



Research Paper

Comparative Evaluation of the Effect of Doxycycline As An Adjunct to Non-Surgical Periodontal Therapy on the Metabolic Control of Poorly Controlled Type 2 Diabetic Subjects with Chronic Generalized Periodontitis – A Clinical Study

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ABSTRACT:

Background: The association between diabetes and periodontal disease has long been discussed with conflicting conclusions. Earlier studies demonstrating the relationship between diabetes and severity of periodontal disease has been equivocal. However, recent studies have clearly proven that diabetes increases the risk of periodontal disease progression. Less clear is the impact of periodontal disease on diabetes. It has been hypothesised that periodontal therapy may improve the metabolic control of diabetes.

Aim: To determine the effect of doxycycline as an adjunct to non-surgical periodontal therapy in improving the metabolic control of poorly controlled type 2 diabetic subjects with chronic generalized periodontitis.

Method: 30 poorly controlled type 2 diabetic subjects with chronic generalized periodontitis and receiving antidiabetic therapy were selected for the study. The subjects were randomly allotted to either of two treatment groups containing 15 subjects each: Group 1 (scaling and root planing(SRP)+ 15 days Doxycycline) or Group 2 (scaling and root planing(SRP)). The Glycated haemoglobin (HbA1c) values, Gingival Index(GI), and Probing pocket depth of both the groups were assessed at baseline and after 3 months.

Results: Both the treatment groups exhibited reductions in HbA1c, G I and Probing pocket depth compared to baseline over time. The amount of reduction in the glycated haemoglobin and gingival parameters was higher in Group 1 compared to group 2 after 3 months.

Conclusion: Both treatments improved glycemic control in patients with type 2 diabetes; however, the reduction in HbA1c values reached statistical significance only in the group receiving doxycycline as an adjunct to scaling and root planing.

Keywords: Chronic periodontitis, Doxycycline, Glycated haemoglobin, Non-surgical periodontal therapy

I. INTRODUCTION

Diabetes mellitus and periodontal disease are closely associated and highly prevalent chronic diseases with many similarities in pathobiology. Type 2 diabetes is a major public health problem of global importance. Patients suffering from diabetes mellitus are known to have increased susceptibility to infections. Infections, as they lead to poor metabolic control in diabetes, are of great concern since it has been shown that hyperglycaemia and poor metabolic control result in increased diabetic complications of eye, kidney and nerves. Periodontitis is defined as an “inflammatory disease of the supporting tissues of the teeth caused by specific microorganisms or groups of specific microorganisms, resulting in progressive destruction of the periodontal ligament and alveolar bone with increased probing depth formation, recession or both.”(Carranza 2011). It is well established that diabetic subjects have increased susceptibility to periodontal disease.^{2,3,4} Abrupt periodontal destruction and more severe periodontitis are observed in individuals with uncontrolled diabetes compared to individuals with well controlled blood glucose level⁵

Less clear is the impact of periodontal disease on diabetes. It has been hypothesized that periodontal therapy may improve the metabolic control of diabetes via improved insulin sensitivity by reducing the peripheral TNF α concentration⁶. Several studies have shown that treating periodontal infections could have a

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beneficial effect on glycemic control in either type 1 or type 2 diabetes^{7,8}. It has been observed that nonsurgical periodontal therapy (scaling & root planing) has positive effects on glycemic control of subjects with type 2 diabetes⁹. But complete elimination of all subgingival bacteria is not achievable by nonsurgical therapy alone and re-colonization occurs over a period of time. The use of adjunctive systemic medication has been shown to improve the healing response following mechanical periodontal therapy. The use of systemic antibiotics can be effective in decreasing the total count of bacteria in periodontal infection, with ensuing down-regulation of the inflammatory mediators leading to an improvement of glycemic control in type 2 diabetes mellitus subjects. Doxycycline may be preferred because it inhibits metalloproteinase activity in addition to its antimicrobial effects.¹⁰

The present study was undertaken to determine the efficacy of systemic doxycycline as an adjunct to nonsurgical periodontal therapy in improving the metabolic control of poorly controlled type 2 diabetes subjects with chronic generalized moderate or severe periodontitis.

II. MATERIALS AND METHODS

Poorly controlled type 2 diabetic patients (HbA1c values ≥ 8) with chronic generalized periodontitis and receiving antidiabetic therapy were selected for the study. 30 subjects who satisfied the inclusion criteria and who were willing to participate in the study were included.

Inclusion criteria

- Male and female subjects, with age groups ranging from 30 to 70 years
- Subjects with moderately and poorly controlled type 2 diabetes mellitus (HbA1c $\geq 10\%$) and receiving antidiabetic therapy
- Patients with chronic generalized moderate or severe periodontitis with attachment loss of 3mm or more on at least 8 sites on different teeth as defined by AAP

Exclusion criteria

- Subjects with any systemic disease other than type 2 diabetes
- Subjects presenting with major diabetic complications
- Presence of any concomitant chronic or acute infection
- Subjects with history of any systemic antibiotic administration or periodontal treatment within the previous six months
- Any history of allergic reaction to tetracycline

The study was approved by the Institutional Ethics and Research Committee and subjects were asked to sign consent forms and complete a questionnaire regarding personal data and medical history. The subjects were randomly allocated to either of two groups containing 15 subjects each: Group 1 (Treatment group) or Group 2 (Control group) by block randomization. The Glycated haemoglobin (HbA1c), Probing pocket depth, and Gingival Index (GI) were recorded at baseline in both the groups and oral hygiene instructions were given. Patients in the treatment group received full mouth scaling and root planing followed by 0.12% chlorhexidine mouthwash for two weeks and systemic antibiotic for 15 days (Doxycycline 100mg BD 1st day followed by 100mg OD for 14 days). Patients in the control group received full mouth scaling and root planing followed by 0.12% chlorhexidine mouthwash for two weeks. Patients were asked to strictly follow the diet as instructed by the Diabetologist. Patients in both the groups were recalled after 1 month to clinically evaluate whether they maintained good oral hygiene and oral hygiene methods were reinforced if necessary. Patients in both the groups were recalled after 3 months. During this visit, HbA1c values, Probing pocket depth and Gingival index were recorded in both the groups.

III. STATISTICAL ANALYSIS

The mean and standard deviation values per site of the clinical parameters for each group were calculated at each examination and grouped per subject per group. The change in HbA1c values and probing pocket depth after 3 months were compared to baseline using the paired 't' test. The change in GI after 3 months was compared to baseline using the Wilcoxon test. The Mann-Whitney test was used to determine significant differences between the two groups. The difference in HbA1c values between the groups was measured using analysis of covariance (ANCOVA). *P* values < 0.05 were considered statistically significant.

IV. RESULTS

A total of 30 subjects were selected for the study. Sixteen subjects were men and 14 were women. Their mean age was 54.6 years. Both groups had similar mean values for age, gender, GI, probing pocket depth and HbA1c at baseline (Table 1).

Periodontal parameters

After 3 months, there was a reduction in the GI and Probing depth (PD) in both the groups. The overall results showed a mean PD reduction of 1.3 mm. The GI decreased by 38%. The PD reductions for the SRP+Doxy group was 1.7mm and for the SRP group was 0.8 mm. Thus there was a statistically significant difference between the groups after 3 months (Table 1). Similarly there was a statistically significant difference in GI between the groups after 3 months: SRP+Doxy showed a reduction of 43.6% and SRP showed a reduction of 36%.

Metabolic parameter

In our study, the mean HbA1c value was 11.5% for SRP + Doxy group and 10.8 for the SRP group at baseline. Diabetes was poorly controlled in both the groups. After 3 months, there was a reduction in the average HbA1c levels in both the groups (Table 1). The difference in HbA1c levels after 3 months were 1.3± 0.7

Table 1. Characteristics of Study Population and Monitored Parameters (mean± SD) at Baseline and 3 months after periodontal therapy

Variable	Experimental group	Control group	p Value
Male(n)	9	7	
Female(n)	6	8	
Mean age(years)	53.9 ± 5.8	55.3 ± 6.3	0.746
GI			
Baseline	2.71 ± 0.65	2.82 ± 0.53	0.787
3 months	1.43 ± 0.36	2.16±0.48	0.001
P value	0.0001	0.001	
PD			
Baseline	6.96 ± 3.82	6.84 ± 4.13	0.171
3 months	5.26± 3.12	6.03± 3.82	0.04
P value	0.001	0.03	
HbA1c			
Baseline	10.8± 2.1	11.5± 1.3	0.620
3 months	9.5± 0.7	11.2±1.4	0.001
P value	0.0001	0.126	

PD – Probing depth

GI – Gingival index

HbA1c- Glycated Hemoglobin

p-value < 0.05 statistically significant

and 0.3± 1.4 for SRP+Doxy group and SRP group respectively, with a statistically significant difference between the two groups(Table 1).

V. DISCUSSION

The two way relationship between diabetes and periodontal disease has long been established. There is sufficient evidence that periodontal infection affects diabetes control. Many studies have corroborated that non-surgical periodontal therapy may ameliorate periodontal parameters and improve glycemic control. Our study also clearly shows that in patients with poorly controlled type 2 diabetes mellitus, treatment of periodontal disease incorporating systemic doxycycline and topical antimicrobial results in a significant reduction in periodontal infection and inflammation and a reduction in levels of HbA1c. An improved clinical response as defined by reductions in gingival inflammation and probing pocket depth was seen in both the groups after 3 months. The clinical improvement was accompanied by a reduction in the glycated haemoglobin values in both the groups. However, this reduction was statistically significant only in the SRP+Doxy group.

Some studies have failed to produce an enhanced effect of doxycycline on the probing depth^{13,14}. The mean values of probing depth has been refuted as an ideal parameter to assess the positive effects of doxycycline for the following reasons:

Shallow pockets are less likely to respond to non-surgical periodontal therapy and their mean values will also be included in the recall visits The antibiotics may effectively penetrate deep pockets. PD changes after therapy are more evident in the sites with deep pockets.

The hypothesis that periodontal therapy using adjunctive systemic antibiotics can improve glycemic control (HbA1c) was substantiated in the present study. In addition to the improvement in periodontal

parameters there was also a significant reduction in HbA1c levels. It has been proposed that tetracyclines including doxycycline inhibit the glycation of proteins in diabetics, acting by the anticollagenase property. These antibiotics prevent the activation of latent pro- MMPs, de-escalate MMP expression and counteract oxidative mechanisms responsible for periodontal tissue destruction¹⁵.

This evidence has provided a basis for therapeutic approach in controlling periodontal disease in diabetic individuals using tetracycline and its derivatives. In the present study the authors could not observe any adverse effects to systemic doxycycline in any of the subjects in the SRP+Doxy group. These findings are similar to those of Llambes et al¹⁴ who used the same drug regimen.

In the present study, HbA1c was used as the parameter to determine the metabolic control because unlike urine or plasma glucose, HbA1c gives an idea of the long term glycemic control. HbA1c predicts the average glucose level over the 30-90 days preceding the test and it does not account for short term fluctuations in plasma glucose levels. On intergroup comparison of SRP+Doxy and SRP groups, there was significant reduction in HbA1c in the SRP+Doxy group after 3 months. Grossi et al¹⁶ in their study noted a similar reduction in HbA1c values after 3 months. However studies by Jones et al¹⁷, O'Connell et al¹³ failed to demonstrate a significant reduction in HbA1c values in the Doxy group after 3 months. The possible cause for lack of significant differences in HbA1c values after 3 months may be due to the reduction of the antimicrobial drug effect.

VI. CONCLUSION

The present study found a clinically significant association between clinical improvement in periodontal condition and improved metabolic control of diabetes in both the treatment groups after 3 months. However the reduction in the HbA1c values in the SRP group after 3 months was not statistically significant. On intergroup comparison, adjunctive use of doxycycline showed improvement in both periodontal parameters and HbA1c levels which was statistically significant. Further studies with larger sample size and longer duration are required to substantiate the long term effects of these findings.

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