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The effect of full-mouth tooth extraction on glycemic control among patients with type 2 diabetes requiring extraction of all remaining teeth: a randomized clinical trial

Y. S. Khader[1], R. Al Habashneh[2], M. Al Malalheh[2], A. Bataineh[3]

[1]Departments of Public Health, Community Medicine and Family Medicine, Jordan University of Science and Technology, Irbid, Jordan and [2]Preventive Department and [3]Oral Medicine and Oral Surgery Department, Faculty of Dentistry, Jordan University of Science and Technology, Irbid, Jordan

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Background and Objective: Several studies have shown that periodontitis can complicate the severity of diabetes by worsening the degree of glycemic control. The purpose of this study was to determine the effect of full-mouth tooth extraction on glycemic control among type 2 diabetic patients.

Material and Methods: A total of 58 patients with type 2 diabetes mellitus and advanced periodontitis who were requiring extraction of all remaining teeth were randomized consecutively into treatment (full-mouth tooth extraction) and control groups (no treatment). Eight patients were lost to follow-up or reported use of antibiotics, leaving 50 patients to be included in the analysis. All patients had all their remaining teeth in a hopeless condition. Relevant data were collected, and glycosylated hemoglobin (HbA_{1c}) and fasting blood glucose levels were measured at baseline and at follow-up times of 3 and 6 mo.

Results: At baseline, the mean (SD) HbA_{1c} level was 8.6% (1.24) in the treatment group and 7.7% (0.87) in the control group. In the treatment group, the mean HbA_{1c} level decreased significantly from 8.6% at baseline to 7.4% after 3 mo of denture treatment, and continued to decrease to 7.3% after 6 mo. In the control group, the mean HbA_{1c} decreased from 7.7% at baseline to 7.5% after 3 mo, and remained almost the same after 6 mo. After adjusting for the baseline HbA_{1c}, the mean reduction in HbA_{1c} after 3 mo in the treatment group [1.23% (0.79)] was significantly higher than the mean reduction in the control group [0.28% (0.87)].

Conclusion: Full-mouth tooth extraction resulted in an improvement in glycemic control among diabetic patients. Large-scale multicentre clinical trials are needed to confirm the current evidence.

Dr Rola Al Habashneh, Preventive Department – Periodontics, College of Dentistry, Jordan University of Science and Technology, PO Box 3030, Irbid 22110, Jordan
Tel: +962 2 7278 662
Fax: +962 2 7278 962
e-mail: rolaperio@yahoo.com

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Diabetes and its related complications represent one of the most significant and growing chronic health problems worldwide. In Jordan, the prevalence of type 2 diabetes and impaired fasting glycemia is high (17.1 and 7.8%, respectively), and it increased over the last 10 years by 31.5% (1). Over the last decade, there have been numerous case–control and longitudinal studies that explored the association between periodontal disease and diabetes mellitus. A recent meta-analysis of the association between periodontal disease and diabetes showed that diabetes is associated with increased severity of periodontal disease (2). In patients with poor glycemic control, periodontal infection has more damaging effects on teeth and associated structures (3–9).

Several studies have shown that periodontitis can complicate the severity of diabetes by worsening the degree of glycemic control (10–17). In some studies, periodontal therapy aimed at eliminating infection and reducing inflammation has shown, at least in the short term, improvement in diabetes control (18–20). In other studies, no effect of periodontal treatment was seen on glycemic control in diabetic patients, especially when no antimicrobials have been used during periodontal treatment (18,21–23). However, small sample sizes, noncomparable study populations and the use of various parameters to assess treatment of periodontitis and improvement in diabetes make it difficult to interpret the study findings. The meta-analyses of 10 intervention studies by Janket *et al*. (24) found a nonsignificant 0.38% reduction in glycated hemoglobin (HbA_{1c}). A more recent meta-analyses carried out by Teeuw *et al*. (25) showed that diabetic patients experienced a greater reduction in HbA_{1c} by about 0.4% compared with the no-treatment control group. It is noteworthy that authors recommended that changes in HbA_{1c} percentage must be interpreted with care owing to heterogeneity among studies.

Since some residual periodontal inflammation may remain after periodontal therapy and may progress and exacerbate, especially around hopeless teeth, the full-mouth hopeless teeth clearance idea has been suggested as the only way in which the complete elimination of infection is achievable. An early study showed that removing teeth with advanced decay (a source of possible inflammatory mediators) improved glycemic control (26). In contrast, two later studies found that complete, definitive and irreversible elimination of dental infections through full-mouth dental extractions did not lower coronary heart disease risk or serum levels of C-reactive protein (27,28). However, a significant decrease in serum levels of C-reactive protein, plasminogen activator inhibitor-1 and fibrinogen, and white cell and platelet counts was noticed after full-mouth tooth extraction (29). Since the effect of periodontal treatment on glycemic control is not clear, we hypothesized that complete elimination of periodontal infection by full-mouth tooth extraction when all teeth are diagnosed to have hopeless prognosis would result in better glycemic control. Therefore, this study was conducted to determine the effect of removal of all the infected teeth by full-mouth tooth extraction on glycated hemoglobin and blood sugar levels in patients with type 2 diabetes mellitus.

Material and methods

Participants

All patients with type 2 diabetes mellitus who attended the endocrinology clinics in King Abdullah University Hospital and Princes Basma Hospital in the period between May and December 2008 were approached, assessed and examined for eligibility. Patients were eligible for the study if they met the following inclusion criteria: diagnosed with type 2 diabetes mellitus; having a baseline HbA_{1c} level of at least 7% (30); having at least eight remaining teeth; and having all teeth in a hopeless condition according to Becker *et al*. (31). Every tooth was considered hopeless if it had at least two of the following: loss of 75% supporting bone; pocket depth > 8 mm; class III furcation involvements using Glickman index (Glickman, 1953); class III mobility using Miller index (Miller, 1950); poor crown-to-root ratio; root proximity with minimal interproximal bone; history of repeated periodontal abscesses; and usefulness for prosthetics and restorative.

For those who met the inclusion criteria, the condition of their teeth was confirmed as periodontally compromised to the point of being hopeless and indicated for extraction for periodontal reasons. Patients were excluded from the study if they needed antibiotic prophylaxis or they had coronary heart disease, malignancies or rheumatoid arthritis.

Interventions

A total of 58 patients were randomized consecutively to one of the two groups: treatment group and control group (Fig. 1). Patients in the treatment group received a full-mouth tooth extraction under local anesthesia within a period of 2 wks by the same dentist (M.M) and received the usual postoperative instructions. No antibiotics or mouthwashes were given to them. For some multiple extraction cases, suturing was done as needed, and sutures were removed after 1 wk. Special care given to patients taking anticoagulants, in the form of additional laboratory tests for bleeding time and prothrombin time, but without changing their regimen. After 2 mo, all treated patients were referred to prosthodontic clinics for construction of complete dentures. All patients in the treatment group had received successful full dentures within 3–4 mo after full-mouth tooth extraction. The control group did not receive any dental treatment during the study period and they only received oral hygiene instructions. All participants in the control group received full-mouth tooth extraction and complete dentures after completion of the study. None of the patients in the control group developed problems around the hopeless teeth during the study period.

Sample size

Using a two-sided 0.05 level of significance and a probability of 85% (the

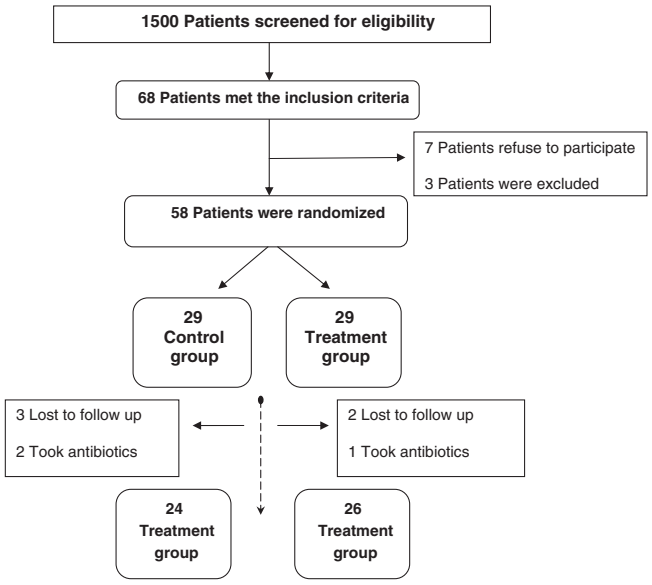

Fig. 1. Flow chart of recruitment and assessment.

power) that the study will detect a treatment difference, if the true difference in the reduction of HbA_{1c} between the treatment and control groups is 0.7 units, the sample size required was calculated as 50. This was based on the assumption that the standard deviation of the reduction in HbA_{1c} is 0.80 units.

Data collection

This study was approved by the Institutional Review Board of Jordan University of Science and Technology. Informed verbal consent was obtained from all eligible participants. Personal interviews were held to collect the baseline data from each participant using a prestructured questionnaire. Sociodemographic data, including age, sex, level of education and income, were collected. Detailed medical history was obtained from all patients. Information about diabetes was collected, including duration of diabetes, type of treatment, diabetes self-care management, blood glucose testing regimens and patients' adherence to their current medications, diet therapy and any physical activities. Barriers to adherence to diabetes regimen were assessed using a scale that was developed by Glasgow *et al.* (32). The original scale consisted of 15 items. Respondents were asked to rate how frequently they experienced various barriers to self-care activity using a five-point scale. Six items were dropped in our study because they were only asked once, and not in a repeated manner. The scale was scored by adding the responses across the items, with minimal score of nine and a maximal score of 45. Attitude to diabetes was recorded using the scale of Fitzgerald *et al.* (33) for diabetes attitude. The scale consisted of 10 items. The first six items were negatively worded, which required reverse scoring. The total score ranged from 10 up to 50. The higher scores on this scale indicate a negative attitude toward diabetes and patients who have possible problems coping with diabetes on daily basis. The support provided by family and friends concerning diabetes and its management was measured by the family and friends support scale developed by Fitzgerald *et al.* (33). The scale consists of 11 items; two of them were negatively worded, which required reverse scoring. Score ranged from 11 to 55, with higher scores indicating more support from family and friends regarding diabetes.

The same questionnaire used to collect data at baseline was used to collect similar information at follow-up time points. In addition, changes in eating habits, medications, smoking status and weight were noted.

Clinical examination

A thorough clinical and radiographic full-mouth examation were conducted. Probing depth and clinical attachment level were measured at six sites (mesial, distal and middle sites of the buccal and lingual sides) per tooth using a William periodontal probe. Plaque index (Silness & Loe; 34), gingival index (Loe & Silness; 35) and mobility (Miller's mobility index; 36) were recorded. The patient's oral hygiene practices, including brushing and any further oral hygiene tools, were also assessed. Based on the clinical and radiographic findings, a consensus between a periodontist, prosthodontist and endodontist about the condition of teeth was reached.

Outcomes

The primary end-points were the average reduction in HbA_{1c} and fasting blood glucose (FBG) from baseline to 3 and 6 mo after successful complete denture treatment. At baseline and after 3 and 6 mo of successful denture treatment in the treatment group and at corresponding times in the control group, blood samples were taken for all patients. Glycated hemoglobin level was assessed using a diagnostic reagent for quantitative *in vitro* determination of hemoglobin A_{1C} in whole blood on photometric systems (HbA1C; DiaSys Diagnostic Systems GmbH, Holzhiem, Germany) on an Automated Selectra E clinical chemical analyzer (Vital Scientific Dieren, The Netherlands). The DiaSys HbA1C assay is based on the principle of the particle-enhanced immunoturbidimetric test, and HbA_{1c} is determined directly without measurement of total hemoglobin. The assay is standardized according to the approved International Federation of Clinical Chemistry (IFCC) reference method, 2002. The FBG level was assessed using a diagnostic reagent for quantitative *in vitro* determination of glucose in whole blood on photometric systems (Glucose GOD-PAP; DiaSys Diagnostic Systems GmbH) on an

Automated Selectra E clinical chemical analyzer (Vital Scientific).

Statistical analysis

The Statistical Package for Social Sciences software (SPSS, version 15, Chicago, IL, USA) was used for data processing and analysis. Patients' characteristics were described using a frequency distribution for categorical variables and mean and standard deviation for continuous variables. The difference between parameters at the baseline between groups was analyzed using Student's unpaired *t*-test or chi-square wherever appropriate. The change in HbA_{1c} and FBG over time was analyzed using the General Linear Model repeated-measure procedure. The difference in the average reduction in HbA_{1c} between treatment and control groups was tested using the GLM Univariate procedure, which provides regression analysis and analysis of variance for the reduction in HbA_{1c} after adjusting for baseline HbA_{1c}. The analysis was adjusted for the baseline HbA_{1c} because the average was higher in the treatment group than in the control group. The same analysis was repeated for FBG. The effects of all other studied variables and the two-way interaction were tested in the multivariate analysis, and none was shown to be significant. A *p*-value of < 0.05 was considered statistically significant.

Results

Characteristics of participants

At baseline, a total of 58 Jordanian patients diagnosed with type 2 diabetes mellitus were enrolled in this study. All subjects had advanced periodontitis and required full-mouth tooth extraction for periodontal reasons. Eight patients (three patients in the treatment group and five patients in the control group) were lost to follow-up or reported use of antibiotics, leaving 50 patients to be included in the analysis. The age of the patients in the treatment group ranged from 42 to 73 years with a mean (SD) of 57.1 (6.9) years, and the age of patients in the control group ranged between 37 and 72 years with a mean of 55.6 (7.9) years. The sociodemographic and relevant characteristics for both groups are shown in Table 1. Patients in both groups did not differ significantly in age, anthropometric measurements, oral hygiene and diabetes-related clinical characteristics, including duration of diabetes, diabetes care profile, treatment of diabetes and diabetes complications. All patients maintained the same dietary habits, medications and smoking status over the entire follow-up period. Weight did

Table 1. Sociodemographic, anthropometric, clinical and relevant characteristics of participants in the treatment and control groups

Variables	Treatment group	Control group	*p*-value*
Age (years; mean (SD))	57.1 (6.9)	55.6 (7.9)	0.470
Sex			
Male (*n* (%))	10 (38.5)	12 (50)	0.412
Female (*n* (%))	16 (61.5)	12 (50)	
Occupation			
Employed (*n* (%))	5 (19.2)	7 (29.2)	0.039
Not employed (*n* (%))	21 (80.8)	17 (70.8)	
Weight (kg; mean (SD))	81.3 (13.9)	82.9 (12.9)	0.957
Body mass index (kg/m^2; mean (SD))	30.2 (5.8)	30.7 (4.7)	0.398
Smoking			
Current smoker (*n* (%))	6 (23.1)	5 (20.8)	0.950
Past smoker (*n* (%))	6 (23.2)	5 (20.8)	
Nonsmoker (*n* (%))	14 (53.8)	14 (58.4)	
Oral health			
Plaque index (mean (SD))	2.96 (0.77)	2.96 (0.55)	0.987
Gingival index (mean (SD))	2.65 (0.69)	2.75 (0.44)	0.564
Probing pocket depth (mm; mean (SD))	5.39 (0.86)	5.67 (1.16)	0.341
Clinical attachment level (mm; mean (SD))	7.33 (0.62)	7.31 (1.14)	0.944
Percentage of teeth with grade 3 mobility	100.0	100.0	1.000
Duration of diabetes (years; mean (SD))	7.7 (4.2)	8.1 (4.5)	0.749
Complication of diabetes			
Hypertension (*n* (%))	10 (38.5)	15 (62.5)	0.089
Atherosclerosis (*n* (%))	3 (11.5)	4 (16.7)	0.600
Nephropathy (*n* (%))	2 (7.7)	1 (4.2)	0.950
Retinopathy (*n* (%))	8 (30.8)	8 (33.3)	0.846
Neuropathy (*n* (%))	13 (50)	10 (41.7)	0.555
Cardiovascular disease (*n* (%))	7 (26.9)	3 (12.5)	0.203
Diabetes care profile			
Barrier to adherence score (mean (SD))	26.7 (2.6)	26.1 (2.2)	0.353
Negative attitude score (mean (SD))	17.6 (3.36)	15.4 (3.06)	0.018
Positive attitude score (mean (SD))	12.46 (2.1)	12.71 (1.27)	0.621
Support score (mean (SD))	33.92 (3.1)	33.08 (3.3)	0.360

p-value refers to the significance of difference between treatment and control group.

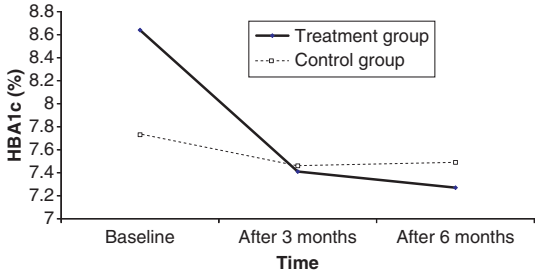

Fig. 2. Glycated hemoglobin (HbA_{1c}) level trend changes from the baseline to 3 and 6 mo.

not change significantly in both groups over the follow-up periods.

Changes in HbA_{1c} over time

At baseline, HbA_{1c} level in the treatment group ranged from 7.4 to 11.2% with a mean (SD) of 8.6% (1.24), and HbA_{1c} level in the control group ranged from 7.2 to 12.6% with a mean of 7.7% (0.87). The averages of HbA_{1c} and FBG were significantly higher in the treatment group. The General Linear Model repeated-measures procedure showed that the change in HbA_{1c} over time differed between the treatment and control groups (Fig. 2). In the treatment group, the mean HbA_{1c} level decreased significantly from 8.6% at baseline to 7.4% after 3 mo of denture treatment, and continued to decrease to 7.3% after 6 mo. *Post hoc* test showed that means at 3 and 6 mo of denture treatment were significantly lower than the mean at the baseline. The difference in the mean HbA_{1c} after 3 and 6 mo of denture treatment was not significant. In the control group, the mean HbA_{1c} decreased from 7.7% at baseline to 7.5% after 3 mo (of denture treatment in the treatment group), and remained almost the same after 6 mo. The change in HbA_{1c} from baseline to 3 mo was not significant. At baseline, the mean (SD) FBG for the treatment and control groups was 12.5 (3.5) and 9.8 (3.3) mM, respectively. A similar pattern of change to that for HbA1c was seen for FBG in both groups (Fig. 3).

Multivariate analysis

Since the average of HbA_{1c} at baseline was significantly higher in treatment group compared with the control group, the changes in HbA_{1c} after 3 and 6 mo of denture treatment were analyzed in the general linear model to adjust for the baseline HbA_{1c} measurements. In the multivariate analysis (Table 2), the mean reduction in HbA_{1c} after 3 mo of denture treatment in the treatment group [1.23% (0.79)] was significantly higher than the mean reduction in the control group [0.28% (0.87); $p = 0.001$]. The same finding was obtained when the average reduction in HbA_{1c} after 6 mo of denture treatment was analyzed. A similar pattern of change was seen for FBG in the multivariate analysis after adjusting for the baseline FBG measurements.

Discussion

Understanding the association between periodontal disease and diabetes and the effect of periodontal treatment on glycemic control may aid health professionals in the prevention, early detection and treatment of these common diseases. The influence of diabetes on periodontal disease is well established, but the effect of periodontitis and its treatment on the control of diabetes remains unclear. To the best of our knowledge, this is the first study investigating the definitive and irreversible elimination of dental infections through full-mouth tooth extractions on glycated hemoglobin in patients with type 2 diabetes.

In this study, a total of 58 patients requiring extraction of all remaining teeth were randomized consecutively to one of the two groups: the treatment group, in which patients received a full-mouth tooth extraction followed by complete dentures, and the control group, in which patients received oral hygiene instructions only. The extraction of teeth with a hopeless prognosis is a definitive and long-term therapeutic option to eliminate chronic dental infections, eliminates all tooth-associated infections and re-establishes an intact epithelial barrier. The study design should not imply that no treatment is an option, because hopeless teeth need to be extracted. The experience of the control group illustrates what would have happened to glycemic control among diabetic patients if they had not received the treatment. For the purpose of comparison, extraction of teeth with a hopeless prognosis in the control group was delayed until the end of the study, and then all patients were treated. None of the patients in the control group developed problems around the teeth with a hopeless prognosis during the study period.

A number of studies have indicated that glycemic control can be improved by nonsurgical periodontal treatment, especially when combined with systemic antimicrobial therapy (18,19,21–23,37–43). However, the comparison of the their findings is very difficult because of the variations in study design, population, diagnosis of periodontal diseases, length of the study period, type of periodontal treatment, use of adjunctive therapy (including antibiotics), inclusion criteria and

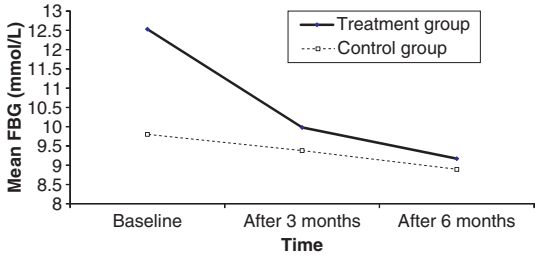

Fig. 3. Fasting blood glucose level trend changes from the baseline to 3 and 6 mo.

Table 2. The changes in glycated hemoglobin (HbA_{1c}) over time for treatment and control groups

Variable	Treatment (mean ± SD)	Control (mean ± SD)	*p*-value[a]
Baseline	8.64 ± 1.24	7.73 ± 0.87	0.005
After 3 mo	7.41 ± 0.72	7.46 ± 1.46	0.895
After 6 mo	7.27 ± 1.009	7.49 ± 1.3	0.564
Δ (Baseline to 3 mo after denture treatment)	1.23 ± 0.79	0.28 ± 0.87	0.001
Δ (Baseline to 6 mo after denture treatment)	1.37 ± 1.003	0.28 ± 0.7	< 0.001
p-value[b]	< 0.005	0.128	
p-value[c]	< 0.005	0.068	

[a]*p*-value refers to the significance of difference between treatment and control group (independent *t*-test).
[b]*p*-value refers to the significance of change in HbA_{1c} (baseline to 3 mo after denture treatment) within each group after adjusting for baseline measurements of HbA_{1c}.
[c]*p*-value refers to the significance of change in HbA_{1c} (baseline to 6 mo after denture treatment) within each group after adjusting for baseline measurements of HbA_{1c}.

parameters used to assess treatment of periodontitis and improvement in diabetes. Furthermore, small sample size and residual effect of confounders might contribute to the inconsistencies of the findings.

Total elimination of periodontal infection is difficult to achieve with periodontal therapy. Periodontal diseases as well as diabetes are affected by many factors, and multiple criteria are needed to assess whether the disease progression has stopped or not. Although that the use of strict inclusion criteria limited the sample size in our study, it helped in assessment of the effect of possible confounding factors.

There was a statistically significant improvement in glycemic control after extraction of severely infected teeth. During the follow-up period, a detailed assessment for most variables that might affect diabetes status was carried out, and none of them changed significantly over the period of follow-up. The average reductions in HbA_{1c} in the treatment group were 1.23% at 3 mo of denture treatment and 1.37% at the end of the study. This reduction was higher than that reported by earlier studies that investigated nonsurgical periodontal treatment (15,39). Previous studies had short follow-up periods (15,16,20,20,30,39,43,44), and this may explain the insignificant changes in glycemic markers, which might require a longer time to change significantly. In this study, a follow-up period of 6 mo after denture treatment was chosen for the evaluation of glycemic control to allow us to notice any possible relapse.

The study population was limited to patients with type 2 diabetes because type 1 diabetes has a different pathogenesis, being a chronic disease affected to a minimal level by periodontal treatment (20). Patients who had taken antimicrobial drugs in the previous 3 mo from the starting point of the study and during the period of follow-up were excluded because the use of antibiotics might affect the results. The metabolic assessment was based on the blood level of glycated hemoglobin because it reflects the glycemic control over the past 30–90 d (45).

Our findings are comparable to results reported by Taylor *et al.* (29), who found a significant decrease in blood levels of C-reactive protein, plasminogen activator inhibitor-1 and fibrinogen, and white cell and platelet counts after full-mouth tooth extraction.

Periodontal disease needs to be viewed more broadly in terms of systemic inflammation, either as a consequence of an underlying hyperinflammatory trait or as a factor contributing to systemic inflammation (28). Patients with diabetes are likely to benefit from programmes aimed at encouraging behaviors toward achieving optimal periodontal health. Physicians caring for patients with diabetes may need to adopt a more vigorous approach for diabetes control and should include a periodontal evaluation in their diabetes risk assessment.

Although we analyzed the change in HbA_{1c} in the multivariate analysis after adjustment for the baseline HbA_{1c} measurements, one should consider that the average of HbA_{1c} at the baseline was significantly higher in the treatment group compared with the control group. Future studies should consider a larger sample size to achieve successful randomization and consider other methods of randomization, such as stratified randomization, to achieve balance among groups in terms of participants' baseline characteristics. Large-scale multicentre clinical trials are needed to confirm the current evidence. In conclusion, the present study showed that full-mouth tooth extraction resulted in a significant improvement in glycemic control among diabetic patients.

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