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ORIGINAL ARTICLE

The effect of periodontal therapy on uncontrolled type 2 diabetes mellitus in older subjects

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OBJECTIVE: The purpose of this study was to examine the effect of periodontal therapy on glycemic control in older type 2 diabetic patients.

METHODS: Fifty-two diabetic patients, age 55–80 years (mean age = 61 years), with glycated hemoglobin (HbA1c) 7.5–11.0% (mean ± s.d. = 8.98 ± 0.88) and severe periodontitis were included in the present study. The treatment group received mechanical periodontal treatment combined with systemic doxycycline, 100 mg day^{-1} for 14 days. The control group received neither periodontal treatment nor systemic doxycycline. Clinical periodontal parameters, fasting plasma glucose (FPG), and HbA1c levels were measures at baseline and 3 months.

RESULTS: Periodontal treatment significantly improved periodontal status of the treatment group ($P < 0.05$), however the reduction in the level of FPG and HbA1c did not reach significance. In the control group, no significant changes in clinical periodontal parameters, FPG and HbA1c levels were observed, except for significant increase in attachment loss ($P < 0.05$). Comparing the two groups, although the 3-month level of HbA1c of the treatment group was lower than that of the control group, the difference did not reach significance.

CONCLUSIONS: The results of the present study indicate that the periodontal condition of older Thais with uncontrolled diabetes is: (a) significantly improved 3 months after mechanical periodontal therapy with adjunctive systemic antimicrobial treatment, and (b) rapidly deteriorating without periodontal treatment. The effect of periodontal therapy on the glycemic control of older uncontrolled diabetics will require further studies that will have to include much larger sample sizes.

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Introduction

It is generally accepted that there is an association between periodontitis and diabetes mellitus. Several studies reported poorer periodontal health in patients with type 2 diabetes mellitus (Cianciola *et al*, 1982; Emrich *et al*, 1991; Safkan-Seppala and Ainamo, 1992). Type 2 diabetes mellitus patients were 2.8 times more likely to have destructive periodontal disease (Emrich *et al*, 1991) and 4.2 times more likely to have alveolar bone loss progression (Taylor *et al*, 1998a). The increased risk of developing periodontal disease could not be explained on the basis of age, gender or hygiene. Periodontal disease has been considered to be another complication of diabetes mellitus (Löe, 1993) and evidence also supports poorer glycemic control contributing to poorer periodontal health (Ainamo *et al*, 1990; Unal *et al*, 1993; Novaes *et al*, 1996; Taylor *et al*, 1998b).

Grossi and Genco have proposed that the relation of periodontitis and diabetes is bi-directional (Grossi and Genco, 1998). One possible biologic mechanism is that glucose-mediated advanced glycation end products (AGEs) accumulation impairs chemotactic and phagocytic function of polymorphonuclear leukocytes (Wilson and Reeves, 1986; Marhoffer *et al*, 1992). Additionally, when AGE-protein binds to its macrophage receptors, it induces production of IL-1, and TNFα (Vlassara *et al*, 1988). These proinflammatory cytokines play a role not only in the pathogenesis of diabetic complications (Vlassara *et al*, 1988) but also in the pathogenesis of periodontitis, and may explain why diabetic patients have more severe periodontitis. Gram-negative periodontopathic bacteria in periodontal pockets, in turn, serve as a chronic source of systemic challenge. The interaction of bacterial products with mononuclear phagocytic cells and fibroblasts results in elevated secretion of IL-1β, PGE2, TNFα, and IL-6 (Offenbacher,

1996; Kornman *et al*, 1997). TNFα is a proinflammatory cytokine that has been implicated in insulin resistance. One possible mechanism is via suppression of insulin induced tyrosine phosphorylation of insulin receptor substrate-1 (IRS-1) (Kanety *et al*, 1995). Conceptually, if TNFα is a key molecule mediating insulin resistance, successful periodontal treatment that reduces the TNFα levels (Heasman *et al*, 1993) should improve insulin sensitivity and metabolic control in diabetic patients. Periodontal therapy consisting of mechanical treatment combined with systemic or local antimicrobial administration has been shown to improve diabetic status (William and Mahan, 1960; Miller *et al*, 1992; Grossi *et al*, 1997, Iwamoto, 2001). While both periodontitis and diabetes mellitus have higher prevalence with increasing age (Locker and Leake, 1988; Grossi *et al*, 1995; Kenny *et al*, 1995), studies evaluating the effect of periodontal therapy on diabetic status in older adults are scarce (Stewart *et al*, 2001). Therefore, it was our interest to study the relation of these two diseases in an older group of patients. The purpose of this study was to investigate the effect of combined mechanical and systemic antibiotic periodontal therapy on the diabetic control in older adults.

Materials and methods

Study population

Sixty patients, aged 55–80 years, were recruited from the Diabetic Clinic of Rajavithi Hospital, Bangkok, Thailand. All patients had uncontrolled type 2 diabetes mellitus [glycated hemoglobin (HbA1c) values between 7.5 and 11.0%]. Additionally, each patient had at least 14 teeth with severe periodontitis as defined by at least eight sites with pocket depth ≥5 mm and clinical attachment level ≥5 mm. Patients with the following conditions i.e. oral infections or periapical pathology as assessed by clinical and radiographic examinations, smoking, allergy to tetracycline derivatives, severe systemic diseases, previous history of antibiotic intake and/or periodontal therapy within 3 months were not included in the study. All diabetic patients were under care of a physician. Their diabetic medications included oral medication only, insulin only, or both. The patients were advised to strictly control their diet and their medications. If, during the course of the study, the physician opted to change a patient's medical care (type and/or dose of medication) for improved management of the disease, then the patient was exited from the study. Patients who refused periodontal treatment were automatically placed in the control group; others were randomly assigned to either treatment or control group by tossing a coin. The details of the study were explained to the patients and all participants provided informed consent. The Institutional Review Board of Mahidol University approved the study protocol and informed consent form. Using Altman's nomogram (Petrie *et al*, 2002), it was decided to have at least 15 subjects in each group in order to have a 90% chance of detecting a difference in mean HbA1c of 1% at the 5% level of significance, assuming the standard deviation of HbA1c value of 0.6 from previously reported study (Grossi *et al*, 1997).

Treatment regimen

The treatment group received periodontal treatment including oral hygiene instruction, and removal of supra and subgingival calculus. Each tooth was thoroughly scaled and root planed with ultrasonic and hand instruments in four sessions within 2 weeks. Subjects in this group received systemic doxycycline, 100 mg day^{-1} for 2 weeks, starting on the first session. Patient compliance with 2-week course of antibiotic in the treatment group was evaluated by interview. Subjects in the control group received neither oral hygiene instruction and periodontal treatment nor systemic doxycycline nor placebo.

Clinical assessments

Periodontal status was assessed at baseline and 3 months and included plaque assessment (Machtei *et al*, 1992), bleeding on probing (BOP) (Ainamo *et al*, 1990), measurement of probing depth (PD) and the distance from cemento-enamel junction to gingival margin (CEJ-GM) on all teeth present in the mouth at mesiobuccal, midbuccal, distobuccal, mesiolingual, midlingual, and distolingual areas. Clinical attachment levels were calculated from PD + (CEJ-GM) measurements. Probing measurements were performed with standard manual periodontal probe (PCPUNC 15; Hu-Friedy®, Chicago, IL, USA).

Determination of plasma glucose and glycated hemoglobin

Venous blood samples were collected at baseline and at 3 months and assayed for fasting plasma glucose (FPG) using glucose oxidase method and HbA1c using immunoassay method at Rajavithi Hospital central laboratory.

Statistical analysis

Mean and standard deviation for plaque score, BOP, PD, clinical attachment level, plasma glucose and HbA1c were calculated at baseline and at 3 months. Paired *t*-test and independent *t*-test were used to test changes from baseline and differences between groups. The treatment group was also divided into two subgroups on the basis of the response for each of the four periodontal parameters, using median values as cut off points, and repeated the comparisons. Subgroup analysis of changes of HbA1c from baseline levels was performed using Chi-square test. The data were analyzed using SPSS for windows software program (SPSS Inc., Chicago, IL, USA).

Results

Eight patients did not complete the study and their baseline data were excluded from analysis; five (two in the treatment group and three in the control group) did not comply with the 3 months evaluation appointment and three suffered diabetic complication. At the end of the study, there were 27 and 25 patients who completed

Table 1 Demographic information of patients at baseline

	Treatment group (n = 27)	*Control group (n = 25)*
Age		
Mean ± s.d.	61.11 ± 5.83	61.64 ± 5.81
Range	55–80	55–73
Gender		
Male (*n*)	11	8
Female (*n*)	16	17
Duration of DM (years)		
Mean ± s.d.	8.30 ± 4.21	14.36 ± 7.57
Mode	10	10
Range	2–20	4–30

the study without changes in medical care in the treatment and control groups, respectively. Table 1 shows the demographic information of the patients in both groups. The periodontal status, levels of FPG, and HbA1c of both groups at baseline are shown in Table 2. At baseline, 24 of 27 patients in the treatment group and 22 of 25 patients in control group had HbA1c ≥8%. There were no significant differences in PD, attachment loss, and the level of HbA1c between groups. However, the mean plaque score and BOP of the treatment group were higher than the control, while the level of FPG was lower.

At 3 months after treatment, the periodontal status of the treatment group apparently improved. All of the patients in this group had decreased plaque score, BOP, and PD. Three patients of the treatment group showed increased attachment loss. There were significant reductions in plaque score, BOP, PD and attachment loss ($P < 0.05$). However, the reduction in the levels of FPG ($P = 0.60$) and HbA1c ($P = 0.185$) did not reach significance (Table 3). Analyzing the data by subgroups of the treatment group, on the basis of the response for each of the four periodontal parameters using medians as cut off points, again did not find the beneficial effect of periodontal treatment on glycemic control (data not shown). Six patients previously had HbA1c level ≥8% became <8% after periodontal treatment. One patient increased HbA1c level to ≥8 %.

At 3 months evaluation of the control group, more attachment loss was observed ($P < 0.05$) with no significant changes in PD, plaque score and BOP during 3-month observation period. No significant change in the level of FPG and HbA1c was found in this group (Table 3). Two patients in this group previously had HbA1c level ≥8% had decreased HbA1c level to <8%. Even though, 16 patients in the treatment and 14 patients in the control groups demonstrated decreased HbA1c level, subgroup analysis of changes in HbA1c level found no association between periodontal treatment with adjunctive antimicrobial treatment and changes in HbA1c levels ($\chi^2 = 0.056$, $P = 0.812$, Table 4).

Comparing the periodontal status between the treatment and control group at 3 months, the treatment group had significant shallower PD and less attachment loss than the control group. Although the reduction of the level of HbA1c from baseline of the treatment group was more than that of the control group, the difference did not reach significance (Table 4).

Discussion

In order to better understand the relationship between periodontal disease and diabetes mellitus, the present

Table 2 Periodontal and diabetic status of patients at baseline

	PD (mm)	*CAL (mm)*	*Pl (%)*	*BOP (%)*	*FPG (mg dl^{-1})*	*HbA1c (%)*
Treatment	3.22 ± 0.69	4.03 ± 1.03	91.48 ± 5.22*	61.57 ± 15.99*	151.4 ± 23.6*	8.98 ± 0.88
Control	3.27 ± 0.49	4.10 ± 0.79	86.16 ± 7.50	49.79 ± 15.32	171.6 ± 34.7	9.17 ± 1.02

Values are given as mean ± s.d.
PD, probing depth; CAL, clinical attachment level; Pl, plaque score; BOP, bleeding on probing; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin.
*Statistically significant difference compared with control group ($P < 0.05$).

Table 3 Changes in periodontal and diabetic status of the treatment and control groups between baseline and 3 months

	PD (mm)	*CAL (mm)*	*Pl (%)*	*BOP (%)*	*FPG (mg dl^{-1})*	*HbA1c (%)*
Treatment						
3 months	2.28 ± 0.35[a]	3.58 ± 1.21[a]	68.25 ± 13.37[a]	24.35 ± 8.77[a]	147.81 ± 28.88	8.78 ± 1.24
Changes	0.94 ± 0.41	0.45 ± 0.50	23.23 ± 13.54	37.22 ± 14.69	3.63 ± 35.55	0.19 ± 0.74
Control						
3 months	3.28 ± 0.54[c]	4.34 ± 0.86[b, c]	87.74 ± 7.67	49.78 ± 16.28	171.80 ± 46.67	9.28 ± 1.50
Changes	−0.01 ± 0.24	−0.24 ± 0.45	−1.58 ± 7.32	0.01 ± 9.85	−0.2 ± 54.22	−0.12 ± 1.05

Values are given as mean ± s.d.
PD, probing depth; CAL, clinical attachment level; Pl, plaque score; BOP, bleeding on probing; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin.
[a]Statistically significant decrease compared with baseline ($P < 0.05$).
[b]Statistically significant increase compared with baseline ($P < 0.05$).
[c]Statistically significant difference compared with the treatment group ($P < 0.05$).

Table 4 Distribution of patients at 3 months stratified by changes in glycated hemoglobin (HbA1c) from baseline levels

	Treatment group ($n = 27$)	*Control group* ($n = 25$)
Decrease in HbA1c levels	16	14
No change or increase in HbA1c levels	11	11

Chi-square test, $\chi^2 = 0.056$, $P = 0.812$.

study aimed to investigate the effect of periodontal therapy in older patients with both chronic periodontitis and diabetes mellitus, in the absence of any changes in medical therapy during the study period. We chose to focus on older patients because aging is associated with increased prevalence of periodontal disease (Locker and Leake, 1988) and increased insulin resistance (Paolisso *et al*, 1998, 1999). Additionally, the incidence and severity of diabetes increase with advancing age (Barbagallo *et al*, 1997; Perry, 1999). Our results clearly demonstrate that mechanical periodontal treatment combined with systemic doxycycline, 100 mg day^{-1} for 14 days, improved periodontal status of uncontrolled type 2 diabetic patients. PD reduction and clinical attachment gain of the treatment group were 29.19 and 11.17% respectively. Similar to previous studies (Grossi *et al*, 1997; Iwamoto *et al*, 2001; Stewart *et al*, 2001), we found that levels of HbA1c in the treatment group decreased, yet, contrary to these other studies, the decrease did not reach statistical significance. Conventional mechanical therapy has been shown to effectively treat chronic periodontitis (Drisko, 1996), while the adjunctive use of systemic doxycycline provided a modest improvement beyond that obtained by scaling and root planning (Ng and Bissada, 1998). Although inconclusive, adjunctive antimicrobial periodontal treatment has been reported to significantly reduce circulating TNF α and HbA1c levels (Grossi *et al*, 1997; Iwamoto *et al*, 2001). Because of these earlier findings, we chose the adjunctive use of systemic doxycycline.

The magnitude of pocket depth reduction and clinical attachment gain found in our study (0.94 and 0.45 mm, respectively) is similar to the response to non-surgical periodontal therapy in non-diabetics, whether treated by mechanical therapy alone (Badersten *et al*, 1981; Lindhe *et al*, 1982; Proye *et al*, 1982) or with adjunctive systemic doxycycline treatment (Ng and Bissada, 1998). The improvements in periodontal parameters reported here are higher than those reported in doxycycline-treated uncontrolled diabetic middle-aged patients with comparable baseline pocket depth and clinical attachment level (Grossi *et al*, 1997). It is interesting that the short-term (3 months) response to non-surgical periodontal therapy in uncontrolled diabetics was similar to that reported in non-diabetics. However, long-term response to non-surgical periodontal therapy in poorly controlled diabetics should be further investigated as Tervonen reported higher recurrence of sites with PD ≥4 mm in Type 1 diabetic patients with poor metabolic control or multiple complications compared with diabetics with good control and no complication, 1 year after therapy (Tervonen and Karjalainen, 1997).

In contrast to the periodontal health improvements observed in the uncontrolled diabetic older patients receiving periodontal therapy, the clinical attachment level of the patients who did not receive periodontal therapy significantly increased within 3 months. One interesting finding was the magnitude of the deterioration of periodontal health. The non-treated diabetics lost 0.24 ± 0.45 mm of periodontal attachment in 3 months. The rate of attachment loss, 0.96 mm year^{-1}, in diabetic older patients was almost the same as the annual loss of attachment rate, 1 mm year^{-1}, in the rapidly progressing disease group of Sri Lankan tea workers who had never been exposed to dental treatment and tooth brushing (Löe *et al*, 1986). The results of the present study suggest that, without periodontal treatment, uncontrolled older diabetics are at risk of rapidly losing their periodontally-affected teeth.

At baseline, the treatment group had higher mean plaque score and BOP than the control group. After periodontal therapy, mean plaque score and BOP of the treatment group decreased by 25 and 60%, respectively, while those of the control group remained unchanged. Despite this significant 25% reduction in plaque score in the treatment group, the improvement in plaque control in these older diabetic patients was far less than the plaque control level expected of treated periodontal patients (DeVore *et al*, 1990). We found that the older patients had diminished manual dexterity as well as lesser ability to learn new oral hygiene technique, such as brushing and use of interdental device, to prevent disease than younger adults as previously reported (Banting, 1986). It has also been previously reported that diabetic patient compliance with dental recommendations is related to HbA1c levels, with better compliance among those with better glycemic control (Syrjälä *et al*, 1999). Therefore, for reasons that include age and systemic health control (the latter probably being an indicator of overall health behavior), the population of the present study, i.e. older and poorly controlled diabetics, appear to represent a particular challenging group of periodontal patients in term of the therapist's ability to motivate them and alter their oral health behavior.

There are many factors influencing the short-term glucose level of a diabetic patient, and one of these is medical care. To determine the relative contribution of periodontal therapy in glycemic control of poorly controlled older diabetics, the present study was designed to include such patients that did not receive any change in their diabetic control regimen during the 3-month study period. Even though long-term study would have been preferable, the ethical dilemma of withholding any change in medical treatment for a period significantly longer than 3 months in patients with poorly controlled diabetes made such a longer-term study impossible. The results suggest that periodontal therapy, consisting of non-surgical mechanical therapy with adjunctive systemic antibiotics in older Thai

subjects, does not result in significant improvement of glycemic control, as determined by HbA1c levels. The present findings are in contrast to the results obtained by Stewart *et al* (2001). They conducted a study in type 2 diabetic older patients and found that level of HbA1c decreased after non-surgical periodontal treatment. However, unlike in the present study, the method of diabetes control was changed during the study period of Stewart *et al* (2001). Therefore, the relative contribution of periodontal therapy in improving the glycemic control of type 2 older diabetics remains unclear.

Significant reduction of HbA1c value has been reported 1 month after the completion of antimicrobial periodontal therapy (Iwamoto *et al*, 2001). In longer observation, significant reduction of HbA1c value was reported at 3 months; however, this significance could not be observed at 6 months (Grossi *et al*, 1997). There are several differences that could account for the discrepancy between the findings of the present study and those by Grossi *et al* (1997) and Iwamoto *et al* (2001). The study of Grossi and coworkers included a wide age range (25–65 years) of Native Americans with significant predisposition for type 2 diabetes (Grossi *et al*, 1997), while the present study was conducted on significantly older (age range: 55–80 years) Thai patients. The much younger (age range: 19–65 years) and much better controlled (baseline HbA1c levels: 7.96 ± 1.94%) diabetic patients in the study by Iwamoto *et al* (2001) received topical antimicrobial therapy for a month. The less than ideal reduction in plaque scores in the treatment group may be another reason for the lack of significant reduction in HbA1c levels in the present study. Despite the differences between the present study and the previous studies discussed above (Grossi *et al*, 1997; Iwamoto *et al*, 2001; Stewart *et al*, 2001), the trends observed in the present study, i.e. a decrease in HbA1c levels for the treatment group and a slight increase in the control group, are in line with the direction of the previous studies' results.

One of the inevitable drawbacks of design of present study is that the provided periodontal treatment makes blinding procedures impossible for the examiners at 3-month evaluation point, because of the absence of calculus and inflammation after periodontal treatment. Therefore, examiner bias, although unintentionally, could have impacted the periodontal measurements at the 3-month time point. Other additional sources of possible bias could be the lack of randomization of all subjects, the control group included patients refusing periodontal treatment. Also, missing data due to loss to follow-up at the 3-month evaluation of some patients is another problem for analysis and interpretation. Intention to treat analysis should be applied to randomized controlled trial. However, without outcome data, serial measurements, or sufficient data to allow estimation for intention to treat analysis, complete case analysis was performed in this study. This approach can lead to bias as well. The variation in HbA1c levels found in the present study (standard deviation of 1.24), when compared with previous studies in younger subjects [standard deviation of 0.6 for Grossi *et al* (1997)] suggested that a larger sample size is needed for any future study in older poorly controlled diabetics. Taking all together, the aforementioned factors may explain the lack of statistically significant effect of periodontal therapy on glycemic control of type 2 diabetic older patients in this study.

In conclusion, the results of the present study indicate that, in the absence of any medical intervention, the periodontal condition of older Thais with poorly controlled diabetes is: (a) significantly improved 3 months after mechanical periodontal therapy with adjunctive systemic antimicrobial treatment, and (b) rapidly deteriorating without periodontal treatment. Furthermore, the results suggest that documenting an independent effect of periodontal therapy on the glycemic control of older poorly controlled diabetics will require further studies that will have to include much larger sample sizes.

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