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## Periapical healing outcome following single visit endodontic treatment in patients with type 2 diabetes mellitus

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### Abstract

**Background:** The prevalence of apical periodontitis in diabetes mellitus patients is high. The altered immunity in diabetes affects the healing process of periapical tissue. Single visit endodontic treatment has shown to increase the periapical healing rate with better patient compliance. Hence the present study aims at evaluating the clinical and radiographic healing outcome of single visit endodontic treatment, in type 2 diabetes mellitus patients with periapical disease.

**Material and Methods:** Eighty patients with periapical disease were divided into 2 groups of 40 each: Group I, Control subjects and Group II, Type 2 diabetics. Glycosylated hemoglobin levels were assessed preoperatively and at follow up intervals in diabetics. Pre-operative assessment of periapical status was done using CPDR (Clinical periapical diagnosis of root), QLDR (Qualitative radiographic diagnosis of tooth) and QTDR (Quantitative radiographic diagnosis of tooth) criteria. Postoperative healing was evaluated following single-visit endodontic treatment by Strindberg criteria.

**Results:** Group 2 subjects had chronic and exacerbating lesions with significantly larger lesions ( $p=0.029$ ). 100 % clinical healing outcome in diabetic group was seen in two months. Group 2 showed 85% success in one year on radiographic evaluation. Poor controlled diabetics showed failure compared to fair and good controlled.

**Conclusions:** Type 2 diabetics had chronic and larger sized lesions when compared to control subjects. The periapical lesions in patients with poor diabetic control showed failure. The clinical and radiographic healing outcome of single visit endodontic therapy was delayed in diabetic patients.

**Key words:** Apical periodontitis, diabetes mellitus type 2, endodontics, periapical lesion, strindberg criteria.

### Introduction

Diabetes mellitus is a common metabolic disorder characterized by various phenotypes of hyperglycemia. It is broadly categorized into Type 1 and Type 2 diabetes

mellitus, among which type 2 is the commonest. The alteration in neutrophil function and failure to deliver the humoral and cellular components of the immune system in diabetic patients increases the risk of episodes of in-

fection (1). Diabetes mellitus has its effects on pulp and periapical diseases and their treatment outcome (2). The prevalence of periapical infection is greater in diabetics in comparison to non-diabetics (3). The prevalence of apical periodontitis in type 2 diabetics is found to be 81.3% (4). Similar finding was observed by Marroto *et al.* and Lopez *et al.* in their research projects (5,6).

The tooth with apical periodontitis is managed by root canal therapy. The success rate of root canal treatment has been generally regarded as 87% (7). The scientifically documented procedure for the best results in canal disinfection is based on complete debridement, irrigation and obturation of root canal in single visit, reducing the risk of inter-appointment infection (8). Single visit root canal treatment has several advantages such as reduced flare-up rates (9), good patient acceptance and practice management, and is more effective in teeth with apical periodontitis with 6.3% higher healing rate than multiple visits (10).

Hence the present study was performed to evaluate both clinically and radiographically the periapical condition of the teeth in type 2 diabetic patients and thereby assess the healing outcome of single visit endodontic treatment in them.

## Material and Methods

80 subjects aged 20-60 years with irreversible pulpitis and apical periodontitis, requiring endodontic therapy were selected and divided into 2 groups.

-Group I - Control group: 40 normal subjects with no history of systemic disease and normal glycosylated hemoglobin levels ( $HbA1c >6.5 <7.5$ ).

-Group II- Diabetic group: 40 subjects with diabetes mellitus, diagnosed by glycosylated hemoglobin  $> 7.5\%$ , without any habits and other systemic diseases.

The approval was obtained from the institutional ethical committee to conduct the study and informed consent was taken from all the subjects. Diagnosis of apical periodontitis was done by clinical and radiographic examination. Pre-operative assessment of periapical status which included pain, apical tenderness & sinus tract was done using CPDR (Clinical periapical diagnosis of root), QLDR (Qualitative radiographic diagnosis of tooth) and QTDR (Quantitative radiographic diagnosis of tooth) criteria (11). The method of viewing the radiograph was standardized. Single-rooted teeth were diagnosed according to these criteria and in multi rooted teeth, most severely affected root was considered.

In group II Glycosylated Hb levels were assessed both preoperatively and at follow up intervals postoperatively. Preoperative, post-obturation, and follow-up radiographs were made in a 70 kVp, 10 mA IOPAR machine using paralleling technique. Standardized processing technique was used in order to obtain optimal diagnostic quality of the radiographs.

## -Procedure for single sitting root canal therapy

The selected tooth was anesthetized with 2% Lignocaine. Single visit endodontic treatment was carried out with strict aseptic measures. Working length was confirmed and adjusted as needed by using straight and angled radiographs using Ingle's method. The root canals were instrumented in a crown down technique (12) with protaper rotary NiTi file (Dentsply) and RC Prep; canals were irrigated with sodium hypochlorite & chlorhexidine. Protaper gutta-percha master cone was selected corresponding to that of last protaper finishing file (13) used & confirmatory IOPAR and RVG were taken. The obturation was completed with zinc oxide eugenol sealer.

Postoperative evaluation of healing was done at first week, second week, first month, second month, sixth month and after one year, using Strindberg criteria (14) The results were statistically evaluated using Student unpaired T test, Chi-Square test and Freidman's test.

## Results

The mean age of Group I patients was 34 yrs and Group II was 44 yrs. Unpaired t test showed no significant difference between the groups ( $p=0.087$ ). In Group I, 24 were males and 16 were females and Group II 18 were males and 22 were females. Chi-square test showed no significant difference between groups.

On preoperative assessment of glycosylated hemoglobin patients with  $HbA1c >6.5 <7.5$  were included in Group I. Among Group II patients six were poor controlled [ $\geq 9.5\%$ ] diabetics, 26 were fair [ $8.5-9.5\%$ ] and eight had good control [ $7.5-8.5\%$ ].

The preoperative assessment of pain, sinus tract and apical tenderness using Friedman's test showed statistically significant improvement in both groups over a period of 6 months (Table 1).

Based CPDR and QTDR criteria, the acute lesions were more in group I, whereas chronic lesions were more in group II (Table 2). Preoperative assessment of periapical status according to, QLDR Criteria (Qualitative radiographic diagnosis of tooth showed increased occurrence of periapical disease in group II (Table 3). The group II subjects had significantly larger sized lesions compared to those in group I (Table 4).

A significant difference was observed in the size of periapical radiolucency from first month to one year. The lesions  $\leq 1$  mm healed within 6 months, whereas only few teeth with large periapical lesions healed completely by one year of evaluation. Higher failure rate was seen in larger sized lesions (Table 5).

The clinical evaluation of periapical healing outcome using Strindberg criteria showed 100% success in group I within 1 month, however it was observed after 2 months in Group II (Table 6).

The radiographic evaluation of periapical healing outcome over a period of 1 year using Strindberg criteria

**Table 1.** Healing outcome of teeth with Preoperative pain, sinus tract and apical tenderness using Friedman's test.

			Pre-op	1wk	2wk	1mon	2mon	6mon	Friedmans test	
<b>Group I</b>	Pain	yes	30	10	4	0	0	0	56.522	vhs
		no	10	30	36	40	40	40		
	Sinus tract	yes	14	10	6	2	0	0	23.846	vhs
		no	26	30	34	38	40	40		
	Apical tenderness	yes	32	16	6	0	0	0	58.178	vhs
		no	8	24	34	40	40	40		
<b>Group II</b>	Pain	yes	24	20	16	4	0	0	44.167	vhs
		no	16	20	24	36	40	40		
	Sinus tract	yes	18	18	16	6	0	0	36.948	vhs
		no	22	22	24	34	40	40		
	Apical tenderness	yes	34	18	16	4	0	0	56.441	vhs
		no	6	22	24	36	40	40		

Vhs: very highly significant.

**Table 2.** Preoperative assessment of periapical status according to, CPDR Criteria and QTDR.

CPDR Criteria	Group I	Group II
Acute	6	4
chronic	4	12
Exacerbating	30	24
QTDR Criteria	Group I	Group II
Normal Periapex	4	0
Acute apical periodontitis	6	4
Chronic resorbing and exacerbating apical periodontitis	30	36

CPDR Criteria  $\chi^2=2.636$   $p=0.621$  not significant (ns); QTDR Criteria  $\chi^2=2.565$   $p=0.632$  ns.**Table 3.** Preoperative assessment of periapical status according to, QLDR Criteria.

QLDR Criteria	Group I	Group II
Normal Periapex	4	0
Diseased	36	40

 $\chi^2=2.105$   $p=0.349$  ns.

**Table 4.** Preoperative size of periapical lesion in all subject groups.

Size	Group I		Group II		Total	
	Count	%	Count	%	Count	%
< 1mm	18	45	6	15	24	30
1mm	8	20	8	20	16	20
2mm	8	20	12	30	20	25
≥3mm	6	15	14	35	20	25
Total	40	100	40	100	80	100

X<sup>2</sup>=4.749 =0.029 significant.**Table 5.** Relation between preoperative size of periapical radiolucency and treatment outcome.

Duration				1month		2month		6month		1 year	
Size	Gr I	Gr II	Total	Success	Failure	Success	Failure	Success	Failure	Success	Failure
<1mm	18	6	24	10	14	24	0	24	0	24	0
1mm	8	8	16	6	10	12	4	16	0	16	0
2mm	8	12	20	0	20	6	14	14	6	18	2
≥3mm	6	14	20	0	20	4	16	10	10	14	6

GroupI Vs Group II: X<sup>2</sup>=4.749 *p*=0.029 sig. 1 month: x<sup>2</sup>=15.02 *p*=0.0018 highly significant(hs); 2 month: x<sup>2</sup>=27.51 *p*<0.001 vhs; 6 month: X<sup>2</sup>=18.333 *p*=0.004 hs; 1year: X<sup>2</sup>=9.381 *p*=0.02 significant.

**Table 6.** Evaluation of periapical healing outcome clinically over a period of 6 months: (adopted from Strindberg).

Duration		1 week		2 week		1 month		2 month		6 month	
Group	Outcome	No.	%	No.	%	No.	%	No.	%	No.	%
Group I n=40	Success	30	75	36	90	40	100	40	100	40	100%
	Failure	10	25	4	10	0	0	0	0	0	0
Group II n=40	Success	20	50	24	60	36	90	40	100	40	100
	Failure	20	50	16	40	4	10	0	0	0	0

1 month: x<sup>2</sup>=4.772 *p*=0.092 ns; 2 month: x<sup>2</sup>=2.105 *p*=0.349 ns; 6 months: x<sup>2</sup>=0 *p*=1 ns; 1 year: x<sup>2</sup>=0 *p*=1 ns.

showed significantly (*p*= 0.0026) low success rate in the first month which improved to 85% over a period of one year. However a success rate of 100% was observed in group I in 6 months (Table 7).

On one year follow up, six patients had poor controlled diabetes, 20 showed fair control and 14 had good control. Clinically healing was observed in all diabetic patients; and radiographically, all patients except the poor controlled diabetic patients showed successful healing. Mean HbA1c % preoperatively was 8.6800 and after one year it was 8.3300 with a mean difference of 0.3500. No statistical difference was seen between preoperative evaluation and after one year of evaluation of HbA1c %.

## Discussion

In the present study the average age of patients ranged from 30-40 yrs with no statistically significant difference. Moreover gender differences were also not significant. Irreversible pulpitis with apical periodontitis is the most common infection of the root canal system. The prevalence of apical periodontitis increases with age and it may rise to 62% in individuals over 60 years (7).

In the group II, majority of patients had fairly controlled diabetes. In the present study the preoperative HbA1c levels ranged from 7.8 to 10.4% with a history of diabetes ranging from 3-11 years.

The periapical status of each tooth in the present study

**Table 7.** Evaluation of periapical healing outcome radiographically over a period of 1 Year: (adopted from Strindberg.

Duration		1 month		2 month		6 month		1 year	
Group	Outcome	No.	%	No.	%	No.	%	No.	%
Group I n= 40	Success	18	45	36	90	40	100	40	100
	Failure	22	55	4	10	0	0	0	0
Group II n=40	Success	2	5	24	60	32	80	34	85
	Failure	38	95	16	40	8	20	6	15

1 month:  $\chi^2=11.875$   $p=0.0026$  hs; 2 month:  $\chi^2=4.772$   $p=0.092$  ns; 6 month:  $\chi^2=4.205$   $p=0.122$  ns; 1 year:  $\chi^2=3.055$   $p=0.217$  ns.

was evaluated according to the 3 indices: (i) The clinical periapical diagnosis of root (CPDR), based on the diagnosis of the pulp and the root with the most extensive periapical involvement; (ii) Qualitative radiographic diagnosis of tooth (QLDR), the actual radiographic status of each individual root apex and differentiates between radiographically normal and diseased periapex; and (iii) Quantitative radiographic diagnosis of tooth (QTDR), the extent of periapical pathosis in millimeters (11).

#### -Preoperative assessment

In the present study pain was more common in Group I, whereas presence of sinus tract and apical tenderness were frequent in diabetic group (Table 1). As per CPDR and QTDL criteria, in the present study, chronic and exacerbating lesions were seen more in type 2 diabetics (Table 2). Falk, Hugoson and Thorstensson found similar correlation, who demonstrated long duration diabetics exhibit teeth with greater extent of periapical lesions than non diabetics (15). Elfving *et al.*, found diabetics with poor glycemic control have a higher rate of asymptomatic tooth infection (16).

Qualitative assessment using QLTR criteria showed more number of teeth with diseased periapex in diabetics than control (Table 3). The compromised circulation within pulp due to endarteritis obliterans and lack of collateral circulation along with altered polymorphonuclear activity in diabetics are considered to result in an increased risk for infection or pulp necrosis (17).

Uncontrolled diabetes has been hypothesized to have statistically significant association with apical periodontitis (4). The group II subjects had significantly larger sized lesions compared to those in group I (Table 4). The results are in accordance with the study conducted by Iwama *et al.*, which showed that larger periradicular lesions were more and alveolar bone resorption was most severe in diabetics (18).

#### -Post-treatment Healing outcome

The endodontic treatment of infected teeth aims at elimination of bacteria from the root canal, thereby providing a favourable environment for healing. Several clinical studies report a success rate of endodontic therapy ranging from 87.4% to 94.5% (19,20). Single-visit RCT has been recommended for use in cases with pulpal infla-

mmation, traumatic pulpal exposure, and necrotic pulp with a sinus tract (21,22).

In our study standard endodontic treatment protocol (23) was implemented in terms of root canal isolation, preparation and obturation. We used the new Progressively Tapered (ProTaper) NiTi rotary files for preparation of root canals. These files represent a revolutionary progression in root canal preparation procedures as they provide superior flexibility, unmatched efficiency and greater safety (13).

It has been hypothesized that pulpal necrosis in diabetics harbor a more virulent microbial profile, with significant increase in *Prevotella intermedia*, *Porphyromonas gingivalis*, *F. nucleatum*, *P. micros* & *Streptococcus* (23). Hence diabetics should be treated with effective antimicrobial root canal regimens. Chlorhexidine and sodium hypochlorite (NaOCl) have been shown to be the most effective root canal irrigants (24). In this regard, in our study these irrigants were used to irrigate the root canals. The history of pain, presence of sinus tract and apical tenderness play a significant role in the outcome of endodontic treatment. The assessment of pain, sinus tract and apical tenderness using Friedman's test showed very highly significant healing outcome over a period of 6 months (Table 1). The success rate of teeth with preoperative sinus tract was less compared to teeth with no preoperative sinus tract. Our results were in agreement with the study performed by Chugal *et al.*, who found that success rate of teeth with a preoperative sinus tract was only 37.5% compared with a 62.7% success for teeth without sinus tract (11). The presence of sinus tract and apical tenderness was more common in Group II. The resolution of pain and apical tenderness in Group I was seen in one month, however in group II resolution of signs and symptoms took two months.

In the present study the smaller lesions showed successful healing outcome within six months, however the success rate of 70% ( 14 out of 20 patients) over a period of one year was observed in  $\geq 3$ mm sized lesions (Table 5). Friedman *et al.* in their review found that the success rate of teeth with apical periodontitis after initial treatment or retreatment was 74% to 86% (25). In the



review, the follow up studies had varied periods of assessment ranging from six months to ten years. Bystrom *et al.* in their study suggested that as long as there is continuous decrease in the size of the lesion, the lesion need not be labeled as failure (26). Hence in our study, if the follow up period was more we would have expected higher success rates.

Clinical evaluation of periapical healing outcome over a period of six months using Strindberg criteria showed no statistical significance among both the groups over a period of six months. 100% success was observed in group I within 1 month, however it was observed after 2 months in Group II (Table 6).

On radiographic evaluation a success rate of 90% in Group I and 60% in Group II were attained in 2 months. 15 % of Group II showed failure even after one year follow up, wherein 100 % of Group I had already achieved success in six months. Diabetic subjects with good and fair glucose control showed better healing than poor controlled diabetic subjects. Cheraskin and Ringsdort showed radiographic healing of periapical lesion following root canal treatment in a low glucose group were reduced by an average of 74% compared with a reduction of only 48% for a high glucose group (27). The lower success rates in diabetic patients could probably be due to impaired healing capacity and increased susceptibility to infection (28,29).

## Conclusions

The present study showed that patients with diabetes mellitus have more complex and compromised presentation of periapical disease and the condition poses a significant effect on the healing outcome of single visit endodontic treatment. The diabetic patients were more prone for chronic periapical disease with larger lesions. The periapical lesions were more prevalent in diabetic patients than in non diabetics. Smaller sized lesions healed faster whereas larger sized lesions showed higher failure rate. Healing outcome at the end of one year was poor in poor controlled diabetics when compared to fair and good controlled diabetics in group II. The clinical and radiographic healing outcome of single visit endodontic therapy was delayed in diabetic patients. Although few lesions still persisted over a period of one year radiographically, long term follow up would probably have shown further decrease in lesion size, adding to the success rate. Hence long term follow up studies are required to assess periapical healing and to determine effective treatment outcome.

## References

1. Delamaire M, Maugeudre D, Moreno M, Le Goff MC, Allannic H, Genetet B. Impaired leucocyte functions in diabetic patients. *Diabet Med.* 1997;14:29-34.
2. Chakravarthy PVV. Diabetes mellitus: An endodontic perspective. *European Journal of General Dentistry.* 2013;2:241-45.
3. Bender IB, Bender AB. Diabetes mellitus & dental pulp. *J Endod.* 2003;29:383-9.

4. Segura-Egea JJ, Jimenez-Pinzon A, Rios-Santos JV, Velasco-Ortega E, Cisneros-Cabello R, Poyato-Ferrara M. High prevalence of apical periodontitis among type 2 diabetic patients. *Int Endod J.* 2005;38:564-9.
5. Marroto PS, Fontes TV, Armada L, Lima KC, Rocas IN, Siquerira JF Jr. Type 2 diabetes mellitus and the prevalence of apical periodontitis and endodontic treatment in an adult Brazilian population. *J Endod.* 2012;38:297-300.
6. Lopez Lopez J, Jane Salas E, Estrugo Devasa A, Velasco-Ortega E, Martin Gonzalez J, Segura Egea JJ. Periapical and endodontic status of type 2 diabetic patients in Catalonia, Spain: A cross sectional study. *J Endod.* 2011;37:598-601.
7. Erikson HM. Epidemiology of apical periodontitis. In: Orstavik D, Ford TRP, ed. *Essential Endodontology. Prevention and treatment of apical periodontitis.* London: Blackwell Science. 1998:179-91.
8. Trope M, Delano EO, Orstavik D. Endodontic treatment of teeth with apical periodontitis: single vs. multiple visit treatment. *J Endod.* 1999;25:345-50.
9. Walton R, Fouad A. Endodontic interappointment flare-ups: a prospective study of incidence and related factors. *J Endod.* 1992;18:172-7.
10. Sathorn C, Parashos P, Messer HH. Effectiveness of single-visit versus multiple-visit endodontic treatment of teeth with apical periodontitis: a systemic review and meta-analysis. *Int Endod J.* 2005;38:347-55.
11. Chugal NM, Clive JN, Spangberg LS. A prognostic model for assessment of the outcome of endodontic treatment: Effects of biologic and diagnostic variables. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2001;91:342-52.
12. Morgan LF, Montgomery S. An evaluation of the crown-down pressureless technique. *J Endod.* 1984;10:491-8.
13. Ruddle CJ. The Protaper Technique. *Endodontic topics.* 2005;10:187-90.
14. Strindberg LZ. The dependence of the results of pulp therapy on certain factors. *Acta Odontol Scand.* 1956;14(Suppl 21):1-175.
15. Falk H, Hugoson A, Thorstensson H. Number of teeth, prevalence of caries & periapical lesions in insulin dependent diabetes. *Eur J Oral Sci.* 1989;97:198-206.
16. Elfving NG, Ljunggren JG, Tomson K. Symptom free dental infections-a common cause of poor sugar balance in diabetics. *Lakartidnngen.* 1979;76:717-9.
17. Tennenberg SD, Finkenauer B, Dwivedi A. Absence of lipopolysaccharide-induced inhibition of neutrophils apoptosis in patients with diabetes. *Arch Surg.* 1999;134:1229-34.
18. Iwama A, Nishigaki N, Nakamura K, Imaizumi I, Shibata N, Yamasaki M, et al. The effect of high sugar intake on the development of periradicular lesions in rats with type 2 diabetes. *J Dent Res.* 2003;82:322-5.
19. Barbakow FH, Cleaton-Jones P, Friedman D. An evaluation of 556 cases of root canal therapy in general dental practice. Part 2: postoperative observations. *J Endod.* 1980;6:485-9.
20. Morse DR, Esposito JV, Pike C, Furst ML. A radiographic evaluation of the periapical status of teeth treated by the gutta-percha-eucapercha endodontic method: a one-year follow-up study of 458 root canals. Part III. *Oral Surg Oral Med Oral Pathol.* 1983;56:190-7.
21. Albashaireh ZS, Alnegrish AS. Postobturation pain after single and multiple visit endodontic therapy- A prospective study. *J Dent.* 1998;26:227-32.
22. Iqbal A, Akbar I, Qureshi B, Sghaireen MG, AL-Omiri MK. A Survey of Standard Protocols for Endodontic Treatment in North of KSA. *ISRN Dentistry.* 2014;2014:1-4.
23. Fouad AF. Diabetes mellitus as modulating factor of endodontic infections. *J Dent Educ.* 2003;67:459-67.
24. Siqueira JF Jr, Rocas IN, Santos SRLD, Lima KC, Magalhães FAC, Uzeda M. Efficacy of instrumentation techniques and irrigation regimens in reducing the bacterial population within root canals. *J Endod.* 2002;28:181-4.
25. Friedman S, Mor C. The success of endodontic therapy- Healing and Functionality. *J Calif Dent Assoc Journal.* 2004;32:493-503.

26. Bystrom A, Happonen RP, Sjogren U, Sundqvist G. Healing of periapical lesions of pulpless teeth after endodontic treatment with controlled asepsis. *Endod Dent Traumatol.* 1987;3:58-63.
27. Cheraskin E, Ringsford WM Jr. The biology of the endodontic patient. 3. Variability in periapical healing and blood glucose. *J Oral Med.* 1968;23:87-90.
28. Bender IB, Seltzer S, Freedland JB. The relationship of systemic diseases to endodontic failures and treatment procedures. *Oral Surg Oral Med Oral Pathol.* 1963;16:1102-15.
29. Freedland JB. The systemic considerations in endodontic therapy. *Int Dent J.* 1963;13:31-45.

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