Tontesh S. Tawady
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Education

University of Maryland Dental School Endodontic Residency **Summer 2013 – Summer 2016**
Certificate of Endodontics Completion June 2016
Master of Science Completion June 2016

Philadelphia Veterans Affair Medical Center GPR Resident **Fall 2012 – Spring 2013**
General Practice Residency Certificate
Completion Date: June 2013

University of Maryland Dental School **Fall 2008 – Spring 2012**
Doctor of Dental Surgery
Graduation Date: May 2012

University of Maryland, Baltimore County (UMBC), **Fall 2003 – Spring 2007**
Bachelor of Science: Biological Sciences
Graduation Date: May 2007.

Professional Experience

Teaching Resident–University of Maryland **Spring 2014 – Current**

- Teach 2nd year dental students to basics of endodontics in a pre-clinical course
- Supervise 3rd and 4th year dental students in their treatment of patients

Clerk – University of Maryland **Fall 2011 – Spring 2012**

- Competitively selected to become a special patient clerk
- Practice at several different settings, including the dental school, Veteran's Affairs Medical Center, and nursing homes.
- Treat patients from homeless, mentally challenged, geriatric, and those in drug rehabilitation

Research Experience

Resident, University of Maryland Dental **Spring 2014 – Current**

The relationship between Short Term Healing of periapical lesions and glycemic control

- Mentor: Dr. Ashraf Fouad
- Awarded an AAE Foundation research grant
- Clinical research pertaining to the relationship between periapical healing and glycemic levels

Resident, University of Maryland Dental **Summer 2013 – Spring 2014**

Volumetric analysis of residual periapical lesions in diabetic and non-diabetic patients

- Mentor: Dr. Ashraf Fouad
- Used a novel software to compare periapical lesion volume and diabetic status
- Awarded the American Association of Endodontists/Dentsply Resident Award

Resident, University of Maryland Dental **Summer 2013 – Spring 2014**

The Correlation Between Periapical Healing and Glycemic Control

- Mentor: Dr. Ashraf Fouad
- Poster presentation at 2014 AAE national conference
- Analyzed immediate post root canal treatment periapical images of diabetic and non-diabetic patients with recall periapical images, to determine a correlation

Licensure

State of Maryland Dental License **Fall 2015 - Current**

Professional Memberships and Affiliations

Resident Member of the American Association of Endodontics **Summer 2013 - Current**

- Attended the annual session, and resident symposium

Resident Member of the Penick Endodontic Study Club **Summer 2013 - Current**

- Endodontic based study club in Bethesda, Maryland

Treasurer, University of Maryland Student Body **Summer 2011 - Summer2012**

- Work with faculty and students to plan academic and social events

Treasurer, Class of 2012 **Fall 2008 – Spring 2010**

- Freshmen, Sophomore, Junior Year
- Assisted in organizing many events, and managing the class funds

Executive Board, American Student Dental Association **Fall 2010 – Spring 2012**

- Represented UMB Dental at the Pittsburgh ASDA conference
- Planned Lunch and Learn events for dental school students

Member, Psi Omega Fraternity **Fall 2008 – Spring 2012**

- Participated in many community outreach programs
- Assisted other members in providing welcome packets used during orientation

Other Community and Service Activities

- Mission of Mercy – Endodontic Volunteer
  - Provided endodontic care to an underserved rural population
- Crest Healthy Smiles
  - Provided education and oral health care products to elementary school students
- Americas Walk For Juvenile Diabetes
  - Helped set up and pass out refreshments to participants
- Multiple Sclerosis 5K run
  - Assisted in passing out refreshments

Abstract

Title: The Relationship between Short Term Healing of Periapical Lesions and Glycemic Control

Tontesh Tawady, Master of Science 2016

Thesis Directed By: Dr. Patricia A. Tordik, DMD

Aim: This study aimed to examine the relationship between HbA1c level and short-term healing of periapical lesions.

Methods: Patients were recruited for the study (n=21). After RCT, the final radiograph was taken, and the patient's blood was drawn for HbA1c analysis. The patients returned in six months for a recall examination. The Periapical Index (PAI) scoring system was used to compare the difference in the periapical status from the initial appointment and at the recall appointment.

Results: Out of 21 recruited patients, eight patients returned for recall. To investigate the rate of healing and how it related to the patients' Hba1c levels, Pearson's r was done with the HbA1c of the recall patients (N=8) and the level of healing (difference in PAI). This correlation was r= -.474.

Conclusion: There was a negative correlation between HbA1c level and the level of healing of periapical lesion, this correlation was not statistically significant.

The Relationship between Short Term Healing of Periapical Lesions and Glycemic Control

By
Tontesh S. Tawady

Thesis submitted to the Faculty of the Graduate School of the
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Introduction

The association between endodontic pathosis and systemic disease has not been studied thoroughly. Areas that have been explored include: cardiovascular disease(1), diabetes mellitus (2), sickle cell anemia (3), systemic allergies (4), and viral infections (5). There has been a lot of interest in diabetes and the role it plays in pathogenesis of endodontic infections and healing following endodontic treatment (2, 6). Diabetes is a metabolic disease in which the patient develops glycemia, due to either reduced insulin levels or insulin resistance. Diabetics are at significantly higher risk of bacteremia compared to non-diabetics (7). Moutschen et al. (8) have shown that diabetic patients have an increased risk of having an impaired immune system because of hyperglycemia. It has been shown that this impairment is attributed to activation of co-regulatory immune responses (9). Bacteremias have been known to increase in diabetics(8) however the effects of diabetes and/or glycemic control on periapical lesions is poorly studied.

Understanding the disease and healing process of periapical lesions and the relationship to diabetic status is clinically important since it can influence the prognosis of treatment that both clinician and patient should be aware of. Instead of looking at the diabetic status, this study will look at the glycemic control status of each patient. One older study has explored the link between glycemic control and endodontic infections, and found that carbohydrate metabolism appeared to be a predictor in healing of periapical disease(10). However, this study used postprandial glycemia as the measure of glycemia, rather than

the more accurate HbA1c, did not control for confounding variables and did not use the PAI, which is a validated radiographic index. (11, 12)

It is believed, by the authors, that the progression and healing of periapical lesions is affected, more so, by the degree of glycemia rather than the presence of diabetes. Even among diabetic patients there is a wide range of glycemic control, which would affect healing. There are approximately 29.1 million diabetic patients in the United States, of which almost a third are unaware that they have the disease.(13, 14) A recent study (15) demonstrated that 47% of patients who reported themselves as non-diabetic actually had an HbA1c level, which would classify them as Pre-Diabetic or Diabetic.

There are several advantages to the examination of glycemic control as opposed to diabetes mellitus. These advantages include the ability to perform the study on a larger number of patients, reduce the effects of hypoglycemic medications that diabetics take ((for example Metformin may actually stimulate bone deposition (16, 17)) and the ability to explore further a specific mechanism (hyperglycemia) that may affect the healing without the confounding effects of other diabetic co-morbidities, complications, and dietary and other behavioral changes. In addition, studies that investigate healing of periapical lesions need long-term follow up time and subsequently end up with high attrition of patients. Therefore, a short-term study with a larger population would allow the generation of data in a more efficient manner.

Review of Literature

Animal Studies

The relationship between Diabetes and endodontic infection has been studied in animal models. Fouad et al. (6) induced periapical lesions in diabetic and non-diabetic mice to study the effect of diabetes on the pathogenesis of periapical lesions. They also measured the periapical lesion size histomorphometrically. They found that the diabetic mice had a higher mortality rate, and when looking at the periapical lesion size of the mice who survived to the pre-determined time periods, there was no statistical difference in the periapical lesion size.

Iwama et al. (18) studied the effect of diabetes in experimentally induced periapical lesions in Goto-Kakizaki rats with diabetes and Wistar rats as controls. This study showed that the diabetic rats, which were given a sucrose diet, had the most severe bone resorption and the periapical lesions were the largest in this group.

Another study by Garber et al. (19) looked at the effects of Mineral Trioxide Aggregate on pulp caps in two groups of rats either receiving saline injections (control) or streptozotocin injections to induce diabetes (diabetes group). The diabetic rats had increased pulpal inflammation as well as decreased dentin bridge formation compared to the control rats. The authors concluded that hyperglycemia has an adverse effect on pulpal healing in rats.

Human Studies

Many older studies involving humans have examined diabetes using blood glucose levels, glucose tolerance tests, and fasting blood glucose. Fasting blood glucose, or oral glucose

tolerance tests simply gauge a moment of a single day and may be misleading when determining a patients long standing glycemic index. (20). Bonoro et al. have recently shown that glycosylated hemoglobin (HbA1c) levels equal the assessment of hundreds (virtually thousands) of individual measures of fasting glucose levels, and therefore are more accurate measurement for diabetes(20). The HbA1c test is an index of serum glucose for 90 days prior to the measurement and is a more accurate assessment of a patient's glycemic status than a fasting blood glucose reading.

The HbA1c test eliminates the daily fluctuations seen in fasting plasma glucose or oral glucose tests. The American Diabetes Association classifies diabetes as having an HbA1c of 6.5 or above, pre-diabetes as 5.7-6.4 and normal HbA1c level being about 5(21). Many people are unaware they have diabetes. It is estimated that the prevalence of diabetes in the United States is approximately 29.1 million people, of whom approximately 8.1 million are unaware of their disease(13, 14). A recent study completed at the University of Maryland examined the relationship of Diabetes and periapical lesion size. From this sample 87.5% of the self-reported non-diabetic patients had an HbA1c above 5.7; defined as diabetic or pre-diabetic (22). This study showed that the size of residual periapical lesion 2-4 years after root canal treatment was correlated with HbA1c and not the reported diabetic status of the patient.

The effect of periodontal health on glycemic control has been exhaustively studied. It is known that diabetes has a strong detrimental effect on periodontal health. In addition, Sgolastra et al(23) did a meta-analysis looking at the effects of scaling and root planing

on improving glycemic and metabolic control in patients with Type 2 diabetes and chronic periodontitis. The meta-analysis showed that scaling and root planning could improve glycemic control (reduce HbA1c) in patients with chronic periodontitis and type II diabetes mellitus. These are indicative of a possible bidirectional relationship between oral health and systemic glycemic control. Although this study does not aim to assess the effect of endodontic treatment on HbA1c, longitudinal data will be available for analysis of this important phenomenon in endodontics, and the effects of periodontal disease will be controlled for in the analysis of the results.

Previously, blood glucose was shown to have an effect on the healing of periapical lesions. Chearaskin and Ringsdorf(10) examined postprandial blood glucose in 55 routine endodontic patients. They were able to measure the periapical lesion size every 2 weeks up to 10 weeks then every month up to 30 weeks via a periapical radiograph. They demonstrated that postprandial glycemia was a good predictor for endodontic treatment outcomes. Based on the results of this study, the reduction in periapical lesion size after 30 weeks was 74% in the lower blood glucose group, whereas a 48% reduction occurred in the higher blood glucose group. This study concluded that carbohydrate metabolism (as measured by two-hour post-prandial blood glucose) is a predictor or periapical healing after root canal therapy. This seminal work prompted our re-examination with a different technology.

Falk et al. (24) studied the prevalence of periapical lesions in type 1 diabetics. They observed that women who had long-term diabetes exhibited more endodontically treated

teeth with a periapical lesion as compared to women with short-term diabetes or women without diabetes. This means that diabetes may accentuate the progression of endodontic disease in long-term diabetic patients.

Britto et al (25) investigated the prevalence of periapical lesions in endodontically treated teeth and untreated teeth in patients with and without diabetes. They showed that men with type II diabetes who had root canal therapy were more likely to have residual lesions. Another retrospective study by Segura-Egea et al. (26) looked at the prevalence of periapical lesions in patients with and without type II diabetes. They showed that at least one tooth was found to have a periapical lesion in 81.3% of diabetic patients and in 58% of the non-diabetic patients. This same group (27) observed the possible association between apical periodontitis and the glycemic control of type 2 diabetic patients in a cross-sectional study. The records of 83 diabetic patients were examined for periapical lesions using the PAI scale and this was compared with the patients HbA1c levels. Results showed that a worse periapical status (higher PAI score) was significantly correlated with HbA1c levels ≥6.5 (odd ratio = 3.8; 95% confidence interval, 1.1–13.0; P = .03)

Fouad and Burleson 2003 (2) evaluated 540 non-surgical endodontic cases with at least a 2-year follow up; all cases were assessed retrospectively, using an electronic record system. They found that patients with diabetes had increased periodontal disease in teeth that were endodontically involved compared to non-diabetics. They also determined, through a 2-year follow up, that the likelihood of success of endodontic treatment in

cases with pre-operative periradicular lesions was reduced in patients with diabetes, especially after controlling for a number of confounding factors, including periodontal disease.

Wang et al. (28) investigated the impact of systemic diseases on the risk of tooth extraction after non-surgical root canal therapy (NSRCT). The study included 49,334 teeth, of which 1592 were extracted during the 2-year follow-up. They showed that diabetes was a significant risk factor for tooth extraction after NSRCT was completed.

A Longitudinal study by Doyle et al (29), showed no significant difference between diabetics and non-diabetics when looking at the outcomes of implants and endodontic restorations. This study relied on a patient's self reported status of diabetes. Endodontically treated teeth were considered successful if the tooth was present in the mouth without the presence of apical periodontitis or symptoms.
However, a prospective study by Ng et al (30) demonstrated that the presence of diabetes resulted in a three times higher chance of tooth loss compared to non-diabetics. This study also relied on the patients self-reported diabetic status.

An HbA1c level is a more reliable indicator of blood glucose than reported diabetic status (22). A study in 2014 assessed the feasibility of screening for diabetes and pre-diabetes in dental practices. This study evaluated a population of patients at 11 general and periodontal specialty clinics in Providence, Rhode Island. The results of this study showed that 40.7 percent of patients who did not know their glycemic status had an

HbA1c blood level of 5.7 percent or greater (31). In the study completed at the University of Maryland(22), it was shown that the average HbA1c of non-diabetic patients was 6.46%, with 87.5% in the hyperglycemic range. Therefore, hyperglycemia is very prevalent in the inner city dental patient population, and many "non-diabetic" patients have glycemic levels that fall in the prediabetes or diabetes range.

Another aspect of this study involved analysis of periapical radiographs for healing assessment. Periapical lesions have been measured using periapical radiographs according to a Periapical Index (PAI). This index was first introduced by Orstavik (32) as a scoring system for radiographic assessment of apical periodontitis. This index, which is based on a histologic study of the lesions imaged (33), involves rating a periapical lesion on a scale of one to five, one and two being healthy and 3-5 being diseased.
Changes in the Periapical index (PAI) have been validated (11, 12) and used for the assessment of healing of periapical lesions using different criteria. Several studies have used PAI for evaluating outcomes in Endodontics. Waltimo et al (34)utilized the changes in PAI score to analyze healing with or without bacterial elimination. Other studies used the PAI score changes in order to study healing in 1 versus 2-visit root canal therapy (35, 36). PAI scoring by blinded evaluators is the most objective way of evaluating healing.

This study was a prospective study with a follow up time of six months (baseline = day of treatment completion, follow up = six months after treatment). The success rate of root canal treatment in cases with periapical lesions at 2-6 years post-operatively is reported as 75-86% (37-40). Since the healing of periapical lesions is still an area of concern in the

field of endodontics and this concern is more prominent for diabetic patients, performing a prospective study on the healing process of periapical lesions based on the HbA1c level would provide new information.

Purpose

The aim of this prospective study was to evaluate the relationship between the HbA1c level and short-term healing of periapical lesions.

Hypothesis

There is a significant negative correlation between HbA1c levels and short term healing of periapical lesions; thus patients with a higher level of HbA1c would display poorer healing of periapical lesions in endodontically treated teeth in a short-term recall than patients with a lower HbA1c level.

Materials and Methods

Research Design

This study was a prospective observational examination of the relationship of glycemia and short-term healing of periapical lesions. After IRB approval, patients were recruited from those who presented for treatment at the Post-Graduate Endodontic Clinic in the School of Dentistry, University of Maryland.

Inclusion Criteria

- Patient must have pulp necrosis (or previous treatment) and a periapical lesion at least 3 mm in diameter (measured by ruler in radiology software), determined by a periapical radiograph, associated with the tooth being treated
- Treatment being provided must be primary RCT or retreatment
- Permanent tooth with closed apices
- Teeth with favorable prognosis at the time of treatment
- Teeth planned for permanent restoration following treatment
- Patient must have well-performed root canal treatment
    - Obturation 0-1mm from the apex in all canals
    - No significant voids in root canal filling
    - No missed canals determined from pre-operative and post-operative periapical film

Exclusion Criteria

- Teeth without a treatment plan for a final restoration
- Patients diagnosed with a malignancy, liver or kidney disease or any other systemic condition that compromises the immune response.
- Patients who present at the recall with a fractured restoration/tooth

All patients received standardized root canal treatment from an endodontic resident for a diagnosis of pulp necrosis (or previous treatment) and asymptomatic or symptomatic apical periodontitis, with or without abscess formation.

Using Power and Precision a power analysis was performed. No prior research has been done on our hypothesis; therefore, in order to run a power analysis the HbA1c levels were dichotomized to a high and low HbA1c groups. The following power analysis was formulated using Power and Precision software (Biostat, Englewood, NJ). The expected pattern of response of the high HbA1c group is Healed (PAI =1) 10 %, Fairly Healed (PAI=2) 15%, Mild Disease (PAI=3) 20%, Moderate Disease (PAI=4) 25% and Severe Disease (PAI=5) 30%. The expected pattern of response of the low HbA1c group is Healed 35%, Fairly Healed 25%, Mild Disease 20%, Moderate Disease 10%, and Severe Disease 10%. Taking into account the mean difference between the groups and the dispersion of response it was determined that our sample size for each group would be 22 subjects.

With a sample of 22 subjects per group we would have had a power of 80%. This means that there is an 80% likelihood that the study will yield a statistically significant effect and allow us to conclude that there is a difference between HbA1c level and change in Periapical index score.

Procedures

Patients presented to the Endodontic Postgraduate Clinic for conventional endodontic treatment and evaluated for inclusion in the study.

Probing depths, clinical attachment level, percussion sensitivity, palpation sensitivity and vitality tests were recorded for each patient. A pre-operative periapical radiograph was taken; if a periapical lesion was visible on the periapical radiograph the patient was given the option to take part in the study. Upon acceptance to participate, the IRB approved consent and HIPAA forms were reviewed and signed.

Periodontal status was classified based on clinical attachment level (CAL) and pocket depth (PD). An epidemiological study by Borrell (41) investigated the CAL and PD at the mesial buccal and mid buccal sites for every tooth in two randomly selected quadrants (1 maxillary and 1 mandibular). They defined "periodontitis" as a dentition with at least 3 sites with CAL $\geq$ 4mm and at least 2 sites with PD $\geq$ 3mm, not necessarily on the same tooth.

An endodontic resident then initiated root canal therapy following a standard protocol under surgical operating microscope. Following anesthesia and rubber dam isolation, access cavity preparation, working length determination using electronic apex locator was performed. Instrumentation using crown down and rotary instruments using Vortex instruments (Tulsa, Dentsply) was done with irrigation using 2.5% NaoCl. After drying the canals using absorbent points, root canal obturation was completed via vertical condensation technique. AH plus sealer was used for obturation. The treating endodontic resident restored all teeth that needed a simple composite or amalgam restorations. If a crown was needed, the tooth received a sterile sponge or polytetrafluoroethylene (PTFE) tape, Cavit and Fuji IX restoration. Cotton pellet was not used since it has been shown inadequate seal that can cause bacterial leakage(42).

Immediately after RCT the patient had a final radiograph taken with a customized stent in place. Bite registration was applied to an XCP, the patient closed their mouth and a reproducible alignment was fabricated(43). These stents were then disinfected and stored until the recall appointment. This stent allowed for a reduction in the magnification factor of periapical images.

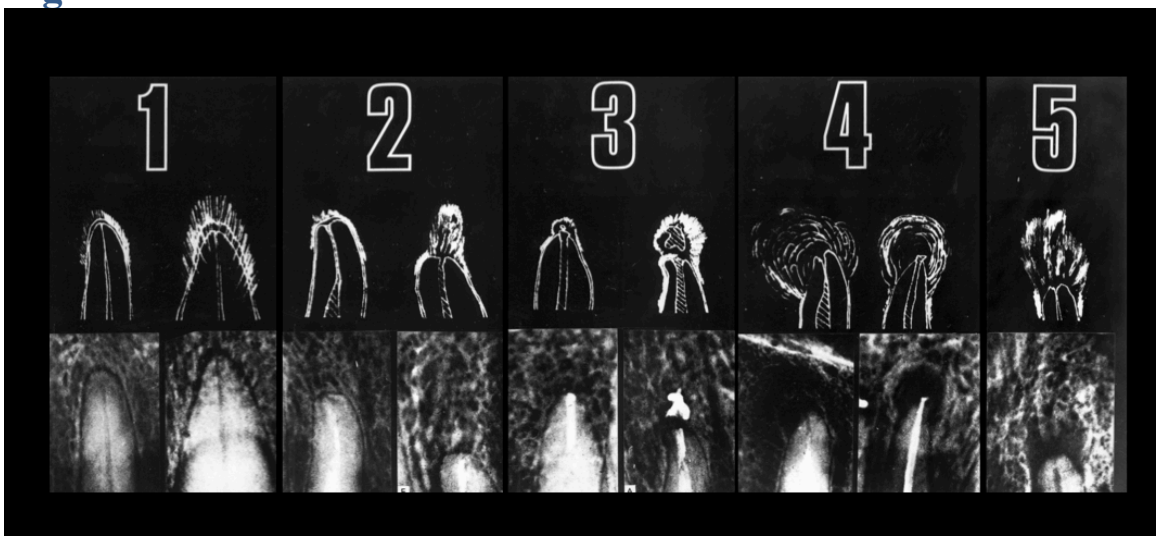
Also after completion of the RCT the patient had blood drawn by a dental school nurse. The blood sample was sent to the University of Maryland Medical System Pathology Laboratory to obtain the patient's HbA1c value. Patients with an HbA1c level of 5.7% or higher were referred to their physicians for further examination and possible diagnosis of diabetes or pre-diabetes.

The patients were called six months after completion of the root canal therapy for a recall examination. Probing depths, clinical attachment level as well as percussion and palpation sensitivity were recorded for the tooth of interest. A periapical radiograph was taken using the previously mentioned radiographic stent. Also, at the time of recall the patient had blood drawn by a dental school nurse. This sample was sent to the University of Maryland Medical System Pathology Laboratory to have the HbA1c determined.

Analysis of Images

Observer calibration was conducted twice using a set of 100 images provided by Dr. Orstavik. Two dentists who were involved in the creation of this system determined the true scores of these images. Each of the observers were given a reference image (Fig 1) and the following written instructions:

Fig 1



1. Find the reference radiograph where the periapical area most closely resembles the periapical area you are studying. Assign the corresponding score to the observed root.
2. When in doubt, assign a higher score.
3. For multi-rooted teeth, use the highest of the scores given to the individual roots.
4. All teeth must be given a score.

The 100 images were analyzed individually by 2 observers (board certified endodontists). Then the author had a brief meeting with each of the observers to review the images that were rated more than one from the true score. Then the observers reviewed the images again a few days after the meeting. The weighted Kappa's were determined before and after calibration when using the true score as reference. The observation of the study radiographs then followed. The quality and type of restoration was masked from the observer, and the order of the images were randomized.

Results

An initial power analysis determined 44 patients were needed for this study,
A total of 21 patients were enrolled and eight patients returned for a recall examination. One patient was excluded due to the observers declaring no radiolucency was present at the start of treatment. For the eight subjects who returned for a recall examination, the average of their initial and recall HbA1c levels were used for analysis. Also the difference in the Initial PAI score and recall PAI score was used to determine the level of healing, a larger negative difference indicating a better healing outcome. The HbA1c levels were dichotomized into 2 groups; HbA1c $\geq$ 5.7 was classified as Pre-Diabetic/Diabetic (Group 1) and HbA1c < 5.7 was classified as Non-Diabetic (Group 2)

Of the 20 enrolled patients, 19 were self reported non-diabetics and one was a self-reported diabetic. Of the self-reported non-diabetics 74% (14/19) had an HbA1c that would classify them as pre-diabetic or diabetic. Out of these 14 patients, 11 fell in the range of pre-diabetic and three fell in the range of diabetic.

After the calibration exercise both observers competence at using the PAI index improved (Table 1). The average weighted kappa after calibration was .66. Similar calibration exercises from other studies resulted in average weighted kappa's of .6 (12) and .59 (36).

Table 1:

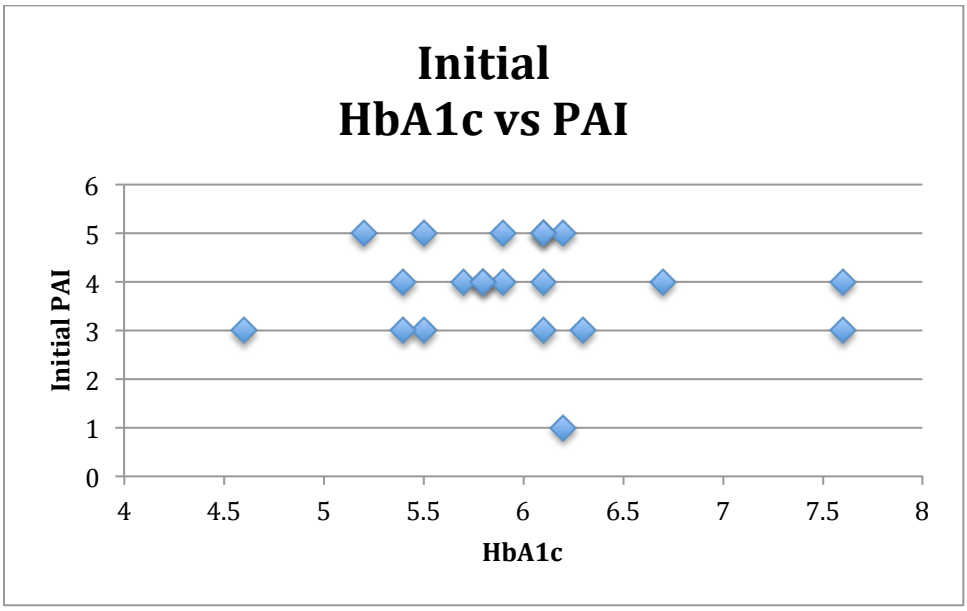
	Pre Calibration	Post Calibration
Observer 1	0.51	0.64
Observer 2	0.62	0.68

Results of initial data

A Pearson's r was completed, correlating the HbA1c and the initial PAI score (N=20).

This showed a correlation of r=-.05 (p=.423; Table 2, Fig2).

Fig 2



Results of recall data

To investigate the rate of healing and how it related to the patients Hba1c levels, another Pearson's r was done with the HbA1c of the recall patients (N=8) and the level of healing (difference in PAI). This correlation was r= -.474 (r^2=-.23, p=.118; Table 1, Fig3). The Post-hoc power analysis was completed using Pearson's r with a correlation of .47. This analysis determined that we needed 23 patients to achieve significance. Even with a small sample size of N=8 the p-value approached significance.

In a second analysis, instead of using HbA1c values, Pre-Diabetic/Diabetic was labeled as group 1 and Non-Diabetic was considered as group 2. These values (N=8) were correlated with the healing rate (difference in PAI score). This showed a correlation of r=-.494 (r^2=.24, p=.107; Table 1).

Fig 3

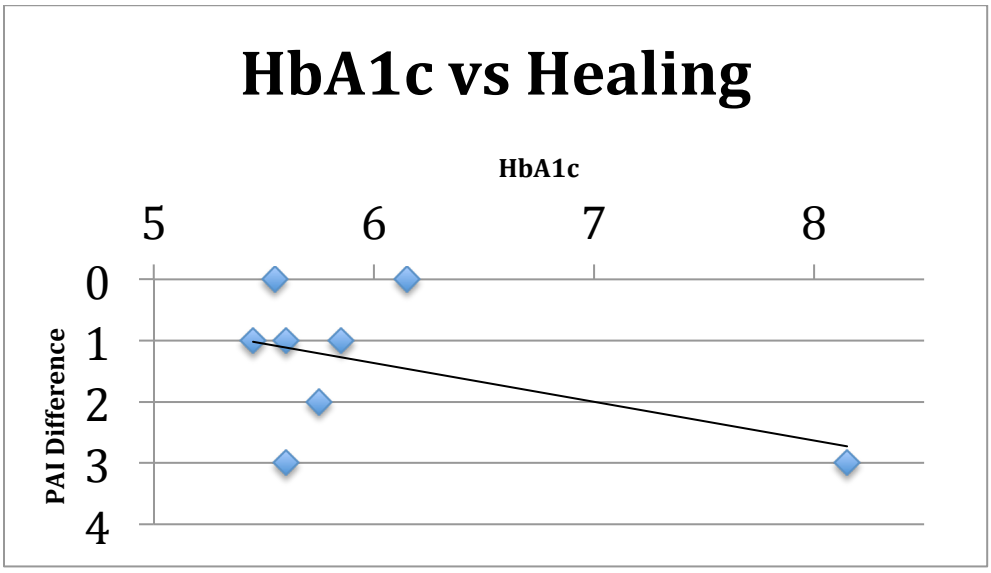


Table 2:

	N	r	r2	P
Patient Recruited	20	0.05	0.006	0.423
Patients who returned for recall	8			
HbA1c		0.474	0.23	0.118
Dichotomized		0.494	0.24	0.107

Results of Healing Data

The cases that reduced in PAI score from 3,4, or 5 to a PAI score of 1,2 were classified as healed and cases which remained at a PAI score of 3,4,5 were classified as not healed. Of the 8 cases 3 were classified as healed and 5 were classified as not healed. The average HbA1c of the healed group was 6.53 and the average of the not healed group was 5.72. The HbA1c difference between the groups was not statistically significant ($F=1.76$, $p=.233$).

Logistic Regression

A logistic regression was attempted. Due to the small sample size (N=8), no combination of these variables (age, gender, race, tooth type, periodontal disease, self-reported diabetic status, CVD, smoking, and days till recall) produced significant results ($p>.05$

Discussion

Our initial power analysis determined we needed 44 patients, however the post-hoc power analysis determined we needed 23 patients. This means we had a stronger correlation than expected and therefore required a smaller sample size to find significant results. The total patients that were recalled were eight; however, the p-value (.118) approached significance.

Pearson's r is reported in the literature, however the r^2 is used as an interpretation between the relationship of HbA1c and difference in PAI. The HbA1c was correlated to difference in PAI ($r=-.474$; $r^2=-.23$). This means that the HbA1c values contributed to 23% of the PAI difference (healing) of each patient.

Initial Data Discussion

Sanchez-Dominguez et al. (27) demonstrated, through a logistic regression on the initial clinical findings, that patients who had an HbA1c ≥ 6.5 showed worse periapical lesions (increased PAI score). Our data showed a very small, non-significant correlation ($r=-.05$, $p=.423$) between initial HbA1c and PAI score, and therefore did not support the significant findings of Sanchez.-Dominguez. The authors believed that initial lesion size depends on the microbial content more so than the patient's host response. The initial HbA1c would affect the host response in endodontic healing. Therefore, no distinct correlation was anticipated when looking at the initial HbA1c and initial PAI scores.

Recall Data Discussion

The sample size of this study was only 8 patients however a negative correlation (r=-.474, p=.118) between healing and HbA1c levels was present. This means that patients with higher levels of HbA1c showed the lower level of healing. The current study supports the findings of Cheraskin and Ringsdorf. Their study found that patients with lower blood glucose levels showed better endodontic healing outcomes compared to patients with higher blood glucose levels. While they did not have the benefit of using HbA1c , their use of blood sugar was still important.

Our results showed that the patients with higher HbA1c levels showed lower levels of healing. This might be because the patients with lower HbA1c levels may be more conscious about their health including better diet and more exercise. Exercise and good diet have been related to better periodontal conditions (44). Although no direct link has been reported between diet and exercise with endodontic disease, such relationship may exist.

Dichotomizing the patient into two groups had a similar correlation to using the patient's HbA1c values on a continuous scale (r=-.49 vs. r=-.47). This was surprising, since lowering the level of data from measured data (HbA1c) to categorical data (Pre-Diabetic/Diabetic and Non-Diabetic) would expect a lower correlation, however the correlations were similar. The difference between .49 and .47 is not clinically meaningful; both values emphasize a strong relationsh
ip between HbA1c and healing.

Discussion of Healing Data

The average HbA1c of the not healed group was lower than the healed group (HbA1c = 5.72 vs. 6.53). This was not expected as we hypothesized that the lower HbA1c group would demonstrate better healing. There was one case in the healed group that had an average HbA1c of 8.15. This represented an outlier in the data set, which can be an explanation for why the data was not as expected. Also, the difference between the groups was not statistically significant ($F=1.755$, $p=.233$), this can be due to the small sample size and one significant outlier.

The large percentage (74%) of self reported non-diabetics who fell in the pre-diabetic/diabetic range might be attributed to the area of the country from which the study population was collected. In Baltimore city, approximately 63.7% of the population is African American(45). The CDC has reported that diabetes is most prevalent in this race(46). Therefore our sample may not reflect the population as a whole.

Study Limitations

The sample size was the main limitation in this study. The post-hoc analysis showed that an additional 15 patients were required to provide significant results. A recall rate (N=8) of 38% was very low, despite the fact that each recall patient was offered a financial incentive ($70) to cover his or her transportation and time costs. The financial incentive

was mentioned at the initial appointment and again after sixp months when the first author called to schedule the recall appointment.

Another limitation was the time difference between the patient's HbA1c tests. HbA1c displays plasma glucose concentration over 90 days. In the present study the tests were completed over a minimum of 180 days. Although there were no marked differences between the HbA1c at the time of treatment and recall for any of the 8 patients, a third HbA1c test 90 days after treatment may have provided a better idea of the patient's glycemic status.

In our study the use of HbA1c was chosen to represent the patients average plasma glucose over a span of approximately 90 days. However, the use of HbA1c is questionable when diagnosing diabetes. HbA1c represents the glycation of proteins in the blood, which secondarily results in high blood glucose. In medicine, looking at the primary increase in blood glucose is emphasized more than the transient response of blood glucose due to glycation of proteins (20). Therefore, a high A1c is observed after blood glucose is already high, resulting in a delay in diagnosis compared to blood glucose assessment. There is also an increased risk of misdiagnosis in patients with end-stage renal disease or heavy alcohol consumption(47). For our purposes, the HbA1c was used because it was the best method to determine the patients average glycemic control over a long period of time rather than a single fasting blood glucose or oral glucose tolerance test value.

Future Directions

The PAI index has been validated (11, 12) and used for healing outcome studies (35, 36). There is no study using PAI score for measurement of a lesion's volume. The volume of a lesion should more accurately represent the initial size and level of healing.

The use of the Cone Beam Computed Tomography (CBCT) has increased tremendously in the field of dentistry. Paula-Silva (48) examined the imaging results of Periapical radiography and CBCT imaging while using histopathology as the gold standard when identifying presence of a lesion. Their results showed that diagnoses based on CBCT scans were more accurate compared to those of periapical radiographs ($p=0.028$)(49). This study demonstrated that analyzing healing via a CBCT is currently accepted to have a higher sensitivity and specificity than periapical radiography.

If the current study was to be redone using CBCT imaging at time of treatment and at a recall exam, this might provide a better assessment of the level of healing.

Conclusion

Among adult self-reported non-diabetic endodontic patients, 74% had HbA1c in the diabetes or pre-diabetes ranges. Although there was a negative correlation between HbA1c level and the level of healing of periapical lesion, this correlation was not significant.

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