ORIGINAL ARTICLE

Correlation Between Fasting Plasma Glucose, Post Prandial Glucose and Glycated Haemoglobin and Fructosamine

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Summary

This study was done to determine the correlation between glucose monitoring by fasting blood glucose or 2 hours postprandial blood glucose with HbA1c and fructosamine in type 2 diabetic patients. A total of 82 patients from the Primary Care Clinic were enrolled in the study. Fasting blood was drawn for fasting plasma glucose (FPG), glycated haemoglobin (HbA1c) and fructosamine. Two hours after a standard breakfast, blood was again drawn for prandial plasma glucose (PPG). Both PPG and FPG significantly correlated with both HbA1c and fructosamine but PPG showed better correlation to HbA1c than FPG (r= 0.604 vs.0.575) whereas that of FPG and PPG were equally correlated to fructosamine (r= 0.566 vs. 0.551). In predicting good glycaemic control (HbA1c < 7.0%), the sensitivity, specificity and positive predictive value of PPG were 75.0%, 80.6% and 82.5% whereas FPG were 81.8%, 58.3% and 70.6% respectively. These results show that PPG correlated better than FPG to HbA1c and both equally correlated to fructosamine levels. Thus, PPG predicted overall glycaemic control better than FPG. Compared to HbA1c, fructosamine correlated least well with mean glucose profiles. Hence, using HbA1c in monitoring overall glycaemic control is better than fructosamine.

Key Words: Type 2 Diabetes, Plasma Glucose, Glycated Haemoglobin, Fructosamine

Introduction

Glycaemic control is an important aspect in managing diabetes in order to prevent acute or chronic complications of diabetes mellitus. Many randomized, prospective clinical trials in type 1 and 2 diabetes have clearly shown that achieving glycaemic control or reducing hyperglycaemia significantly decrease the microvascular complications of diabetes. In the Diabetes Control and Complications Trial[1] (DCCT) and Kumamoto Study[2], there was a significant reduction of both eye and kidney diseases by 50-70%. An epidemiological analysis of the UKPDS cohort also showed an approximate 14% reduction in macrovascular complications for every 1% reduction in HbA1c[3]. Fasting blood glucose concentration is often used to monitor progress since it correlates well with HbA1c values[4]. Fasting blood glucose concentrations are fairly stable in type 2 diabetic patients but can vary by about 15 percent from day to day[5]. Therapeutic goals for HbA1c and pre-prandial glucose levels have been established based on the results of controlled clinical trials. It was noted that elevated postprandial glucose concentrations may contribute to suboptimal glycaemic control[6]. An important role for postprandial glucose monitoring with therapy aimed at achieving postprandial glucose targets is suggested by teleological argument, biochemical information, epidemiologic

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study and limited clinical data[7]. Data from the National Health and Nutrition Examination Survey showed that patients who had 2-hour postprandial glucose levels of 194mg/dL had a threefold increase in the incidence of retinopathy despite normal fasting glucose level[9]. HbA1c level is considered the gold standard of long – term glycaemic control[1,2,9]. HbA1c is a measure of the degree to which hemoglobin is glycosylated in erythrocytes and is expressed as a percentage of total hemoglobin concentration. The half-life of the circulating red blood cell is approximately 60 days and the half-life of the HbA1c is approximately 34 days. So it reflects mean glycemic values in the previous 2-3 months, incorporating both pre and postprandial glycaemia. Fructosamine is the general name for the stable, rearranged product of glucose and protein amino group that is currently called glycated serum protein. It's measurement monitors the glucose status over 1-3 weeks. It is useful in conditions that affect glycohemoglobin. Epidemiological studies have shown stronger correlation between incidence of cardiovascular event and postprandial glucose levels than with pre-prandial levels as in the Diabetes Intervention Study (DIS)[10]. Recent research on PPG measurements indicates that not only are they potentially more accurate reading of blood glucose concentrations but that high PPG levels may forecast cardiovascular risk. Indeed, investigators have suggested that postprandial glycaemia may better correlate with HbA1c levels than fasting glycaemia. On the other hand, there are also insufficient data to determine accurately the relative contribution of the FPG and PPG to HbA1c. It appears that FPG is somewhat better than PPG in predicting HbA1c, especially in type 2 diabetes. However, there is still an argument whether postprandial glucose monitoring is superior to fasting blood sugar. The aim of this study is to determine the correlation between fasting plasma glucose, postprandial glucose and glycated haemoglobin and fructosamine in patients with type 2 diabetes mellitus.

Materials and Methods

Subjects

A total of 82 patients (38 men, 44 women) with type 2 diabetes mellitus from Primary Care Clinic, Hospital Universiti Sains Malaysia, were enrolled into the study. The subjects' age ranged from 35 to 70 years and signed informed consent was obtained from all of them before the start of the study. Excluded were subjects who had serious medical condition such as above stage 2 hypertension, coronary artery disease, arrhythmias, recent stroke/ cerebrovascular accident and chronic renal failure, serious diabetic complications and psychiatric illnesses; subjects who had medical conditions that are known to alter HbA1c levels (haemolytic diseases and haemoglobinopathies) and serum fructosamine levels (haemolysis, icterus, lipemia / dysproteinaemic state and recent acute illness); subjects with very poor diabetic control - (HbA1c > 10%); subjects with newly diagnosed diabetes (less than 6 months) and subjects with type 1 diabetes mellitus or type 2 diabetes mellitus on insulin. All patients were asked to come to the clinic after an overnight fast and blood was taken for fasting plasma glucose (FPG), HbA1c and fructosamine.

All patients were served with standard breakfast, which consisted of ¾ cup of rice (about 30g weight), fish (about 40g weight) in coconut milk (about 30g weight). The meal was approximately equivalent to 30gm carbohydrate, 10gm protein and 10gm of fat (300kcal)[11]. Blood was drawn for postprandial glucose (PPG) determination 2 hours after the breakfast.

Plasma Glucose:

Blood was collected into sodium fluoride/ potassium oxalate containers and then sent immediately to the laboratory for measurement of plasma glucose using glucose oxidase method on a Chemistry Analyser (Hitachi 912 – Roche Diagnostics).

HbA1c

HbA1c was measured in heparinized whole blood using cation-exchanged, low pressure liquid chromatography method using Drew Scientific All 8's (DS5 machine).

Fructosamine

Fructosamine was measured in plasma, using Fructosamine Calorimetric Test Unimate FRA (Roche Reagent Unimate FRA) on a centrifugal analyzer (Roche Diagnostics – Hitachi 912) based on the ability of ketoamines to reduce nitroblue tetrazolium in alkaline solution. The reaction rate was measured by photometry at 550 nm.

Statistical Analysis

Evaluation of simple correlation coefficients of overall HbA1c and fructosamine with fasting and postprandial plasma glucose were done using bivariate correlation analysis followed by linear regression. Scatter plot graphs were then plotted and estimated calculation for an increase in 1% HbA1c and 1μmol/L in fructosamine

level that would increase plasma glucose levels were done based on that graphs.

Stata version 7 was used to analyze the sensitivity, specificity and positive predictive value in predicting good control of HbA1c (HbA1c≤7.0 %), for good (FPG < 6.1 mmol/l: PPG ≤8 mmol/l) and poor (FPG > 6.1 mmol/l and PPG >8 mmol/l) plasma glucose categories.

Results

The majority of the participants in this study were Malays (98.8%) with mean age of 56.7 ± 7.8 years and mean body mass index was 27.2 ± 3.9 kg/m². The majority of them were diagnosed to have diabetes mellitus between 5 to 10 years before. FPG and PPG were significantly well correlated (p=0.001) with HbA1c. However, PPG showed slightly better correlation compared to FPG (r=0.604 vs. 0.575) (Figures 1 and 2). Based on regression analysis, every increase of 0.36 mmol/l postprandial glucose and 0.31 mmol/l fasting plasma sugar will increase HbA1c by 1%.(Figures 1 and 2). FPG and PPG were significantly well correlated (p=0.001) with fructosamine. Both showed almost equal correlation with fructosamine. The results are presented in Figures 3 and 4. Based on regression analysis, every increase of 15.6 mmol/l postprandial glucose and 15.8mmol/l fasting plasma sugar will increase fructosamine by 1μmol/L (Figures 3 and 4). Fasting plasma glucose showed better sensitivity (81.8% vs. 75.0%) than postprandial glucose whereas postprandial glucose showed higher specificity (80.6% vs. 58.3%) and positive predictive value (82.5% vs. 70.6%) compared to fasting plasma glucose (Table I).

Table I: Sensitivity, specificity and positive predictive value of fasting and postprandial glucose in predicting good glycaemic control

Plasma Glucose	Sensitivity (%)	Specificity (%)	Positive Predictive value (%)
Fasting Blood Glucose	81.8	58.3	70.6
Postprandial Blood Glucose	75.0	80.6	82.5

Good control of HbA1c was defined as <7.0%

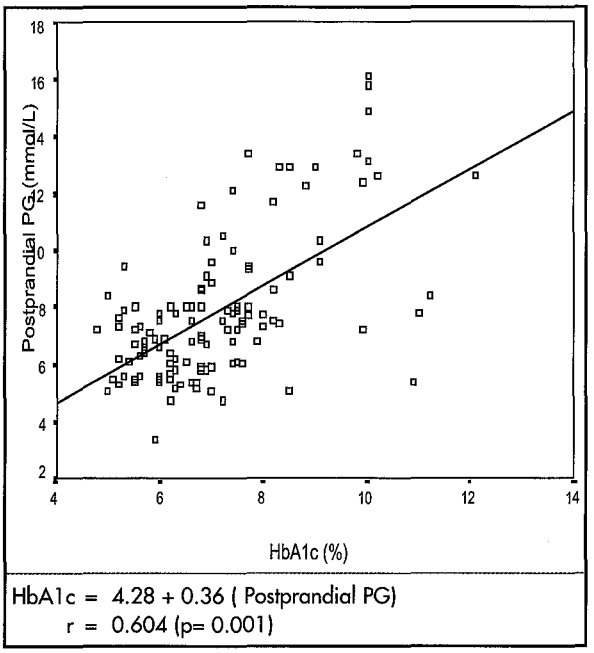

Fig. 1: Scatter plot for correlation between HbA1c and Postprandial Glucose

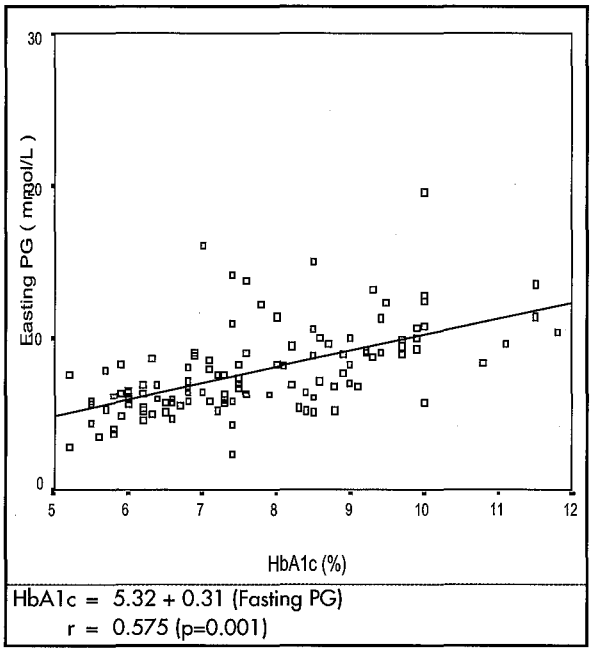

Fig. 2: Scatter plot for correlation between HbA1c and fasting blood glucose

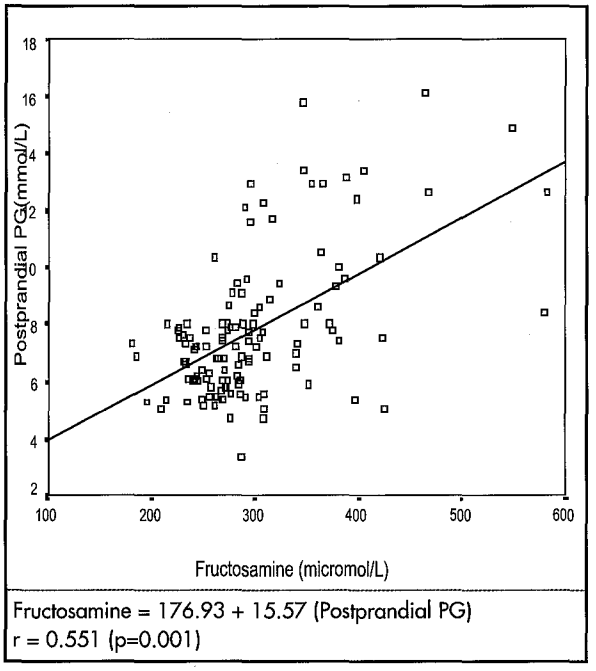

Fig. 3: Scatter plot for correlation of fructosamine with postprandial glucose

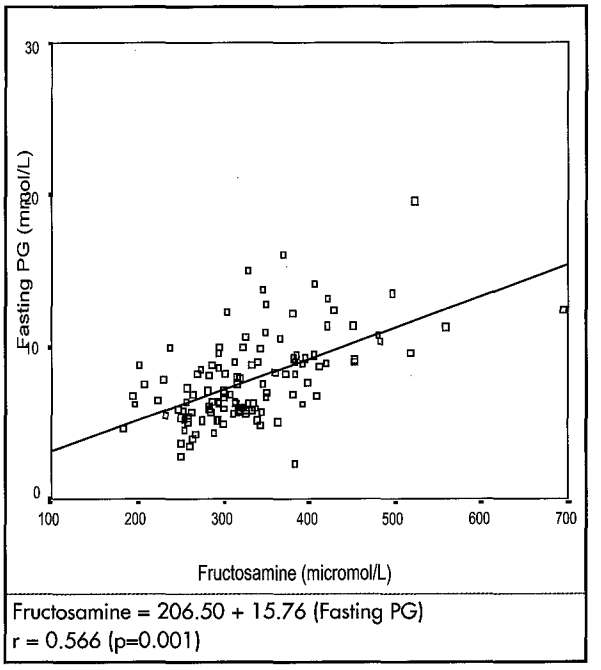

Fig. 4: Scatter plot for correlation of fructosamine with fasting plasma glucose

Discussion

The relative contribution of fasting and postprandial glycaemia to HbA1c has been the subject of increased interest in recent years, since there has been no sufficient data to determine this accurately. Until now, HbA1c has been the main indicator in the metabolic control of diabetic patients although fructosamine is cheaper. It has been used as a guide in therapeutic intervention studies on type 1 diabetic patients, as in the Diabetes Control and Complications Trial (DCCT)[1] and on type 2 diabetic patients, as in the U.K. Prospective Diabetes Study (UKPDS) [9].

Fasting glycemia has traditionally been considered the main HbA1c marker as suggested by the American Diabetes Association (ADA) and World Health Organisation (WHO). Recently, however, the validity of this has been questioned, and it has even been suggested that the main marker is postprandial glycemic level[12]. Postprandial glycemia has also been described as being more related to the development of macroangiopathy than fasting glycemia[2,10]. Regarding correlation between plasma glucose profile with HbA1c, we found that HbA1c was better correlated to postprandial glucose levels than fasting plasma glucose, with moderate correlation (r= 0.604 vs.0.575). The finding of postprandial glucose levels being better correlated to HbA1c than fasting glucose levels are supported by Avignon *et al.*[13] and Bastyr *et al.*[14]. Avignon *et al.* [13] found that prebreakfast, prelunch, postlunch, and extended postlunch PG values were all significantly correlated with HbA1c. Multiple linear regression analysis demonstrated that postlunch PG and extended postlunch PG correlated significantly and independently with HbA1c, but the prebreakfast PG and prelunch PG did not. Bastyr *et.al.*[14] also reported similar findings with stronger correlation of 2-hour postprandial blood glucose (r=0.400,p<0.001) than FBG (r=0.260,P=0.004). A study done by Soonthornpun *et al.*[15], also concluded that strong correlation with HbA1c value was seen with 2-hour postprandial PG (r=0.51) for near normal FPG (FPG < 7.8 mmol/L). However, the results in the present study were not consistent with the conclusions reached by a panel of experts designated by the American Diabetes Association to review the available data on postprandial glucose[6]. Fructosamine levels correlate less well with glucose profiles (FBS and

PPG) compared to HbA1c. These results are supported by a study done by Hom *et al.*[16].

In conclusion, postprandial plasma glucose correlated better than fasting plasma glucose with HbA1c and postprandial glucose also predicted overall glycaemic control better than fasting glucose. Compared to HbA1c, fructosamine correlated less well with glucose profiles. Hence using HbA1c in monitoring overall glycaemic control is better than fructosamine.

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