Glycated Hemoglobin Levels and Prevalence of Apical Periodontitis in Type 2 Diabetic Patients

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Abstract

Introduction: The purpose of this investigation was to study the possible association between the prevalence of apical periodontitis (AP) and the glycemic control of type 2 diabetic patients. **Methods:** In a cross-sectional study, the radiographic records of 83 type 2 diabetic patients were examined. Glycemic control was assessed by the mean glycated hemoglobin (HbA1c level). AP was diagnosed as radiolucent periapical lesions (RPLs) using the periapical index score. The Student *t* test, chi-square test, and logistic regression analysis were used in the statistical analysis. **Results:** Based on the HbA1c levels, 2 groups of diabetic patients were established: the HbA1c good control group (GCG, $n = 24$, HbA1c <6.5%) and the HbA1c poor control group (PCG, $n = 59$, HbA1c ≥6.5%). In the total sample, RPLs in 1 or more teeth were found in 62.7%, and no significant differences between GCG and PCG groups were observed ($P = .13$). At least 1 root-filled tooth was found in 32.5% of diabetic patients; this percentage was comparable in both HbA1c groups ($P = .68$). The prevalence of RPLs in RFT (29.6%) was similar in the GCG compared with the PCG ($P = .94$). Multivariate logistic regression analysis showed that worse periapical status correlated significantly with HbA1c levels ≥6.5% in type 2 diabetic patients (odd ratio = 3.8; 95% confidence interval, 1.1–13.0; $P = .03$). **Conclusions:** HbA1c levels of diabetic patients are associated with periapical status. Data reported in the present study, together with the results of previous studies, further support a relationship between glycemic control and periapical inflammation in diabetic patients. *(J Endod 2015;41:601–606)*

Key Words

Apical periodontitis, diabetes mellitus, endodontics, glycemic control, glycosylated hemoglobin, periapical inflammatory response

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Apical periodontitis (AP) is an acute or chronic inflammatory lesion around the apex of a tooth caused by bacterial infection of the pulp canal system (1). Periapical inflammatory response provokes a characteristic local periradicular osteolytic radiolucent lesion, but AP is not exclusively a locally limited phenomenon. Lipopolysaccharide from anaerobic gram-negative bacteria causing AP activates the broad axis of innate immunity interacting with Toll-like receptor 4 on macrophages and neutrophils (2), up-regulating proinflammatory cytokines such as interleukin (IL)-1β, IL-6, IL-8, tumor necrosis factor α, and prostaglandin E_2 (PGE_2). These cytokines may be released into systemic circulation (3), inducing or perpetuating an elevated chronic systemic inflammatory status (4, 5).

Diabetes mellitus (DM) is a clinically and genetically heterogeneous group of disorders affecting the metabolism of carbohydrates, lipids, and proteins in which hyperglycemia is a main feature (6). Glycated hemoglobin (HbA1c) has been used as a "gold standard" for mean glycemia and as a measure of risk for the development of DM complications (4, 6). The American Association of Clinical Endocrinologists considers HbA1c levels ≤6.5% as a goal for optimal glycemic control in diabetic patients (7).

DM is caused by a deficiency in insulin secretion caused by pancreatic β-cell dysfunction and/or insulin resistance in liver and muscle (8). It has been shown that proinflammatory status resulting from the activation of innate immunity pathways contributes to insulin resistance (9, 10). Therefore, it has been suggested that the ongoing cytokine-induced acute-phase response, a low-grade inflammation that occurs through activation of the innate immune system in chronic oral inflammatory processes such as periodontal (4) and endodontic diseases (11), could contribute to increased insulin resistance and poor glycemic control in diabetic patients.

Some studies have investigated the association between periodontal disease and diabetes-related inflammatory status (4, 12, 13). Moreover, the relationship of HbA1c levels with periodontal disease has been extensively analyzed, and several studies have been conducted to assess the possible effect of nonsurgical periodontal treatment on serum glycated hemoglobin in diabetic patients (13, 14). In the case of AP, several investigations have studied, both in animals (15, 16) and humans (17–24), the possible association between AP and DM, with inconclusive results (11). However, as far as we know, no study has investigated whether AP is connected to the metabolic control of diabetic patients, analyzing the correlation of HbA1c levels with the periapical status of diabetic patients.

The purpose of this investigation was to study the possible association between the prevalence of AP, diagnosed as radiolucent periapical lesions (RPLs), and the glycemic control of type 2 diabetic patients assessed by the mean HbA1c level. We tested the null hypothesis that "AP is not associated with glycemic control in diabetic patients."

Materials and Methods

Patients

Participants were recruited among patients presenting consecutively seeking routine dental care (not emergency care) at the University of Barcelona dental clinic between the years 2011 and 2013. Subjects reporting a history of type 2 DM, diagnosed according to the criteria of the American Diabetes Association (2010) (6), were asked to voluntarily participate. Inclusion criteria were as follows: patients older than 18 years having at least 8 remaining teeth with HbA1c levels recorded in the last week who agreed to a radiologic examination. Exclusion criteria were patients younger than 18 years old, patients having less than 8 remaining teeth, patients without HbA1c levels recorded in the last week, and patients who did not agree to a radiologic examination. A total of 83 subjects (66.0 ± 10.6 years), 41 men (49.4%) and 42 women (50.6%), who agreed and met the inclusion/exclusion criteria were included in the study. Questionnaires were filled out for each patient, eliciting information on medical and dental history, the most recent measurement of HbA1c levels, smoking status, periodontal status, and coronary heart disease.

The criteria used to determine the presence of periodontal disease were those previously established by Machtei et al (25); patients showing more than 5% gingival bleeding with clinical attachment loss higher than 6 mm in 2 or more sites and with 1 or more sites with a probing depth ≥5 mm were diagnosed as having periodontal disease.

The ethics committee of the faculty of dentistry approved the study, and all the patients provided written informed consent. The research was conducted in full accordance with the World Medical Association Declaration of Helsinki.

Glycemic Control Assessment

To determine the metabolic control status of diabetic patients, HbA1c was registered. Adequate glycemic control was defined according to the American Association of Clinical Endocrinologists as HbA1c <6.5% (7) using the most recent HbA1c measurement before the visit date obtained from the patient's record on the public health service. Based on the HbA1c levels, 2 groups were established: the HbA1c good control group (GCG) (HbA1c <6.5%) and the HbA1c poor control group (PCG) (HbA1c ≥6.5%).

Radiographic Examination and Evaluation

Radiographic periapical status was diagnosed on the basis of examination of digital panoramic radiographs of the jaws. Two trained radiographic technicians, with over 10 years of experience, took the panoramic radiographs using a digital orthopantomograph machine (Promax, Planmeca, class 1, type B, 80 KHz; Planmeca, Helsinki, Finland).

All teeth, excluding third molars, were recorded. Teeth were categorized as root-filled teeth (RFTs) if they had been filled with a radiopaque material in the root canal(s). For each subject, the number of teeth present, the number and location of RFTs, and the number and location of teeth having identifiable RPLs were recorded.

The periapical status was assessed using the periapical index (PAI) score (26) as described previously (27). A score greater than 2 (PAI ≥3) was considered to be a sign of AP. The worst score of all roots was taken to represent the PAI score for multirooted teeth.

Observer Calibration

Three observers with extensive clinical experience in endodontics examined the radiographs. Before evaluation, the observers participated in a calibration course for the PAI system, which consisted of 100 radiographic images of teeth, some root filled and some not, kindly provided by Dr. Ørstavik. Each tooth was assigned to 1 of the PAI scores by using visual references (also provided by Dr. Ørstavik) for the 5 categories within the scale. After scoring the teeth, the results were compared with a "gold standard atlas," and a Cohen kappa was calculated (0.79–0.87).

Intraobserver reproducibility was evaluated for each examiner. Every observer scored the panoramic radiographs of 20 patients (10 in each group, randomly selected). Then, 1 month after this first examination, the observer was recalibrated in the PAI system and repeated the scoring of the radiographs of the same 20 patients. The intraobserver agreement test on PAI scores on the 20 patients produced a Cohen kappa ranging from 0.82 to 0.93.

Finally, intraobserver reproducibility was also determined by comparing the PAI scores on the 20 radiographs provided by each observer. The agreement test produced a Cohen kappa ranging from 0.84 to 0.91. The Cohen kappa for interobserver variability ranged from 0.80 to 0.89. The consensus radiographic standard was the simultaneous interpretation by the 3 examiners of the panoramic radiograph of each patient.

Statistical Analysis

The minimal sample size (adjusted $n = 72$) was calculated for the comparison of proportions with nQuery Advisor (version 7.0; Statistical Solutions Ltd, Cork, Ireland), taking into account a 2-sided significance level of 5% ($\alpha = 0.05$, $Z\alpha = 1.960$) and an 80% statistical power ($\beta = 0.20$, $Z\beta = 0.842$) to detect a hypothesized difference between groups of 25 points and a 15% dropout rate.

Raw data were entered into Excel (Microsoft Corp, Redmond, WA). All analyses were performed in an SPSS environment (version 11; SPSS, Inc, Chicago, IL). Data are reported as mean ± standard deviation. The Student *t* test and chi-square test were used to determine the significance of differences between groups. Logistic regression analysis was performed to measure the strength of the association between HbA1c levels and the presence of RPLs, adjusting for the presence of covariates. A value of $P < .05$ was considered significant.

Results

The characteristics and dental status of diabetic type 2 patients in relation with their HbA1c levels are shown in Table 1. In the total sample, 49% were men and 51% were women, and the mean age was 66.6 ± 10.6 years. The average number of teeth per subject was 21.1 ± 6.1, and the mean number of RFTs and teeth with RPLs per subject was 0.7 ± 1.3 and 1.7 ± 2.2, respectively. Twenty patients (24.1%) were smokers, 67 (80.7%) had coronary heart disease, and 72 (86.7%) had periodontal disease. According to HbA1c levels, patients were classified into 2 groups: 24 (28.9%) were included in the HbA1c GCG (HbA1c <6.5%), and 59 (71.1%) were classified in the HbA1c PCG (HbA1c ≥6.5%). No statistically significant differences between the 2 groups were observed in age, sex, smoking habits, coronary heart disease, periodontal status, number of teeth, number of RFTs, or number of teeth with RPLs ($P > .05$).

The relationship between glycemic control of diabetic patients, assessed as HbA1c levels, and radiographic periapical status was analyzed (Table 2). RPLs in 1 or more teeth were found in 52 diabetic patients (62.7%); 40 patients (67.8%) showed at least 1 RPL in the PCG, whereas this percentage was only 50.0% in the GCG (odds ratio = 2.1; 95% confidence interval [CI], 0.8–5.5; $P = .13$). The frequency of root canal treatment was 32.5% (27 diabetic patients) in the total sample, and no statistically significant differences between the PCG and GCG were observed (odds ratio = 1.2; 95% CI, 0.4–3.5; $P = .68$). Finally, among diabetic patients with RFTs, 8 (29.6%) had at least 1 RFT showing RPL, but the prevalence of RPLs was not significantly higher in the PCG compared with the GCG (odds ratio = 1.2; 95% CI, 0.2–7.5; $P = .94$).

Multivariate logistic regressions were run with age, sex, smoking habits, number of teeth, periodontal status, periapical status, and endodontic status as independent explanatory variables and HbA1c levels as the dependent variable (0 = HbA1c <6.5%; 1 = HbA1c ≥6.5%)