targeted. These reactions are also affected by risk factors which cause release of cytokines and matrix metalloproteinase involved in destruction of host connective tissue. Thus, periodontal therapy involves elimination of etiologic factors and risk factors and use of tissue matrix metalloproteinase inhibitors.

In this study, three clinical parameters (PD, RAL and BOP) were studied. The difference between these parameters was not statistically significant and the severity of disease was similar between both groups at baseline. The mean probing depth at baseline was 3.82 mm and 3.98 mm in case and control groups respectively. During the study probing depth decreased

significantly in both groups in the first 3 months (P-value>0.0001). These results were found to be consistent with the previous studies done by Morrison [4] Proye[5] Cobb[6] Lindhe[7]. Reduction in probing depth subsequent to sub-gingival scaling and improvement in oral hygiene appears to be due to the combination of reduction of inflammation in connective tissues [8] and formation of long junctional epithelium[9, 10].

At the end of 6 months probing depths again decreased to 1.95 mm in the case and 2.94 mm in the control group, while the reduction of probing depth was more significant in case group than control group(P value>0.0001). This result was according to Philip *et al*. in 2004, Gulnur *et al*. in 2004, Caton *et al*. in 2001, which can be attributed to the effect of SDD in the reduction of host response [11-13]. Considering the inhibitory effect of Tetracyclines on matrix metallo-proteinase and specifically better absorption of Doxycycline and its more effectiveness in the reduction of of collagenase activity in GCF, this drug was used. SDD increases the predictability of clinical response to mechanical treatment and improves the cost/effectiveness of surgical and non-surgical treatment compared with conventional treatment.

BOP, was 74.28% and 75.80% in case and control groups *respectively*, which at 3 months decreased to 51.64% and 61.17% respectively, and at the end of 6 months decreased to 40.05% and 58.80%. Reduction in the first 3 months can be attributed to mechanical treatment and reduction of inflammation in the periodontal tissues. Also, effectiveness of SDD must be considered in reduction of inflammation in case group. These results were according to the results of previous studies [14]. Reduction of BOP is more related to the improvement of the integrity of collagen structure in periodontal pocket.

RAL in case group was 3.84 mm and 4.02 mm in the control group which after 3-month of the study, decreased to 2.64 mm in the case group and 3.01 mm in the control group, in the next 3 months decreased to 2.01 mm and 2.95 mm, respectively, in the case and control group. Attachment gain subsequent to sub-gingival scaling appears to be due to the formation of long junctional epithelium and increased content of collagen fibers in gingival connective tissue [15]. This can also be attributed to effectiveness of SDD.

CONCLUSION

SDD can be regarded as effective adjunct to NSPT in treatment of chronic periodontitis as appreciated by improvement in clinical parameters.

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