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Efficacy of non-surgical treatment accompanied by professional toothbrushing in the treatment of chronic periodontitis in patients with type 2 diabetes mellitus: a randomized controlled clinical trial

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ABSTRACT

Purpose: The present study aimed to evaluate the clinical benefit of additional toothbrushing accompanying non-surgical periodontal treatment on oral and general health in patients with type 2 diabetes mellitus (T2DM).
Methods: We conducted a doubled-blind randomized controlled trial in 60 T2DM patients between June 2013 and June 2014. The patients were randomly assigned to the scaling and root planing (SRP) group; the scaling and root planing with additional toothbrushing (SRPAT) group, in which additional toothbrushing was performed by toothpick methods; or the control group. Microbiological and oral examinations were performed for up to 12 weeks following treatment. Non-surgical treatment was conducted in the experimental groups. The SRP group received scaling and root planing and the SRPAT group received additional toothbrushing with the Watanabe method once a week from the first visit through the fifth visit. The primary outcomes were changes in haemoglobin A1c (or glycated haemoglobin; HbA1c) levels, serum endotoxin levels, and interleukin-1 beta levels. Periodontal health status was measured by periodontal pocket depth, the calculus index, and bleeding on probing (BOP).
Results: Both the SRP and SRPAT groups showed improvements in periodontal health and HbA1c, but the SRPAT group showed significantly less BOP than the SRP group. Furthermore, only the SRPAT group showed a statistically significant decrease in serum endotoxin levels.
Conclusions: Non-surgical periodontal treatment was effective in improving HbA1c and serum endotoxin levels in T2DM patients. Furthermore, non-surgical treatment with additional tooth brushing had a more favourable effect on gingival bleeding management.
Trial RegistrationClinical Research Information Service Identifier: KCT000416

Keywords: Diabetes mellitus; Glycated hemoglobin A; Interleukins; Periodontitis; Toothbrushing

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Conflict of Interest
No potential conflict of interest relevant to this article was reported.

INTRODUCTION

The prevalence of diabetes mellitus among the adult population has increased to 8.5% globally, and the World Health Organization (WHO) has estimated that diabetes is the seventh leading cause of death globally [1]. Periodontal disease, which is recognized as the sixth major complication of diabetes [2], is a common chronic disease that causes symptoms such as gingival bleeding and recession, periodontal pocket formation, and alveolar bone destruction in most adults with diabetes [3-5].

The local inflammatory response is associated with periodontal disease and results in the activation of the immune system in response to factors such as bacteria and antigens. Pro-inflammatory molecules and cytokine networks are known to play a vital role in this response [6]. As mediated through inflammation, periodontal disease may be a risk factor for metabolic diseases such as diabetes, dyslipidaemia, and heart disease [7-10].

The bacteria that cause chronic periodontal disease secrete inflammatory mediators and trigger an inflammatory response that induces cell proliferation and variants, reduces the ability to adapt to oxidative stress, and suppresses apoptosis [11]. The secondary promotion of inflammatory molecules through increased levels of these toxins has been reported to cause damage to pancreatic beta cells, increasing insulin resistance and consequently impairing blood glucose regulation [12].

A patient with diabetes who maintains rigorous glycaemic control with regular medical care generally can receive any indicated dental treatment [13]. Adults with well-managed diabetes who do not have systemic complications are treated the same as patients without diabetes. Additionally, antibiotics are not prescribed unconditionally for non-invasive procedures [14]. However, since dental practitioners may treat patients with diabetes at any time, they must be familiar with the correlations among the oral signs and symptoms of the disease, oral health, and glycaemic control in order to ensure that these patients are properly managed [15].

Patients who present multiple sites with significantly increased probing depth and bleeding on probing (BOP) even after surgical periodontal treatment are more likely to have active infections, meaning that the treatment modality employed might not have been adequate [16]. People with diabetes have an especially high risk of serious infections, even during non-surgical periodontal treatment, which represents a considerable population-level burden [17].

Professional toothbrushing, which is carried out to remove inflammatory substances on the surface of the tooth, reduces the risk of infection by reducing oxidative stress throughout the circulatory system [18] and enhancing capillary gingival circulation [19-21]. It has been reported that mechanical stimulation by the toothpick toothbrushing method increases the proliferation of gingival basement cells by approximately 2.5 times compared to using a scaler [22]. Thus, the histometric changes induced by toothbrushing resemble the repair phase of wound healing [23].

Based on the hypothesis that treatment with additional toothbrushing concurrently with non-surgical periodontal therapy could reduce the risk of systemic infection, we evaluated changes in oral health, improvements in glycaemic control, and changes in systemic markers of inflammation in patients with type 2 diabetes mellitus (T2DM). Through this study, we hope to establish an optimal non-surgical periodontal treatment method for patients with diabetes.

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MATERIALS AND METHODS

Study population

The Institutional Review Board of Seoul National University School of Dentistry approved this clinical trial (S-D20130016, 30/05/2013), and it was also registered with the Korean Clinical Research Information Service (KCT000416). Written informed consent was obtained from each subject. We evaluated 60 patients with T2DM. The patients recruited for this study were maintenance patients from a community health care centre (Gwangjin-gu Public Health Centre, Seoul, Korea). Subjects were included in the study if they had: 1) teeth with sites with a PD >5 mm and attachment loss in at least 2 quadrants; 2) BOP at these sites; 3) at least 20 remaining teeth; 4) a haemoglobin A1c (or glycated haemoglobin; HbA1c) level ≥6.5%; and 5) non-smoking status. Additionally, all patients were diagnosed with periodontitis [24]. The exclusion criteria were 1) current abuse of alcohol or drugs; 2) chronic liver disease including hepatitis; and 3) a body mass index (BMI) ≥40 kg/m^2. Patients' age, BMI, HbA1c level, endotoxin level, interleukin-1 beta (IL-1β) level, and oral health status were recorded (Table 1). Patients were randomly assigned in equal proportions to the control (CTR) group, the scaling and root planing (SRP) group, which received general non-surgical periodontal treatment only, or the scaling and root planing with additional toothbrushing (SRPAT) group, which received non-surgical periodontal treatment accompanied by toothbrushing. At the end of the study, all participants, including the CTR group, were provided proper oral health care.

Diagnosis of T2DM

T2DM was diagnosed according to the WHO criteria: 1) HbA1c ≥6.5%; 2) symptoms of diabetes mellitus and a random blood sugar concentration ≥200 mg/dL; 3) fasting blood sugar ≥126 mg/dL on more than 1 occasion; or 4) a 2-hour postprandial plasma glucose concentration ≥200 mg/dL during an oral glucose tolerance test. As part of follow-up visits for diabetes, blood samples were collected from participants once every 3 months. No additional blood collection was performed for this study. Additionally, serum levels of inflammatory molecules were analysed.

Table 1. Clinical characteristics of the study participants at baseline

Characteristics	SRP	SRPAT	Control	Total	*P* value
Sex					
Male	10 (50.00)	10 (50.00)	10 (50.00)	30 (50.00)	-
Female	10 (50.00)	10 (50.00)	10 (50.00)	30 (50.00)	-
Age (years)	71.15±8.61	72.45±8.20	74.15±7.21	72.58±7.99	0.645[a]
BMI (kg/m^2)	24.17±2.14	24.57±2.97	24.15±2.55	24.30±2.54	0.748[a]
HbA1c (%)	6.64±0.29	6.68±0.23	6.76±0.39	6.69±0.31	0.379[a]
IL-1β (pg/ml)	0.73±0.83	0.66±0.83	0.59±0.47	0.66±0.72	0.931[a]
Endotoxin level (EU/mL)	1.48±1.29	1.70±1.35	1.49±0.94	1.56±1.19	0.866[a]
No. of teeth	25.50±2.54	24.75±3.43	25.05±2.89	25.10±2.94	0.819[a]
Decayed teeth	0.10±0.31	0.20±0.52	0.20±0.62	0.17±0.49	0.861[a]
Missing teeth	2.20±2.46	2.35±3.27	2.10±2.71	2.22±2.79	0.962[a]
Filled teeth	1.85±2.52	2.70±3.11	3.15±4.31	2.57±3.38	0.589[a]
DMFT	4.15±3.51	5.25±4.81	5.45±5.84	4.95±4.77	0.836[a]
PD	3.32±0.29	3.42±0.67	3.44±0.48	3.39±0.50	0.705[b]
PD ≥4 mm sites[c]	4.60±2.46	4.85±3.30	4.15±2.52	4.53±2.75	0.724[b]
CI	3.30±2.74	3.05±1.32	3.10±1.07	3.15±1.83	0.688[a]
BOP rate (%)	18.93±15.76	22.25±15.96	21.29±15.44	20.82±15.52	0.790[b]

Data shown are number (%) or mean±standard deviation.
SRP: scaling and root planing, SRPAT: scaling and root planing with additional toothbrushing, BMI: body mass index, Hb: haemoglobin, IL: interleukin, DMFT: decayed, missing, filled teeth, PD: pocket depth, CI: calculus index, BOP: bleeding on probing.
[a]*P* value was determined by the Kruskal-Wallis test for continuous variables. [b]*P* value was determined by 1-way analysis of variance for continuous variables. [c]PD ≥ 4 mm sites: number of sites with a periodontal pocket depth of 4 mm or more.

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Intervention

SRP group

After a baseline oral examination, oral health education including toothbrush instruction was conducted to eliminate bias in oral health behaviours. In the SRP group, supragingival scaling was performed only on the first visit by 2 trained dentists working together simultaneously. After 2 weeks, root planing was performed to remove the subgingival calculus. At 12 weeks, patients were recalled to re-check their oral health status. If they required additional periodontal treatment, it was done at 12 weeks.

SRPAT group

After a baseline oral examination, oral health education including toothbrush instruction was conducted to eliminate bias in oral health behaviours. In the SRPAT group, additional toothbrushing (Watanabe method) with a 2-row toothbrush was applied on the first visit by a trained dentist. On the second visit, subgingival calculus was removed as appropriate according to the patient's oral health condition. Additional toothbrushing (Watanabe method) was performed once a week from the first visit through the fifth visit.

CTR group

The CTR group received no other treatments beyond medical screening for diabetes. However, all groups received oral health education including toothbrush instruction at the baseline visit to eliminate intergroup bias associated with routine oral health behaviours. After the study was completed, the necessary dental treatment was provided to the patients who wished to receive it.

Measurements

This study is a preliminary report of a randomized, parallel-design, double-blinded, controlled clinical trial. HbA1c levels, which are a major indicator of improvement in diabetes, reflect the average blood glucose level over the course of 2 to 3 months, which is the life span of red blood cells. Therefore, to evaluate improvements in HbA1c levels in this study, we set a minimum evaluation period of 12 weeks, taking into account the safety of participants undergoing non-surgical periodontal procedures and the impact of the study on the participants. The examinations were carried out using a portable dental unit equipped with a dental light, mouth mirrors, and periodontal probes. To assess participants' oral health status, all teeth were examined by 2 trained dentists using the WHO dental caries examination criteria [25], and the decayed, missing, filled teeth (DMFT) variable was used to assess the prevalence of dental caries. The DMFT is a simple count of the number of decayed, missing (due to caries only), and restored teeth (due to caries only). The gold standard was a dentist who had sufficient experience in national oral examinations and screening studies before the study, and repeated training on screening was conducted for the 2 dentists who carried out the measurements. Intra-examiner reproducibility was calculated using the kappa index, which was 0.976 for repeated scores.

Periodontal health was examined in the maxillary right first molar, maxillary right incisor, maxillary left first molar, mandibular left first incisor, mandibular left first molar, and mandibular right first molar. Measurement was assessed buccal and lingual site. Full-mouth periodontal probing was performed by dentists using a periodontal probe (University of North Carolina No. 15 probe; Hu-Friedy, Chicago, IL, USA). The periodontal pocket depth (PD) was measured at 6 sites for each tooth (mesio-labial, mid-labial, disto-labial, mesio-lingual, mid-lingual, disto-lingual) as the distance from the gingival margin to the bottom of the sulcus. BOP was measured at the gingival margin surrounding individual teeth, which were divided into buccal, lingual, mesial, distal, and median regions. Based on an observation of whether bleeding occurred at those sites,

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the arithmetic mean of BOP was calculated. The calculus index (CI) was measured using oral hygiene index criteria [26] based on 12 numerical determinations, representing the amount of calculus found on the buccal and lingual surfaces of each of 3 segments of each dental arch.

Laboratory parameters

HbA1c analysis

Blood samples were taken by a medical laboratory technologist at the health centre. At the first visit and last visit, blood was collected in a serum separator tube (SST) and an ethylenediaminetetraacetic acid plasma tube, respectively. To analyse HbA1c levels, blood samples were immediately analysed by an immunoturbidimetric assay (COBAS INTEORA 400 plus; Roche Diagnostics GmbH, Mannheim, Germany).

Endotoxin and IL-1β analysis in serum

To analyse serum levels of endotoxin and IL-1β, which are inflammatory molecules, the blood aliquoted in the SST on the day of the visit was centrifuged at 3,500 rpm and 22°C for 10 minutes, then placed in a 2-mL tube and stored at −80°C until a quantitative analysis was conducted. To prevent deformation of samples, the serum samples were dissolved on ice after which an enzyme-linked immunosorbent assay (human IL-1β high-sensitivity ELISA kit; eBioscience, San Diego, CA USA) was conducted and a quantitative analysis using the Pyrotell®-T kit was performed using the turbidimetric method (Pyros Kinetix®; Associates of Cape Cod Inc., East Falmouth, MA, USA).

All microbiological and immunological laboratory procedures were performed by blinded analysts, who did not have any knowledge of the clinical status of the study subjects.

Sample size and statistical analysis

We estimated that a total of 72 patients with diabetes would be needed to detect a difference among 3 groups, with an α of 0.05, a (1-β) of 0.80, and an effect size of 0.40, with a drop-out rate of 10%. All data were analysed with IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA). The threshold for statistical significance was set at a *P* value of 0.05. The type of periodontal treatment received by the clinical trial participants was the explanatory variable, which was compared using the continuous variables of oral health status, inflammatory molecules, and HbA1c levels among the groups. Intragroup comparisons for each non-surgical treatment method between the baseline and 12 weeks were performed using repeated-measures analysis of variance (ANOVA) to compare different time points. For comparison of basic characteristics among groups 1-way ANOVA was tested, and continuous variables with a non-normal distribution were analysed using the Kruskal-Wallis test. For statistical testing of changes between the first visit (1 week) and last visit (12 weeks), continuous data with a normal distribution were evaluated via the paired t-test, and paired continuous data with a non-normal distribution were evaluated using the Wilcoxon signed-rank test. For multiple comparisons, continuous data with a normal distribution were tested using the Tukey *post hoc* test, and continuous variables with a non-normal distribution were tested using the Mann-Whitney test.

RESULTS

Characteristics of participants

The participants were randomly assigned by rolling a dice to the SRP group, the SPRAT group, or the CTR group. During the study period, 15 participants dropped out of the study

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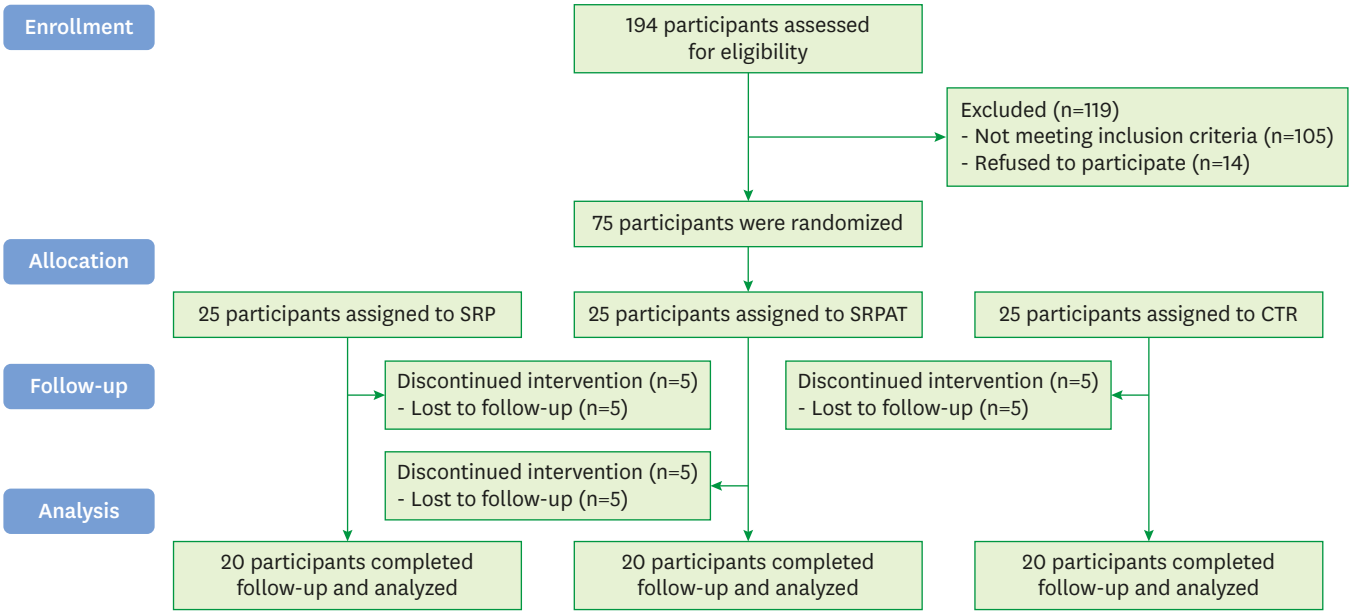

Figure 1. Flowchart of the participants through the study (CONSORT flow diagram).
CTR: control, SRP: scaling and root planning, SRPAT: scaling and root planing with additional toothbrushing.

(Figure 1) due to old age and the long intervention period. Finally, data were analysed from 60 participants (20 in each group). The characteristics of the participants at baseline are presented in Table 1. Sex, age, BMI, HbA1c levels, IL-1β levels, endotoxin levels, number of teeth, DMFT, PD, BOP, and CI values were not significantly different among the 3 groups (P>0.05).

Correlation between circulating molecules and periodontal status

The correlations of baseline circulating levels of HBA1c, IL-1β, and endotoxins with variables reflecting baseline oral health status are presented in Table 2. Significant positive correlations were found between levels of endotoxins and PD. The data were analysed for relationships between changes in circulating molecule levels and changes in periodontal status after the last visit (Figure 2, Table 3). No significant relationships were found between changes in oral health status and IL-1β levels. However, changes in endotoxin and HbA1c levels showed significant positive correlations with PD, CI, and BOP.

Table 2. Correlations between circulating levels of HbA1c, IL-1β, endotoxin, and oral health status variables[a)]

Variables	PD	CI	BOP	DMFT	NT
HbA1c					
Correlation coefficient	0.118	−0.074	0.210	−0.062	0.025
P value	0.370	0.576	0.107	0.640	0.852
IL-1β					
Correlation coefficient	0.090	0.177	0.037	−0.117	0.026
P value	0.495	0.175	0.777	0.374	0.846
Endotoxin					
Correlation coefficient	0.809	−0.100	0.025	0.232	0.232
P value	0.000[b)]	0.446	0.851	0.075	0.075

PD: pocket depth, CI: calculus index, BOP: bleeding on probing, DMFT: decayed, missing, filled teeth, NT: number of remaining teeth, HbA1c: haemoglobin A1c, IL: interleukin.
[a)]Each cell contains a Spearman rho value for pairs of variables and the probability that the correlation is significant. [b)]P value <0.05.

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Table 3. Correlations between changes in participants' biochemical variables and oral health status variables[a)]

Variables	PD change	CI change	BOP change
HbA1c change			
Correlation coefficient	0.496	0.351	0.321
P value	0.000[b)]	0.006[b)]	0.012[b)]
IL-1β change			
Correlation coefficient	0.009	0.257	0.125
P value	0.944	0.048[b)]	0.342
Endotoxin change (LAL assay)			
Correlation coefficient	0.485	0.332	0.367
P value	0.000[b)]	0.010[b)]	0.004[b)]

PD: pocket depth, CI: calculus index, BOP: bleeding on probing, HbA1c: haemoglobin A1c, IL: interleukin.
[a)]Each cell contains a Spearman rho value for pairs of variables and the probability that the correlation is significant. [b)]*P* value <0.05.

Effects of periodontal treatment and additional toothbrushing on metabolic assessments and inflammatory molecules

HbA1c levels were not significantly different among the groups at baseline (Table 1). However, HbA1c levels significantly decreased in both intervention groups after non-surgical periodontal treatment (Figure 3, Table 4). Significant differences were found between the intervention and CTR groups at each point during the follow-up period ($P<0.05$).

Serum IL-1β levels were not significantly different among the intervention and CTR groups at baseline. No significant changes were observed either within any group or among the 3 groups during the follow-up period.

Serum endotoxin levels in the intervention and CTR groups are shown in Table 4. No significant differences in serum endotoxin levels were observed among the intervention and CTR groups at baseline. Significant changes were observed within the intervention and CTR group and SRPAT group during the follow-up period ($P<0.05$). Additionally, there were significant differences among the intervention and CTR groups at each visit ($P<0.05$).

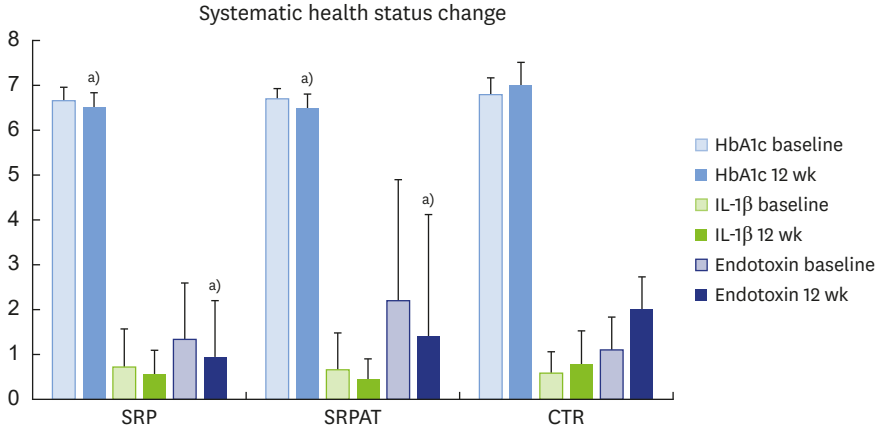

Figure 2. Changes in systemic health status after each treatment (baseline and after 12 weeks).
HbA1c, IL-1β, and endotoxin levels in the serum were analysed. *P* values were calculated by repeated-measures analysis of variance with use of the Bonferroni-Holm adjustment for multiple comparisons.
SRP: scaling and root planing, SRPAT: scaling and root planing with additional toothbrushing, CTR: control, HbA1c: haemoglobin A1c, IL-1β: interleukin-1 beta.
[a)]Significant difference from the control group ($P<0.025$).

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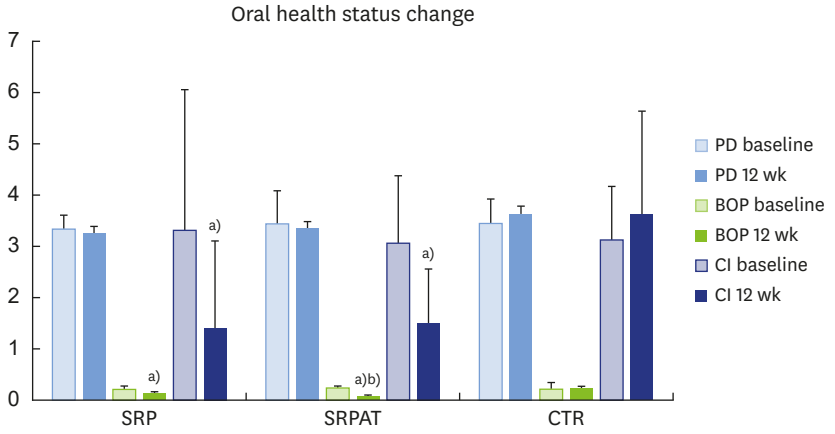

Figure 3. Changes in oral health status after each treatment (baseline and after 12 weeks).
PD, BOP, and CI decreased significantly. *P* value were calculated by repeated-measures analysis of variance with use of the Bonferroni-Holm adjustment for multiple comparisons.
PD: pocket depth, BOP: bleeding on probing, CI: calculus index, SRP: scaling and root planing, SRPAT: scaling and root planing with additional toothbrushing, CTR: control.[a]Significant difference from the control group ($P<0.025$). [b]Significant difference from the SRP group ($P<0.025$).

Effects of non-surgical periodontal treatment and additional toothbrushing on periodontal health

In both intervention groups, PD, CI, and BOP had significantly improved at the last visit compared with the baseline values, and these improvements were significant compared with the CTR group (Figure 2, Table 4). In the CTR group, PD values had increased at the last visit compared with the baseline values (Figure 2, Table 4).

DISCUSSION

Many oral health complications are caused by diabetes mellitus, including gingivitis, xerostomia, and a burning sensation. Although many studies have investigated associations between oral diseases and the systemic health of patients with metabolic diseases, there have not been any studies of appropriate periodontal treatment methods tailored to the specific needs of patients with particular diseases. Therefore, in this study, the effects of oral hygiene on general health according to the use of different non-surgical periodontal treatment methods were evaluated in adult patients with diabetes.

Inflammation plays a role in inducing cell proliferation and variants, reducing the body's ability to adapt to oxidative stress, suppressing apoptosis, and increasing the secretion of inflammatory mediators [11]. The bacteria that cause chronic periodontal disease secrete inflammatory mediators and trigger an inflammatory response, which results in toxin secretion in tissues [12]. Secondary promotion of inflammatory mediators through increased levels of these toxins has been reported to cause damage to pancreatic beta cells, increasing insulin resistance and consequently impairing blood glucose regulation [13].

Non-surgical periodontal treatment and regular oral hygiene care are generally considered to be effective methods of periodontal treatment that facilitate the removal of inflammatory substances. Horiuchi et al. [22] and Sakamoto et al. [27] reported that mechanical stimulation through toothbrushing resulted in histological effects on periodontal tissue

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Table 4. Changes in concentrations of HbA1c, circulating IL-1β, endotoxins, and oral health status variables

Variables	Baseline	3 months	Change	*P* value
HbA1c				
SRP	6.64±0.29	6.47±0.34	−0.17±0.27[d]	0.009[a]
SRPAT	6.68±0.23	6.43±0.35	−0.25±0.25[d]	0.001[a]
Control	6.76±0.39	6.98±0.51	0.22±0.28	0.001[a]
P value			0.000[c]	
IL-1β				
SRP	0.73±0.83	0.54±0.55	−0.19±0.85	0.506[a]
SRPAT	0.66±0.83	0.45±0.44	−0.21±0.87	0.243[a]
Control	0.59±0.47	0.76±0.75	0.18±0.81	0.360[a]
P value			0.404[c]	
Endotoxin				
SRP	1.48±1.29	1.08±0.76	−0.39±1.22[d]	0.287[a]
SRPAT	1.70±1.35	0.92±0.77	−0.78±1.22[d]	0.003[a]
Control	1.49±0.94	2.35±1.57	0.91±1.26	0.004[a]
P value			0.000[c]	
PD				
SRP	3.32±0.29	3.23±0.37	−0.08±0.18[f]	0.043[b]
SRPAT	3.42±0.67	3.34±0.74	−0.09±0.18[f]	0.039[b]
Control	3.44±0.48	3.62±0.64	0.18±0.21	0.001[b]
P value			0.000[e]	
CI				
SRP	3.30±2.74	1.40±1.70	−1.90±2.65[d]	0.006[a]
SRPAT	3.05±1.32	1.50±1.05	−1.55±1.70[d]	0.001[a]
Control	3.10±1.07	3.60±2.04	0.50±1.43	0.181[a]
P value			0.000[c]	
BOP (%)				
SRP	18.93±15.76	11.66±8.86	−7.27±11.90	0.013[b]
SRPAT	22.25±15.96	5.73±5.70	−16.52±14.38[f,g]	0.000[b]
Control	21.29±15.44	22.66±13.62	1.37±9.43	0.524[b]
P value			0.000[e]	

SRP: scaling and root planing, SRPAT: scaling and root planing with additional toothbrushing, PD: pocket depth, CI: calculus index, BOP: bleeding on probing, HbA1c: haemoglobin A1c, IL: interleukin.
[a]*P* value was determined by the Wilcoxon signed rank test between the baseline and 3-month variables. [b]*P* value was determined by the paired t-test between the baseline and 3-month variables. [c]*P* value was determined by the Kruskal-Wallis test for continuous variables. [d]*P* value was determined by the Mann-Whitney test in comparison with the control group. [e]*P* value was determined by 1-way analysis of variance for continuous variables. [f]*P* value was determined by the *post hoc* Tukey test in comparison with the control group. [g]*P* value was determined by the *post hoc* Tukey test in comparison with the SRP group.

in addition to plaque removal. In those studies, repeated professional toothbrushing (at least 3 times) using Watanabe's method had a statistically significant effect on gingival fibroblast proliferation through activation of fibroblasts, procollagen-positive fibroblasts, and proliferating cell nuclear antigen-positive fibroblasts in periodontal tissue and promoted the proliferation of fibroblasts and the junctional epithelium. Therefore, the group with additional brushing in this study also received non-surgical periodontal treatment once a week, at least 3 times. Numerous clinical reports have also shown that Watanabe's toothbrushing method helps to alleviate periodontal tissue inflammation. In conclusion, regular oral health care with professional toothbrushing using Watanabe's method was effective in relieving gingival inflammation in patients with periodontitis.

Soorya et al. [28] reported that non-surgical periodontal treatment decreased the levels of the inflammatory cytokine tumour necrosis factor alpha (TNF-α) collected from gingival crevicular fluid after 3 months of application However, Talbert et al. [29] reported that levels of local inflammatory cytokines, such as TNF-α and IL-6, in gingival crevicular fluid did not significantly change after performing SRP. It has been reported that periodontal treatment may cause systemic stress, spreading throughout the blood circulation.

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However, it is challenging to determine changes in the inflammation index throughout the whole body, as most studies have examined changes in local inflammatory mediators by analysing gingival crevicular fluid. Therefore, in this study, blood was collected from the upper arm to evaluate indexes of systemic inflammation; although IL-1β levels did not change, the systemic endotoxin level was significantly different between the control and intervention groups. The serum endotoxin level significantly decreased in the SRPAT groups. These 2 non-surgical periodontal treatments are suitable for patients with diabetes because they led to significant changes in the levels of inflammatory substances compared to the CTR group. Bacterial contamination affects the systemic immune system through inflammatory mediators [30]. The spread of these mediators into the bloodstream has been suggested to be one of the main factors involved in systematic diseases such as diabetes [31]. Zekeridou et al. [32] reported that periodontitis is an inflammatory disease that stimulates the immune response through a cascade of local and systemic cytokines that are not limited to the diseased sites. In addition, bacteria produce cell-destructive substances, which include acids, enzymes, antigens, and toxins, with endotoxin from Gram-negative bacteria being the most prevalent [33]. The destruction of the epithelial attachment to the teeth and pocket lining contributes to endotoxaemia and bacteraemia. As a result, metabolic endotoxaemia dysregulates the inflammatory tone and triggers body weight gain and diabetes [34]. Thus, stress due to the effects of periodontal treatment can be an important factor affecting the concentration of inflammatory mediators throughout the whole body, especially in people with systemic illnesses such as diabetes.

HbA1c is a significant index of blood glucose control in patients with diabetes. Discordant findings have been reported regarding changes in HbA1c after non-surgical periodontal treatment. An increase in HbA1c levels was found in the study of Christgau et al. [35] in patients who received non-surgical periodontal treatment, and no significant effect was found compared to the CTR group in terms of improvement in oral health. Furthermore, in the study of Chen et al. [36] only a decrease in high-sensitivity C-reactive protein was observed to result from non-surgical periodontal treatment, whereas changes in HbA1c levels, fasting plasma glucose levels, TNF-α levels, and the lipid profile were not observed. However, Iwamoto et al. [37] found that HbA1c levels were significantly reduced (by approximately 0.84%) after 8 weeks through a clinical trial of non-surgical periodontal treatment in patients with diabetes, and Gaikwad et al. [38] reported more significant improvements in the average PD, gingival index, clinical attachment loss, oral hygiene, and HbA1c in the SRP group with doxycycline than in other groups. According to a systematic review of the effect of non-surgical treatment on these outcomes [16], it was reported that HbA1c was reduced by approximately 0.4% by non-surgical periodontal treatment. These results are similar to the trend observed in this study for HbA1c to decrease after non-surgical periodontal treatment (Table 4).

It was found in this study that non-surgical periodontal treatment improved oral and systemic health, but an important problem in the dental treatment of patients with diabetes is their susceptibility to infection. Since controlling dental plaque plays a vital role in preventing the spread of inflammatory substances, the toothpick toothbrushing method is effective in removing plaque between teeth, and continuous plaque removal through this method suppresses the occurrence of periodontal disease [39].

Another finding of this study is that the BOP rate in the group with additional tooth brushing was significantly less than that in the group that received non-surgical periodontal

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treatment alone. Therefore, additional brushing can help to effectively control infection problems due to bleeding in patients with diabetes, and it was confirmed that mechanical stimulation could positively affect periodontal tissue healing. Tomofuji et al. [40] reported that mechanical stimulation of the gingiva through toothbrushing can help healing by stimulating proliferation, and this cell division results in an increased number of fibroblasts in periodontal tissue.

As a result of examining the effects of the most commonly used non-surgical periodontal treatments (SRP and SRPAT) on oral health and systemic health status, it was found that both non-surgical periodontal treatments yielded improvements in oral health and HbA1c levels. These techniques are both suitable for patients with diabetes, as they do not cause an increase in concentrations of inflammatory substances in the body.

In particular, SRPAT led to a greater decrease in BOP than was observed for SRP alone or in the CTR group. Therefore, incorporating additional toothbrushing is considered to be a beneficial treatment for patients with diabetes who face problems such as infection risk or bleeding due to their high susceptibility to disease.

Some limitations of this study should be noted. First, the patients were relatively old due to their characteristics (e.g., the average age of visitors to the studied public health centre was high), and older individuals often have complex chronic systemic diseases. This raises the possibility of bias due to changes in indicators of general health. Because of the long participation period and the age of the participants, some discontinued participation in the study. Nonetheless, from a statistical perspective, a sufficient number of participants was secured to ensure normality of changes in the main indicators. The study also took into account the minimal systemic risks that non-surgical periodontal treatment can pose to patients with diabetes by limiting the analysis to the shortest period in which the effects of the intervention could be evaluated. Based on previous studies, the histological effects of professional toothbrushing become evident 3 weeks after treatment initiation and require at least 3 visits. However, providing professional toothbrushing only as a comparison group with the same number of visits for periodontal disease was not possible because there is no usual treatment. Therefore, this study was designed to evaluate only the effect of additional toothbrushing accompanying PAT, in light of safety considerations and ethical concerns. In order to receive additional toothbrushing, the SRPAT group had more visits than the SRP group. Therefore, further clinical studies are required with a standardized design suitable for monitoring the relevant metabolic disorders, providing participants with the stimulation expected to result in benefits, and tracing the participants over a longer-term follow-up with the same number of visits. Moreover, it is considered that prognostic observations to support the appropriate duration and details of treatment will be necessary. Another limitation of this study is that all the participants, including the CTR group, had an interest in their health because they regularly visited the public health centre for diabetes treatment. In addition, the same oral health education was provided for all groups to eliminate the influence of daily oral health care, but their relatively high concern regarding health may have been a source of bias.

In conclusion, this study investigated the effects of non-surgical periodontal treatment methods on changes in oral health and general health conditions with the goal of determining the most suitable non-surgical periodontal treatment method for adult patients with diabetes. In total, there were 60 participants, and the following conclusions were obtained.

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1. Two types of non-surgical periodontal treatment (in the SRPAT and SRP groups) resulted in improvements in oral health and HbA1c levels (P<0.05).
2. Among the methods of non-surgical periodontal treatment that were evaluated, the SRPAT group showed a significant reduction in BOP compared with the SRP group (P<0.05).
3. The SRPAT group showed a statistically significant decrease in serum endotoxin levels (P<0.05).

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