Effect of Periodontal Therapy on Metabolic Control and an Inflammatory Mediator in Type 2 Diabetic Subjects: A Report on 17 Consecutive Cases

Carlos Serrano[1], Clara Pérez[2] and Diego Sabogal[1]
[1]Department of Oral Medicine and Basic Science, School of Dentistry, and [2]Division of Lipids and Diabetes, School of Medicine, Universidad Nacional de Colombia

Abstract

Background: A reciprocal relationship between diabetes mellitus and chronic periodontitis has been described, whereby chronic periodontal infection could affect diabetic metabolic control. Therefore, periodontal therapy could influence metabolic control or systemic inflammation leading to diabetic complications. This case report series presents the effect of therapy on periodontal indices, glycated hemoglobin (HbA_{1c}) and high-sensitivity C-reactive protein (hs-CRP) in a group of type 2 diabetic patients. **Methods:** Seventeen diabetic patients diagnosed with moderate to severe chronic periodontitis received periodontal therapy. All patients received a hygienic phase of treatment and were re-examined 3 months later. At re-examination, subjects judged to need periodontal surgery were treated and re-examined after a further 3 months. A complete clinical examination and measurements of HbA_{1c} and hs-CRP were evaluated. **Results:** Periodontal treatment led to a significant improvement in periodontal indices; only five patients required periodontal surgery. The percentage of bleeding on probing was reduced by nearly 40%; percentage of pockets $\geqslant$ 5 mm was less than half baseline values; mean pocket depth reduction was 1.21 mm (0.58) and attachment level gain was 0.74 mm (0.69). Nevertheless, no changes were present for HbA_{1c}; a reduction in hs-CRP of 1.37 mg/L (2.67) was present. **Main finding:** Periodontal therapy in this case series group produced a significant improvement in the clinical condition, but did not affect metabolic control. It led to a decrease in hs-CRP.

Key words: Chronic periodontitis, diabetes mellitus type 2, glycated hemoglobin A, C-reactive protein

Introduction

Diabetes mellitus represents a growing health problem worldwide, with approximately 300 million affected individuals in the year 2010, a figure that could rise to 500 million people if proper public health actions are not taken (International Diabetes Federation, 2009). While mortality from communicable diseases and infant and maternal mortalities are decreasing in developing countries, increasing prevalence of diabetes could lead to a higher medical burden because of associated chronic complications (Wild *et al.,* 2004). In particular, 90% of affected individuals have type 2 diabetes mellitus, a pathology characterized by pancreatic β-cell dysfunction and peripheral insulin resistance. Major complications of diabetes mellitus are mainly macrovascular and microvascular diseases, both a consequence of accelerated atherogenesis (Sturnvoll *et al.,* 2005). Shared pathological mechanisms promote endothelial dysfunction in the macrovasculature as well as in the microvasculature of diabetic patients, among them hyperglycemia, dyslipidemia, hypertension, elevated levels of fatty acids or cytokine-mediated inflammation (Krentz *et al.,* 2007). In particular, it has been hypothesized that periodontal infection could cause indirect damage to the vascular system by releasing inflammatory mediators and eliciting different host reactions, such as monocyte hypersensitivity (Meurman *et al.,* 2006). A meta-analysis study including more than 3500 individuals showed more severe periodontal conditions in subjects with diabetes than in non-affected individuals (Papapanou,

Corresponding author: Carlos Serrano Universidad Nacional de Colombia, Facultad de Odontología, Ciudad Universitaria, Carrera 30 # 45-03, Building 210, Office 301 Bogotá, Colombia.
Tel: 57-1-6352633 Fax: 57-1-3165226
caserranom@unal.edu.co

1997). A population-based study of 4343 subjects included in the Third National Health and Nutrition Examination Survey (NHANES III) compared the prevalence of severe periodontitis in poorly and better controlled diabetics to that of unaffected individuals, finding a tendency toward higher prevalence of periodontitis in the better controlled diabetics, odds ratio 1.56 (CI 0.90-2.68), and a significantly higher prevalence in the poorly controlled, odds ratio 2.90 (CI 1.40-6.03) (Tsai *et al.,* 2002).

A further reciprocal relation between periodontal disease and diabetes has been described. It is based on the fact that infections could lead to poor metabolic control of diabetes, including the chronic Gram-negative anaerobic periodontal infection; hence periodontal therapy could lead to improvement in the level of glycated hemoglobin percentage measurements (HbA_{1c}) (Grossi *et al.,* 1997; Stewart *et al.,* 2001). During recent years multiple reports have analyzed the effect of periodontal treatment on HbA_{1c} percentage, showing conflicting results. On one hand, reports have shown a significant long- and short-term reduction in HbA_{1c} levels after periodontal therapy, whether supplemented by antimicrobial therapy or not (Grossi *et al.,* 1997; Stewart *et al.,* 2001; Rodrigues *et al.*, 2003; Kiran *et al.,* 2005; Faria-Almeida *et al.,* 2006), leading to a proposal that diabetes and periodontitis shared a "two-way" relationship. On the other hand, others have not found any significant reductions in the level of HbA_{1c}, even if therapy had obtained improvement of periodontal conditions (Aldridge *et al.,* 1995; Westfelt *et al.,* 1996; Jones *et al.,* 2007).

The presence of acute- and chronic-phase inflammatory mediators is common to periodontitis and type 2 diabetes mellitus (Schmidt *et al.,* 1999; Ebersole and Cappelli, 2000). In particular, an acute-phase molecule of great interest is high-sensitivity C-reactive protein (hs-CRP), because of longitudinal studies linking it to cardiovascular disease as a risk predictor (Ridker and Silvertown, 2008). A systematic review by Paraskevas *et al.* (2008) found modest evidence concerning the effect of periodontal therapy in lowering the levels of hs-CRP, with a mean difference between baseline and re-examination ranging between 0.0 and 0.6 mg/L for experimental groups, compared to a non-effect of -0.1 to 0.0 mg/L for control groups. Studies on the effect of periodontal therapy on hs-CRP levels have focused mainly on the general population, and studies on type 2 diabetic patients are scarce.

The present case series reports the effect of therapy on periodontal indices, HbA_{1c} levels and hs-CRP in a group of 17 consecutively treated type 2 diabetic patients affected by chronic periodontitis.

Case series report

Patients

A group of 17 type 2 diabetic patients adhering to the Diabetes Treatment Program at the Medical School, Universidad Nacional de Colombia received comprehensive periodontal treatment. Patients in the program included active or retired academic or administrative university personnel. Patients diagnosed with chronic periodontitis during a routine periodontal examination were offered comprehensive periodontal therapy. Specific criteria used for subject inclusion were: age $\geqslant$ 35 years; diagnosis of type 2 diabetes mellitus; adherence to treatment protocols at the Diabetes Treatment Program, Division of Lipids and Diabetics, Medical School, Universidad Nacional de Colombia; presence of at least six treatable teeth; and diagnosis of moderate to advanced chronic periodontitis according to a modification of the Center for Disease Control Periodontal Surveillance Workgroup Definition Criteria (Page and Eke, 2007). A modification was introduced to the original criteria in that the presence of $\geqslant$ 2 proximal sites with $\geqslant$ 4 mm clinical attachment loss (CAL), and the presence of $\geqslant$2 proximal surfaces with $\geqslant$ 5 mm probing pocket depth (PPD) were required, instead of either one or the other condition. Patients had to be willing to participate in a follow-up visit after six months. Exclusion criteria were: type 2 diabetes mellitus related to pregnancy, pancreatitis or alcoholism; uncontrolled systemic conditions or a requirement for prophylactic antibiotics to receive dental treatment; previous specialist periodontal treatment. Approval for this case report study was obtained from the Ethics Committee, Dental School, Universidad Nacional de Colombia. All subjects signed an informed consent form before the start of the study.

Examination of subjects

A full-mouth periodontal examination was performed on all subjects at baseline, after the hygienic phase, and after the corrective phase for the subjects in need of periodontal surgery. Periodontal probing was done by a single examiner, independent of treatment procedures (coauthor DS). All measurements were recorded at six sites per tooth: mesio-buccal, mid-buccal, disto-buccal, mesio-lingual, mid-lingual and disto-lingual. The following measurements were taken in addition to recording the number of teeth: bleeding upon periodontal probing (BoP) to the bottom of the pockets in a period of 10 seconds was recorded and the percentage of sites that bled was calculated. Probing pocket depth (PPD) was measured with a manual probe to the closest millimeter. The gingival margin (GM) level was measured with a manual probe from the free gingival margin to the cemento-enamel junction or the margin of a restoration; in case of a gingival recession, the gingival margin acquired a negative value. The clinical attachment level (CAL) was calculated as CAL= -PPD $\pm$ GM. The percentage of pockets $\geqslant$ 5 mm deep was calculated.

Table 1. Demographic characteristics of the patient sample (n = 17).

Characteristic	Data
Patient age (years)	66.58 ± 5.83
Gender (male/female)	7/10
Smokers (y/n)	2/15
Time since diabetes diagnosis (months)	98.11 ± 101.23
Body mass index (kg/cm^2)	26.77 ± 3.94

Blood samples for measurement of HbA_{1c} and hs-CRP were taken at baseline, after the hygienic phase, and after the corrective phase in subjects receiving periodontal surgery. Blood samples were taken at 7:00 AM after overnight fasting from the antecubital fossa by venipuncture as part of complete biochemical examinations routinely performed on program patients. A total volume of 7 mL of blood was taken, 10 µL being extracted for HbA_{1c} determination through a standardized immunological technique using monoclonal antibodies against the glycated fraction of hemoglobin (Axis-Shield plc Laboratories, Dundee, Scotland), and read on a Nyco-card photometer (Axis-Shield plc Laboratories). For hs-CRP determination, the blood sample was centrifuged at 3500 rpm for 5 minutes (Clay Adams, New Jersey, USA); and a serum volume of 3 mL was recovered to be used in a standardized turbidometric method for hs-CRP quantification (Helica Biosystems Inc., Fullerton, CA, USA). All samples were stored for one year at -30°C.

Treatment procedures

After baseline examination (BL) all patients underwent a comprehensive hygienic phase of periodontal therapy including scaling and root planing (SRp), oral hygiene instruction, extraction of hopeless teeth and removal of overhanging restorations. Over the course of four weeks, scaling and root planing was performed on a different jaw quadrant each week, using magnetostrictive ultrasonic equipment (Cavitron, Dentsply, York, PA, USA) and manual curettes (Hu-Friedy, Chicago, IL, USA). Oral hygiene instructions were given and reinforcements were performed during the hygienic phase. They included proper toothbrushing, use of proximal tooth floss and mouthrinsing twice a day (Colgate Total 12 hours, Colgate, NJ, USA; Plax mouthrinse, Colgate). Teeth judged not treatable due to advanced caries destruction or periodontal disease were extracted and not included for analysis. Overhanging restorations were removed and replaced by properly contoured provisional or definitive restorations. Three months after the hygienic phase, a periodontal re-examination was performed (Re-ex 1).

At re-examination, the need for further periodontal therapy was assessed. Subjects presenting with remaining deep periodontal pockets judged in need of periodontal therapy were surgically treated using the modified Widman flap operation with osteoplasty procedures (Ramfjord and Nissle, 1974). Other treated subjects were included in maintenance phase activities. At all times, plaque control evaluations were performed and needed oral hygiene reinforcements were made. In subjects receiving periodontal surgery, a re-examination was performed three months after the procedures (Re-ex 2).

Statistical analysis

Means and standard deviations were calculated for all periodontal and medical laboratory variables.

Results

Patient description

The group of 17 patients diagnosed with chronic periodontitis received periodontal therapy; 11 patients had moderately severe periodontal involvement, and another six patients had advanced periodontitis. The mean age was 66.58 years, range 60 to 75 years (*Table 1*). All patients received a complete hygienic treatment phase. At re-examination, it was judged that only five patients required the corrective treatment phase, mainly those affected by advanced disease at baseline; three patients had one periodontal surgery; two other patients received two periodontal surgeries.

All patients were being treated at the Diabetes Treatment Program of the Division of Lipids and Diabetes, Medical School, Universidad Nacional de Colombia. The mean time since diagnosis of diabetes was approximately eight years, though it encompassed a wide range. Not all patients were receiving pharmacological treatment: five patients were controlled only with physical exercise, diet and continuous monitoring. The other 12 patients had additional pharmacological therapy, 10 patients receiving only oral hypoglycemic drugs, the remaining two patients receiving oral hypoglycemic drugs plus insulin. During the course of treatment one patient had a dosage increase of their hypoglycemic medication, a second patient had a change of insulin type; the other 10 patients had an unchanged diabetic medication

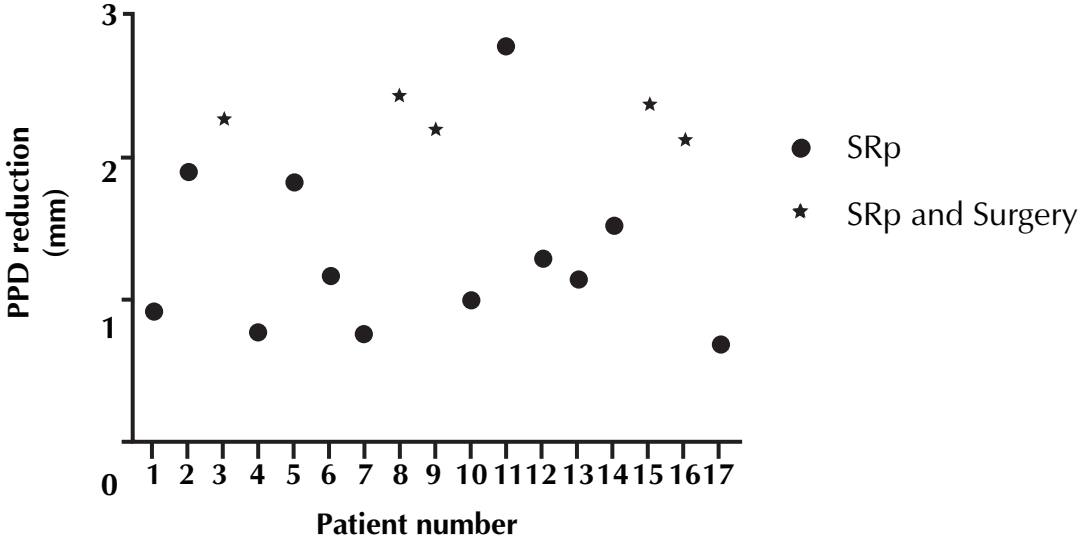
Table 2. Change in periodontal parameters between baseline and re-examination 1 for all patients.

	Percentage BoP (mean ± SD)	PPD (mm) (mean ± SD)	Percentage of pockets ≥ 5 mm (mean ± SD)	CAL (mm) (mean ± SD)
Baseline	70.79 ± 18.26	4.65 ± 0.34	14.91 ± 13.72	4.25 ± 1.51
Re-examination1	30.92 ± 19.37	3.44 ± 0.66	6.32 ± 9.91	3.34 ± 1.47
Change	39.86 ± 25.07	1.21 ± 0.58	8.58 ± 9.86	0.90 ± 0.89

Table 3. Change in periodontal parameters for the five patients receiving periodontal surgery between baseline, re-examination 1 and re-examination 2.

	Percentage BoP (mean ± SD)	PPD (mm) (mean ± SD)	Percentage of pockets ≥ 5 mm (mean ± SD)	CAL (mm) (mean ± SD)
Baseline	75.27 ± 14.35	5.05 ± 0.16	24.90 ± 15.88	4.58 ± 1.30
Re-examination 1	45.66 ± 22.48	4.09 ± 0.61	15.31 ± 15.05	4.24 ± 1.14
Re-examination 2	28.94 ± 15.51	3.35 ± 0.35	4.92 ± 3.18	4.24 ± 1.12
Change (BL - Re-ex 2)	46.32 ± 11.41	1.69 ± 0.37	19.98 ± 16.12	0.34 ± 1.09

Figure 1. Individual probing pocket depth (PPD) change in all 17 treated patients. SRp, scaling and root planing.



dosage. The mean sample body mass index was 26.77 kg/cm^2, ranging from 21.50 to 37.36 kg/cm^2. Five patients had a normal weight, nine were overweight and three were obese (*Table 1*).

Periodontal parameters

At baseline, patients had a mean number of 19.76 teeth (6.15), ranging from 7 to 28 teeth. Only one tooth was extracted during treatment due to poor periodontal prognosis. Periodontal treatment produced a significant improvement in recorded periodontal indices for all patients. Bleeding upon periodontal probing and percentage of pockets ⩾ 5 mm deep were reduced to less than half baseline values. Mean PPD reduction amounted to 1.21 mm (0.58), with a mean CAL gain of 0.74 mm (0.69) (*Table 2, Figures 1 and 2*).

Separate analysis of the five patients who received periodontal surgery revealed a gradual improvement in clinical parameters between baseline, re-examination 1 and re-examination 2, with significant improvements for all clinical parameters except CAL (*Table 3*).

Figure 2. Individual clinical attachment loss (CAL) change in all 17 treated patients. SRp, scaling and root planing.

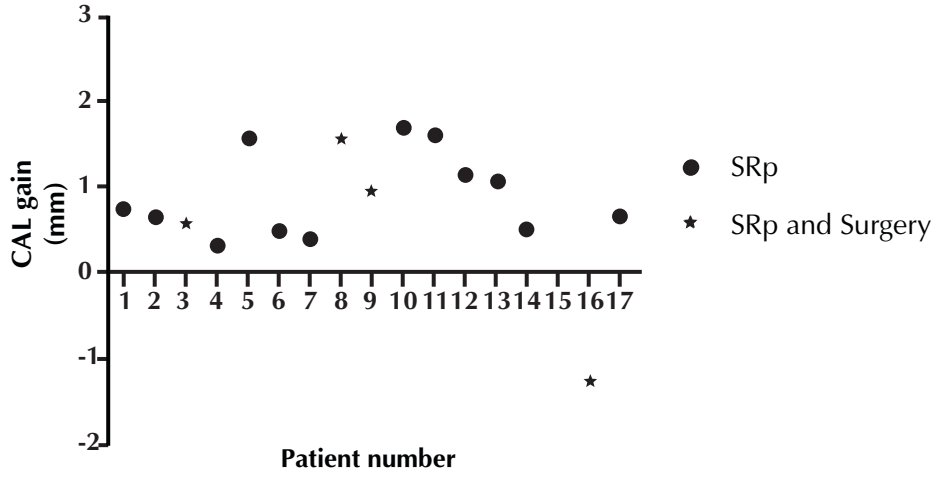


Figure 3. Changes in glycated hemoglobin (HbA_{1c}) after hygienic phase in 17 patients, and after hygienic and corrective phase in five patients. BL, baseline; re-ex, re-examination.

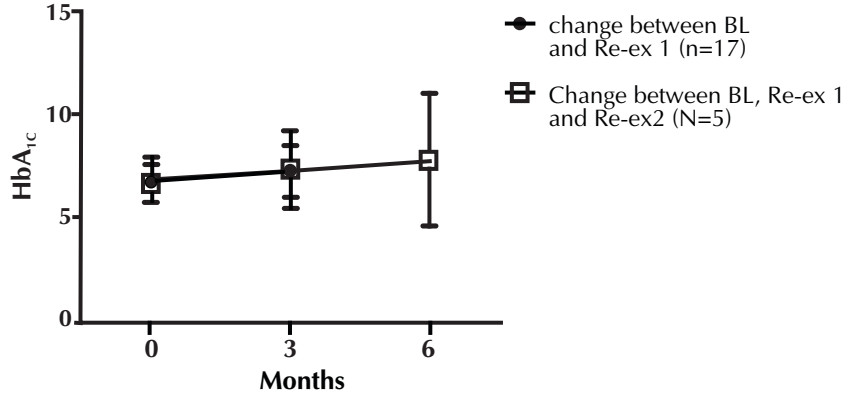
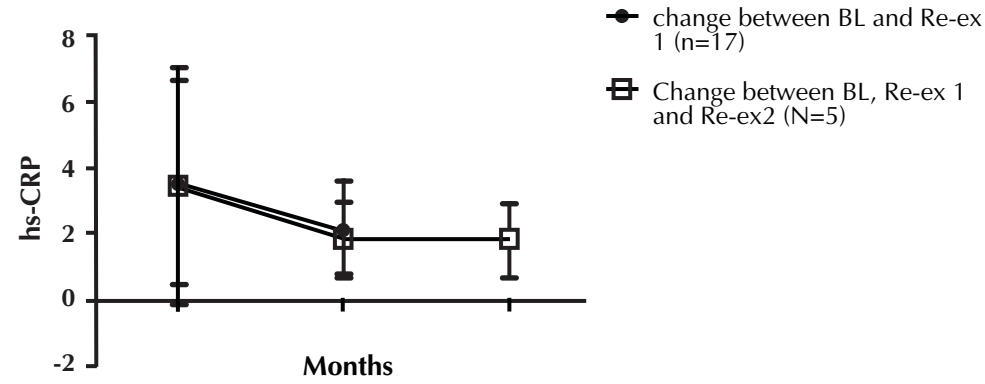


Figure 4. Changes in high-sensitivity C-reactive protein (hs-CRP) after hygienic phase in 17 patients, and after hygienic and corrective phase in five patients. BL, baseline; re-ex, re-examination.



Biomarker parameters

Baseline mean HbA_{1c} was 6.85% (1.12), revealing adequate metabolic control of diabetes. Eleven patients had good metabolic control with HbA_{1c} values < 7%, three patients had fair metabolic control with values between 7 and 7.9%, and the other three patients had poor metabolic control with values ⩾ 8%. Periodontal treatment did not produce any significant change in HbA_{1c} levels, either for the 17 diabetic patients receiving the hygienic phase, or for the five diabetic patients receiving the hygienic and corrective phases of treatment (*Figure 3*).

Baseline mean hs-CRP was 3.50 mg/L (3.11), representing a high risk for cardiovascular events, according to established criteria (Pearson *et al.,* 2003). The hygienic phase of periodontal treatment led to a decrease in hs-CRP to 2.13 mg/L (1.48) (*Figure 4*). In 10 subjects, hs-CRP decreased at re-examination 1, in four subjects hs-CRP stayed the same, and in three subjects hs-CRP increased. The change in hs-CRP for each

Table 4. Change in hs-CRP and main periodontal parameters after hygienic phase of periodontal treatment.

Subject	BL hs-CRP	Re-ex 1 hs-CRP	BL BoP	Re-ex 1 BoP	BL % pockets ≥ 5mm	Re-ex 1 % pockets ≥ 5 mm
1	1.67	0.34	74.64	42.75	10.86	3.62
2	3.45	5.28	85.26	29.49	10.25	0.64
3	0.42	2.13	66.67	38.46	17.30	3.84
4	1.10	1.17	82.50	13.33	7.50	5.00
5	0.89	0.95	75.76	10.61	9.48	3.03
6	10.14	4.33	39.81	18.52	1.85	0
7	2.70	1.21	43.86	41.23	6.14	9.64
8	2.50	1.06	67.26	30.95	25.59	8.33
9	9.15	2.35	75.76	30.95	16.66	10.60
10	2.72	2.80	63.19	16.67	3.47	0.72
11	5.50	0.76	91.67	2.38	36.90	0
12	1.13	0.72	69.44	22.22	2.77	0
13	2.39	2.01	41.27	50.00	3.17	0.79
14	8.89	3.72	100.00	85.42	28.57	4.76
15	4.52	3.27	100.00	34.09	52.08	41.66
16	0.68	0.49	66.67	27.78	12.87	12.12
17	1.75	3.60	59.72	30.93	7.63	6.32

subject is depicted along with clinical parameters representing inflammation of the periodontal tissues; for the majority of subjects, decreases in hs-CRP were concomitant with reduction in BoP and percentage of pockets (*Table 4*). For the five subjects who received hygienic and corrective treatment phases, larger decreases were present at the hygienic phase, having a baseline mean hs-CRP of 3.45 mg/L (3.58) reduced to 1.86 mg/L (1.09), and a slight decrease when receiving periodontal surgery, mean hs-CRP 1.82 mg/L (1.14) (*Figure 4*).

Discussion

The clinical results of this group of type 2 diabetic subjects showed a successful outcome of therapy in periodontal indices; percentage of bleeding on probing was reduced by nearly 40%, mean PPD reduction was 1.21 mm (0.58), with a CAL gain of 0.74 mm (0.69). These figures agree with the results of systematic reviews on the effect of non-surgical periodontal therapy on the general population, showing a mean PPD reduction ranging from 0.7 to 1.7 mm for pockets initially ⩾ 5 mm, and a gain in CAL ranging from 0.42 to 1.50 mm for the same baseline pocket depth category (Van der Wejden and Timmerman, 2002). Specific results from periodontal therapy for type 1 and 2 diabetic patients showed that positive results could be maintained with a long-term 5-year follow-up, demonstrated by a drastic reduction in percentage of pockets at different PPD categories and reduction in BoP percentage similar to the present study, even with subjects having a poorer degree of metabolic control (Westfelt *et al.,* 1996). Two other studies confirmed an equally large improvement of periodontal conditions after non-surgical periodontal therapy (Ternoven *et al.,* 1991; Christgau *et al.,* 1998). In the present study, periodontal surgery was performed on five subjects affected by severe chronic periodontitis, still showing deep pockets at re-examination 1. Surgery was effective in obtaining a further reduction in percentage of sites bleeding on probing, percentage of deep pockets and mean PPD. A fairly small need for periodontal surgery after successful non-surgical therapy was also observed in the five-year study by Westfelt *et al.,* (1996), as only 9 out of 20 treated diabetic patients were in need of periodontal surgery. Mean baseline HbA_{1c} values of the

present group revealed adequate metabolic control, which could have contributed to a successful outcome of periodontal therapy. Other studies comparing treatment response in well-controlled and poorly controlled diabetics have shown greater CAL loss or radiographic bone loss in the poorly controlled patients in a 2-year follow-up (Seppala *et al.,* 1993; Seppala and Ainamo, 1994).

Recently, several studies have analyzed the effect of non-surgical periodontal therapy on HbA_{1c} levels in diabetic patients. An early hallmark project by Grossi *et al.* (1997) evaluated the effect of periodontal therapy on HbA_{1c} levels. Significant HbA_{1c} reduction in the three groups receiving systemic doxycycline adjunctive to conventional non-surgical therapy was observed three months after treatment, the largest reduction being 0.94%; nevertheless this effect was not present at the six-month re-examination.

Lately, contradictory results have been found by different research groups (Aldridge *et al.,* 1995; Westfelt *et al.,* 1996; Stewart *et al.,* 2001; Rodrigues *et al.,* 2003; Faria-Almeida *et al.,* 2006; Jones *et al.,* 2007). A meta-analysis study on 10 studies in the field found a non-significant 0.57% reduction in HbA_{1c} for type 2 diabetics (Janket *et al.,* 2005). Studies have varied in: diabetes type subject inclusion, degree of baseline HbA_{1c}, inclusion of systemic antibiotics for periodontal treatment and follow-up time. Similar to the present study, reports have mainly included type 2 diabetes, probably due to its increased global prevalence and the influence of chronic inflammation on insulin resistance. Chronic infection and inflammation can enhance insulin resistance by macrophage activation leading to increased secretion of inflammatory markers such as CRP and plasminogen activator inhibitor-1, among other cytokines (King, 2008). However, the study by Aldridge *et al.* (1995) focused on type 1 diabetics, and the study by Christgau *et al.* (1998) included a mixed type 1 and 2 diabetic sample: none of them found any significant effect of periodontal therapy on HbA_{1c}.

Baseline HbA_{1c} values have varied greatly among studies on the subject, while the majority of the studies have not included a specific inclusion criterion of HbA_{1c} levels, similar to the present study. Others have focused on poorly controlled diabetics (Jones *et al.,* 2007), or well-controlled subjects (Kiran *et al.,* 2005). As stated by Jones *et al.* (2007), bad metabolic control leaves room for improvement, supporting a baseline HbA_{1c} inclusion criterion of $\geqslant$ 8.5%. However, periodontal therapy is less effective in poorly controlled diabetic subjects (Seppala *et al.,* 1993; Seppala and Ainamo, 1994), and bad metabolic control could reveal a failure of pharmacological and non-pharmacological measures for disease control. Self-care behaviors of diabetic patients include following a meal plan, exercise, medication intake, monitoring blood glucose levels and responding to diabetes-related symptoms (McNabb, 1997). The present patients mostly revealed adequate metabolic control: baseline HbA_{1c} level was 6.85% (1.12). They came from a small treatment clinic with over 130 diabetic subjects, where the general HbA_{1c} value was 7.9%. In this study, patients diagnosed with chronic periodontitis were consecutively treated if willing to do so, regardless of the metabolic control values. Being adequately controlled could hamper finding further HbA_{1c} percentage reduction. However, a study by Kiran *et al.* (2005) including subjects with baseline HbA_{1c} values from 6-8% found a reduction in the experimental group of 0.86%. A study by Stewart *et al.* (2001) found a reduction in HbA_{1c} levels of 1.9% for the experimental group and of 0.8% for the control group; both changes were statistically significant. The authors mention changes in the protocol for diabetes management, with the inclusion of HbA_{1c} levels as a guide for medication changes as a possibility for the improvement in the control group. The treatment protocol of the current study patients was standardized, laying great emphasis upon medical and self-care activities contributing to an acceptable mean metabolic control. Administration of systemic doxycycline has been suggested to improve the outcome of periodontal therapy in diabetic subjects, based on its antimicrobial and anti-inflammatory properties (Martorelli de Lima *et al.,* 2004; Llambés *et al.,* 2005). Nevertheless, the current results of therapy were satisfactory. In subjects with continued deep pockets periodontal surgery contributed to further disease resolution.

A systematic review and meta-analysis of C-reactive protein in relation to periodontitis by Paraskevas *et al.* (2008) calculated a reduction in hs-CRP ranging from 0.00 - 0.60 mg/L after periodontal therapy. Reductions after the hygienic phase in the present study were larger than the meta-analysis result, 1.37 mg/L (2.67). This reduction could have clinical significance, as it represents a reduction from high to moderate vascular risk, according to the Center for Disease Control and Prevention and the American Heart Association Clinical Guidelines (Pearson *et al.,* 2003). Reduction of hs-CRP was present in the majority of subjects, but a greater hs-CRP reduction came from subjects affected mainly by severe periodontitis and successfully treated, subjects 7, 10, 12 and 15. Studies on larger general population samples about the effect of periodontal therapy on hs-CRP found mean reductions of about 0.4 mg/L and 0.5 mg/L after intensive periodontal therapy, including: scaling and root planing over 24 hours, local antibiotic application and oral hygiene instruction (D'Aiuto *et al.,* 2004; D'Aiuto *et al.,* 2005). Changes in the present study patient population are of the same magnitude.

Few reports have analyzed the effect of periodontal therapy on systemic inflammation in

diabetic subjects. A pilot study by Lalla *et al*. (2007) treated 10 periodontally affected diabetic subjects, finding significant reductions in the levels of sE-selectin, vascular cell adhesion molecule-1 and hs-CRP. A study by Correa *et al*. (2010) treating 23 affected individuals found significant reductions in the levels of tumor necrosis factor-α and fibrinogen, but a non-statistically significant decrease in hs-CRP. On the contrary, a study by Karagiri *et al*. (2009) using adjunctive topical antibiotics did not find a mean change in hs-CRP in an intervention group of 32 patients; when analyzing only those subjects having hs-CRP reduction this was concomitant with a reduction in HbA_{1c} levels. Similar to the present study, reports have analyzed the effect of non-surgical therapy on limited samples of diabetic patients. In contrast, great variations in baseline HbA_{1c} and hs-CRP levels were present, emphasizing the variation in medical control of the diabetic condition.

Within the limits of this study, the periodontal therapy provided to this group of type 2 diabetic subjects produced a marked improvement of the periodontal condition, but did not affect HbA_{1c} levels. Levels of hs-CRP were diminished, especially because of a reduction in subjects affected by severe periodontitis.

Acknowledgments

The authors would like to offer thanks for the valuable work of the following undergraduate research assistants: Angela Carrero, Angelica López, Ana Marulanda, Claudia Méndez and Casandra Valencia. This study was supported by a grant from the Research Office, Universidad Nacional de Colombia, and a research award from Colgate-Palmolive, Colombia. Dr. Perez and Dr. Sabogal do not have any financial relationship to any products used in the present study. Dr Serrano has been a speaker for Colgate-Palmolive, Colombia.

References

Aldridge JP, Lester V, Watts TLP, Collins A, Viberti G and Wilson RF. Single-blind studies of the effects of improved periodontal health on metabolic control in type 1 diabetes mellitus. *Journal of Clinical Periodontology* 1995; **22**:271-275.

Christgau M, Palitzsch KD, Schmalz G, Kreiner U and Frenzel S. Healing response to non-surgical periodontal therapy in patients with diabetes mellitus: clinical, microbiological, and immunologic results. *Journal of Clinical Periodontology* 1998; **25**:112-124.

Correa FOB, Goncalves D, Figueredo CMS, Bastos AS, Gustafsson A and Orrico SRP. Effect of periodontal treatment on metabolic control, systemic inflammation and cytokines in patients with type 2 diabetes. *Journal of Clinical Periodontology* 2010; **37**:53-58.

D'Aiuto F, Parkar M and Andreou G. Periodontitis and systemic inflammation: Control of the local infection is associated with a reduction in serum inflammatory markers. *Journal of Dental Research* 2004; **83**:156-160.

D'Aiuto F, Nibali L, Parkar M, Suvan J and Tonetti MS. Short-term effects of intensive periodontal therapy on serum inflammatory markers and cholesterol. *Journal of Dental Research* 2005; **84**:269-273.

Ebersole JL and Cappelli D. Acute-phase reactants in infections and inflammatory diseases. *Periodontology 2000*; 2000; **23**:19-49.

Faria-Almeida R, Navarro A and Bascones A. Clinical and metabolic changes after conventional treatment of type 2 diabetic patients with chronic periodontitis. *Journal of Periodontology* 2006; **77**:591-598.

Grossi SG, Skrepcinski FB, DeCaro T, *et al*. Treatment of periodontal disease in diabetics reduces glycated hemoglobin. *Journal of Periodontology* 1997; **68:**713-719.

International Diabetes Association. Diabetes Atlas, 4th edition. International Diabetes Federation. Brussels, 2009.

Janket SJ, Wightman A, Baird AE, Van Dyke TE and Jones JA. Does periodontal treatment improve glycemic control in diabetic patients? A meta-analysis of intervention studies. *Journal of Dental Research* 2005; **84**:1154-1159.

Jones JA, Miller DR, Wehler CJ, *et al*. Does periodontal care improve glycemic control? The department of veteran affairs dental diabetes study. *Journal of Clinical Periodontology* 2007; 34:46-52.

Katagiri S, Nitta H, Nagasawa T, *et al*. Multi-center intervention study on glycohemoglobin (HbA_{1c}) and serum high-sensitivity CRP (hs-CRP) after local anti-infective periodontal treatment in type 2 diabetic patients with periodontal disease. *Diabetes Research and Clinical Practice* 2009; **83**:308-315.

King GL. The role of inflammatory cytokines in diabetes and its complications. *Journal of Periodontology* 2008; **79**:1527-1534.

Kiran M, Arpak N, Unsal E and Erdogan MF. The effect of improved periodontal health on metabolic control in type 2 diabetes mellitus. *Journal of Clinical Periodontology* 2005; **32**:266-272.

Krentz AJ, Clough G and Byrne CD. Interactions between microvascular and macrovascular disease in diabetes: pathophysiology and therapeutic implications. *Diabetes Obesity Metabolism* 2007; **9**:781-791.

Lalla E, Kaplan S, Yang J, *et al.,* Effects of periodontal therapy on serum C-reactive protein, sE-selectin, and tumor necrosis factor-α secretion by peripheral blood-derived macrophages in diabetes. A pilot study. *Journal of Periodontal Research* 2007; **42**:274-282.

Llambés F, Silvestre FJ, Hernández-Mijares A, Guiha R and Caffesse R. Effect of non-surgical periodontal therapy with or without doxycycline on the periodontium of type 1 diabetic patients. *Journal of Clinical Periodontology* 2005; **32**:915-920.

Loe H. Periodontal disease: The sixth complication of diabetes mellitus. *Diabetes Care* 1993; **16**:329-334.

McNabb WL. Adherence in diabetes: Can we define it and can we measure it? *Diabetes Care* 1997; **20**:215-218.

Martorelli de Lima AF, Cury CC, Bazan Pallioto D, Mendes Duro A, Carvalho da Silva R and Wolff LF. Therapy with adjunctive doxycycline local delivery in patients with type 1 diabetes mellitus and periodontitis. *Journal of Clinical Periodontology* 2004; **31**:648-653.

Meurman JH, Sanz M and Janket SJ. Oral health, atherosclerosis and cardiovascular disease. *Critical Review in Oral Biology Medicine* 2004; **15**:403-413.

Page RC and Eke PI. Case definitions for use in population-based surveillance of periodontitis. *Journal of Periodontology* 2007; **78**:1387-1399.

Papapanou PN. Periodontal diseases: Epidemiology. *Annals of Periodontology* 1996; **1**:1-36.

Paraskevas S, Huizinga JD and Loos BG. A systematic review and meta-analysis on C-reactive protein in relation to periodontitis. *Journal of Clinical Periodontology* 2008; 3**5**:277-290.

Pearson TA, Mensah GA, Alexander RW, *et al*. Markers of inflammation and cardiovascular disease: Application to clinical and public health practice: A statement for healthcare professionals from the Centers for Disease Control and Prevention and the American Heart Association. *Circulation* 2003; **107**:499-511.

Powers AC. Diabetes Mellitus. In: Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, Loscaldo J.,eds. *Harrison´s Principles of Internal Medicine*. McGraw Hill 1998, Chapter 333: 2467-2499.

Ramfjord SP and Nissle RR. The modified Widman flap. *Journal of Periodontology* 1974; **45**:601-607.

Ridker PM and Silvertown JD. Inflammation, C-reactive protein and atherothrombosis. *Journal of Periodontology* 2008; **79**:1544-1551.

Rodrigues DC, Taba Jr. M, Novaes Jr. AB, Souza SLS and Grisi MFM. Effect of non-surgical periodontal therapy on glycemic control in patients with type 2 diabetes mellitus. *Journal of Periodontology* 2003; **74**:1361-1367.

Schmidt MI, Duncan BB, Sharret AR, *et al.* Markers of inflammation and prediction of diabetes mellitus in adults (Atherosclerosis risk in communities studies): A cohort study. *Lancet* 1999; **353**:1649-1652.

Seppala B, Seppala M and Ainamo J. A longitudinal study on insulin-dependet diabetes mellitus and periodontal disease. *Journal of Clinical Periodontology* 1993; **20**:161-165.

Seppala B and Ainamo J. A site-by-site follow-up study on the effect of controlled versus poorly controlled insulin-dependent diabetes mellitus. *Journal of Clinical Periodontology* 1994; **21**:161-165.

Stewart JE, Wager KA, Friedlander AH and Zadeh HH. The effect of periodontal treatment on glycemic control in patients with type 2 diabetes mellitus. *Journal of Clinical Periodontology* 2001; **28**:306-310.

Sturnvoll M, Goldstein BJ and van Haeften TW. Type 2 diabetes: principles of pathogenesis and therapy. *Lancet* 2005; **365**:1333-1346.

Ternoven T, Knuuttila M, Pohjamo L and Nurkkala H. Immediate response to non-surgical periodontal treatment in subjects with diabetes mellitus. *Journal of Clinical Periodontology* 1991; **18**:65-68.

Tsai C, Hayes C and Taylor GW. Glycemic control of type 2 diabetes and severe periodontal disease in the US adult population. *Community Dental and Oral Epidemiology* 2002; **30**:182-192.

Van der Wejden GA and Timmerman MF. A systematic review on the clinical efficacy of subgingival debridement in the treatment of chronic periodontitis. *Journal of Clinical Periodontology* 2002; **29**(Suppl.3):55-71.

Westfelt E, Rylander H, Blohmé G, Jonasson P and Lindhe J. The effect of periodontal therapy in diabetics. *Journal of Clinical Periodontology* 1996; **23**:92-100.

Wild S, Roglik G, Green A, Sicree R and King H. Global prevalence of diabetes. *Diabetes Care* 2004; **27**:1047-1053.