Diabetes *Mellitus* and its Influence on the Success of Endodontic Treatment: A Retrospective Clinical Study

Diabetes *Mellitus* e sua Influência no Sucesso do Tratamento Endodôntico: Um Estudo Clínico Retrospetivo

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ABSTRACT

Introduction: Diabetes *mellitus* is an endocrine disease in which are involved the hormones produced by the islets of Langerhans. The diabetes *mellitus* can affect various functions of the immune system of the individual, predisposing them to chronic inflammation, progressive degradation of tissues and decreased tissue repair. The changes caused by this disease at the level of the oral cavity can highlight xerostomia, dysgeusia, periodontal alterations, increased susceptibility to infection and changes both in the dental pulp and periapical tissues.

Objectives: The aim of this study is to evaluate the influence of diabetes *mellitus* at the periapical tissues and the success of endodontic treatment in these patients.

Material and Methods: We analyzed 737 cases treated in consultation Area of Dental Medicine, which were made nonsurgical endodontic treatments, between the years 2003 and 2012. These were selected patients with diabetes *mellitus*, a total of 32, of whom 23 were willing to come to the consultation and to participate in this study. The data collected were analyzed using the Statistical Package for the Social Sciences, version 19, at a significance level of 5%.

Results: A total of 37 teeth in the test group and 25 in the control group. For the analyzed parameters related to the diagnosis pulp, mobility, fistula, pain on percussion horizontal and vertical evaluation of final restoration and the time interval between the query and the final restoration shutter and / or the control visit, there were no differences statistically significant ($p > 0.05$). Regarding the assessment of the success of endodontic treatment, this was 62% in the test group and 80% in the control group ($p > 0.05$).

Conclusions: The results of this study are inconclusive regarding the increasing prevalence of apical periodontitis in diabetic patients. Regarding the evaluation of the success of endodontic treatments examined it was found that the success rate in diabetic patients is lower, though not statistically significant. For this reason and given the limitations of this study, we cannot state that patients with diabetes *mellitus* have a greater predisposition to the development of periradicular lesions or that the success of endodontic treatment in these patients is compromised. It is important, however, that further studies are developed to characterize the pulp and periradicular changes and to assess the prevalence of apical periodontitis and progression in patients with diabetes *mellitus*.

Keywords: Dental Restoration, Permanent; Diabetes *Mellitus*; Diabetes Complications; Periapical Periodontitis; Portugal; Root Canal Therapy.

RESUMO

Introdução: A diabetes *mellitus* é uma doença endócrina onde estão envolvidas as hormonas produzidas pelos ilhéus de Langerhans. A diabetes *mellitus* pode afetar várias funções do sistema imunitário do indivíduo, predispondo-o para a inflamação crónica, degradação progressiva dos tecidos e diminuição da reparação tecidular. Das alterações provocadas por esta doença ao nível da cavidade oral pode-se destacar a xerostomia, disgeusia, alterações periodontais, aumento da suscetibilidade à infeção e alterações tanto ao nível da polpa dentária como nos tecidos periapicais.

Objetivos: O objetivo deste trabalho é avaliar a influência da diabetes *mellitus* ao nível dos tecidos periapicais e no sucesso dos tratamentos endodônticos nestes doentes.

Material e Métodos: Foram analisados 737 casos clínicos tratados na consulta da Área de Medicina Dentária, a que foram feitos tratamentos endodônticos não cirúrgicos, entre os anos de 2003 e 2012. Destes foram selecionados os doentes com diabetes *mellitus*, num total de 32, dos quais 23 se dispuseram a vir à consulta e a participar neste estudo. Os dados recolhidos foram analisados no *software* Statistical Package for the Social Sciences, versão 19, a um nível de significância de 5%.

Resultados: Foram avaliados 37 dentes no grupo teste e 25 no grupo controlo. Para os parâmetros analisados relativos ao diagnóstico pulpar, mobilidade, presença de fístula, dor à percussão horizontal e vertical, avaliação da restauração definitiva e intervalo de tempo entre a consulta de obturação e a restauração definitiva e/ou a consulta de controlo, não foram verificadas diferenças estatisticamente significativas ($p > 0,05$). Em relação à avaliação do sucesso dos tratamentos endodônticos realizados, este foi de 62% no grupo de teste e de 80% no grupo controlo ($p > 0,05$).

Conclusões: Os resultados deste estudo não são conclusivos em relação ao aumento da prevalência da periodontite apical nos doentes diabéticos. Em relação à avaliação do sucesso dos tratamentos endodônticos analisados verificou-se que a percentagem de sucesso nos doentes diabéticos é mais baixa, embora não seja estatisticamente significativa. Por este motivo e dadas as limitações deste estudo, não se pode afirmar que doentes com diabetes *mellitus* têm maior predisposição para o desenvolvimento de lesões periradiculares ou que o sucesso dos tratamentos endodônticos nestes doentes esteja comprometido. É importante, no entanto, que sejam desenvolvidos mais estudos de forma a caracterizar as alterações pulpares e periradiculares e a avaliar a prevalência da periodontite apical e sua progressão em doentes com diabetes *mellitus*.

Palavras-chave: Complicações da Diabetes; Diabetes *Mellitus*; Periodontite Apical; Portugal; Restauração Dentária Permanente; Tratamento do Canal Radicular.

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INTRODUCTION

Diabetes *mellitus* is an endocrine disease involving the hormones produced by the islets of Langerhans. It develops when the pancreas is unable to produce enough insulin or when our body is unable to efficiently use the insulin it produced. In type 1 diabetes, often referred as insulin-dependent, there is a total absence of insulin production due to the destruction of β-cells in relation to an autoimmune response. Type 2 diabetes, which is more frequent, relates to insulin-producing β-cell dysfunction or to organic resistance to the produced insulin.[1-3]

Chronic hyperglycaemia is the most frequent effect of diabetes and the major underlying cause for the associated complications. Diabetes induces severe lesions, mainly affecting renal and eye function, peripheral nerves and blood vessels.[1-4] In Portugal, the prevalence of diabetes is 12.4%, affecting patients between 20 and 79 years of age. There is also a strong association between an increase of diabetes prevalence and population ageing.[2] Diabetes affects several functions of the immune system, making the patient more vulnerable to chronic inflammation, to progressive tissue damage and reduction of tissue repair.[1-6] Regarding oral damage related with diabetes, we wish to emphasize the association with xerostomia, dysgeusia, periodontal disease and an increase in susceptibility to infection and dental pulp or periapical tissue disease.[4-6]

There is strong scientific evidence regarding diabetes impact on periodontal disease prevalence and severity, mainly in patients with uncontrolled glucose levels.[5-8] Apical periodontitis is a chronic inflammatory lesion with a pulp origin, affecting periapical tissues.[8-10] Periodontal disease and apical periodontitis have some similarities, both being chronic infections mainly involving anaerobic Gram-negative bacteria and occurring in the context of a significant increase in inflammatory mediators.[9,10] Therefore, it may be stated that diabetes is a potential modulator of endodontic pathology and may be associated with a high prevalence of periapical lesions or an increase in endodontic treatments in these patients.[10-12] In addition, the regression of preoperative periapical lesions seems to be slower in diabetic patients.[12,13] Wang et al studied the success rate of teeth submitted to non-surgical endodontic treatment. This study found that in patients with diabetes the risk of exodontia two years upon treatment was approximately 30% higher than in non-diabetic patients.[14]

Regarding dental pulp lesions, histopathological studies describing detailed effects of diabetes on dental pulp in humans are still scarce. Due to compromised collateral circulation and reduced pulp tissue microvascularisation[15] together with inhibition of polymorphonuclear microbicide activity,[16] an increase of the risk of infection and pulp necrosis is predictable in patients with diabetes.[12,15,16] Nevertheless, evidence supporting pathogenesis, progression and resolution of endodontic lesions in patients with diabetes is altogether scarce and undetermined.

The aim of our study is the assessment of diabetes influence on periapical tissues and to estimate its impact upon the successful achievement of non-surgical endodontic treatment.

MATERIAL AND METHODS

We analysed 737 patients attending to the Dental Medicine Department at the *Faculdade de Medicina da Universidade de Coimbra* (FMUC), submitted to non-surgical endodontic treatments carried out between 2003 and 2012. Thirty-two patients with diabetes were selected from these and were contacted by phone and by mail, in order to come for an appointment for evaluation and treatment follow-up. From these, two patients were already deceased, it was not possible to contact one patient and from the remaining patients, only 23 attended and accepted to join the study.

Upon clarification and presentation of the informed consent form, we collected data on general health, habits and diabetes medical data. We also completed an oral general evaluation including lost teeth and an endodontically-treated teeth evaluation, analysing panoramic imaging and clinical record, as well as periapical imaging. Peri-radicular tissue evaluation was carried out with panoramic imaging and in the case of endodontically-treated teeth with retro-alveolar imaging obtained at follow-up. Endodontically-treated teeth evaluation included horizontal and vertical percussion sensitivity tests, mobility and associated fistulae evaluation, as well as evaluation of depth of cure and sealing of definitive restoration. All endodontically-treated teeth were submitted to periapical imaging, in order to assess the Ørstavik periapical index (PAI) and limits and quality of dental fillings.

A control group of patients was randomly selected, including non-diabetic patients alone. The time gap between treatments was taken into consideration, as well as the average age, in order to resemble the study group as much as possible. We analysed the same parameters for this group of patients, considering the available data in the clinical records.

Data were subsequently analysed, using the Statistical Package for the Social Sciences (SPSS), version 19 software, in order to identify the presence of statistically significant differences between both groups, for the considered parameters. The tests were evaluated at a significance level of 5%.

RESULTS

Characteristics of the sample

Our study included 46 patients, from which 23 were diabetic – Study group – and 23 were non-diabetic – Control group. (Table 1)

In the study group, 73.9% of the patients presented with type-2 diabetes and the remaining presented with type 1 diabetes. All patients were regularly followed by their GP or endocrinologist. All patients with type-1 diabetes followed insulin therapy and only 12% of the patients with type-2 diabetes had to use insulin for blood sugar control. The remaining patients were treated with oral hypoglycaemic

medications.

Regarding the number of years of disease progression, i.e. from the moment of diagnosis until the moment of the study visit, the patients with type-1 diabetes presented on average 19.5 years of disease progression, while patients with type-2 diabetes presented 9.12 years.

As regards the age of the patients, we found a statistically significant difference between both groups (p = 0.001), with an average age of 64.43 in the study group and 50.39 in the control group.

Overall oral assessment

Thirty-seven teeth were assessed upon endodontic therapy in the study group and four teeth had already been extracted at the time of the study visit. Patients in this group presented on average 1.61 endodontically-treated teeth and 54% of these were posterior teeth. Twenty-five teeth were evaluated in the control group; two of them had also been extracted, with an average per patient of 1.09. Of these, 52% were posterior teeth.

Most already extracted teeth subjected to prior

Table 1 - Patient distribution regarding gender and age

	Control Group (n = 23)	Study Group (n = 23)	p
Gender			
M	8 (34.8%)	10 (43.5%)	0.763*
Age			
Mean	50.39	64.43	0.001
Standard deviation	12.409	12.978	
Min	32	28	
Max	74	85	

* Chi-square test of independence with Yates' correction for continuity

Table 2 – Number of missing teeth, teeth submitted to RET, with AP and with RET+AP in both groups

		Control Group (n = 23)	Study Group (n = 23)	p
Nº Missing teeth	Mean	7.57	10.35	0.123§
	Max	22.00	23.00	
Nº teeth submitted to RET	Mean	1.35	1.70	0.451§
	Max	3.00	7.00	
Nº teeth with AP	Mean	0.17	0.39	0.104§
	Max	2.00	2.00	
Nº teeth with RET + PA	Mean	0.17	0.22	0.713§
	Max	1.00	1.00	

§ Mann-Whitney – RET: radicular endodontic treatment; AP: Apical periodontitis

endodontic treatment in our Department did not have any Information on the hospital record, as extraction was completed in private clinics. These patients referred periodontal compromise and definitive dental restoration impossibility as reasons for exodontia.

The numbers of missing teeth, endodontically-treated, with periapical lesion and endodontically-treated and with periapical lesion in each group of patients are presented in Table 2. Third molars were excluded from these numbers. None of these parameters presented any statistically significant difference between the evaluated groups ($p > 0.05$).

Endodontically treated teeth evaluation

As regards pulpal diagnosis, previously assessed before endodontic treatment and according to the available data from patient's medical record, 37.8% of treated teeth were due to irreversible pulpitis, 27% due to pulpal necrosis and 10.8% due to pulpal necrosis with chronic apical periodontitis (Fig. 1). Regarding pulpal diagnosis, we did not find any statistically significant differences (Mann-Whitney U = 296.0; Z = -1.962; $p = 0.105$) between both groups.

Regarding horizontal and vertical percussion sensitivity (Mann-Whitney U = 347.5; Z = -0.876; $p = 0.381$), mobility (Fisher exact test; $p = 1.000$) and the presence of fistulae (Fisher exact test; $p = 1.000$), there were no statistically significant differences between both groups.

Probing depth evaluation was performed in four dental aspects (mesial, distal, vestibular and oral) of each tooth, using a millimeter probe. An increase was found in 15.2% of the measurements in the study group.

Regarding sealing evaluation of the definitive restoration, we found 5.4% of evaluated teeth were not submitted to a definitive restoration, keeping the interim therapeutic restoration performed during the dental filling visit. There were no statistically significant differences (Mann-Whitney U = 354.5; Z = -0.8260; $p = 0.795$) between groups regarding definitive filling.

The time period between the filling and the definitive restoration and between filling and the control visit was also analysed. We did not find statistically significant differences between both groups (Mann Whitney U = 176.0; Z = -1.819; $p = 0.069$) regarding the time period between filling and definitive restoration. We found that approximately 59% of the patients were submitted to a definitive restoration more than one month after the filling was applied.

We also found that 57% of the patients in the study group had not been previously evaluated. In the patients that were evaluated, the evaluation took place mostly between one and three years after the filling application. When comparing both groups, there are no statistically significant differences (Mann Whitney U = 249.0; Z = -0.781; $p = 0.435$) between them regarding this parameter.

Radiological Assessment

The quality of the dental filling, its limits and the Ørstavik periapical index were assessed using retro-alveolar radiographies. As to the "filling quality" parameter, only three of the studied teeth failed to condense the filling material, in posterior teeth. The remaining teeth in both groups presented a correct vertical condensation obturation, with correct sealing. Regarding this parameter, there are statistically no significant differences (Mann-Whitney U = 360.0; Z = -0.728; $p = 0.467$) between groups.

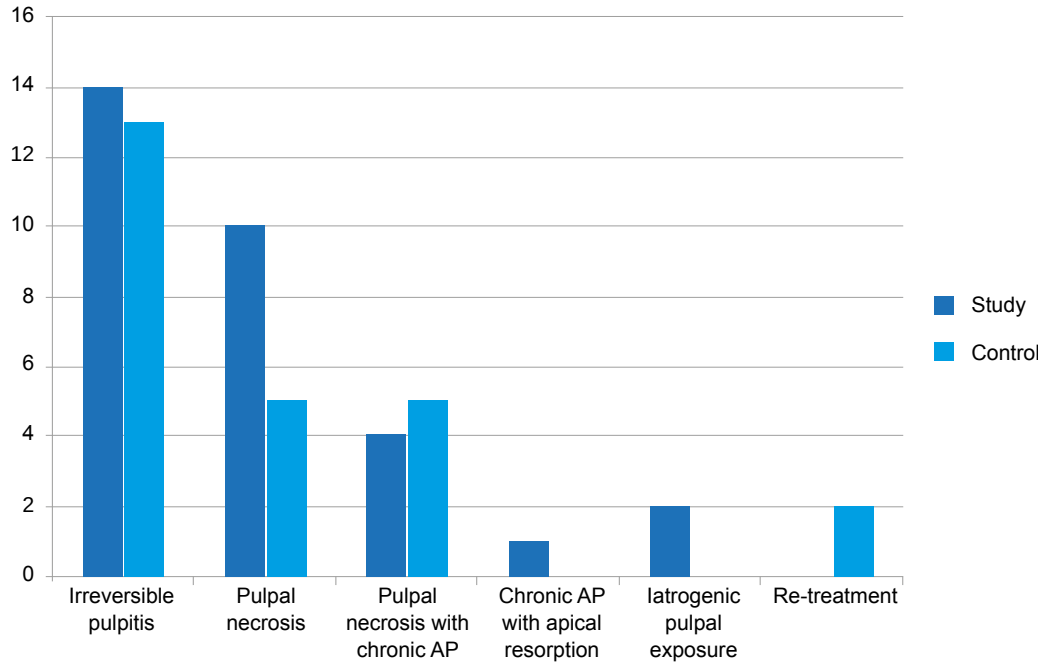

Figure 1 – Pulpal diagnosis in both patient groups

Table 3 – Periapical index of assessed teeth

PAI	Control Group (*n* = 23)	Study Group (*n* = 33)
1	16	23
2	4	7
3	3	2
4	0	0
5	0	1

(PAI- periapical index)

In the control group of patients, all evaluated teeth presented a correct limit of obturation (0-2 mm). In the study group, we found that 6.25% of the teeth presented an under-extension and 3.13% an over-extension. There were statistically no significant differences (Mann-Whitney U = 345.0; Z = -1.473; p = 0.141) between both groups regarding the limit of obturation.

Regarding periapical tissue evaluation, studied teeth were classified according with the Ørstavik periapical index. This radiological classification system of peri-radicular lesions presents a scale ranging from 1 to 5, according with periodontal space and peri-radicular bone changes (Table 3).There are statistically no significant differences (Mann-Whitney U = 376.0; Z = -0.072; p = 0.943) between both groups regarding periapical index evaluation.

In this study, from the 37 teeth initially selected, four had already been extracted before the study visit and two did not present any clear diagnosis with an indication for exodontia. From the assessed teeth, 10 were associated with a poor prognosis, mainly due to a definitive restoration failure and to periodontal compromise.

The success or failure of endodontic treatment was based on the analysis of all parameters previously described, for each assessed tooth in both groups (Fig. 2). The group of teeth considered as "failure" included the teeth that were already missing in the study visit, even when the reason for extraction could not be confirmed.

Even though success evaluation seems lower in the study group, there were no statistically significant differences (Mann-Whitney U = 449.5; Z = -0.215; p = 0.830) between both groups.

DISCUSSION

Endodontic treatment success criteria were established in 1994 by the European Society of Endodontology and included the absence of pain, swelling and fistula, the maintenance of tooth function as well as the presence of radiological evidence of a normal periodontal ligament space, absence of apical periodontitis or radicular resorption.[17] The parameters that we chose to assess in our study tried to meet these criteria, in order to infer on the success of non-surgical endodontic treatment performed in patients with diabetes.

This retrospective clinical study aimed to evaluate the

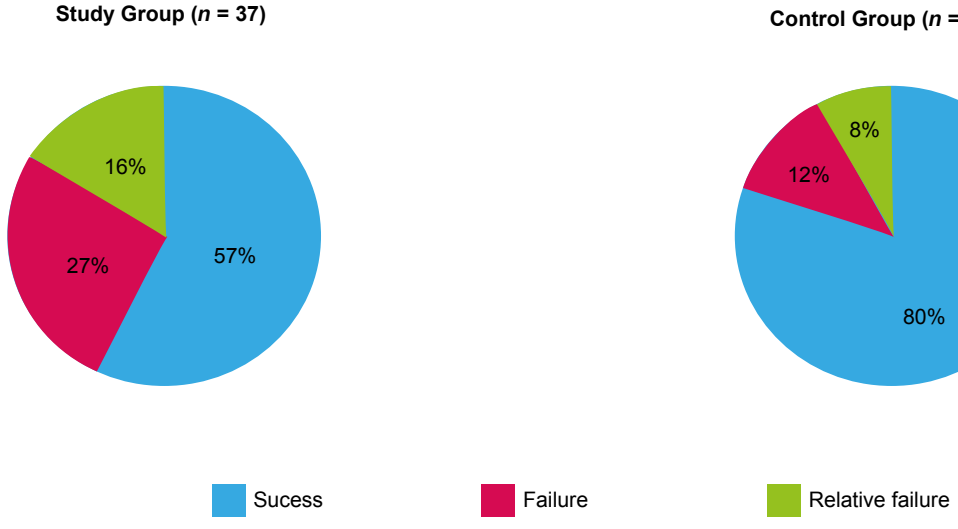

Figure 2 – Assessment of the success of endodontic treatments in both patient groups

success of endodontic treatment performed in diabetic patients, namely regarding the prevalence of these treatments and the prevalence of peri-radicular changes in these patients. All the patients included in our study were followed in our department, which could have caused a bias in the study results. Our group of patients is mainly from a low social-economic background, a population where oral health is not always a priority. This is important as a source of constraint on the treatment plan, as well as in the follow-up. This study also has some other limitations related to the small number of patients that we were able to assess, as these are usually followed in the Dental Department at the *Centro Hospitalar e Universitário de Coimbra*. Regarding the age, there is a significant difference between both groups, due to the fact that type-2 diabetes is more prevalent in older patients.[2,7,14]

In the current literature, there are some studies highlighting a prevalence increase of periapical changes in patients with diabetes.[3,4,10,11,18] These studies are mainly focused on patients with type-1 diabetes, mostly related with a longer clinical progression, and in patients with less satisfactory blood sugar control. In our study, the patients with diabetes only included patients with an adequate glucose control. The published studies have also highlighted that glucose levels may interfere with the repair process of periapical changes and patients with diabetes submitted to dental procedures, namely endodontic treatment, showed less ability for wound repair.[4,10,11,18] The evolution of periapical changes before non-surgical endodontic treatment was not assessed, due to the frequent loss of initial radiological records which were mostly unavailable.

Fouad and Burleson showed in a study with patients with diabetes that the success of the endodontic treatment is compromised in these patients, mainly in the presence of pre-operative periapical change. These authors also found that pre-operative pain is more frequent in patients with type-1 diabetes, as well as flare-up occurrence.[11] López-López et al in their 50-patient study, described that adult patients with type-2 diabetes are significantly more susceptible to apical periodontitis and the need for radicular endodontic treatment.[3]

A study using Wistar mice, aimed to assess dental pulp and periapical tissue histological changes upon pulpal exposure, found that mice with diabetes present significantly more serious peri-radicular changes when compared to healthy mice. The histological examination also revealed that diabetic mice are more likely afflicted with extensive peri-radicular changes, eventually due to a reduction in defence capacity against microbial agents.[19]

A study on extracted non-decayed teeth in patients with diabetes suggested that, despite the presence of clear calcifications on the pulp vascular system of both groups of patients (with or without diabetes), these were more frequent, more specific and sickle-shaped, in patients with diabetes.[15] Bissada and Sharawy also suggested that the pulpal vascular changes need more time to be evident in patients with diabetes than periodontal tissue vascular changes.[20]

Some studies have already been carried out in order to compare the success of endodontic treatments and prevalence of peri-radicular changes in patients with diabetes and in non-diabetic patients.[3,4,18] A study carried out at the University of Florida assessed 30 patients with type-1 and 2 diabetes and found that these present a higher risk for endodontic treatment failure. Another study assessed the radiological status of 50 adult patients with controlled type-2 diabetes. This study aimed to assess apical periodontitis prevalence in teeth submitted to non-surgical endodontic treatment and in teeth submitted to endodontic treatment and associated apical periodontitis. With the data obtained, the authors found an association between diabetes and the presence of apical periodontitis, although they acknowledge the need for more epidemiological studies in order to establish the relationship between endodontic pathology and diabetes.[18] Apical periodontitis and endodontic treatment prevalence was also studied in a Brazilian group of patients with type-2 diabetes. Thirty patients with diabetes and 60 non-diabetic patients were analysed, including panoramic and retro-alveolar radiographies, allowing for the conclusion that apical periodontitis was significantly more prevalent in patients with diabetes and that the teeth submitted to endodontic treatment were also more seriously affected. This fact led the authors to suggest that diabetes may act as an apical periodontitis modifier agent and patients with diabetes are more likely affected by periapical changes than non-diabetic individuals.[10]

We were not able to find significant differences between the groups regarding periapical change prevalence affecting teeth submitted or not to endodontic treatment. Nevertheless, we wish to emphasize a slightly higher number of missing teeth in the group of patients with diabetes. We also found that, from the 37 teeth initially selected for our study, four teeth had been already extracted before the study visit, two presented a poor prognosis and 10 presented an uncertain prognosis mainly due to definitive restoration failure and/or to periodontal compromise. In the present study, regarding pulpal diagnosis and bearing in mind that diabetes affects endodontic infections,[9,11,12,16] we found that irreversible pulpitis was more prevalent, followed by pulpal necrosis.

Regarding data collection, aimed to assess time periods between endodontic obturation and definitive restoration, this study showed that it was longer than one month in 59% of the studied teeth, in comparison to 57% in the control group were not previously evaluated. These parameters are also important for the success of endodontic treatments[9,11,13] and may also affect the results obtained.

Regarding the outcome of endodontic treatment, we found that the success rate in patients with diabetes was 62%, while in non-diabetic patients was 80%. Despite a statistically non-significant difference between both groups (Mann-Whitney U = 449.5; Z = -0.215; p = 0.830), we should remark the number of "relative failures" were mainly due to difficulties in peri-radicular changes healing process. For this reason and due

to the limitations of our study, we may not say that patients with diabetes have higher predisposition for peri-radicular changes or that the success of endodontic treatments in these patients is compromised.

Regarding the new therapy possibilities and new avenues for research, it has been suggested that vitamin D may have an important biological effect on glucose control, improving the response to insulin. This has been considered essential for diabetes pathogenesis control. Vitamin D may also have a major role in alveolar bone regeneration as well as in peri-radicular tissue inflammation. One study on this issue found that vitamin D may have a therapeutic role in endodontic treatment to patients with diabetes[21] and may be used as a therapeutic approach in this group of patients, despite the need of a more thorough study of the mechanism involved.

CONCLUSIONS

Diabetes crucially affects oral tissues, influencing inflammatory mediators as well as metabolic changes of pulpal tissues.[2,5,6,9,12,15,16,22] In addition, when pathology arises, diabetes increases the development of infections, intensifying necrosis and its consequences on pulpal , as well as on peri-radicular tissues.[7,9,11,15,16]

Although several studies show the correlation between pulpal infections and diabetes, there remain several gaps in the current literature, such as a role of the several virulence factors in the host inflammatory pathway and the effects of different pulpal pathogenic agents.

The results of our study were not entirely conclusive regarding the increase in prevalence of apical periodontitis in patients with diabetes. Regarding the assessment of the success of endodontic treatments in this group of patients, the results should not be considered separately. Therefore, we consider that the healing of peri-radicular changes is crucial for the success of endodontic treatments, with a need for periodical follow-up and evaluation in order to monitor the healing process. The quality of endodontic treatments seemed also important for peri-radicular tissue response although, in our study, the quality of definitive restoration is mostly related to failure.

It is important to assure an adequate follow-up of these patients before and following radicular endodontic treatments.[9,11,22,23] In this study, 59% of the patients in the study group did not attend a follow-up visit, itself a worrying aspect.

Considering that this is a retrospective study that assessed a small group of patients, the results that we found must be considered taking into account these constraints. For this reason and given the limitations of the study, we are not able to state that in patients with diabetes there is a clear change of response of periapical tissue and therefore we cannot state that the success of endodontic treatment in these patients is compromised. Nevertheless, we wish to emphasize the importance of follow-up in patients with systemic pathologies, namely diabetes, taking into account the potential risks of treatment.

We conclude that more studies are needed in order to characterize pulpal and peri-radicular changes, as well as epidemiological studies to assess the prevalence of apical periodontitis, its progression and all the aspects related with endodontic treatment in patients with diabetes.

CONFLICTS OF INTEREST

The authors wish to declare that there was no conflicts of interest in writing this manuscript.

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