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Comparative evaluation of Plasma glucose and salivary glucose in Type 2 Diabetes Mellitus patients

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Abstract

Aim: To determine whether salivary glucose levels could be used as a noninvasive tool to monitor glycemic status in Type 2 Diabetes mellitus

Materials and Methods: 120 study subjects were selected from outpatient Department of Diabetic Centre, Tellicherry, Kerala. 80 Type 2 Diabetes mellitus patients were enrolled in the study and were divided into two groups based on the level of plasma glucose. 40 healthy age matched subjects were included in the study. Plasma glucose levels and salivary glucose levels were estimated using glucose oxidase peroxidase method.

Results: The results were analyzed using chi square test followed by a post hoc procedure, Multivariate ANOVA and correlations using Pearson coefficient.Statistically significant ($p<0.01$) correlation was obtained between random plasma glucose and unstimulated whole salivary glucose levels in Type 2 uncontrolled DM group.

Conclusion: Salivary glucose level reflect the random plasma glucose level when the plasma glucose levels are high which confirms the effects of diabetic membranopathy leading to raised percolation of glucose from blood to saliva thus altering the salivary composition.

Keywords: Diabetes Mellitus, Plasma glucose, salivary glucose.

Introduction

Diabetes mellitus is a clinically and genetically assorted group of ailments affecting the metabolism of carbohydrates, lipids and proteins.[1] It is one of the most common endocrine diseasesdistressingthe almost 6% of the world's population with majority having Type 2 Diabetes Mellitus.

Currently we have 40.9 million people suffering from Diabetes and the projected estimate by the year 2025 is around 70 million.[3]In Diabetes Mellitus an important aspect of glycemic control is steady monitoring of blood glucose. The current measures result in pain and uneasiness to the patient.[4]Research has been enduring in the past two to three decades for substitute methodologies which includeintegrating various other body fluids. This could provide aperception for the potentials of them being used as an auxiliary for blood for diagnostic purposes.For the past two decades salivary diagnostic approaches have been developed to monitor oral diseases such as periodontal diseases and to assess caries risk. Recently the combination of emerging biotechnologies and salivary diagnostics has protracted the range of saliva-based diagnostics from the oral cavity to the whole physiologic system as most composites found in blood also exist in saliva.[5]

For many years the query of presence of glucose in saliva has been a subject of discussion. Studies have shown both positive and negative association between plasma glucose and salivary glucose. Salivary estimation of glucose is mainly investigated because of its simple and noninvasive method of collection of the sample. The interest has been increasing recently in noninvasive diagnostic testing.

As saliva is an ultrafiltrate of blood, evaluations based on salivary constituents have already made substantial roads into diagnosis.So, this study explores the possibility of using saliva to reflect the glucose concentration in blood and thereby making estimation of blood glucose noninvasive.

Materials and Methods

Objective of the study was to estimate plasma glucose and unstimulated whole salivary glucose enzymatically using GOD-POD method by Digital photo colorimeter, to detect salivary pH levels in diabetic and non-diabetic subjects and to judge any relationship between the salivary and blood glucose.

Study population and data source

The study subjects were selected from outpatient Department of Diabetic Centre, Tellicherry, Kerala. 80 Type 2 Diabetes mellitus patients and 40 control subjects in the age group of 30-60 years were selected after taking informed consent from each patient. Study subjects were divided into two groups based on the level of plasma glucose level.

Each group comprised of 40 subjects:

Group1: Patients with random plasma glucose level >120mg/dl &<200mg/dl

Group 2: Patients with random plasma glucose level >200mg/dl

Control group: comprised 40 non diabetic subjects of comparable age and gender Patients with Type 2 Diabetes Mellitus having blood glucose levels as per the criteria established by the expert committee on diagnosis and classification of Diabetes Mellitus 2005. (Symptoms of diabetes + random non fasting plasma glucose levels less than 200mg/dl and more than 120mg/dl for controlled diabetes and more than 200mg/dl for uncontrolled diabetes) were included.

Patients with other systemic diseases like patients with hyperthyroidism, severe diabetic complications who are hospitalized, Pregnancy, Chronic kidney failure, Heart attack /stroke, Cushing syndrome, Acromegaly, Pancreatitis & pancreatic cancer, Patients on medications Steroids, Tricyclic antidepressants, Epinephrine, Diuretics etc. were also excluded.

Blood samples were collected from the median cephalic vein of the forearm of the subjects. The samples were immediately transferred into 2ml non vacuum fluoride oxalate blood collection tube and the test tube was gently twisted for complete mixing. The samples were centrifuged at 20rpm for 5 minutes. 10 microliters of the plasma sample were drawn in a micropipette and was added to 1ml test reagent in a cuvette and incubated at 37degree Celsius for 10 minutes. Absorbance values were recorded using semi-automated analyzer. Un-stimulated salivary samples were collected by suction method. 10 microliters of the sample were mixed with the test reagent in 1:3 ratio and incubated for 37degree Celsius for 5minutes. Absorbance values of sample are measured in a semi-automated analyzer.

Salivary glucose estimation was done using the formula

$$\text{Salivary glucose in mg/dl} = \frac{\text{Absorbance of sample X concentration of the sample}}{\text{Absorbance of standard}}$$

Statistical analysis: SPSS for Windows (version 16.0) was used for statistical analysis. Statistical analysis was done using chi square test followed by a post hoc procedure, Multivariate ANOVA and Correlations using Pearson coefficient. Concentration of the standard glucose was 100mg/dl.

Results

In the present study, a total of 120 subjects of which 40 Type 2 controlled, 40 uncontrolled DM and 40 healthy controls were included. Random plasma Glucose and UWSG levels were estimated and correlations between these were assessed in 30-60-year age group along with salivary pH.

The mean plasma glucose in the control group, controlled diabetes and uncontrolled diabetes were 96.25mg/dl, 158.82mg/dl and 286.05mg/dl respectively. (Table 1)The mean plasma glucose levels were higher in both the study groups (more in uncontrolled Type 2 Diabetics) compared to control group. The mean unstimulated whole salivary glucose levels in the control group, controlled diabetes and uncontrolled diabetes were 3.648mg/dl, 5.408mg/dl and 6.672 mg/dl respectively (Table 2). The mean salivary glucose levels were higher in the study group consisting of Type 2 Diabetics when compared to the control group.

The Pearson correlation between Random plasma glucose and unstimulated whole salivary glucose levels were found to be statistically highly significant ($P< 0.01$) in both the control group (Table 3) and uncontrolled diabetes group (Table 5). However, it was found to be statistically insignificant in controlled diabetes group (Table 4). Following were the key result of the study.

- Statistically significant ($p<0.01$) correlation was obtained between random plasma glucose and unstimulated whole salivary glucose levels in healthy control.
- Statistically significant ($p<0.01$) correlation was obtained between random plasma glucose and unstimulated whole salivary glucose levels in Type 2 uncontrolled DM group.
- Statistically insignificant ($p>0.01$) correlation was obtained between randomplasma glucose and

unstimulated whole salivary glucose levels in Type 2 controlled DM

Discussion

According to American Dental Association (ADA) a fasting glucose more than 126 mg/dl or a random glucose or post oral glucose challenge value more than 200 mg/dl meet criteria for diabetes. A major challenge in dealing with the burden of diabetes is inability to easily and conveniently detect diabetes in population due to lack of noninvasive tests. Routine blood examination for glucose assessment can be traumatizing to the patient, hence other alternatives have been explored. Various body fluids like saliva, tear and sweat have been explored for the estimation of glucose levels in DM of which salivary diagnostic approaches have been developed recently. Unlike whole blood, saliva is easy to collect, less painful to patient and is less infectious to the health care provider. Successful development of salivary testing for diabetes will have a significant impact on the effective management of this critical public health crisis. Various other body fluids like tear, sweat have been explored for estimation of glucose levels in Type 2 DM. However, more research studies are necessary in using these as diagnostic fluids in estimating glucose levels in Diabetics.[6] It has been long recognized that saliva serves as a mirror of body's health as it contains proteins, antibodies and other molecules that are frequently measured in standard blood test to monitor health and disease.[7]

Studies in the past have used different methodologies for the assessment of unstimulated salivary glucose and random blood glucose. In the present study plasma glucose levels were estimated using the glucose oxidase peroxidase methodin accordance with studies done by shehlan amer et al.[8]

In the present study random plasma glucose levels in controlled, uncontrolled Type 2 DM and healthy controls were 158.82mg/dl, 286.05mg/dl and 96.25mg/dl respectively. In the present study correlation between random plasma glucose and unstimulated salivary glucose levels were assessed in controlled and uncontrolled type 2 Diabetes Mellitus. A statistically highly significant correlation ($P<0.01$) was observed between random plasma glucose and unstimulated salivary glucose levels in uncontrolled diabetes mellitus subjects. This correlates with study done by Radhika S et al,[9]however statistically significant correlation was not observed between random plasma glucose and unstimulated salivary glucose levels in controlled Diabetes Mellitus. Correlation between random plasma glucose and unstimulated salivary glucose levels in uncontrolled diabetes could be due to leakage of glucose from blood across the basement membrane of salivary glands especially the parotid glands. Saliva samples collected in the present study represent whole mouth fluid and therefore reflects glucose levels not only due to leakage across basement membrane of major and minor salivary glands but also from the gingival crevicular fluid. Recognition that salivary glucose exhibits a threshold response can aid in the interpretation of the diagnostic potential of salivary glucose. First, it means that salivary glucose levels are likely to be useful only for diagnosis of high glucose conditions. It is commonly reported in the salivary glucose literature that there is a significant correlation between plasma and salivary glucose levels under conditions in which hyperglycemia is expected, such as in subjects with uncontrolled diabetes, but that there is little or no correlation under conditions where hyperglycemia may not be expected, such as in healthy subjects and in patients with controlled diabetes.

This fact becomes understandable if blood glucose levels are at or below the value of the salivary glucose concentration threshold. [10]

Considering the limited amount of studies that evaluate the concentration of glucose in saliva and the controversy that exists in relationship between the salivary glucose and glycemia, we have proposed this study to determine the concentration of salivary glucose comparing it with plasma glucose in Type 2 diabetes patients. In the present study, a total of 120 subjects of which 40 Type 2 controlled, 40 uncontrolled DM and 40 healthy controls were included. Random plasma Glucose and UWSG levels were estimated and correlations between these were assessed in 30-60-year age group along with salivary pH.

Unstimulated Whole Salivary Glucose

Reagents used in estimation of salivary glucose are generally GOD-POD/ GOD-PAP and Hexokinase. In the present study Unstimulated whole salivary glucose (UWSG) was estimated using GOD-POD method and a semi-automated analyser. In the present study unstimulated salivary glucose levels were significantly ($P<0.01$) higher in the Type 2 uncontrolled DM than the healthy subjects. The mean UWSG levels in control, controlled and uncontrolled diabetes subjects were 3.648mg/dl, 5. 408.mg/dl and 6.672mg/dl respectively. Similarly, significant difference in salivary glucose levels between Type 2 DM and controls were observed by various other authors. Carolina A ***et*** al in his study noted salivary glucose levels of 14.03 ±16.76mg/dl and 6.35 ± 6.02mg/dl in diabetics and controls. [11]

Campbell MJA estimated salivary glucose levels in both diabetic and control subjects which were 0.44 ± 6.33mg/dl and 0.24± 3.33mg/dl[18] respectively. [12]Bakianian V et al also compared the salivary glucose levels in diabetic and control group which was found to be 18.67 ± 16.5mg/dl and 15.61 ± 9.10mg/dl [13]and Sreedevi et al have shown the salivary glucose values of 3.10 ± 1.04mg/dl and 1.0 ± 0.1mg/dl in diabetic and control subjects.[1]

Even though varying levels of salivary glucose was observed in these studies they seem to reflect the blood glucose levels respectively. However, the study done by Amer S et al.[14] could detect the presence of salivary glucose in whole saliva of only in Type 2 DM patients and not in healthy controls. However, in contrast to the present study various other authors Carolina A et al, [11]CampbellMJAcould not establish any correlation between random plasma glucose levels and unstimulated salivary glucose levels.[12]

Salivary Ph

In the present study there was significant difference in the mean salivary pH between control subjects, controlled, and uncontrolled Type 2 DM patients with their mean salivary pH 6.6052, 5.025 and 4.115 respectively. Similar studies were done by Jawed M et al wherein the pH levels in Type 2 DM and controls were 6.08 ± 0.31 and 7.03 ± 1.23[15]Few of the researchers have investigated the levels of normal pH in healthy subjects. According to Henry Starr's study the estimations of pH revealed to be 5.75 to 7.05[16].However, study by Fenoll C et al estimated the salivary pH to be 6.7 to 6.8 in the healthy populations they studied. When the pH falls below the critical level 5.5, hydroxyapatite begins to dissolve freeing phosphates that attempt to restore the pH balance. Certain proteins such as Sialin or histatin and alkaline products generated by metabolic activity of bacteria on amino acids, peptides, proteins and urea are also important for controlling the pH of saliva.[17]

Conclusion

From this study it can be concluded that salivary glucose level reflects the random plasma glucose level when the plasma glucose levels are high which confirms the effects of diabetic membranopathy leading to raised percolation of glucose from blood to saliva thus altering the salivary composition. Further studies with larger sample size are warranted to substantiate correlation between blood glucose and salivary glucose so as to devise salivary based tests for diagnosing Diabetes Mellitus. This study made some novel observations that will unquestionably contribute to providing a platform for further research.Limitation of our study would be relatively smaller sample size included. Further studies with larger sample size are warranted to substantiate correlation between blood glucose and salivary glucose so as to devise salivary based tests for diagnosing Diabetes Mellitus. This study made some novel observations that will unquestionably contribute to providing a platform for further research.

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