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SALIVARY GLUCOSE CONCENTRATIONS IN PATIENTS WITH DIABETES MELLITUS – A MINIMALLY INVASIVE TECHNIQUE FOR MONITORING BLOOD GLUCOSE LEVELS

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ABSTRACT

Salivary and blood glucose concentrations were determined in non-diabetic healthy individuals and patients with diabetes mellitus (type II). Glycosylated haemoglobin A1c was also determined in some of the patients (n=25) and a significant correlation (r = 0.82) was found between HbAlc and serum glucose concentrations in these patients, indicating that these patients had average elevated blood glucose concentration over an extended time period. Glucose was only found in the saliva of patients with diabetes mellitus (n=135), while the salivary samples of age matched non-diabetic subjects (n=25) did not show the presence of glucose. A significant correlation (r=0.78) was found between salivary and blood concentrations in the diabetics. This finding suggests that saliva can be used reliably for reflecting and monitoring the blood glucose concentration in the patients of diabetes mellitus.

INTRODUCTION

Interest has been increasing recently in non-invasive diagnostic testing. Some of this storms from the AIDS epidemic in the west, which has provided a new rationale for haemophilia, while other factors include new development in home based diagnostic tests and a demand of samples collected in the home or work place. Diagnostic tests based on fluid generally use blood and urine and less frequently the esoteric fluids such as saliva, sweat and tears.

It is becoming increasingly apparent to investigators and clinicians in a variety of disciplines that saliva has many diagnostic uses and is especially valuable in the young, the old and infirm and in large-scale screening and epidemiological studies. The highly sensitive test procedures that are now commonplace make it practical to quantitate, despite very low concentrations a large number of hormones and drugs in saliva. Indeed, all steroids of diagnostic significance in routine clinical endocrinology can now be readily measured in saliva (Mandel, 1990).

Tests based on saliva have already made substantial inroads into diagnosis. For some molecules – for example, antibodies, unconjugated steroids, hormones and certain drugs – the techniques are sufficiently sensitive to reflect blood concentrations of the substance accurately (Malamud, 1992). The following study explores the possibility of using saliva to reflect the glucose concentration in blood, thereby making self-measurement of glucose less invasive.

MATERIALS AND METHODS

Collection of Samples

Normal healthy individuals of both sexes (n=25) aged 35-45 years were selected as the non diabetic control group for this study. Blood and whole salivary samples (unstimulated) were collected from these individuals during resting condition. All volunteers were asked to thoroughly wash their mouth before collection of the salivary samples in clean sterile containers. Blood and whole salivary samples were also obtained under similar conditions from patients of non-insoline-dependent diabetes mellitus (NIDDM, Type II) of both sexes (n=135) aged 35-50 years. These patients were attending the Diabetic OPD Clinic of the Liaquat National Hospital, Karachi. The samples were obtained from individuals who volunteered to participate in this study.

Sodium Flouride (BDH A.R.) was added in minute quantities to all the blood and salivary samples obtained from the non diabetic and the diabetic subjects.

Serum and salivary glucose determination

Serum and salivary glucose was assayed by the use of an enzymatic colorimetric test kit, GOD-PAP (Plasmatec, U.K.)

Glycohaemoglobin (HbA1c) determination

HbA1c level was determined by the use of two channelled test kit BM (Boehringer Mannheim, Germany).

Data and Statistical Analyses

All values presented in this paper are presented as mean ± SEM. The difference in serum and salivary glucose concentrations between the controls and the diabetics was determined using Standard Z test (Standard Normal Distribution). Significance was accepted at $P<0.005$. Correlation coefficient (r) was calculated between serum glucose concentrations and HbA1c levels (n=25) and between serum and salivary glucose concentrations (n=135) obtained from the patients of diabetes mellitus.

RESULTS

A comparison of the serum and salivary glucose concentrations in normal individuals, compared with the uncontrolled diabetes type II is represented in Fig. 1. Glucose could not be detected in the salivary samples obtained from the non-diabetic control subjects whose random serum glucose concentrations were significantly higher ($P<0.005$) than the serum glucose concentrations of the non diabetic control subjects. Out of the total 135 patients of diabetes mellitus HbA1c level was determined for 25 patients and a positive correlation ($r=0.82$) was found between the serum glucose concentrations and the HbA1c (Fig. 2).

Glucose could only be detected in the salivary samples with diabetes mellitus, where as none of the salivary samples from the non-diabetic control subjects showed the presence of glucose (Fig.1). The salivary glucose concentration showed a parallel increase with an increase in the serum glucose concentration. Hence a positive correlation ($r=0.78$) was found between the salivary and serum glucose concentration among the diabetics (Fig. 2).

DISCUSSION

The present study was undertaken with the aim of suggesting saliva as the diagnostic fluid especially in the diabetics. The levels of HbA1c were also determined in 25 patients. Studies on the role of HbA1c indicate that it reflects the average blood glucose concentration over an extended period of time and remains unaffected by short-term fluctuations in blood sugar levels. HbA1c levels in these patients correlated significantly with their serum glucose concentrations.

The salivary samples of the non-diabetic control subjects did not show the presence of glucose even in the slightest concentrations, while the samples obtained from the diabetics showed significant concentrations of glucose in the saliva. The salivary glucose concentrations seem to correlate with the serum glucose concentration in the patients of diabetes mellitus as also indicated earlier by Darwazeh *et al*. (1991) and Swanljung *et al.* (1992). A significant glucose concentration in saliva from the patients with Insulin-dependent diabetes mellitus (IDDM type I) was also reported by Twetman *et al*. (1992). The presence of glucose in the saliva of the diabetics probably reflects the high serum glucose concentrations. An earlier study indicated that the salivary glucose concentration was lower during the period of better metabolic control (Reuterving *et al.,* 1987). Therefore, in well-controlled individuals with altered glucose metabolism, salivary gland function is not significantly impaired (Peppers *et al.,* 1992).

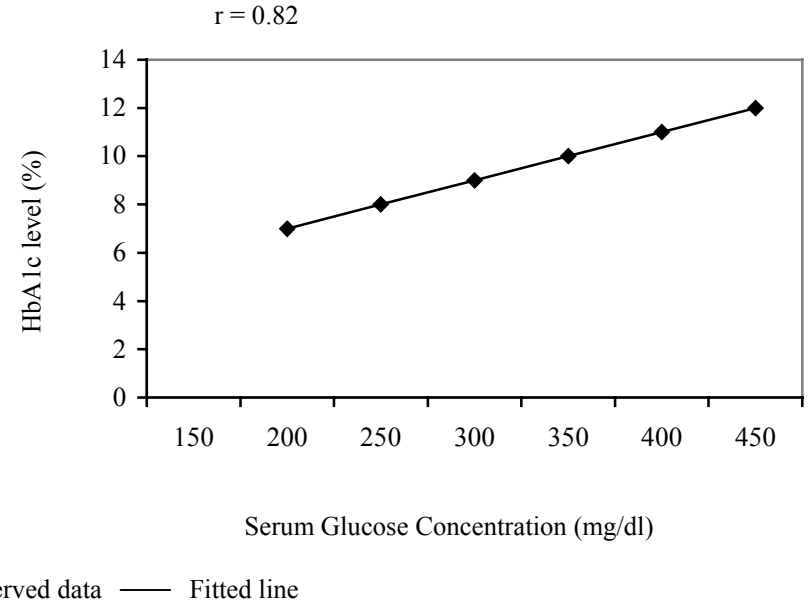

Fig. 1: Relation between serum glucose concentration and HbA1c levels in the patients of diabetes mellitus.

In the light of these results the present study supports the use of saliva as a diagnostic fluid in diabetes where it would especially prove valuable. Self-measurement of glucose is an integral part of diabetes mellitus therapy. As many as 50% of the diabetic people are reported to perform some degree of self monitoring and approximately 20-30% do so frequently (Ginsberg, 1992). Most

patients are therefore anxious for less invasive methods for glucose measurement. Methods are being developed for minimally invasive glucose monitoring which use body fluids other than blood e.g., saliva. Salivary glucose determinations may also be successfully performed in patients of IDDM especially in children. Significant concentrations of glucose were reported in saliva in children with IDDM, suggesting that changes in salivary composition may together with estimation of glucose levels may play a helpful role in the children with IDDM (Belazi *et al.,* 1998). As Butler (1992) puts it "I am convinced that its advantages especially in children, over weigh the drama of blood, sincerity of sweat and awkwardness of urine, moreover, the terror of the needle and the need even to shed a tear are avoided. Marchetti *et al.* (1989) in their report have suggested that the measurement of salivary glucose concentration may also represent a simple, quick, and inexpensive method for screening of diabetic autonomic neuropathy. Further investigations in these directions could well prove the value of salivary glucose measurements in all these conditions.

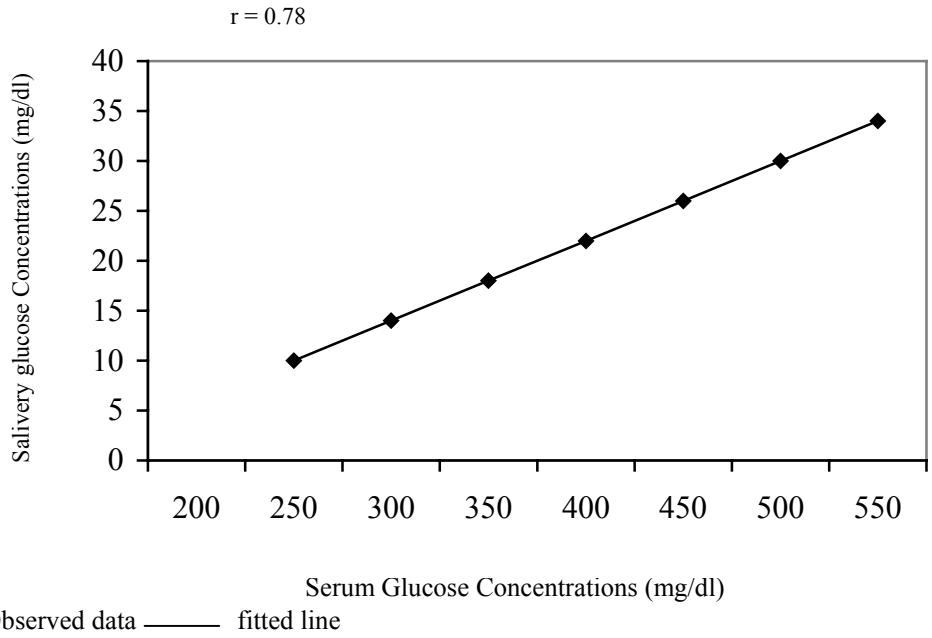

Fig. 2: Relation between serum and salivary glucose concentrations in patients with diabetes mellitus.

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