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Original Research

In Office Gingival Crevicular Blood Glucose Monitoring In Diabetic Patients

Dr. Harpreet Kaur Narula[1], Dr. Jasvinder Singh Narula[2], Dr. Vipin Bharti[3], Dr. Harinder Gupta[4]

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Affiliation:

1. Reader, Department Of Periodontology and Oral Implantology, Yamuna Institute of Dental Sciences and Research, Gadhouli, Yamunanagar, India.
2. Professor and Head, Department OfPeriodontology and Oral ImplantologyYamuna Institute of Dental Sciences and Research, Gadhouli, Yamunanagar, India.
3. Principal, Professor & Head, Department of Periodontolgy, Government Dental College & Hospital, Patiala, Punjab, India.
4. Professor and Head, Department of Periodontology, Government Dental College & Hospital, Amritsar, Punjab, India

Corresponding author:

Dr. Harpreet Kaur Narula

Email:narulas@hotmail.com

ABSTRACT

Background – Diabetes Mellitus (DM) remains undiagnosed in approximately half of the patients actually suffering from the disease. In addition, the prevalence of DM is more than twice as high in patients with periodontitis as compared to periodontally healthy subjects. These patients do come for periodontal examination and treatment in dental office setup.

Objective – To test the feasibility of using gingival crevicular blood (GCB) collected during routine periodontal examination to estimate blood glucose levels using a self monitoring device (Glucometer).

Material & Method– During routine periodontal examination, 15 patients with history of Type II DM had gingival crevicular whole blood from periodontal probing collected in a blunt insulin syringe which was transferred to a novel and highly sensitive self monitoringdevice (ReliOn™). At the same time venous blood was collected from patients arm for measurement in a laboratory glucose analyzer. Each laboratory measurement (serum glucose value) was converted to a whole blood glucose value by a function of patient's hematocrit. This corrected glucose valueallowed direct comparison of the laboratory measurement to the intraoral whole blood measurement.

Results – The gingival crevicular blood exhibited a correlation (r) of 0.959 ($p < 0.0001$) to the corrected laboratory standard measurement. The American Diabetic Association recommends that the prediction error of blood glucose monitoring device fall within 15% of the laboratory standard. Using this criteria, 92% of the gingival crevicular measurements fell within 15% of the laboratory value.

Conclusion – The results suggested that blood oozing during routine periodontal examination may be used for monitoring blood glucose levels in known DM cases as well as for DM screening in a dental office setting.

Keywords–Blood Glucose levels, Diabetes mellitus, Gingival crevicular blood, Hematocrit, Periodontal probing

INTRODUCTION

Diabetes Mellitus (DM) is a metabolic disease with

disturbances in the intrinsic production and action of insulin leading to abnormal fat, sugar, protein metabolism. It is characterized by chronic hyperglycemia (high blood glucose levels). DM is one of the most important risk factors for destructive periodontal disease.[1]DM significantly impacts the periodontium producing a number of effects including change in subgingival microbiota, gingival crevicular fluid glucose levels, periodontal vasculature, host response (neutrophil chemotaxis defects) and collagen metabolism.[2]Infact, periodontal disease is considered to be the sixth complication of diabetes. Certain microorganisms in dental plaque are considered to be the main cause of destructive periodontal disease but ignoring established risk factors like smoking or DM would most probably lead to therapeutic failure.[3]

Successful periodontal therapy in diabetic patients must include the stabilization of blood glucose to a near normal range. However, stable blood glucose levels alone will not reduce the degree of periodontal inflammation, unless bacterial etiology of periodontal disease is also treated.[4]

The periodontist frequently manages diabetic patients using limited information about their blood glucose control. The only information available is from a single laboratory test that may not reflect their current blood glucose status. The introduction of self monitoring provided diabetic patients with a simple method for rapid daily monitoring of their disease.

Self-monitoring uses one drop of finger puncture whole blood placed on a test strip impregnated with glucose oxidase, peroxidase as a color indicator. After timing on the reaction strip, the blood is wiped off leaving a shade of color that is similar to the blood glucose concentration.[5]

Originally, the test strip's color was compared to a color chart that estimated the glucose concentration by 40 to 80 mg/dl increments. Later, electronic self monitor replaced the color charts. These new devices optically read color changes on similar test strips with discrimination to the nearest 1mg/dl. This enables diabetic patients to have blood glucose measurements with better accuracy several times each day.[6]

The most recent innovations in self monitoring are instruments that no longer require the patients to time and then wipe blood off the test strip before measurement. The Reli On blood glucose testing system has been developed to allow rapid measurement of blood glucose (D- Glucose) by using an electrochemical detection technique.

Periodontal inflammation with or without the complicating factor of DM is known to produce ample extravasated blood during diagnostic procedures such as periodontal probing.[7]Routine probing during a periodontal examination is more familiar to the practitioner and less traumatic than a more sensitive and painful finger puncture with a sharp lancet. It is possible that gingival crevicular blood from probing may be an excellent source of blood for glucometric analysis using technology of portable glucose monitor. This might be of considerable interest to the dental practitioner since this method if sufficiently accurate, could be a simple and relatively inexpensive in office screening device for monitoring blood glucose levels in known diabetics and for screening patients suspected to have diabetes.

The purpose of this investigation was to:

1. Compare crevicular blood glucose measurements to a standard laboratory venous blood glucose measurement so as to promote it'sin office use, if comparison falls within laboratory standard.
2. Use it as a method for monitoring current blood glucose status in known diabetic patients before starting and during subsequent periodontal therapy.
3. Use it as a method for suspected diabetes screening in patients reporting for routine periodontal examination.

MATERIALS AND METHODS

Materials used were

- Blunt tip insulin syringe (blunted with sterile bur)
- Glucose meter
- Hematocrit measurement
- Laboratory serum glucose measurement.

STUDY POPULATION

A total of non fasting 15 subjects, 7 males and 8 females with age range between 35 to 60 years suffering from Type II DM were selected for the study from those attending OPD of Periodontology at Government Dental College and Hospital, Patiala. All the subjects were diagnosed as suffering from Generalized Chronic Periodontitis, with the requirement that the subjects have atleast one tooth that bled upon periodontal probing.

Exclusion criteria included:-

1. Any bleeding disorder
2. Any medication interfering with the coagulation system
3. Severe systemic disease such as cardiovascular, renal, hepatic or immunological disorders.
4. Current treatment for anemia, polycythemia, gout, dialysis or any other disorder that can cause an abnormally high or low hematocrit.

As the hematocrit value is used in this study, it has been seen that low hematocrit (<30%) may yield a falsely higher result and one with a hematocrit greater than 55% may yield a falsely lower result. Salicylate (aspirin) at toxic levels and severely dehydrated or hypotensive patients may yield falsely lower results.

PROCEDURE

1. Measuring gingival crevicular blood glucose (whole blood)

The Reli On blood glucose testing system (glucometer) based on electrochemical detection technique is used (Fig-1). This biosensor system employs a disposable dry reagent strip technology, based upon the glucose oxidase method for glucose determination. The glucose oxidase (Aspergillusniger) catalyzes the oxidation of glucose in the drop to produce gluconic acid. During the reaction electrons are transferred by an electrochemical mediator to the test strip surface. This in turn generates a current that is measured by the *ReliOn* blood glucose monitor. The size of the current generated is proportional to the amount of glucose present in the blood drop, thus giving an accurate reading of the blood glucose concentration. Each patient was examined intraorally for any sign of periodontal inflammation. Area which seemed inflamed was noticed and isolated with gauze to avoid dilution of blood with saliva. Periodontal probing using standard force, was done in order to know attachment loss and bleeding on probing. A small blood sample of about a drop was collected in an insulin syringe with its needle tip blunted with a sterile/disinfected bur (to prevent pocket wall injury). The needle tip was kept inside the sulcus inorder to obtain whole blood from crevice/pocket (Fig-2). The blood was then placed on circular chemically reactive surface of test strip placed on glucometer. The blood glucose reading on glucose self monitoring device was recorded (Fig-3).

2. Measuring plasma glucose and hematocrit

Venous blood sample was then drawn from patient's antecubital fossa for measurement of serum (plasma) glucose and hematocrit (PCV) in the laboratory. All these measurements are done on the sameday one after the other (Fig-4 & Fig-5)

Hematocrit (Packed cell volume, PCV) is the percentage of blood volume occupied by RBC. This measurement is important because the glucose meter measures whole blood glucose whereas reference laboratory instrument measures glucose in remaining plasma after separation. Hematocrit is used to convert the reference laboratory measurement (plasma glucose) to whole blood glucose value. This corrected laboratory value is now considered the true value of blood glucose and allows for direct comparison of gingival crevicular blood glucose with true laboratory value of blood glucose.

Figure -1: Glucometer - The ReliOn Blood glucose testing system

Figure -2: Insulin syringe needle tip inside the sulcus in order to obtain whole blood

Figure -3: Blood placed on circular chemically reactive surface of test strip placed on glucometer.

Figure -4: Venous blood sample drawn from patient's antecubital fossa

Figure-5 : Measurement of serum (plasma) glucose and hematocrit (PCV) in the laboratory.

RESULTS

Measurements from laboratory glucose analyzer are considered to be the true value for glucose concentration. In laboratory, RBC's were removed and remaining plasma was analyzed for glucose concentration. The two measurements (Lab plasma glucose and hematocrit) are equated by knowing percentage of volume occupied by RBC's.

Hematocrit corrected venous glucose (mg/dl) =Lab(mg/dl) × [1.0 – (0.0024 × Hct)]

Correlation Relationships

Coefficient of correlation (r) was calculated using the corrected venous glucose measurements as the true values for blood glucose. The gingival crevicular blood glucose measurement was correlated to the corrected venous glucose measurements. ($r = 0.959, p < 0.0001$)

Regression Analysis

Regression analysis was calculated for the mean gingival crevicular measurement versus the corrected laboratory venous blood measurements. By using the linear regression data, the predictability of gingival crevicular value in an individual patient can be determined. The coefficient of determination was found to be 0.92. The regression line shows 92% of total regression.(Fig-6, Fig -7)

Unpaired t-test

Significance of difference in means was done by unpaired t-test ($t=0.691$; $p=0.495$). This shows no significant variation between means of gingival cevicular blood glucose and lab values.

Fig. - 6 : Comparison of reference glucose values (Lab Value) and gingival crevicular blood glucose Values (Gum Value)

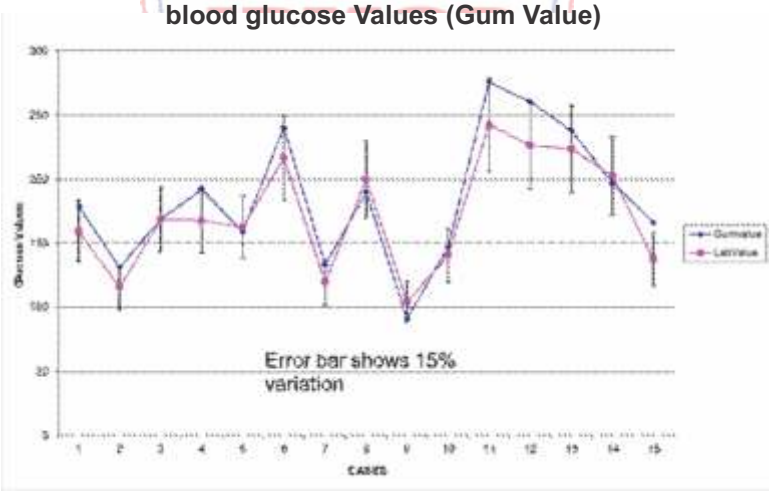
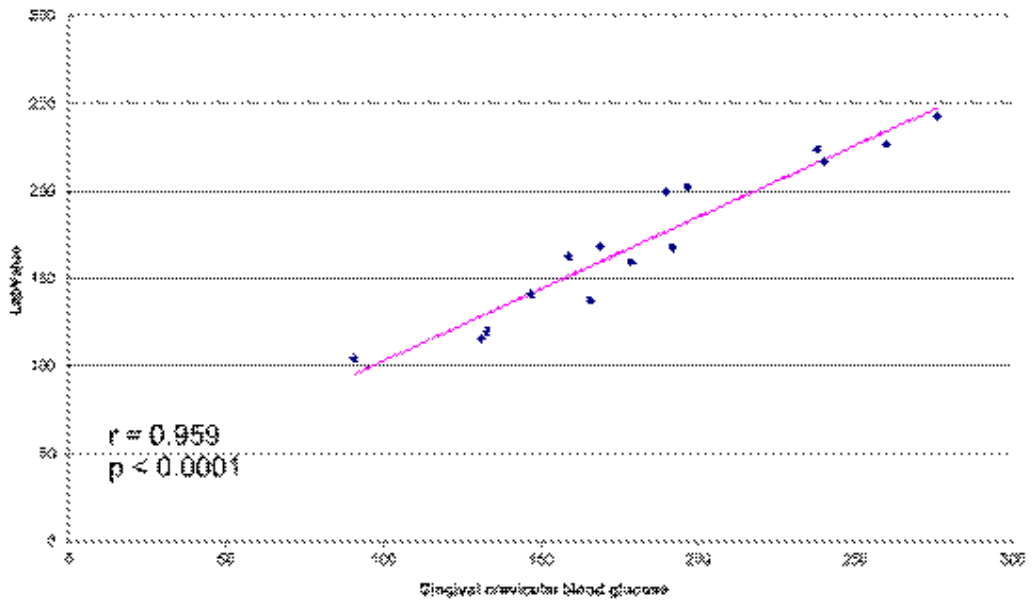


Fig. - 7 : correiation between gingiva crevicular blood glucose value and reference labortary blood glucose value (Lab Value)



DISCUSSION

In this study a new technique was devised for sampling gingival crevicular blood, using a blunt insulin syringe and tip blunted with a sterile bur. The insulin syringe transferred the blood onto a test strip for glucose measurement in a glucose self monitor. Isolating bleeding gingival site with cotton gauze and then rapidly sampling blood with the syringe is an improvement over other methods used in the past intraoral blood glucose studies by Stein Nebbia[8] and Tsutsui et al.[9]They transferred the blood glucose onto the test strip either by wiping blood directly from hemorrhagic gingival tissue with the test strip itself or by rubbing blood onto the test strip from blood ladened dental curette. Hence manual timing of the the test strip reaction and the wiping of the test strip have been identified as the significant sources of error when using glucose self monitors. These sources of error are reduced by using the glucose self monitors, which is self timing and requires no wiping.[10]

Significant contamination may occur from saliva and oral debris present at the wiped gingival area or from plaque and crevicular fluid on the dental curette from its entry into the gingival sulcus. Using the blunt insulin syringe eliminated contamination from saliva, plaque and debris by collecting free flowing blood just inside the gingival crevice. In the past,plastics pipettes have also been used for the collection of gingival crevicular blood. Limited flexibility of pipettes, inappropriate length and diameter of tip, variable force applied to create vaccum pressure are certain limitations that led to the use of blunted insulin syringe in this study as innovative methodology of gingival crevicular blood collection It is suspected that this change of blood collection methodology has the greatest positive effect on the correlation in this study.

Self-monitoring of blood glucose concentration has advanced over the past few years. Glucose values determined by glucometer correlate well with laboratory results. Because of the importance of precision and accuracy of self monitoring blood glucose devices, guidelines for the performance of these devices were recommended in 1987 by the American Diabetes Association(ADA). An ADA consensus conference concluded that the prediction error of blood glucose

monitoring devices should be within 15% of the reference value. Clinically, analytic precision to 20% is considered acceptable. The major error component is the user error, which includes the volume of blood droplet, the accuracy with which the blood drop is placed on the strip, use of test strip after expiry date, timing and effect of temperature and humidity on signal generating reaction etc. The analytic performance of the instrument is important too. The glucometer used in this study had an accuracy profile when used at temperature of 18-30 degree centigrade and at humidity if 20-80% and had self tested correlation of 0.979 with laboratory analyzer.

As glucometer provide instantaneous assessment of blood glucose, they are highly beneficial in the dental office environment. Glucometer monitoring is recommended in hypoglycemic prone patients who may not experience early warning signs along with avoidance of severe hypoglycemia.Patients with blood glucose levels at or below lower end of normal before procedures may become hypoglycemic intraoperatively,hence preoperative and emergency management can be done at the same time.Glucometer used in this study has a measuring range of 20-600mg/dl (1.1 to 3.3 mmol/l).As the prediction error of available glucometer should be within + 15%. The usual hypoglycemic symptoms presented by the patients along with glucometer reading may lead to little uncertainty about the reading presenting as “true positive” and little harm done if it is “false positive”.Random blood glucose is considered in this study owing to highly sensitive and technically advanced usage of glucose self monitoring device. It is known by glucose tolerance test that the preprandial and 2 hour postprandial blood glucose levels are quite similar.Known diabetic patients were examined in nonfasting state as random blood glucose is more feasible while diagnosing and treating diabetic patients who most often should come to dental clinic in fed state.Patients undergoing insulin therapy need to be monitored for in-office gingival crevicular blood glucose during periodontal diagnostic, therapeutic and maintenance phase quite often in non-fasting state.

In this study,hematocrit is used to convert the plasma glucose to whole blood glucose.Though hematocrit of venous blood is slightly more than capillary, this difference causes negligible change in viscosity and blood glucose levels in both capillary and vein.Lock et al found that hemoglobin concentration and hematocrit were found to be significantly higher in capillary blood of forearm than in fingertip but the percent of glucose difference between capillary forearm and fingertip was statistically insignificant in non-fasting subjects. No correlation was observed between an individual's hematocrit bias and his/her % of glucose difference as measured by glucometer. Karon B S et al in their study comparing glucometer measured capillary, arterial and venous whole blood glucose levels correlate most closely with laboratory plasma glucose levels in patients receiving intravenous insulin therapy after cardiac surgery

In this study, the glucose measurements of gingival crevicular blood using a self monitor was compared to corrected venous blood measurements using the glucose analyzer. Since the corrected laboratory measurement is considered to be true (or reference) blood glucose value, its comparison to gingival crevicular blood measurements allows the evaluation of accuracy and precision of blood collecting technique and of the self monitoring device. In this study, there was a very strong correlation between the glucose self monitor measurements and the corrected venous glucose measurements. It is noted that crevicular fluid contamination dilutes the glucose concentration producing consistently lower measurements by an average of 4mg/dl. Also, the glucose concentration drops by an average of 3.5mg/dl due to glycolysis that occurs between the capillary and venous blood. The glycolysis correction is not normally taken into account clinically such that average drop in crevicular blood glucose concentration can be ignored.[7]In a study by Khader

YS et al, almost perfect positive correlation between gingival crevicular whole blood glucose and finger puncture whole blood glucose was present suggesting negligible effect of GCF on gingival crevicular blood.In healthy situations glucose levels in GCF is considerably 9 times lower than blood glucose levels and only half time lower than blood glucose in periodontitis subjects.Although the gingival crevicular blood glucose is three times more than that of serum, the amount of GCF (0.0005 ml) is small enough to affect the glucose concentration of gingival crevicular blood after probing (0.16 ml or more).

When a precise reference measurement is available (as in case the laboratory glucose analyzer), using the correlation alone may be considered a poor method to evaluate performance of measuring device or method. In this study, there was a strong correlation between the glucose self monitor measurements and corrected venous glucose measurements. The interest of this study however is in finding the predictability of a single measurement on one patient. Perfect correlation for individual measurement has good clinical significance than the correlation of the whole group.

The result evaluated by the root mean square of the prediction error showed moderate precision for all the self monitor blood glucose measurements. Prediction error is often presented in terms of percentage of the true (or reference) value. An American Diabetes association (ADA) consensus conference concluded that the prediction error of blood glucose monitoring devices should be within 15 % of the reference value. Using this criteria, 92% of the gingival crevicular measurements fall within 15% of the laboratory value.[7]

The clinical application of these findings involves the interrelationship of diabetes mellitus and periodontal disease. Successful resolution of periodontal inflammation in patients suffering from specifically uncontrolled diabetes mellitus involves both improvement in periodontal health and stabilization of blood glucose. Since periodontal treatment often continues from months to years, a single blood glucose report is not sufficient for periodontal management. Whether patient needs to be put on antibiotic therapy, oral hypoglycemic or instructed for diet control and exercise are the major criterias that should be in the knowledge of a periodontist at each visit of the patient for the successful outcome of the periodontal treatment. The periodontist referral to patient's physician regarding diabetic control can positively influence the outcome of treatment for both diabetes mellitus and periodontitis.

The majority of periodontal therapy produces extravasated blood from the gingival crevice due to inflammation. Using the method described in this study, the periodontal therapist can rapidly measure blood glucose many times using the gingival crevicular blood. Multiple measurements of a diabetic patient's blood glucose levels allows the periodontist to better assess the patient's diabetic control as the treatment progresses.

CONCLUSION

Within the limitations of this investigation, the following conclusions can be made:

1. The use of the insulin syringe (tip blunted with sterile bur) is a reliable method for sampling gingival crevicular blood and delivering the blood for testing in the non wipe glucose self monitor.
2. There was a statistically significant correlation (P) between gingival crevicular blood glucose measured by glucose self monitor and venous blood glucose measured by a reference laboratory analyzer.
3. 92% of the gingival crevicular blood glucose measurements were within 15% of the true glucose concentration.
4. The results of this study suggest that gingival crevicular blood can provide an acceptable source for measuring blood glucose in the study's specific glucose self monitor.

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