

Effects of full mouth disinfection procedure and doxycycline on the HbA1c levels among patients of moderate chronic periodontitis with type II diabetes mellitus: A randomised controlled clinical trial.

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Abstract

Chronic periodontitis is a chronic inflammatory destructive disease of the periodontium. The bidirectional relationship between periodontal disease and diabetes mellitus require more research particularly to check the positive effects of periodontal therapy on improvement in metabolic aspects of diabetic patients. Objective of the present study is to determine the effects of full mouth disinfection procedure in combination of systemic doxycycline on hemoglobin A1c (HbA1c) levels in moderate chronic periodontitis patients with type II diabetes. The present study is a 3 months randomized controlled clinical trial. Patients with type II diabetes mellitus taking stable dose of medications had HbA1c \geq 6.5% with untreated moderate chronic periodontitis

patients were included. Total 80 participants were enrolled in the study. All patients were randomly divided into two different groups. Group I treatment group (n=40) in which patients received full mouth disinfection procedure in combination with systemic doxycycline. Group II control group where no periodontal treatment was given. The full mouth disinfection procedure included scaling and root planing during a 24 hour period; brushing the back of the tongue with 1% Chlorhexidine gel for 1 minute; performing the subgingival irrigation of all pockets with 1% chlorhexidine gel; use of mouthwash twice with 10 ml of 0.2% chlorhexidine. Treatment group patients were prescribed 100 mg systemic doxycycline for 14 days. Difference in serum HbA1c levels were checked at baseline and after 3 months follow up period. Other

parameter assessed included measurement of oral hygiene index, probing pocket depth, gingival recession, clinical attachment loss, bleeding on probing and gingival index. The students t test, wilcoxon signed rank test, Mann Whitney U test were used to compare various parameters at intragroup and intergroup level. At 3 months follow up, HbA1c levels has reduced significantly compared with baseline in treatment group (Group I). Probing pocket depth, clinical attachment loss, bleeding on probing and gingival index measures improved at 3 months in treatment group. So it establishes positive effects of full mouth disinfection procedure and systemic doxycycline on HbA1c levels in type II diabetic patients.

Keywords: Full Mouth Disinfection, Diabetes Mellitus, Glycated Hemoglobin, Chronic Periodontitis.

Introduction

Chronic periodontitis is a chronic inflammatory destructive disease of the supporting periodontal structures of the tooth. Dental plaque is considered as primary etiological factor for periodontal disease but there are various local and systemic factors that affects the course and etiopathology of the disease that is why periodontitis is considered as disease with multifactorial etiology[1]. Diabetes mellitus and its association with periodontal diseases has been a topic of scientific research since long time[2]. On one side diabetes mellitus and poor glycemic control lead to an increased incidence of periodontal disease. On other side chronic periodontitis results in a systemic inflammatory state due to persistent bacteremia and increased levels of pro-inflammatory mediators like IL1 β , IL6, TNF α , PGE2 [3]. This increased level of inflammatory mediators will lead to increased insulin resistance in the body and ultimately leads to poor glycemic control. Reduction in systemic inflammation is one of the methods to achieve glycemic control. Proper non surgical periodontal therapy along with systemic

antibiotic will reduce the bacterial load and amount of inflammatory mediators and can be useful as one of the modality for glycemic control in type II diabetic patients. Conventional therapy for management of type II diabetic patients with oral antidiabetic agents and insulin has demonstrated reduction in the level of glycated hemoglobin (HbA1c) [4,5,6]. However, conventional therapies are challenged by the risks of lack of pharmacological responsiveness, developing insulin resistance, and rising production costs. Hence, adjunctive modalities like non surgical periodontal therapy and systemic antibiotics are speculated to improve glycemic control. India ranks second in the global diabetes map, with 65.1 million diabetes patients and majority among them are adult type 2 diabetes mellitus (T2DM) patients [7]. Early diagnosis and treatment of periodontal disease among diabetic patients as an adjunctive modality could potentially help patients in achieving glycemic control [8]. Therefore, the aim of the present study is to evaluate whether nonsurgical periodontal therapy along with systemic doxycycline plays a role in reducing HbA1c levels among type II diabetic patients with moderate periodontitis.

Materials and Methods

The present study was conducted in agreement with ethical standards established by the World Medical Association Declaration of Helsinki for research trials involving human participants. The present study was approved by the local research ethics committee of Manubai Patel Dental College and hospital, Vadodara, Gujarat, India. Eligible participants who fulfilled the inclusion criteria and agreed to the conditions of the research study were invited to sign a written informed consent. All patients were selected from outpatient section of Department of Periodontics, Manubhai Patel Dental College & Hospital, Vadodara, Gujarat, India.

Sample size was determined using the power calculation. It was estimated to be a total of 40 patients per group that provided 80% power for the detection of 1.0 mm of difference in the probing depth between the two groups with a standard deviation of 0.8 mm and type I error adjusted at 0.05 and type II error adjusted at 0.2.

Inclusion criteria

1. Patient's aged ≥ 29 years.
2. Patients who were already diagnosed with type II diabetes mellitus and taking medication prescribed by physician and newly diagnosed patients of type 2 diabetes with criteria for the diagnosis of diabetes mellitus are clinical symptoms of diabetes along with $HbA1c \geq 6.5\%$.
3. Clinical diagnosis of moderate generalized chronic periodontitis defined by loss of clinical attachment of 4 to 6 mm in all quadrants. Radiographically assessed bone loss of 30–50%.
4. Presence of ≥ 10 teeth per dental arch, excluding third molars.
5. No previous periodontal treatment taken.
6. No modification in diabetes medication for 2 months, before or during the study.
7. No major diabetic complication.
8. No history of systemic antibiotic administration within the last 3 months.

Exclusion criteria

1. Presence of any systemic disease that could influence the progression and severity of periodontal disease or hemoglobin levels in the blood.
2. Current smokers or former smokers.
3. Pregnancy or intention to be pregnant during the 6 months of study.

Patients who fulfilled inclusion criteria were randomly divided into two groups using coin toss. Group I

(Treatment Group) received full mouth disinfection therapy with systemic doxycycline (Non surgical periodontal therapy) and Group II (Control Group) did not receive any periodontal therapy.

The full mouth disinfection procedure begins with motivating and instructing the patient about good oral hygiene techniques. The procedure included are as follows
a) scaling and root planing under local anesthesia during a 24 hour period; b) brushing the back of the tongue with 1% Chlorhexidine gel; c) performing the subgingival irrigation of all pockets with 1% chlorhexidine gel; and d) use of mouthwash twice with 10 ml of 0.2% chlorhexidine. At home, the patient has to comply with the recommendations of the dental practitioner (for 2 weeks, the patient has to use mouthwash twice daily with 10 ml of 0.2% chlorhexidine and use brushing aids)[9,10]. Patient in treatment group were prescribed with systemic doxycycline 100 mg/day for 14 days started as 200 mg on the first day.

Clinical parameters included (At baseline & 3 months) Oral Hygiene Index Simplified (Green & Vermillion 1960), Bleeding on Probing, Gingival index (Loe & Silness 1963), Probing pocket depth (With calibrated UNC 15 probe), Gingival recession, Clinical attachment level.

Laboratory parameters included were Glycated hemoglobin level HbA1c, Fasting blood sugar level and 2 hours postprandial blood glucose level.

Statistical Analysis

All clinical periodontal and metabolic parameters were analyzed per individual. Means and standard deviations (SD) were estimated for all parameters. The statistical analysis was performed using SPSS software program. The student t test was used to test the differences of age, sex and duration of diabetes. The changes of OHI S, GI, PPD, CAL, GR and BOP values from baseline to third

month within both groups were compared using wilcoxon signed ranks test. The evaluation of differences for periodontal parameters in time for the treatment and the control groups was compared by using the Mann–Whitney U-test and Student t-test. The significance of the metabolic parameters within the groups was assessed by Wilcoxon signed ranks test. Non-parametric Mann–Whitney U-test was used to compare the changes in metabolic parameters between the treatment and the control groups. In the treatment and the control groups, correlations between HbA1c and BOP changes were assessed using Pearson’s correlation coefficient.

Results

Out of 132 patients screened and enrolled for the study, a total of 80 type II diabetes patients with moderate chronic periodontitis were recruited and randomized in to two study groups. Each group consisted of 40 patients. The demographic details and duration of diabetes (in years) of the study groups are described in Table 1. The mean age of patients in group I and II were 50.72±10.57 years and 51.45±7.71 years respectively. In group I there were equal number of male and female participants. Males were higher in number compared to female in group II. Duration of diabetes recorded for patients in group I is 4.7±2.78 years and for group II is 4.07±2.39 years.

Table 2 shows clinical periodontal parameters at baseline and after 3 months follow-up periods. The clinical periodontal parameters including oral hygiene index, gingival index, bleeding on probing, probing pocket depth and clinical attachment level showed significant reduction from baseline to 3 months follow-up in treatment group (Group I) (p <0.05). No significant difference was found in gingival recession in both groups. No significant difference in any clinical periodontal parameter was observed in control group (p>0.05).

Table 3 shows laboratory investigation values for treatment and control group at baseline and 3 months follow up period. There were no statistically significant differences between the two groups at baseline. At baseline mean with standard deviation value of plasma fasting glucose level was 139.27±39.14 for group I and 142.55±36.44 for group II. There was tendency towards a decrease in the treatment group (128.45±32.91) where as this changes was not found to be statistically significant in control group. Two hour post prandial levels decreased in the treatment group from 159.22±51.23 to 134.31±39.11 whereas this parameter has not changed much significantly in control group.

The normal range for the HbA1c subjects without diabetes is 4.5–6.0%. In our study, population the mean standardized HbA1c values were 7.21±0.71 for the treatment and 7.12±0.52 for the control group. The treatment group showed a reduction in HbA1c to 6.33±0.77. This reduction equates to a level approximately 10.94% of the baseline HbA1c level. The control group showed 4.42% increases in levels of HbA1c compared with baseline whereas this was not found to be statistically and clinically significant.

Table 1: Demographic data of the patients included in the study.

Parameters	Group I (Treatment Group)	Group II (Control Group)	Total
Total number of Participants (n)	40	40	80
Age in Years (mean ±SD)	50.72±10.57	51.45±7.71	50.06±9.20
Gender (Male/Female)	20/20	23/17	43/37
Duration of Diabetes (Years)	4.7±2.78	4.07±2.39	4.39±2.6

Table 2: Clinical periodontal parameters at baseline and after 3 months follow up in both groups.

	OHI S mean±SD	BOP % mean ±SD	GI mean ±SD	PPD (mm) mean ±SD	GR (mm) mean ±SD	CAL (mm) mean± SD
Treatment (Group I)						
Baseline	3.15±1.03	57.68 ±19. 34	1.65± 0.34	3.29± 1.02	0.93± 0.65	4.19±0. 70
3 Months Postop	0.54±0.37	06.34 ±1.2 6	0.25± 0.19	2.10± 0.78	1.02± 0.59	3.15±0. 21
p Value	<0.05	<0.0 5	<0.05	<0.05	>0.05	<0.05
Control Group II						
Baseline	3.06±0.94	58.23 ±21. 12	1.43± 0.26	3.36± 1.09	0.72± 0.40	4.07±0. 88
3 Months Postop	3.77±0.63	59.17 ±21. 78	1.54± 0.31	3.54± 1.11	0.69± 0.33	3.98±0. 95
p Value	>0.05	>0.0 5	>0.05	>0.05	>0.05	>0.05

OHI S= Oral hygiene index simplified, BOP=Bleeding on probing, GI=Gingival Index, PPD=Probing pocket depth, GR=Gingival Recession, CAL=Clinical Attachment Level.

TABLE 3: Laboratory parameters at baseline and after 3 months of periodontal therapy.

	Glycated Hemoglobin HbA1c %	Fasting Plasma Glucose (mg/dl)	2 h Post Prandial Glucose (mg/dl)
Treatment (Group I)			
Baseline	7.21±0.71	139.27±39. 14	159.22±51.23
3 months Postop	6.33±0.77	128.45±32. 91	134.31±39.11
p Value	<0.05	>0.05	<0.05
Control Group II			
Baseline	7.12±0.52	142.55±36. 44	161.2±57.77
3 Months Postop	7.21±1.08	143.45±38. 25	163.45±60.33
p Value	>0.05	>0.05	>0.05

Discussion

The influence of diabetes on periodontal disease has been discussed widely in literature[11,12,13]. A number of studies reported a high incidence and severity of periodontal disease in diabetic patients as compared with non-diabetic controls[14,15,16]. There is substantial evidence to support considering diabetes as a risk factor for poor periodontal health, there is also evidence for periodontal infection adversely effecting glycaemic control in diabetes where this has been less extensively studied[17]. It has been accepted that HbA1c is a reliable laboratory parameter to evaluate diabetes variation over 2 to 3 months time period[18]. Most of the studies compare HbA1c baseline values with the results obtained 3 months after periodontal treatment[19,20,21].

The aim of the present study is to investigate if non surgical periodontal therapy by full mouth disinfection procedure along with systemic doxycycline has effect on improvement in serum HbA1c levels of moderate chronic periodontitis patients with type 2 diabetes. Results of this study suggest that after non surgical periodontal therapy there is improvement in glycemic control in patients with type II diabetes compared to control group where periodontal treatment was not carried out.

All the periodontal clinical parameters like oral hygiene index, gingival index, periodontal pocket, clinical attachment gain has improved after 3 months of non surgical periodontal therapy. This shows good healing response of diabetics to non surgical therapy. This results are in consistent with previous investigations[22,23].

The significant finding of the study is that the data supported the clinical improvement and significant reductions in levels of HbA1c in type II diabetes patients following non surgical periodontal therapy. Elimination of periodontal infection and improvement of periodontal inflammation significantly reduced the HbA1c in short

term. In the present study systemic doxycycline 100 mg was prescribed to patient in treatment group. In our study, population the mean standardized HbA1c values were 7.21 ± 0.71 for the treatment and 7.12 ± 0.52 for the control group. The treatment group showed a reduction in HbA1c to 6.33 ± 0.77 . This reduction equates to a level approximately 10.94% of the baseline HbA1c level. Grossi et al[24] obtained similar numbers after 3 months of a combined non surgical periodontal therapy with doxycycline, and found a 10% reduction from baseline levels of HbA1c. In one of the study by Al-Zahrani et al[25], that compared an additional group using systemic antimicrobial doxycycline showed statistically significantly higher reduction only in the serum hbA1c levels. This could be considered an important key factor that suggests antimicrobials may be used to reduce serum HbA1c in type 2 DM patients. Inflammatory mediators released during chronic inflammation like interleukin 1 β and tumour necrosis factor α produces an insulin antagonism and have important effect on glucose and lipid metabolism[26,27,28]. Full mouth disinfection procedure and systemic doxycycline will reduce the bacteria load and reduce amount of various inflammatory mediators like IL1 β , IL6, PGE2, TNF α thus will minimize the insulin resistance and leads to improvement in glycaemic control.

Conclusions

Periodontitis is a complex multifactorial disease and diabetes has been identified as complicating factor in disease progression. Our results showed that non surgical periodontal treatment along with systemic antibiotics is associated with improvement in glycaemic control in type II diabetes patients. The effect on the metabolic control is a consequence of reduction in bacterial and inflammatory load. Non surgical periodontal treatment along with systemic antibiotics like doxycycline achieves good results in terms healing and in periodontal clinical parameters like

oral hygiene, gingival index, probing pocket depth and clinical attachment gain. Prevention and control of periodontal disease must be considered an integral part of diabetes disease control.

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